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Alignment, Mass and Orthoses in Medial Compartment Knee Osteoarthritis

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by

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Abstract

Biomechanical factors during locomotion are important contributors to knee osteoarthritis (OA). A better understanding of their potential role in intervention strategies is required. The overall purpose of this thesis was to examine the interaction between lower limb alignment and body mass on dynamic knee joint loading, and to examine the effects of knee and foot orthoses, in patients with knee OA. The thesis included three studies. Chapter 2 was a cross-sectional study using three-dimensional gait analysis and full limb radiographs in 487 patients. Using sequential (hierarchical) linear regression, results indicated a statistical interaction between lower limb alignment and body mass on the external knee adduction moment, a proxy for the load distribution across the knee and a strong risk factor for OA progression. The relationship between alignment and the knee adduction moment depended on mass, with a higher association observed in patients with higher mass. Chapter 3 was a systematic review with meta-analysis of the biomechanical and clinical effects of valgus knee braces. Data were extracted from 38 articles. When pooling data, standardized mean differences suggested that braces provided a statistically significant decrease in the knee adduction moment during walking, and in patient-reported measures of pain and function, with overall moderate effect sizes. Substantial issues related to appropriate dosage, patient comfort and compliance were also identified. Chapter 4 was a proof of concept study that tested the combined effects of knee and foot orthoses. Sixteen patients with varus alignment and medial compartment knee OA underwent repeated three-dimensional gait analyses with and without wearing a custom-fit valgus knee brace, custom-fit lateral wedge foot orthotic, and both. Results indicated that the combined use of the knee brace and foot orthotic provided greatest reductions in the knee adduction moment. Overall, the results of this thesis emphasize the importance

of considering alignment and the distribution of loads across the knee during walking when developing intervention strategies for knee OA. The present findings provide rationale for future research examining the combined use of different interventions that target biomechanics, including orthoses tailored to maximize biomechanical effects while maintaining patient comfort.

Keywords: knee osteoarthritis, lower limb alignment, body mass, knee adduction moment, systematic review, meta-analysis, valgus knee braces, lateral wedge foot orthotics, and gait biomechanics

Co-Authorship

This thesis contains material from two published manuscripts (Chapters 2 and 4) and one manuscript that will be prepared for submission (Chapter 3). Rebecca Moyer was the primary author of all chapters contained in this thesis. Chapters were co-authored by T.B. Birmingham, a Professor in the School of Physical Therapy, Faculty of Health Sciences, Western University (Chapters 2-4); B.M. Chesworth, an Associate Professor in the School of Physical Therapy (with adjunct appointment in the Department of Epidemiology and Biostatistics), Faculty of Health Sciences, Western University (Chapter 2); C.E. Dombroski, a Canadian Certified Pedorthist at the Fowler Kennedy Sport Medicine Clinic, Western University (Chapter 4); J.R. Giffin, an Associate Professor in the Department of Orthopaedic Surgery, Schulich School of Medicine, Western University (Chapter 2 and 4); T.R. Jenkyn, an Associate Professor in the Department of Mechanical and Materials Engineering, Western University (Chapter 4); C.O. Kean, a PhD Graduate student at the time of publication, Health and Rehabilitation Sciences, Faculty of Heath Sciences, Western University (Chapter 2); K.M. Leitch, a PhD Candidate in the Department of Biomedical Engineering, Western University (Chapter 3 and 4); K.A. Marriot, an MPT PhD Student in Health and Rehabilitation Sciences, Faculty of Health Sciences, Western University (Chapter 3); and R.F. Walsh, a Canadian Certified Athletic Therapist at the Fowler Kennedy Sport Medicine Clinic, Western University (Chapter 4).

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List of Abbreviations

AP - Anteroposterior

BMI – Body mass index

CI – Confidence interval

CoM – Centre of mass

CoP – Centre of pressure

GRF – Ground reaction force

ICC – Intraclass correlation coefficient

KAM – Knee adduction moment

KL Grade – Kellgren and Lawrence grade of OA severity

KOOS – Knee Injury and Osteoarthritis Outcome Score

MAA – Mechanical axis angle

NRS – Numeric rating scale

Nm – Newton-meters

OA – Osteoarthritis

RCT – Randomized controlled trial

SD – Standard deviation

SMD – Standardized mean difference

VAS – Visual analog scale

%BW*ht – The product of body weight and height expressed as a percentage

1. Introduction: Background and Rationale

The purpose of this chapter is to provide the background and rationale for the thesis objectives. A general description of knee osteoarthritis (OA) is presented, followed by a description of the importance of obesity and lower limb malalignment. Gait analysis and non-surgical treatments targeting those risk factors are also described. Lastly, a brief overview of thesis chapters 2-5 is provided.

1.1 Knee Osteoarthritis

Approximately 17% of people ≥ 45 years of age and 5% ≥ 26 years of age have symptomatic knee OA[1]. Often accompanied by other chronic disabling health conditions, OA is the most common musculoskeletal disease consuming more than 10% of Canada's total economic burden[2-5]. Coinciding with growing life expectancies among an aging population and increasing incidence of obesity[1], the prevalence of arthritis in society is expected to increase substantially, accompanied by a slow deterioration in physical function. Therefore, limiting OA disease progression has become an important public health strategy[6]. Understanding modifiable risk factors for OA and identifying intervention strategies that promote disease self-management and physical independence is paramount.

Knee OA is now recognized as a disease affecting the whole knee joint organ, although the degeneration of articular cartilage is the hallmark of the condition. Articular cartilage deterioration alters the anatomical force distribution between medial and lateral tibiofemoral compartments, modifying contact areas and lubrication, thus causing pain, stiffness and decreased function over time[7]. Normal mechanics of articular cartilage require regular, cyclical loading to maintain its natural protective function. In OA, as pain

increases and physical activity decreases, abnormal joint biomechanics lead to irregular cartilage wear patterns, cartilage degradation, structural changes and bone deformations[8-11]. Weight-bearing joints, such as the knee, are highly susceptible to cartilage degradation. In knee OA, the majority of the degeneration occurs in the medial compartment of the tibiofemoral joint, largely because of how the knee is loaded during walking. In healthy knees with neutral alignment, approximately 70-80% of the weight-bearing load passes through the medial compartment compared to the lateral compartment, and can increase to 100% of the load in the presence of varus malalignment and cartilage breakdown[12-14].

Radiographic and symptomatic classification criteria are considered for knee OA diagnosis. Radiographic criteria most commonly follow the Kellgren and Lawrence grading system, which considers bony changes including osteophytes, joint space narrowing, sclerotic changes and joint deformation[15]. Alternatively, symptomatic criteria often align with Altman's Classification Criteria for OA[7], including 1 of 3 criteria from the following: age greater than 50 years, morning stiffness lasting longer than 30 minutes and joint crepitus. Both standards are commonly used to identify patients with knee OA for research purposes. The cause of disease onset is unclear despite a wide variety of modifiable and non-modifiable risk factors that contribute to the development and/or progression of the disease. Known risk factors that can make an individual susceptible to knee OA include genetics, age, sex, muscle weakness, joint injury, joint loading, obesity and malalignment. This thesis focuses on obesity, malalignment, knee joint loading and non-surgical interventions targeting those risk factors.

1.2 Obesity and Knee Osteoarthritis

Based on measures of mass (kg) or BMI (kg/m^2), obesity is an important modifiable risk factor for OA that has the potential for impact at the population level. Convincing evidence implicates obesity as a main precursor to the development and progression of radiographic disease[16-17]. In obese patients, the development of OA promotes sedentary lifestyles and immobility, which leads to further obesity and further OA progression[16]. This spiral of functional decline associated with obesity suggests that weight loss may protect against incident knee OA[18] and increasing physical activity levels may protect against disease progression[19]. Additional treatment strategies that enable patients with knee OA to engage in activity to achieve these protective benefits are necessary.

Although obesity is considered to be both a systemic and biomechanical risk factor for knee OA, this thesis focuses only on its role in biomechanics. Obesity increases axial loads and can exceed the normal cyclical loads required to maintain natural cartilage function. In OA, the ability to carry increased loads associated with increased body mass can be further compromised, exacerbating knee pain and disability. Therefore, exercise and weight-loss intervention studies are imperative and have received a great deal of attention in the knee OA literature[20-24].

1.3 Malalignment and Knee Osteoarthritis

Static alignment of the lower limb can be measured from full-limb (hip to ankle) standing anteroposterior (AP) radiographs. The mechanical axis angle (MAA or hip-knee-ankle angle) is measured as the included angle between the line connecting the knee and hip joint centres and the line connecting the ankle and knee joint centres. Other measures

of alignment do exist, yet the MAA is considered the gold standard measure of static lower limb alignment and can be highly reliable using digital software programs[25-27] (Figure 1.1). Malignment in the varus direction, also known as bow-legged, is more common in medial compartment knee OA; whereas, malalignment in the valgus direction, also known as knock-kneed, is more common in lateral compartment knee OA[28-32]. Although both forms of knee OA exist, medial compartment knee OA is more common due to the greater loads borne by that compartment during walking[13-14].

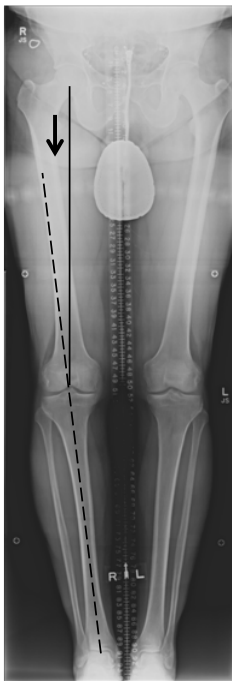

Figure 1.1: The mechanical axis angle (MAA) of the lower limb is measured as the included angle between the line connecting the knee and hip joint centers and the line connecting the ankle and knee joint centers.

Lower limb alignment is a frequently studied risk factor for knee OA[10,12,28,33-38]. Malalignment has been previously correlated with other risk factors for knee OA including joint space narrowing[28,33,36], disease severity[29,39] and various measures to infer

knee joint load distribution[25,34,36,40-45]. In patients with varus malalignment, the distribution of load that is normally greater in the medial compartment is exaggerated further. This can lead to degradation of the medial tibiofemoral articular cartilage[30,46-47], medial joint space narrowing and a further increase in varus alignment. Several authors have previously described this vicious cycle in medial compartment knee OA[37,48] (Figure 1.2). A strong relationship has been consistently identified between varus malalignment and radiographic OA progression[28,39]. Although less consistent, recent evidence suggests that varus alignment is also associated with incident knee OA[39,49-51]. In addition to its independent effects, there is limited evidence to suggest that lower limb malalignment may also interact with other risk factors such as obesity[35,37-38,52].

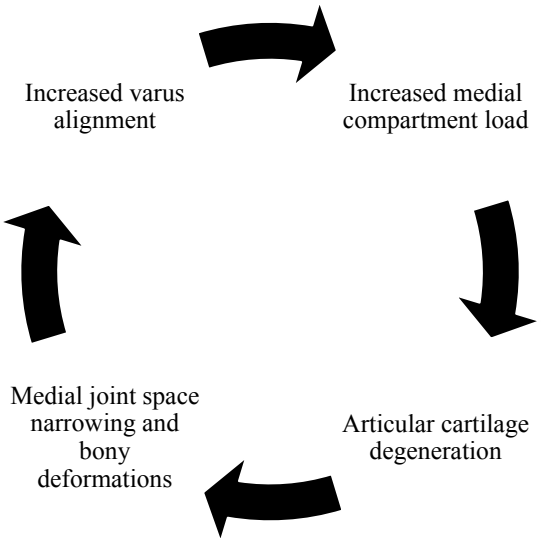

Figure 1.2: A vicious cycle of medial compartment knee osteoarthritis. Varus alignment creates aberrant loads on the medial compartment, leading to structural changes in the joint, decreased medial joint space and further increased varus alignment.

Obesity and lower limb malalignment both contribute to increased loads on the medial tibiofemoral compartment and are reported risk factors for the development and

progression of knee OA. However, limited information exists on the potential interaction between alignment and body mass on medial compartment loading.

1.4 Three-Dimensional Gait Analysis in Knee Osteoarthritis

Walking is the most common activity of daily living with thousands of steps taken per day[53-55]. Three-dimensional gait analysis has proven to be a valuable instrument for the evaluation of biomechanical factors involved in knee OA. Knee joint kinematics and kinetics can provide particularly useful information with respect to the distribution of loads in the medial versus lateral tibiofemoral compartments. Specifically, during the stance phase of walking, the line of action of the resultant ground reaction force (GRF) is directed from the centre of pressure (CoP) under the foot and directed upwards towards the body's centre of mass (CoM). Therefore, this GRF vector passes medial to the knee joint centre during stance, creates a lever arm in the frontal plane and an external adduction moment about the knee (Figure 1.3). In the presence of varus alignment, the frontal plane lever arm increases, the GRF shifts further away from the knee joint centre, and the external knee adduction moment increases.

Although limitations must be acknowledged[32,56-58], the external knee adduction moment has proven to be a valid, reliable and clinically relevant proxy for the distribution of load across the tibiofemoral joint[34,43,56,59]. Perhaps most importantly, high external knee adduction moments predict disease progression[42,60]. Therefore, decreasing the external knee adduction moment (or perhaps the associated lever arm) during walking has become an important target for various intervention strategies.

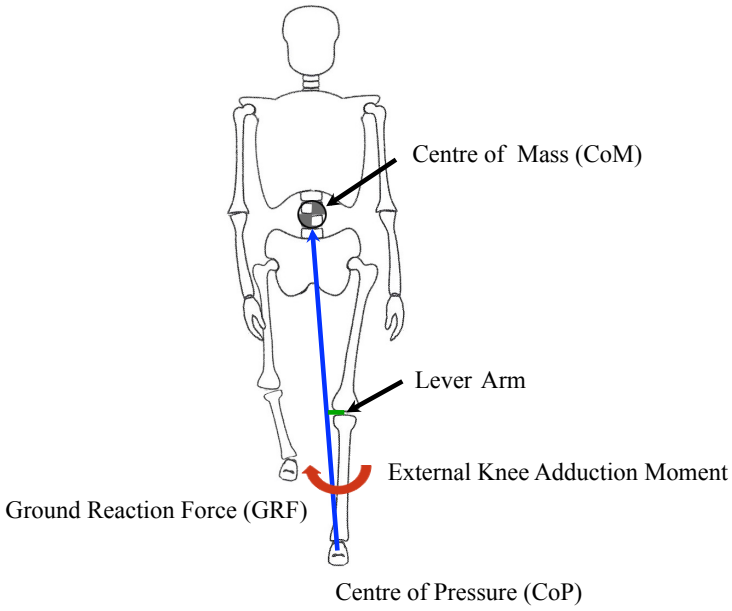

Figure 1.3: During walking, the ground reaction force (GRF) vector originates at the foot's centre of pressure (CoP) and passes medial to the knee towards the body's centre of mass (CoM). This creates a lever arm in the frontal plane and an external knee adduction moment.

1.5 Knee and Foot Orthoses in the Treatment of Knee Osteoarthritis

Clinical practice guidelines have outlined available surgical and non-surgical options for patients with symptomatic knee OA[61-66]. Less invasive treatment options for knee OA, with the aim to slow the rate of disease progression and improve pain and quality of life, are suggested as early treatments. Unloading the medial compartment of the knee is a common goal of conservative treatments. Through different mechanisms, valgus knee braces and lateral wedge foot orthotics both aim to decrease the external knee adduction moment. Although both knee and foot orthoses have been included in clinical practice guidelines, recommendations supporting their use are inconsistent[61-66]. Given the abundance of recently published literature on valgus knee bracing, a systematic review and meta-analysis is warranted.

1.5.1 Valgus Knee Braces

Varus knee braces can be used for patients with valgus alignment and lateral compartment knee OA, while valgus knee braces can be used for patients with varus alignment and medial compartment knee OA. Consistent with the greater prevalence of medial compartment OA, valgus braces are more common. These external devices are worn at the knee to provide a moment to oppose the external knee adduction moment, thereby lessening the load on the medial tibiofemoral compartment (Figure 1.4A). Off-the-shelf and custom-fit designs are available. Custom-fit braces are more expensive, but there is limited evidence to suggest that they can create greater biomechanical effects than off-the-shelf models[67]. Numerous published studies have evaluated various biomechanical effects of valgus braces and have reported mixed results[67-92]. The size of these biomechanical effects is often described as small and the carryover to clinically important benefits remains controversial[67-68,70-74,76,78-80]. Few clinical trials of valgus bracing have also been published and provide inconsistent conclusions[67,86,78,81,93-96]. While some encouraging results exist, discomfort[84-85,90,97-99] and poor long-term brace use[84,99-101] are also sometimes reported. Importantly, the size of biomechanical effects may be directly proportional to the angulation provided by the brace, yet greater angulations may be associated with greater discomfort[71,76,90-91].

1.5.2 Lateral Wedge Foot Orthotics

Lateral wedge foot orthotics are worn in the shoe and are also intended to lessen the load on the medial compartment of the knee (Figure 1.4B). Acting at the foot, lateral wedge orthotics are designed to move the body's CoP laterally on the foot, thereby moving the GRF vector closer to the knee joint center. A direct relationship between

decreases in the knee adduction moment and shortening of the lever arm in the frontal plane has been established[102]. Decreases in the external knee adduction moment have been reported[76,103-110] with no diminishing effects after one month of wear[108], yet the evidence remains inconclusive. Alternatively, randomized clinical trials have not supported the use of lateral wedge foot orthotics due to the lack of clinical improvements in pain and function[110-112]. Although greater wedge inclinations may be associated with greater reductions in the external knee adduction moment, patients have previously reported discomfort with inclinations larger than 10° [104].

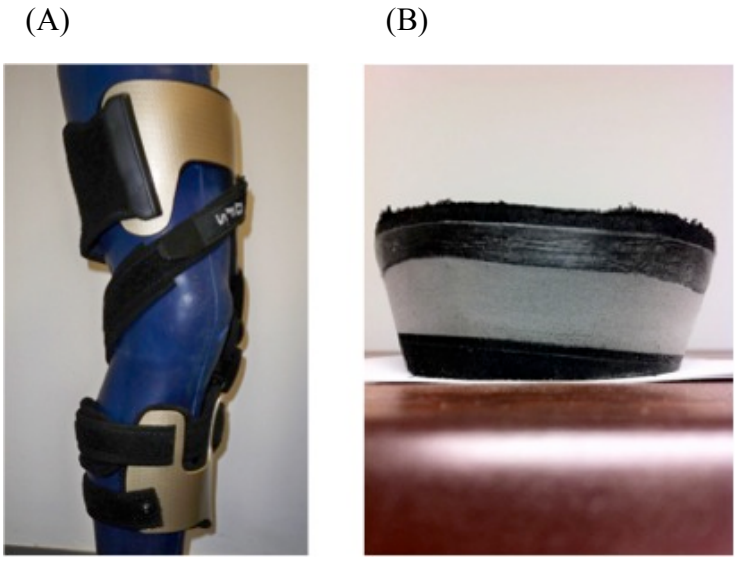

Figure 1.4: (A) Valgus knee brace and (B) full-length lateral wedge orthotic

Although not previously investigated, it is theoretically possible that valgus knee braces and lateral wedge foot orthotics have additive effects on decreasing the external knee adduction moment during walking. Specifically, a valgus knee brace may alter the position of the knee joint center medially, while a lateral wedge orthotic may alter the orientation of the ground reaction force laterally, when worn concurrently.

1.6 Thesis Outline

The overall purpose of this thesis was to examine the interaction between lower limb alignment and body mass on dynamic knee joint loading, and to examine the effects of knee and foot orthoses, in patients with knee OA. The thesis consists of three studies. All studies were completed in the Wolf Orthopaedic Biomechanics Laboratory, Fowler Kennedy Sport Medicine Clinic, Western University.

Chapter 2 (Study 1): Clinical and biomechanical rationale suggest that the effect of body mass on knee joint loading may depend on lower limb alignment, although this potential interaction has not been previously described. The objective of this study was to examine the interaction and relative contributions of frontal plane alignment and body mass on measures of knee joint loading during gait. Results from this study provided further rationale for studying interventions aimed at altering malalignment, including valgus knee braces and lateral wedge foot orthotics.

Chapter 3 (Study 2): Clinical practice guidelines are inconsistent regarding their recommendations for the use of valgus knee braces in the management of knee OA. The objective of this systematic review and meta-analysis was to investigate biomechanical effects, patient-reported outcomes, complications, and compliance with valgus brace use in patients with medial knee OA. Results from this study provided the rationale for investigating the combined use of a valgus knee brace and lateral wedge foot orthotic, where both were custom-fit to doses that ensured patient comfort.

Chapter 4 (Study 3): The primary objective of this proof of concept study was to test the hypothesis that a custom-fit valgus knee brace and custom-made lateral wedge foot orthotic would have greatest effects on decreasing the external knee adduction moment during gait when used concurrently. The secondary objective was to explore changes in the frontal plane ground reaction force and its lever arm.

Chapter 5: A final chapter summarizes the findings of the thesis, provides a general discussion of the studies and offers suggestions for future research.

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2. Alignment, Body Mass and Their Interaction on Dynamic Knee Joint Load in Patients with Knee Osteoarthritis

2.1 Summary

The objective of this study was to examine the interaction and relative contributions of frontal plane alignment and body mass on dynamic knee joint loading in patients with knee osteoarthritis (OA). We completed three-dimensional gait analyses and hip-to-ankle standing anteroposterior radiographs on 487 patients with knee OA referred to a tertiary care center specializing in orthopaedics. Using sequential (hierarchical) linear regression, the interaction term (mechanical axis angle × mass) contributed significantly ($P < 0.001$) to a model (total adjusted $R^2 = 0.70$) predicting the external knee adduction moment, that included mechanical axis angle ($R^2 = 0.37$) and mass ($R^2 = 0.06$) while controlling for age, sex, height, Kellgren and Lawrence grade, pain score during walking, gait speed, toe out angle and trunk lean ($R^2 = 0.25$). When the sample was split into tertiles for mass, mechanical axis angle accounted for 32–54% of explained variance in knee adduction moment. In the tertile with greatest mass, results suggest a 3.2 Nm increase in knee load for every 1° increase in varus alignment. When split into tertiles for mechanical axis angle, mass accounted for 6–10% of explained variance in the knee adduction moment. In the tertile with the most varus alignment, results suggest a 0.4 Nm increase in knee load for every 1 kg increase in mass. Our findings describe the interaction between alignment and body mass on dynamic knee joint loading, with the association between alignment and load highest in patients with the highest mass. Our findings also emphasize the role of malalignment on knee load at all levels of mass, and have implications for better understanding risk factors and intervention strategies for knee OA.

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2.2 Introduction

Approximately 17% of people greater than 45 years of age and 5% greater than 26 years of age have symptomatic knee osteoarthritis (OA)[1]. It is a leading cause of disability and increases the risk of disability due to other medical conditions substantially[2,3]. Knee OA that has progressed beyond the mild stage is responsible for the majority of its burden, which is extensive[2,4,5]. Limiting disease progression is therefore an important public health strategy, and understanding risk factors for progression is imperative.

Malalignment of the lower limb and excess body mass are both proposed risk factors for the progression of knee OA, presumably because of their contributions to increased joint loading[6-11]. Although greater varus alignment is consistently reported to be strongly associated with disease progression[7,11], the effect of body mass is less clear and may depend on the extent of malalignment[6,8,10]. A plausible biomechanical hypothesis is that alignment and body mass produce interaction effects on knee joint loading. Specifically, excess body mass may modify the well-established association between alignment and load on the medial compartment of the tibiofemoral joint[6,9]. We are unaware of previous research that has directly tested for an interaction between alignment and body mass on knee joint load.

If a significant interaction exists, one might expect patients with malalignment and obesity to be at greatest risk for disease progression. However, recent evidence from prospective studies is somewhat inconsistent with respect to the effect of obesity on disease progression in patients with malalignment[6,9,10]. Sharma et al.[9] reported that body mass index (BMI) was related to OA severity in knees with varus malalignment. Felson et al.[6] reported that disease progression was affected by BMI in knees with moderate

malalignment, but not in knees with severe malalignment. Alternatively, Niu et al.[10] reported that obesity had no effect on radiographic progression in knees with varus alignment, and suggested the excess load produced by varus knee malalignment may be sufficient by itself to cause progression. Although this hypothesis is plausible and implies a greater role of malalignment than body mass on knee load, we are unaware of previous research that has evaluated the relative contributions of alignment and body mass to knee joint loading in patients with knee OA.

Several lines of evidence suggest that quantitative gait analysis provides an appropriate means to measure knee joint load during walking. In particular, the external adduction moment about the knee, calculated as the product of the frontal plane components of the ground reaction force magnitude and the lever arm, is a valid and reliable proxy for the dynamic load on the medial compartment of the tibiofemoral joint[12-15]. Importantly, in addition to being affected by one's body mass and lower limb alignment, the knee adduction moment reflects an individual's walking characteristics and arguably represents a functional measure of dynamic knee joint loading. Gait variables most commonly reported to be associated with reduced knee adduction moments in patients with knee OA include decreased walking speed[16-18], increased toe out angle[14,18-20] and increased lateral trunk lean over the stance limb[17]. Pain and disease severity may also influence the knee adduction moment[21]. It is therefore important to consider these covariates when evaluating the effects of alignment and body mass on dynamic knee joint load.

Although clinical and biomechanical rationale suggests that the effect of frontal plane alignment on the knee adduction moment during gait may depend on body mass, this potential interaction has not been previously described. The purpose of this study was

to examine the interaction and relative contributions of frontal plane alignment and body mass on knee joint loading during gait. We hypothesized that while controlling for other factors suggested to alter knee joint load, there would be a statistically significant interaction between alignment and body mass on the external knee adduction moment. In the presence of significant findings we planned to describe the interaction by controlling for effect modification from two perspectives: one where the effect modifier was body mass and the other where the effect modifier was alignment.

2.3 Methods

2.3.1 Participants

We included the first 487 participants in an ongoing gait data registry for patients diagnosed with knee OA who were referred to a tertiary care center specializing in orthopaedics. The diagnosis of knee OA was based on the criteria described by Altman et al.[22]. Patients with rheumatoid arthritis or a concomitant neurological condition were excluded. The study was approved by the institutional research ethics board and all participants provided informed consent.

2.3.2 Gait Analysis

Patients underwent a 3-dimensional gait analysis using an 8-camera motion capture system (Eagle EvaRT; MAC, Santa Rosa, CA) synchronized with a floor-mounted force plate (AMTI, Watertown, MA). Twenty-two reflective markers were placed on the patients in accordance with a modified Helen Hayes marker set[23]. Extra markers were placed bilaterally over the medial knee joint line and medial malleolus during an initial static standing trial on the force platform to determine body mass, marker

orientation, and positions of joint centres of rotation for the knee and ankle. These four additional markers were removed prior to gait testing. During the gait analysis, patients were instructed to walk across the laboratory at their typical walking speed while kinetic (sampled at 1200 Hz) and kinematic data (sampled at 60 Hz) were collected during the middle of several strides. Raw data were filtered using a 4^{th} order Butterworth low pass filter with a cutoff frequency of 6Hz.

The frontal plane component of the GRF was calculated as the resultant force vector of the vertical and mediolateral components of the GRF. The frontal plane lever arm was calculated as the perpendicular distance between the frontal plane GRF and knee joint centre of rotation using custom post-processing and data reduction techniques previously described[24,25]. The external adduction moment about the knee was calculated using commercial software from the kinetic and kinematic data with a process called inverse dynamics (Orthotrak 6.2.4; MAC, Santa Rosa, CA). Each lower limb segment (foot, shank and thigh) was modeled as a rigid body with a local coordinate system that coincided with anatomically relevant axes. Inertial properties of each limb segment were approximated anthropometrically and the translations and rotations of each segment were reported relative to neutral positions as defined during the initial standing static trial.

We used a numeric rating scale to assess pain levels during walking, 0 representing no pain and 10 representing the worst possible pain. Walking speed was calculated as the average walking speed between successive foot contacts of the tested limb. Toe-out (positive angle) was calculated as the angle between a line drawn between the centre of the ankle and the head of the 2^{nd} metatarsal and the forward progression of the body. Lateral trunk lean over the stance limb (positive angle) was calculated as the angle of a line drawn from the midpoint of the anterior superior iliac spines to the

midpoint of the anterior tips of the acromion processes with respect to vertical. All gait variables were calculated by averaging across five trials for each patient. We have previously reported excellent test-retest reliability of the peak knee adduction moment ($ICC_{2,1}$ = 0.86)[15]. We have also previously reported acceptable reliability of gait speed ($ICC_{2,1}$ = 0.92), toe-out angle ($ICC_{2,1}$ = 0.69), and trunk lean angle ($ICC_{2,1}$ = 0.91) measurements[17].

2.3.3 Radiographic Analysis

Frontal plane alignment and Kellgren and Lawrence grades of severity were assessed using hip-to-ankle bipedal standing anteroposterior radiographs and custom computerized software[26,27]. Patients stood with the patellae centered over the femoral condyles and feet straight ahead to control for effects of foot rotation on measures of lower limb alignment[28]. The x-ray beam was centred on the knee at a distance of approximately 2.5m. Beam exposure was determined based on each patient's leg mass. The mechanical axis angle of the lower limb was used to quantify alignment in the frontal plane and was defined as the angle formed between a line drawn from the centre of the hip to the centre of the knee and a line drawn from the centre of the ankle to the centre of the knee[29,30]. Negative values indicated varus alignment. Positive values indicated valgus alignment. The center of the hip was identified as the geometric center of the femoral head using a circular template, the center of the knee was identified as the midpoint of the tibial spines extrapolated inferiorly to the surface of the intercondylar eminence, and the center of the ankle was defined as the mid-width of the tibia and fibula at the level of the tibial plafond. We have previously reported excellent reliability of mechanical axis angle measurements using this method ($ICC_{2,1}$ = 0.97)[27].

2.3.4 Statistical Analysis

We used sequential (hierarchical) linear regression models to test the hypothesis that a statistical interaction exists between alignment and mass on dynamic knee joint load, while controlling for other factors suggested to affect knee loading. Specifically we created an interaction term by multiplying mechanical axis angle by mass (MAA*mass) and tested whether it contributed significantly to a model predicting peak knee adduction moment, that also included mechanical axis angle, mass and other independent variables that affect knee loading[31]. We tested four, hypothesis driven models. Independent variables in the first model included age, sex, height, Kellgren and Lawrence grade, pain score during walking, gait speed, toe out angle and trunk lean angle because these variables have been previously reported to affect knee adduction moments[14,16-21]. We then added mechanical axis angle, mass and the interaction term (MAA*mass) in three separate sequential models to determine the contribution of each of these variables. We repeated these three sequential models while reversing the order of adding mechanical axis angle and mass.

Following a significant interaction, we split the sample into subgroups based on tertiles for mass and mechanical axis angle and calculated descriptive statistics for the peak knee adduction moment for each of the nine subgroups. To investigate the interaction when the effect modifier was body mass, we tested three separate models within each tertile of mass, after excluding mass and the interaction term from the model. Mechanical axis angle was added in a separate step to determine its contribution to the model in each tertile of mass. Similarly, to investigate the interaction when the effect modifier was alignment, we tested three separate models within each tertile of alignment, after excluding alignment and the interaction term from the model. Mass was added in a

separate step to determine its contribution to the model in each tertile of alignment. The SPSS program version 18.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses.

2.4 Results

Participants' demographic, gait and clinical characteristics are presented in Table 2.1. Results of the unstratified regression analyses are presented in Table 2.2. The interaction term (mechanical axis angle*mass) contributed significantly to the full model. There were no substantial differences in results when we repeated analyses while reversing the order of adding mechanical axis angle and mass to the models. Means and standard deviations for the peak knee adduction moment for nine subgroups based on the tertiles for mechanical axis angle and mass are presented in Table 2.3. The regression coefficients and total explained variance for the regression models within each tertile of mass and mechanical axis angle are presented in Tables 2.4 and 2.5, respectively. After controlling for the other variables in the model, the effect of alignment on knee adduction moment was shown to increase from the lowest-to-highest mass tertiles illustrating mass modified the relationship between alignment and knee load (Table 2.4). The addition of the alignment term in these models contributed 32%, 54% and 44% of explained variance, respectively. After controlling for the other variables in the model, the effect of mass on knee adduction moment was shown to remain relatively constant across the alignment tertiles suggesting alignment did not modify the relationship between mass and knee load (Table 2.5). The addition of the mass term in these models contributed 6%, 10% and 9% of explained variance in the knee adduction moment, respectively.

Table 2.1: Participants' demographic, gait and clinical characteristics (n=487)

	Mean (SD)	Min, Max
Age (years)	46 (10)	20.0, 76.0
No. of males	363 (74.5%)	-
Mass (kg)	90.6 (18.3)	43.2, 150.7
Height (m)	1.8 (0.1)	1.5, 2.1
BMI (kg/m^2)	29.5 (5.1)	18.0, 49.0
Gait speed (m/s)	1.1 (0.2)	0.3, 1. 8
Toe-out angle (˚)	12.1 (6.2)	-6.9, 32.0
Trunk lean (˚)	3.0 (2.7)	-4.9, 20.3
Peak adduction moment (Nm)	46.1 (20.6)	-3.1, 127.7
Peak adduction moment (%BWxHT)	3.0 (1.1)	-0.2, 6.4
Mechanical axis angle (˚)	-6.5 (5.6)	-21.0, 22.1
No. varus/valgus limbs*	437/50	-
Pain score during walking (0-10)	3.1 (2.7)	0.0, 10.0
KL Grade [Ŧ]		
No. 1/2/3/4	59/148/147/133	-

* Varus is defined as < 0˚, and valgus as > 0˚.

[Ŧ] Higher Kellgren and Lawrence (KL) grades indicate greater disease severity

Table 2.2: A summary of regression models (dependent variable: peak knee adduction moment)

Model	Adjusted R^2	R^2 Change	P
Trunk Lean + Toe Out + Pain + Height + Age + OA grade + Gait Speed + Gender	0.25	0.25	<0.001
Trunk Lean + Toe Out + Pain + Height + Age + OA grade + Gait Speed + Gender **+ MAA**	0.62	0.37	<0.001
Trunk Lean + Toe Out + Pain + Height + Age + OA grade + Gait Speed + Gender + MAA **+ Mass**	0.68	0.06	<0.001
Trunk Lean + Toe Out + Pain + Height + Age + OA grade + Gait Speed + Gender + MAA + Mass **+ (MAA*Mass)**	0.70	0.02	<0.001

Table 2.3: Mean (SD) for peak knee adduction moment (Nm) for subgroups of patients based on tertiles of mechanical axis angle (MAA) and mass. Negative MAA values represent varus alignment.

	MAA > -5º [mean = 0º]	**MAA -5º to -9º** [mean = -7º]	**MAA < -9º** [mean = -12º]
Mass < 80 kg [mean = 72kg]	26 (10)	39 (10)	50 (13)
Mass 80 to 100 kg [mean = 89kg]	31 (15)	47 (10)	56 (15)
Mass > 100 kg [mean = 111 kg]	37 (16)	56 (16)	72 (22)

Table 2.4: Regression coefficients and total explained variance in the peak adduction moments for mass tertiles

Peak Knee Adduction Moment						
	Mass < 80 kg [R^2=0.66, p<0.01]		**Mass 80 to 100 kg** [R^2=0.69, p<0.01]		**Mass >100 kg** [R^2=0.61, p<0.01]	
Variable	**B-coefficient**	**P**	**B-coefficient**	**P**	**B-coefficient**	**P**
Constant	-48.5 (-87.2, -9.8)	0.014	-94.8 (-139, -50.6)	< 0.001	-109.8 (-169.2, -50.4)	< 0.001
Age	0.1 (-.01, 0. 3)	0.081	0.3 (0.1, 0.5)	0.002	-0.1 (-0.4, 0.2)	0.499
Gender	3.5 (-0.4, 7.3)	0.07	-9.8 (-15.4, -4.2)	0.001	-1.2 (-9.1, 6.8)	0.776
Height	39.3 (16.3, 62.3)	0.001	69.9 (45, 94.9)	< 0.001	80.7 (46.3, 115.1)	< 0.001
Gait speed	4.6 (-3.7, 12.9)	0.272	9.4 (-0.1, 18.8)	0.052	9.9 (-3.2, 23)	0.136
Trunk lean	-0.6 (-1.2, -0.1)	0.02	-1.4 (-2, -0.7)	< 0.01	-0.9 (-1.8, 0.1)	0.054
Toe-out angle	-0.4 (-0.6, -0.2)	< 0.001	-0.2 (-0.5, 0.1)	0.149	0.2 (-0.3, 0.5)	0.454
MAA*	**-1.7** (-2, -1.5)	**< 0.001**	**-2.5** (-2.8, -2.2)	**< 0.001**	**-3.2** (-3.7, -2.7)	**< 0.001**
OA grade	1.1 (-0.6, 2.7)	0.206	-2.4 (-4.1, -0.6)	0.008	-1.9 (-4.9, 1)	0.196
Pain	-0.2 (-0.7, 0.4)	0.583	-0.4 (-1.1, 0.3)	0.229	-0.1 (-1.1, 0.8)	0.772

* The mechanical axis angle (MAA) adds 32% (mass < 80kg), 54% (mass 80 to 100kg) and 44% (mass > 100kg) of explained variance when added to the models.

Table 2.5: Regression coefficients and total explained variance in the peak adduction moments for mechanical axis angle (MAA) tertiles. Negative MAA values represent varus alignment.

Peak Knee Adduction Moment						
	MAA > -5º [R^2=0.25, p<0.01]		**MAA -5º to -9º** [R^2=0.47, p<0.01]		**MAA < -9º** [R^2=0.50, p<0.01]	
Variable	**B-coefficient**	**P**	**B-coefficient**	**P**	**B-coefficient**	**P**
Constant	3.4 (-46.4, 53.2)	0.893	-82.5 (-126.5, -38.4)	< 0.001	-169.5 (-227.3, -111.6)	< 0.001
Age	0.1 (-0.1, 0.3)	0.272	0.1 (-0.1, 0.3)	0.156	0.2 (-0.1, 0.5)	0.144
Gender	8.5 (2.7, 14.4)	0.003	0.1 (-5.6, 5.7)	0.992	-7.5 (-14.6, -0.4)	0.038
Height	-12 (-43.1, 18.9)	0.443	56 (26.9, 85)	< 0.001	103.8 (68.1, 139.5)	< 0.001
Mass*	**0.3** (0.1, 0.4)	**< 0.001**	**0.3** (0.2, 0.5)	**< 0.001**	**0.4** (0.2, 0.5)	**< 0.001**
Gait speed	19.6 (4.3, 34.9)	0.012	4.5 (-4.7, 13.6)	0.334	19.8 (6.6, 32.9)	0.003
Trunk lean	-0.2 (-1, 0.6)	0.615	-0.7 (-1.5, 0)	0.042	-0.9 (-1.7, 0)	0.05
Toe-out angle	-0.5 (-0.8, -0.2)	< 0.001	-0.2 (-0.5, 0.2)	0.32	-0.1 (-0.5, 0.3)	0.71
OA grade	0.6 (-1.7, 3)	0.609	-2 (-4, 0.1)	0.059	-3.1 (-6, -0.2)	0.038
Pain	-0.5 (-0.9, 0.8)	0.909	0.1 (-0.6, 0.8)	0.705	0.1 (-0.9, 1)	0.893

* Mass adds 6% (MAA > -5°), 10% (MAA -5° to -9°) and 9% (MAA < -9°) of explained variance when added to the models.

2.5 Discussion

The present findings describe a statistical interaction between alignment and body mass on dynamic knee joint load in patients with knee OA. Specifically, the association between frontal plane alignment and medial compartment load during walking depends on mass, with a higher association observed in patients with higher mass. For example, in the tertile with highest mass, our results suggest a 3.2 Nm (approximately 6% of the mean value) increase in knee adduction moment for every 1 degree increase in varus alignment.

These findings also describe the major role of alignment in loading the knee's medial compartment during walking. In all regression analyses, mechanical axis angle contributes substantial amounts (32-54%) of explained variance in the knee adduction moment. Even in the tertile with lowest mass, results suggest a 1.7 Nm (approximately 5% of the mean value) increase in peak knee adduction moment for every 1 degree increase towards varus alignment, while controlling for other variables in the model (Table 2.4). Similarly, the means for peak knee adduction moment in the patient subgroups with the lowest mass and more varus alignment (39 Nm and 50 Nm) are greater than in the patient subgroups with the highest mass and least varus alignment (37 Nm) (Table 2.3).

Our results are consistent with the well-established major role of alignment in dynamic knee joint loading[24,32]. Similarly, the described major role of alignment in knee joint loading is consistent with results of a prospective study evaluating obesity as a risk factor for progression of knee OA. Niu et al.[10] report no association between obesity and progression in knees with varus alignment (Relative Risk (RR) = 0.9; 95%CI = 0.7, 0.9) and suggest that the increased load on the medial compartment produced by varus

alignment alone is sufficient to produce progression, and that the excess load conferred by obesity may not be necessary as an additional factor.

Our results also suggest an increase in the knee adduction moment of up to 0.4 Nm (approximately 1% of the mean value) for every 1 kg increase in mass. Although mass explained less variance than alignment, these findings should not lessen the importance of increased mass on excessive knee joint loading, or the importance of mass reduction for patients with knee OA[33-36]. In fact, results from our cross-sectional study are comparable with those of Messier et al.[37] who in a prospective study of mass loss in older adults with knee OA suggested a 0.5 Nm reduction in knee adduction moment for every 1 kg decrease in mass. Messier et al.[37] emphasize that this equates to a four-fold reduction in knee loading per step for every one pound lost, and given the thousands of steps taken per day, is clinically important[37].

Statistical interactions identify a relationship between an independent and a dependent variable that is conditional upon the value of a second independent variable[38]. More specifically, a moderated causal relationship specifies a focal independent variable, a dependent variable and another independent variable that moderates the relationship between the focal independent variable and the dependent variable (i.e. moderator variable)[39]. Table 2.4 and 2.5 illustrate a simple approach to understanding joint loading in patients with knee OA, while accounting for the interaction between mass and alignment using the terminology of a moderated causal relationship. Because the assignment of a variable to a focal or moderating role is a matter of perspective[39], these tables were structured to illustrate each component variable of the interaction term as the effect moderator in the interaction. Inspection of the beta coefficient confidence intervals for mechanical axis angle in Table 2.4 shows that mass moderates the effect of alignment

on knee joint load by increasing this effect at greater body mass. Conversely, the overlapping beta coefficient confidence intervals for mass in Table 2.5 show that alignment does not appear to moderate the effect of mass on knee joint load to the same extent because the effect of mass is relatively constant across increasing amounts of varus deformity. Perhaps the clinical relevance of these two perspectives about the nature of the interaction is a function of treatment objectives. For example, when evaluating the effects of interventions intended to alter alignment as the focal independent variable, it is important to control for mass because it clearly moderates the relationship between alignment and load, as shown in Table 2.4. Conversely, Table 2.5 suggests when evaluating OA treatments intended to decrease mass as the focal independent variable, it may be less critical to control for alignment because it does not appear to moderate the effect of mass on knee joint loading. This knowledge about the nature of the interaction may be clinically useful because weight reduction interventions may not necessarily occur in a setting where knee alignment measures are easily obtained.

Furthermore, our results complement and extend the work of Sharma et al.[9]. They found that much of the association between BMI and radiographic disease severity is explained by alignment, reporting that the partial correlation between BMI and radiographic disease severity is reduced from r=0.24 (95% CI = 0.16, 0.31) to 0.04 (95% CI = -0.040, 0.12) when alignment is added to the model. Our work builds upon this finding because it reveals an interaction between mass and alignment when knee load, a key intervening variable in the obesity-OA relationship, is the dependent variable of interest. Further investigation of this interaction may provide additional insight into the relational paradigm between obesity and knee OA outlined by Sharma et al.[9].

2.5.1 Study Limitations

The present findings provide further rationale for interventions intended to decrease mass, and in particular, to alter alignment in patients with knee OA. However, limitations in the present cross-sectional study design should be acknowledged when inferring changes in knee joint load due to changes in alignment and/or body mass. Potential limitations in the generalizability of findings based on our sample should also be acknowledged. The present sample was recruited from patients with longstanding symptoms referred to a tertiary care centre that specializes in orthopaedics, including surgical interventions. This may also help explain the unusually high proportion of males in our sample, given the overall greater prevalence of knee OA in women than men. Additionally, although the external adduction moment about the knee is a valid and reliable proxy for load on the knee medial compartment[12-15], and is strongly associated with radiographic disease progression[40], it neglects the contribution from muscles and other soft tissues to internal joint loading. Future prospective intervention studies comparing the effects of changes in lower limb alignment and body mass (including their combination) on measures of knee joint load and disease progression are warranted.

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3. Systematic Review and Meta-Analysis of the Biomechanical and Clinical Effects of Valgus Knee Bracing in Patients with Medial Compartment Knee Osteoarthritis

3.1 Summary

Clinical practice guidelines are inconsistent regarding their recommendations for brace use in the management of knee osteoarthritis (OA). The objective of this study was to investigate biomechanical effects, patient-reported outcomes, complications, and compliance with valgus brace use for medial compartment knee OA. Four electronic databases were searched. All English-language articles that reported biomechanical and/or patient-reported outcomes of valgus knee braces in patients with medial compartment knee OA were included. The methodological quality of each study was examined. Data were extracted and meta-analyses were performed where possible using standardized mean differences (SMD) and 95% confidence intervals (95%CI). Studies not included in the meta-analyses were reviewed descriptively. Data were extracted from 38 articles including eight randomized clinical trials. Pooled data from biomechanical studies suggested a significant decrease in the external knee adduction moment during walking while wearing the brace (SMD=0.61; 95%CI: 0.39, 0.83; $p<0.001$). Pooled data from randomized clinical trials suggested significant improvements in pain (SMD=0.46; 95%CI: 0.09, 0.83; p=0.014) and function (SMD=0.39; 95%CI: 0.10, 0.68; p=0.008). The reporting of parameters affecting dosage (i.e. brace angulation and frequency of use) was variable and often unclear. The most common difficulties reported during brace use included slipping, discomfort and poor fit. Complications included skin irritation, swelling, mechanical brace problems, heat and heaviness. Patient-reported brace use varied considerably between studies, but consistently decreased over time. Systematic review with meta-analysis of biomechanical effects and patient-reported outcomes supports the use of valgus knee braces in the management of medial knee OA; however, issues related to their appropriate dosage, patient comfort and compliance remain as substantial challenges to long-term use.

3.2 Introduction

Osteoarthritis (OA) imposes a substantial burden on individuals and society[1,2]. While there is no known cure, clinical practice guidelines have outlined the available treatment options for patients with symptomatic knee OA[3-8]. Risk factors for disease progression, patient needs and preferences should modulate which approach to consider[5]. Initial treatments for knee OA include both pharmacological and non-pharmacological options, while surgical therapies are available to those patients that fail to respond to non-surgical treatment[4-5]. Physical therapy, patient education and joint protection modalities such as valgus knee braces encourage disease self-management to minimize physical disability and improve quality of life for patients, and expose patients to less risk of side effects than pharmacological interventions[9-11].

Valgus knee braces are external, removable devices aimed to redistribute knee loads about the tibio-femoral joint. While varus braces do exist and are intended to shift the load away from the lateral compartment, valgus braces are more common largely due to the greater loads borne by the medial tibio-femoral compartment during walking[12]. Although braces are popular[4,13], their biomechanical and clinical effectiveness in the management of knee OA is still debated. Numerous studies have assessed the proposed mechanisms of bracing; however, results from these biomechanical studies vary widely[14-21]. Similarly, the clinical significance of valgus bracing is unclear despite promising findings from clinical trials with respect to pain and function[22-25].

Many clinical practice guidelines have included comments on knee bracing for patients with malalignment, joint pain and instability. Despite reviewing the same literature, some guidelines support the use of valgus bracing as an appropriate treatment for medial knee OA[3-5], while others suggest inconclusive evidence to support brace use[7-8].

Several bracing studies have been published recently and may contribute to a better understanding of these devices[18-21,24-27,29-35]. Additionally, improving the level of evidence informing future clinical practice guidelines for valgus knee braces might be achieved by conducting a systematic review, with meta-analyses where possible. We are unaware of any previously published meta-analyses examining the biomechanical and clinical effectiveness of valgus knee braces. Therefore, the objective of this systematic review and meta-analysis was to investigate biomechanical effects, patient-reported outcomes, complications, and compliance with valgus brace use in patients with medial knee OA.

3.3 Materials and Methods

3.3.1 Inclusion Criteria and Exclusion Criteria

Studies examining the effectiveness of valgus knee braces in patients with medial compartment knee OA published as full text, English language journal articles since 1990 were included. There were no restrictions on the development or severity of knee OA. Follow-up duration was also not restricted. Subject matter not pertaining to valgus knee bracing, as well as editorials, comments, letters, abstracts, review articles, unpublished material such as theses and dissertations, and animal or cadaveric studies were also excluded.

3.3.2 Search Strategy

Relevant peer-reviewed studies were identified by systematically reviewing the following electronic databases from their inception to February 2013: Web of Knowledge, Medline, Scopus, CINAHL and Embase. Searches were performed using combined and/or truncated key terms including: “knee*”, “osteoarthritis OR arthritis OR

arthrosis", "brace* OR bracing", and "valgus brace* OR valgus bracing". The Medline database search is listed in Appendix A. Studies published before 1990 were manually excluded after database results were combined. Also, reference lists of potentially eligible articles were manually searched. A detailed protocol for this systematic review has not been previously published.

3.3.3 Determining Inclusion

Two authors (RFM and KML) blinded to journal title and authorship independently assessed eligibility in two stages. Title and abstracts were reviewed. Articles that met the inclusion and exclusion criteria were then obtained as full manuscripts and reviewed. Disagreement between reviewers regarding article selection was discussed and consensus was achieved. Details of the literature search are reported using the PRISMA guidelines and checklist (Appendix B)[36].

3.3.4 Methodological Quality Assessment of Included Studies

The methodological quality of each study was evaluated using a modified Downs and Black scale[37]. The scale consists of 27 items across six subscales including Quality Index, Reporting, Internal Validity (Confounding and Bias), External Validity, and Power from which 13 items for Internal Validity were used in the present review (Appendix C). Each item was scored 1-point if the item was satisfied. If all studies scored 0 for a given item, the item was removed. Two authors (RFM and KAM) independently scored each study. Disagreement between reviewers was discussed and consensus was achieved.

3.3.5 Outcome Measures and Data Extraction

Study design, number of patients and their demographics, brace type, duration of use and data for biomechanical effects, patient-reported outcomes, comfort and compliance were extracted from each study by two independent reviewers (RFM and KAM). A standard data extraction form was used (Appendix D). Disagreement between reviewers regarding article selection was discussed and consensus was achieved. Study designs were classified using the operational definitions provided by the Cochrane Collaboration[38]. Outcome measures considered for meta-analysis were subdivided into biomechanical and patient-reported. Means and standard deviations for the outcomes of interest were extracted from each study. We contacted eight authors. Five authors provided additional data not provided in the original study[16,18-19,21-22,26,30,48].

3.3.6 Data Analysis

At each phase of the article selection process, measurement of agreement between reviewers was calculated using the kappa (κ) statistic. For each meta-analyses, calculations were performed with the Comprehensive Meta-Analysis software program (V2, Biostat, Englewood, NJ, USA).

The standardized mean difference (SMD) was calculated to compare results between biomechanical studies using within-patient pre-intervention and post-intervention means and standard deviations for the external knee adduction moment and knee adduction angular impulse. For authors who could not be contacted or no longer had data, we estimated values from figures or imputed missing data using a conservative approach. If a study reported significant findings with a non-exact p value (i.e. $p<0.05$ or $p<0.01$), we assigned p values of $p=0.05$ and $p=0.01$, respectively[38-39]. For non-significant

findings reported with a non-exact p value, a paired correlation value of r=0.5 was used to calculate the SMD[40-43]. Because we were evaluating pre and post intervention means and standard deviations, a correlation closer to zero would have been similar to using post-intervention means only, whereas a correlation closer to one would have been similar to using change scores[40].

Although many studies reported the effects of valgus knee bracing on patient-reported outcomes, we considered findings from high quality randomized clinical trials (RCT) comparing a control group and experimental valgus knee brace group to provide stronger evidence than non-randomized studies. Therefore, the SMD was calculated using reported post-intervention means, standard deviations and/or effect sizes for the RCT's only.

Pooled estimates and 95% confidence intervals for each meta-analysis were obtained using a random effects model. The SMD was interpreted using Cohen's d [44]. Heterogeneity was tested using I^2 [43]. Sensitivity analyses were performed to assess possible effects of outliers and studies with estimated or imputed data. Small-to-moderate heterogeneity was explored using subgroup analyses for laboratory-based studies. We assessed publication bias quantitatively using Egger's Regression test[45].

3.4 Results

3.4.1 Search Results

Of the 1107 articles identified, 38 were included (Figure 3.1). Eligibility agreement for titles and abstracts between reviewers was excellent (κ=0.94). There was disagreement between reviewers for nine titles and abstracts. Eight articles were excluded and one included. Reasons for exclusion were: patents (two studies), non-English

language (one study), healthy populations (two studies), duplicates (one study) and review articles (two studies). Eligibility agreement for full-text articles was good (κ=0.85). There was disagreement between reviewers for seven full-text articles and all were excluded. Reasons for exclusion were: samples of subjects without OA (two studies), outside eligibility criteria (two studies), data from a previously published study (one study), irrelevant outcome measures (one study), and a modeling/technical report (one study). After extracting data for 38 full-text articles, disagreement was recorded for 13 (35%) articles and a consensus was met following a joint reassessment. The outcome measures from all 38 articles were examined descriptively. Data from 16 studies were combined in meta-analyses.

3.4.2 Characteristics of Included Studies

Characteristics of the included studies are described in Table 3.1A, 3.1B and 3.1C. In total, there were 1143 patients with knee OA recruited and enrolled in the studies. Data from 1098 patients were analyzed and reported. Age ranged from 21 to 80 years. Of the 28 (of 38) articles that reported sex, 525 (56%) males and 420 (44%) females were included. Knee OA severity was reported in 20 studies (of 38). Fourteen studies (of 38) used a laboratory-based design to examine the effects of valgus bracing during a single test session with and without wearing the brace (Table 3.1A)[15-16,18,20-21,26-27,31,33-34,53,57,60-61]. Thirteen studies (of 38) used a prospective cohort (single group of patients observed prospectively over time) to evaluate the effectiveness of the brace over time (Table 3.1B)[14,19,29,35,46-52,56,59] and one study (of 38) evaluated both[46]. Two studies (of 38) retrospectively evaluated valgus knee braces[28,54] and one study (of 38) administered a survey[32]. Twenty-six (of 38) studies assessed the biomechanical mechanisms of valgus

knee bracing[14-16,17-21,24,26-27,30-31,33-34,46-49,52-53,55,57,59-61] and 26 (of 38) studies assessed patient-reported outcome measures[14,16-19,22-25,29-31,33,35,46-52,54-55,58-60]. Nineteen studies (of 38) investigated effects of a single brace[14-16,18,20,28-29,32,34-35,46-54]. Ten studies compared valgus bracing with another valgus brace or using the same brace with multiple degrees of valgus angulation[17,19,21,26-27,55-59]. Two studies used a placebo brace[60-61]; five studies compared bracing with lateral wedge insoles[24,26,30-31,33]; one study compared bracing with a neoprene sleeve[22]; one study used a multi-intervention approach[25]; and four studies included a control group (two studies were healthy controls[14,48] and two studies were controls with knee OA[22-23]).

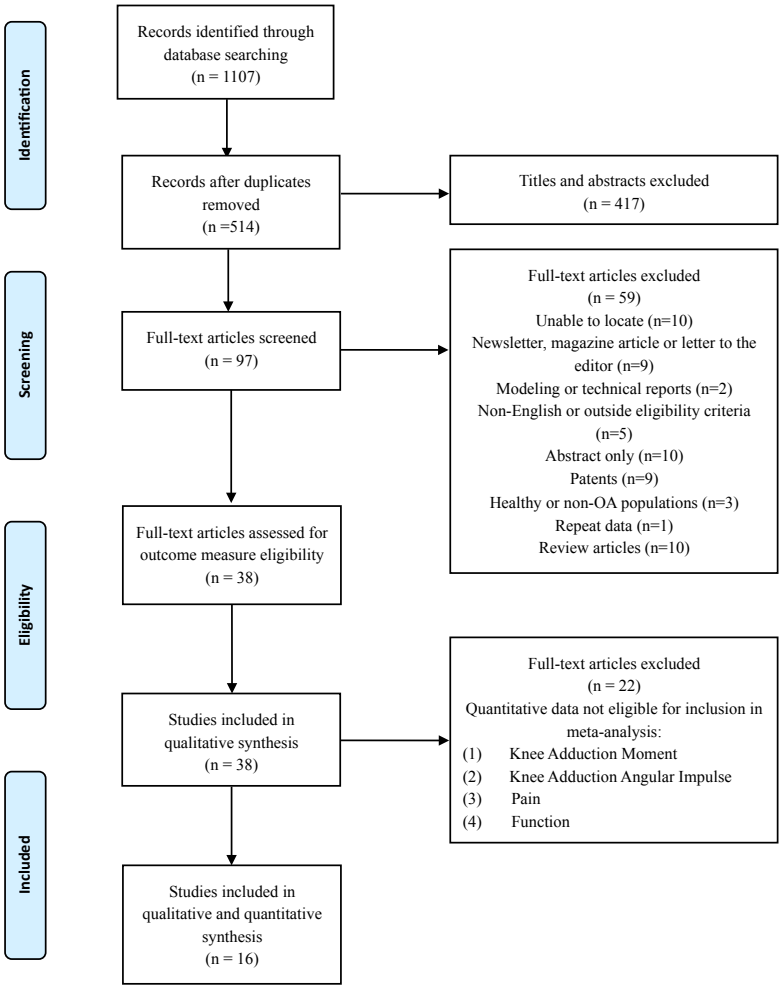

Figure 3.1: The 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flowchart. 38 studies were selected for inclusion in qualitative analysis.

Table 3.1: A detailed summary of included (A) laboratory-based studies, (B) observational cohorts, and surveys, and (C) randomized controlled trials (parallel and crossover).

(A)

Author, Year	Study Design (Sample Size)	Duration in Brace	Clinical Outcome Measures	Biomechanical Outcome Measures	Compliance / Adverse Effects
Komistek *et al*. (1999)	Laboratory (n=15)	Single Day Testing	Yes/No pain report	Joint Space FTA	- / -
Self *et al*. (2000)	Laboratory (n=5)	Single Day Testing	-	KAM Brace Force	- / -
Pollo *et al*. (2002)	Laboratory (n=11)	2 weeks (Single Day Testing)	VAS pain VAS function	KAM Brace Moment	- / -
Anderson *et al*. (2003)	Laboratory (n=11)	Single Day Testing	-	Joint Force	- / -
Nadaud *et al*. (2005)	Laboratory (n=5)	Single Day Testing	-	Joint Space	- / -
Dennis *et al.* (2006)	Laboratory (n=40)	Single Day Testing	-	Joint Space	- / -
Schmalz *et al.* (2010)	Laboratory (n=16)	4 weeks (Single Day Testing)	VAS pain	KAM Brace Moment	Yes / Yes
Toriyama et al. (2011)	Laboratory (n=19)	Single Day Testing	-	KAM	- / -
Fantini Pagani *et al.* (2011)	Laboratory (n=10)	Single Day Testing	-	KAM Impulse Alignment Brace Moment	- / -
Kutzner *et al.* (2011)	Laboratory (n=3)	Single Day Testing	-	Joint Force	- / Yes
Esrafilian *et al.* (2012)	Laboratory (n=2)	Single Day Testing	-	KAM Alignment	- / -
Fantini Pagani *et al.* (2012)	Laboratory (n=12)	Single Day Testing	-	Muscle activation	- / -
Moyer *et al.* (2013)	Laboratory (n=16)	Single Day Testing	VAS pain	KAM Impulse	- / -
Arazpour *et al.* (2013)	Laboratory (n=12)	6 weeks (Single Day Testing)	VAS pain	KAM	Yes / -

(B)

Author, Year	Study Design (Sample Size)	Duration in Brace	Clinical Outcome Measures	Biomechanical Outcome Measures	Compliance / Adverse Effects
Lindenfeld *et al*. (1997)	Prospective Cohort (n=11)	4 weeks (maximum 6 weeks)	CKR System VAS pain	KAM	- / -
Matsuno *et al*. (1997)	Prospective Cohort (n=20)	12 months	JOA Knee Score	FTA	Yes / -
Liu *et al*. (1998)	Prospective Cohort (n=11)	3 to 50 months (Average 1.75 years)	-	-	- / Yes
Hewett *et al*. (1998)	Prospective Cohort (n=19)	4 weeks 9 weeks 12 months	CKR System VAS pain Walking Tolerance	KAM	Yes / -
Katsuragawa *et al*. (1999)	Prospective Cohort (n=14)	3 months	JOA Knee Score	BMD	- / -
Draper *et al*. (2000)	Prospective Cohort (n=30)	3 months	HSS Score	-	- / -
Finger *et al*. (2002)	Prospective Cohort (n=28)	3 months	Resting pain Activity pain Night pain	-	Yes / Yes
Barnes *et al*. (2002)	Prospective Cohort (n=30)	8 weeks	AAOS Arthritis Questionnaire SF 36	Joint Space Alignment	Yes / Yes
Giori *et al.* (2004)	Retrospective Cohort (n=46)	Retrospective	Knee Society Score for Pain and Function	-	Yes / Yes
Gaasbeek *et al.* (2007)	Prospective Cohort (n=15)	6 weeks (with Single Day Testing)	VAS pain WOMAC	KAM	- / -
Ramsey *et al.* (2007)	Prospective Cohort (n=16)	2 weeks in each phase	KOOS pain KOOS function	Muscle activation Alignment	- / Yes
Fantini Pagani *et al.* (2010)	Prospective Cohort (n=11)	2 weeks in each phase	WOMAC 6MWT	KAM Impulse Brace Moment	- / -
Wilson *et al.* (2011)	Retrospective Cohort (n=30)	Retrospective	-	-	Yes / -
Hurley *et al.* (2012)	Prospective Cohort (n=24)	2 week accommodation with 6 months of wear	WOMAC SF 36	-	Yes / -
Briggs *et al.* (2012)	Prospective Cohort (n=39)	6 months	SF 12 WOMAC	-	Yes / -
Squyer *et al.* (2013)	Survey (n=110, 89 responders)	Survey	-	-	Yes / Yes

(C)

Author, Year	Study Design (Sample Size)	Duration in Brace	Clinical Outcome Measures	Biomechanical Outcome Measures	Compliance / Adverse Effects
Horlick *et al*. (1993)	Randomized Crossover (n=19)	6 weeks in each phase	VAS pain Participation Time	FTA Joint Space	Yes / -
Kirkley *et al*. (1999)	Randomized Parallel (n=110)	6 months	WOMAC MACTAR 6MWT	-	- / -
Richards *et al.* (2005)	Randomized Crossover (n=12)	6 months	VAS pain VAS function HSS Score	-	- / Yes
Draganich *et al.* (2006)	Randomized Crossover (n=10)	4 to 5 weeks	WOMAC	KAM Alignment	Yes / -
Brouwer *et al.* (2006)	Randomized Parallel (n=117)	3 months 6 months 12 months	VAS pain HSS Score Walking Distance	-	Yes / Yes
van Raaij *et al.* (2010)	Randomized Parallel (n=91)	6 months	VAS pain WOMAC	Alignment	Yes / Yes
Hunter *et al.* (2012)	Randomized Crossover (n=80)	12 weeks in each phase of the study with 6 weeks washout	WOMAC	-	Yes / Yes
Jones *et al*. (2013)	Randomized Crossover (n=28)	2 weeks in each phase	WOMAC VAS pain	Alignment KAM Impulse	Yes / -

NA = Not Available

VAS = Visual Analog Scale; CKR = Cincinnati Knee Ratings; JOA = Japan Orthopaedic Association knee scoring system; WOMAC = Western Ontario McMaster Arthritis Center; MWT = Minute Walk Test; MACTAR = McMaster Toronto Arthritis Patient Preference Questionnaire; AAOS = American Academy of Orthopedic Surgeons; HSS = Hospital for Special Surgery; KOOS = Knee Injury and Osteoarthritis Outcome Score; QOL = Quality of Life; SF 36 = Short Form 36, SF 12 = Short Form 12

FTA = Femor-tibial Angle; KAM = Knee Adduction Moment; BMD = Bone Mineral Density

Nine different brace angulations were used across 27 studies (of 38) and 11 studies (of 38) did not specify the brace angulation. The following brace descriptions were used: an off-the-shelf (OTS) brace[17,23-25,32,51,56-58,60-61]; a custom brace[14-15,17-18,31-33,47,56]; a neutral brace[19,21,25,27,55,59]; a 10° brace[55]; an 8° brace[16,26-27]; a 6° brace[30]; a 5° brace[29]; a 4° brace[16,19,21-22,26-27,50,59] and a 4° tight brace[16].

Eight RCTs (of 38) were included[17,22-25,30,55,58] and five (of eight) were a randomized crossover design. Three (of five) compared different valgus braces[17,55,58], one (of five) compared valgus bracing to a lateral wedge orthotic[30] and one (of five) investigated the effects of combined interventions including valgus bracing with a motion control shoe and lateral wedge orthotic[25]. Two (of three) randomized parallel design trials compared valgus bracing to a control group[22-23] (one of which also compared bracing to a neoprene sleeve[22]), and one (of three) compared valgus bracing to a lateral wedge orthotic[24]. Sixteen studies (of 38) assessed patient compliance with valgus brace wear or frequency of use and twelve studies (of 38) assessed adverse events and potential reasons for poor compliance.

3.4.3 Methodological Quality Assessment of Included Studies

Four internal validity items were removed because all included studies scored 0. Therefore, the maximum possible score was 9. The average quality appraisal score was 6.5 ± 1.4 (range: 3-9). For 30 laboratory-based, prospective and retrospective studies and a survey, the average quality appraisal score was 6.1 ± 1.2 (range: 3-8). For eight RCTs, the average quality appraisal score was 7.9 ± 1.0 (range: 6-9). No studies were excluded on the basis of quality appraisal (Appendix C). Inter-rater agreement for each item of the methodological quality assessment was moderate to high (κ=0.72-0.91).

3.4.4 Biomechanical Effects

Twenty-six (of 38) articles were analyzed descriptively. Biomechanical parameters evaluated included the external knee adduction moment[14-20,26,30-31,33-34,46,48]; lower limb alignment[17,24,26,30,34,47,52,55,60,62]; the valgus moment created by the brace[15-16,18-19,26]; medial compartment joint space[52,55,57,60-61]; knee adduction angular impulse[19,26,30-31]; medial contact joint forces[27,51]; muscle co-contraction[21,59]; and bone mineral density at the medial and lateral tibial condyles[49].

Fourteen studies (of 26) reported the effect of the brace on the external knee adduction moment during walking. Nine studies (of 14) reported the overall peak knee adduction moment[14-18,33-34,46,48] while five studies reported the first and second peak knee adduction moments separately[19-20,26,30-31]. Extracted data were analyzed and combined in a meta-analysis (n=175). Seven studies (of 14) reported multiple changes in the external knee adduction moment depending on the magnitude of brace angulation, or evaluated the effects of valgus bracing at both peaks of the knee adduction moment curve[16-17,19-20,26,30-31]. For those studies, we only included data with the greatest change in the meta-analysis. The analysis indicated a significant reduction when wearing the brace (Figure 3.2). The SMD with and without the valgus knee brace was 0.61 (95%CI: 0.39, 0.83, $p<0.001$; $I^2=40.8$, $p=0.06$). The Egger's regression test showed significant evidence for publication bias (intercept=2.06, 95%CI: 0.08, 4.03; $p=0.04$).

Sensitivity analysis revealed that removing an outlier[15] had minimal effect on outcome (SMD=0.57; 95%CI: 0.38, 0.76; $p<0.001$), but did reduce heterogeneity from moderate to low ($I^2=24.9$, $p=0.19$). After removal of that study, the Egger's regression test did not show significant evidence for publication bias (intercept=1.37, 95%CI: -1.15, 3.89; $p=0.25$). A second sensitivity analysis revealed that removal of three studies with

estimated and imputed data[20,46,48] had minimal effect on outcome (SMD=0.69; 95%CI: 0.42, 0.96; p<0.001), and did not account for statistical heterogeneity (I^2=45.2, p=0.05). After removal of those studies, the Egger's regression test showed significant evidence for publication bias (intercept=2.27, 95%CI: 0.29, 4.25; p=0.03).

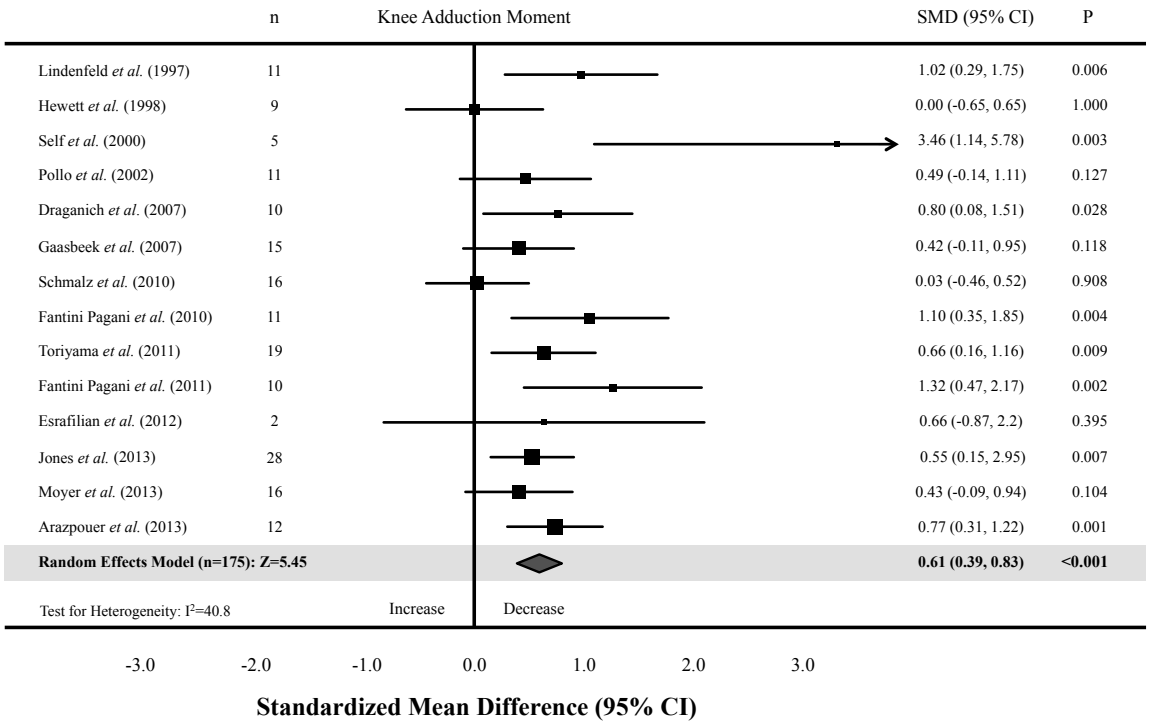

Figure 3.2: Standardized mean difference and 95% confidence intervals for the external knee adduction moment before and after brace wear over time, and with and without a valgus knee brace during single day testing. The diamond represents the pooled effect using a random effects model. The vertical line at 0 represents no difference. Data to the right of 0 represent a decrease in the peak external knee adduction moment.

Nine studies (of 14) examined the effects of bracing with and without the brace during a single testing day[15-16,18,20,26,31,33-34,46], whereas five studies (of 14) examined the effects of bracing before and after brace wear over a longer period of time (14-42 days)[14,17,19,30,48]. Although overall results were similar, the SMD did increase when

analyzing only those studies that examined the effect of valgus brace wear over time. The SMD before and after brace wear over time was 0.65 (95%CI: 0.30, 1.01, p<0.001; I^2=39.0, p=0.16) (Figure 3.3A), and the SMD with and without the valgus knee brace during a single testing day was 0.59 (95%CI: 0.30, 0.89, p=0.000; I^2=47.3, p=0.06) (Figure 3.3B). Subgroup analyses suggested minimal effects on statistical heterogeneity.

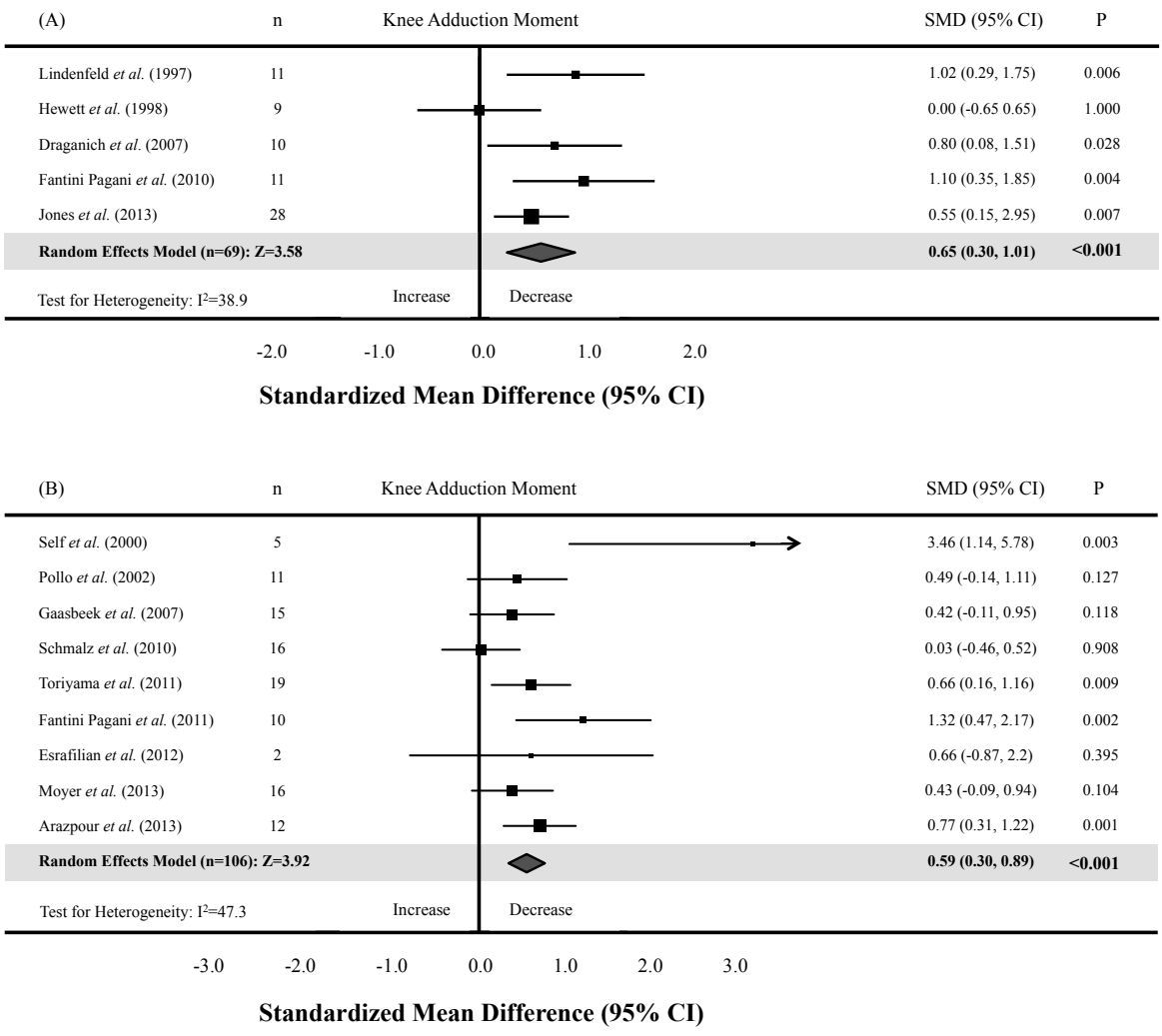

Figure 3.3: Standardized mean difference and 95% confidence intervals for the external knee adduction moment (A) before and after brace wear over time, and (B) with and without a valgus knee brace during single day testing. The diamond represents the pooled effect using a random effects model. The vertical line at 0 represents no difference. Data to the right of 0 represent a decrease in the peak external knee adduction moment.

Five studies (of 26) described the valgus moment provided by the brace to directly oppose the external knee adduction moment[15-16,18-19,26]. One study (of five) reported a maximum valgus brace force of 60N, which remained fairly constant throughout stance[15]. Four studies (of five) described the valgus moment created by the brace, and each suggested that greater valgus moments were associated with greater valgus angulations or strap tensions at both the 1st and 2nd peaks of the knee adduction moment[16,18,19,26]. One study also reported the valgus brace moment relative to the magnitude of the knee adduction moment, suggesting that the mean maximum valgus moment generated by the brace accounted for approximately 10% of the external knee adduction moment during non-brace walking[18].

Four studies (of 26) reported the effects of the brace on the knee adduction angular impulse[19,26,30-31]. This analysis indicated a decrease in the knee adduction angular impulse when wearing the brace (Figure 3.4). The SMD with and without the valgus knee brace was 0.77 (95%CI: 0.32, 1.23, p=0.001; I^2=56.3; p=0.08). The Egger's regression test did not show significant evidence for publication bias (intercept=3.62, 95%CI: -3.31, 10.55; p=0.15).

Five studies (of 26), three laboratory-based[57,60-61], one randomized crossover[55] and one prospective cohort[52], reported the effect of valgus knee bracing on medial compartment joint space. Two studies used standing, hip-to-ankle anteroposterior (AP) radiographs and reported no significant difference in medial joint space between braced and non-braced conditions[52,55]. Means or measures of variability were not reported. Three studies (of five) used fluoroscopic gait analysis to measure knee joint space during walking[57,60-61]. Two studies (of three) reported statistically significant increases in condylar separation while wearing the brace[60-61]. The average increase in medial

compartment separation (mean ± SD) for both studies (n=15, n=40)[60-61] was 1.3mm ± 1.8mm, respectively. In only those patients that had reported improvements in pain (12/15)[60] or an increase in joint space (31/40)[61], the respective average increase in medial compartment separation approached 2.0mm and 1.7mm. One study (of three) did not report whether the change in condylar separation was statistically significant (range: 0.2-0.8mm)[57].

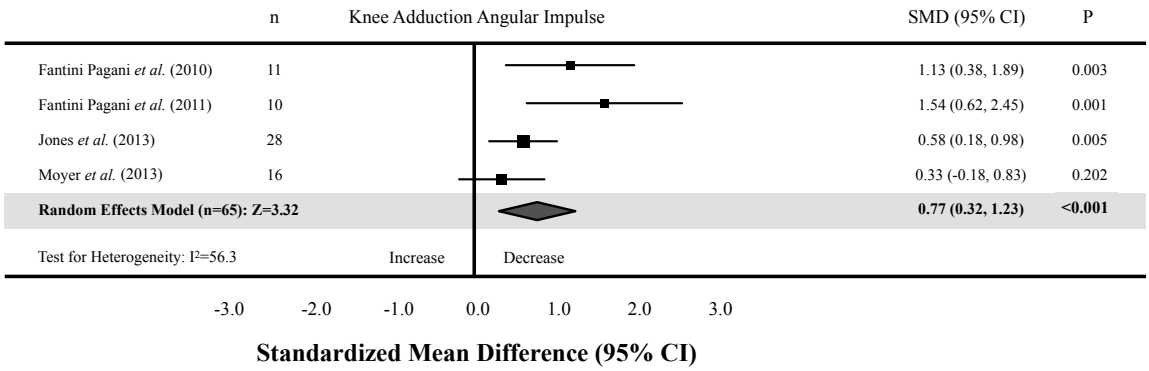

Figure 3.4: Standardized mean difference and 95% confidence intervals for the knee adduction angular impulse before and after brace wear. The vertical line at 0 represents no difference. The diamond represents the pooled effect using a random effects model. Data to the right of 0 represent a decrease in the knee adduction angular impulse.

Ten studies (of 26) reported effects on lower limb alignment[17,24,26,30,34,47,52,55,59-60]. Four studies used the knee adduction angle calculated from three-dimensional gait analysis[26,30,34,59]. Non-significant decreases[59] and significant improvements in lower limb alignment (2.6°)[30] were reported. One study (of four) reported significant and non-significant changes in lower limb alignment when patients wore an 8° and 4° valgus brace, respectively[17]. One study was excluded from further analysis because the values reported occurred during swing[34]. One study used fluoroscopic gait analysis and reported a decrease in varus alignment (2.2°) in 80% of patients (n=12/15), but did not indicate

whether this was a statistically significant change[60]. Five studies used the hip-knee-ankle (or femoro-tibial) angle (FTA) measured on standing AP radiographs[17,24,47,52,55]. Non-significant decreases[24,52,55] and significant improvements in lower limb alignment (1.4°)[47] were reported. One study (of five) reported significant and non-significant changes in lower limb alignment when patients wore a custom fit and off-the-shelf brace, respectively[17]. Across nine (of 10) studies, the change in varus alignment ranged from 0° to 2.6°.

Two studies (of 26) examined the effects a valgus brace on muscle co-contraction during walking[21,59]. Ramsey et al. (2007)[59] and Fantini Pagani et al. (2012)[21] reported decreases in co-contraction ratios for the following muscle pairs: vastus medialias-medial hamstrings (VM-MH), vastus lateralis-lateral hamstrings (VM-MH), vastus medialis-medial gastrocnemius (VM-MG) and vastus lateralis-lateral gastrocnemius (VL-LG). Ramsey et al. (2007)[59] observed a reduction in VM-MH with a 4° brace and VL-LH with both a neutral and 4° valgus setting (100ms prior to initial contact through to the 1st peak knee adduction moment). No changes were observed for either VM-MG or VL-LG co-contractions. Reductions in VM-MH and VL-LH were also reported by Fantini Pagani et al. (2012)[21] for both neutral and 4° brace settings; however, these findings were only noted during the pre-activation phase of the gait cycle (150ms before heel contact). During the loading phase (0-15% stance), reductions in VL-LG were also observed with the 4° brace. No changes were observed for VM-MG co-contractions.

Two studies (of 26) examined the effects of a brace on direct measures of joint loading in vivo[27,53]. Anderson et al. (2003)[53] reported no significant difference on medial compartment load during standing with and without a brace when tested using Tekscan pressure sensors inserted arthroscopically. Authors suggested that their results might be

attributable to sensors shifting. Kutzner et al. (2011)[27] reported decreased medial compartment force during walking with a brace when tested using telemetric implants in three patients after total knee arthroplasty. In neutral, 4° and 8° valgus brace settings, contact force was reduced by 10%, 18% and 23% respectively at the 1st peak knee adduction moment, and was reduced by 9%, 24%, and 30% respectively at the 2nd peak knee adduction moment.

One study (of 26) reported changes in bone mineral density (BMD) over time when patients wore a valgus brace[49]. After wearing a valgus brace, the BMD increased 3% and 7% in the medial and lateral tibial condyles, respectively.

3.4.5 Patient-Reported Outcomes

Eighteen non-randomized studies (of 38) reporting the effects of bracing on pain (15 studies) and function (13 studies) were analyzed descriptively. The effect of valgus bracing on pain was reported using a visual analog scale[14,16,18,31,33,46,48,51], the pain subdomain of questionnaires[19,29,35,53,52,59], or a yes or no response to relief during brace wear[60] (Table 3.1A and 3.1B). Improvements in pain were consistent in thirteen studies (of 15). Two studies (of 15), a laboratory-based study[31] and a prospective observational cohort with a non-randomized crossover design[59] reported no change. No studies reported worse pain after brace wear.

The effect of valgus bracing on function was reported using either a visual analog scale[16], a function subdomain of questionnaires[14,19,29,35,46-50,52,54,59], walking distance[48] or the six-minute walk test[19]. Improvements in function were consistent in eleven studies (of 13)[14,16,19,35,46-50,52,54]. Three prospective observational cohorts studies[19,29,59] reported no change and no studies reported worse function after brace wear. One study (of three)

found inconsistent findings for improvements in function depending on the outcome measure used[19].

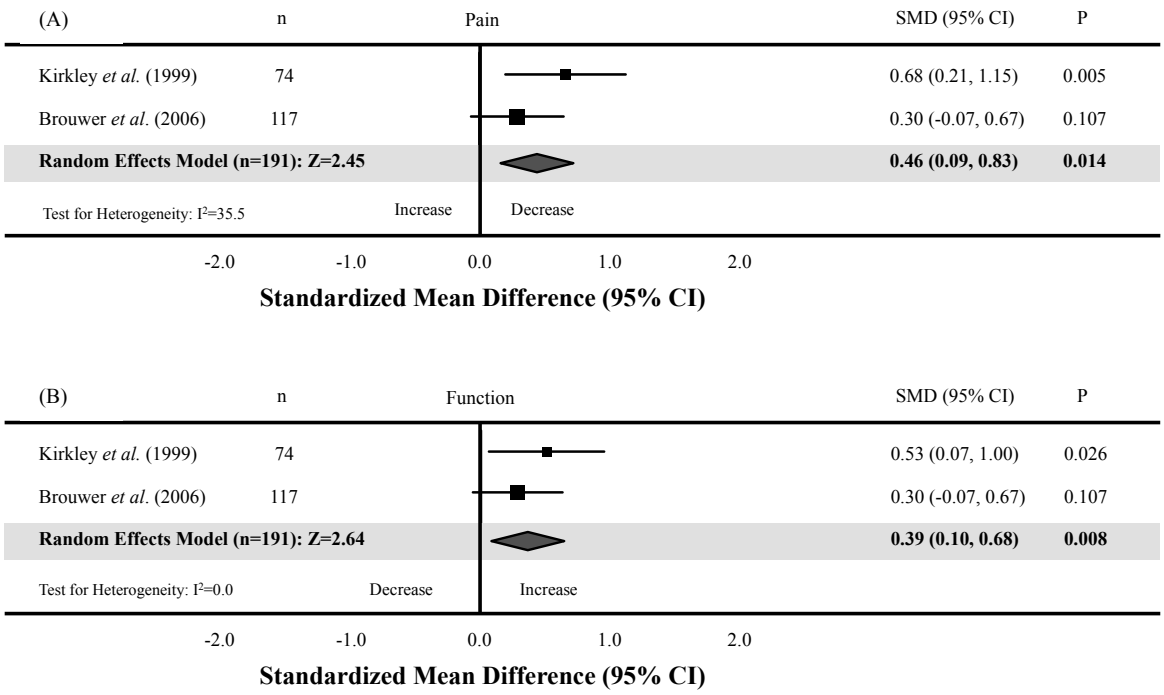

Figure 3.5: Standardized mean difference and 95% confidence intervals for (A) pain and (B) function for two RCTs comparing a control group and a valgus knee brace experimental group. The diamond represents the pooled effect using a random effects model. The vertical line at 0 represents no difference. (A) Data to the right of 0 represent a decrease in pain. (B) Data to the right of 0 represent an increase in function.

Eight studies (of 38) were RCTs and reported significant improvements in both pain and function[17,22-25,30,55,58]. Three RCTs (of eight) were a parallel group design[22-24]. Two RCTs (of three) compared a control group to a brace group[22-23]. Data were extracted from these two studies and combined in separate meta-analyses to compare groups at 6 months follow-up (n=191). Pain was significantly less for the brace group (Figure 3.5A). The SMD between groups was 0.46 (95%CI: 0.09, 0.83, p=0.014; I^2=35.5, p=0.21). Function was significantly greater for the brace group (Figure 3.5B). The SMD between groups was 0.39 (95%CI: 0.10, 0.68, p=0.008; I^2=0.0, p=0.44).

Six (of eight RCTs) could not be included in the meta-analyses due to lack of a non-treatment, parallel control group. These six RCTs reported the effect of bracing on pain using either a visual analog scale[24,30,55], or the WOMAC subdomain for pain[17,25,30] (Table 3.1C). One RCT reported both[30]. Improvements in pain after brace wear were reported in all six trials. The effect of bracing on function was reported using either a visual analog scale[24], a function subdomain of questionnaires[17,25,30,58], or sport participation hours[55]. Improvements in function after brace wear were reported in four trials[17,24,30,58] and three trials reported no change[17,25,55]. One study (of six) found inconsistent findings for improvements in function whether a custom-fit or off-the-shelf brace was used[17].

3.4.6 Complications

Twelve studies (of 38) reported the complications and difficulties experienced by patients using a brace. The reported difficulties included slipping (32/107)[18,25,56], instability or discomfort (42/150)[27,32,51-52,56,59], too constraining, awkward or poor fit (70/231)[23-24,32,52,54,56], mechanical problems with the brace (9/84)[32,54], too hot (9/11)[56], and too heavy (3/11)[56]. One study did not state the number of patients that reported the brace to be bulky[58].

Reported complications resulting from brace use included skin irritation (29/190)[23-24,32,54], blisters (2/46)[24] and swelling (14/190)[23,32,54]. One study reported that a single patient (n=46) developed a pulmonary embolus (PE) shortly after initiating valgus brace wear[54]; however, no direct causal relationship between valgus bracing and PE onset could be made. The number of studies and patients affected are summarized in Figure 3.6.

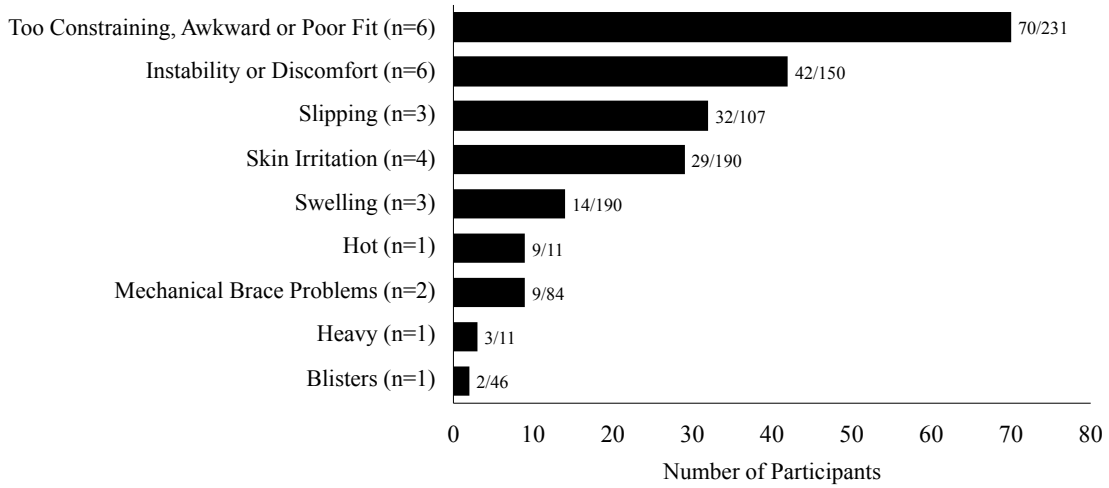

Figure 3.6: The number of studies (n) and patients (number of patients with difficulty/total number of patients) reporting difficulties with valgus brace use and minor complications.

3.4.7 Compliance

Twenty-one (of 38) studies reported details regarding instructions for brace use (i.e. how many days per week and how many hours per day, or for what activities). Instructions varied widely and included wearing the brace all day[16-18,46,58], only during activity[22,30-31,33,54-55], as needed[24,28-29,48,52], one hour per day at least two days per week[32], or a minimum of four hours per day[25]. Three studies indicated that a technician or therapist fit the brace and gave patients donning and doffing instructions, but did not specify type or frequency of use[23,50,59].

Ten (of 21) studies reported the average number of hours per day that patients actually wore the brace. These included 9 hours[17-18], 7 hours[33,48], 5 hours[24,28-29,52], more than 3 hours[25] and less than 4 hours[30]. One study reported that all patients wore the brace for seven days per week, but did not specify the number of hours per day[46]. Seven studies (of 38) reported the number of patients not compliant with the instructions for valgus brace wear[28-29,32,48,51-52,54]. Overall, 22% of patients (62/292) did not comply with the prescribed bracing protocol.

3.4.8 Long Term Brace Use

Eight studies (of 38) reported the number of patients who continued to wear the brace long-term. Overall, 56% of the patients studied (182/327) continued to wear the brace at 6 months[23-24,32,48,51-52,54-55]. Two studies (of eight) also reported the frequency of brace wear at 6 months. Twenty-six percent of patients (11/42) wore the brace all day, and 74% of patients (31/42) wore the brace as needed or during strenuous activity[51,54]. Overall, 43% of patients (139/327) continued to wear the brace at one year, as reported by five studies (of eight)[23,32,48,52,55].

A recent retrospective survey by Squyer et al. (2013)[32] also reported declining trends with brace use. Twenty-eight percent (25/49), 25% (10/40) and 14% (3/14) of patients continued to use the brace regularly at one, two and three years, respectively. Barnes et al. (2002)[52] and Wilson et al. (2011)[28] evaluated the status of brace use in the same sample of patients, reporting 41% of patients were still using the brace at 2.7 years[52] and 0% at 11.2 years[28].

3.5 Discussion

The present systematic review and meta-analyses suggest that valgus knee braces can significantly alter knee joint biomechanics during walking and result in significant improvements in patient-reported outcome measures. Although the methods of investigation vary, the preponderance of biomechanical evidence suggests that valgus braces alter knee joint loading. Results suggest that valgus braces can significantly decrease direct measures of medial compartment load[27], indirect measures representing the distribution of loads across the knee[14-17,19-20,26,30-31,33,46], muscle co-contraction[21,59] and

increase medial joint space during gait[57,60,61]. Potential mechanisms for lessening the load on the medial compartment include the application of a valgus moment at the knee to directly oppose the external knee adduction moment, with or without an alteration in frontal plane alignment of the lower limb, and/or the provision of increased knee joint stability that enables less muscle co-contraction. The most common mechanism studied suggests that a valgus brace opposes the external knee adduction moment that exists during walking[15-16,18-19,26]. Observations of greater reductions in the knee adduction moment with greater brace valgus angulations are consistent with this mechanism[26-27]. Multiple studies failed to show changes in the patient's anatomical alignment with the brace, emphasizing that decreases in alignment are not necessarily required for decreases in medial compartment loading[17,24,52,55,59-60]. Alternatively, load may be transferred to the brace, rather than the knee medial compartment, yet may not necessarily lead to observable decreases in the knee adduction moment[64]. A less commonly suggested mechanism is that the brace stabilizes the knee and thereby enables decreased muscle co-contraction[21,59]. Observations of decreased co-contraction[21,59] with braces in neutral angulation are consistent with this mechanism. Based on the studies reviewed, valgus braces likely provide a combination of these biomechanical mechanisms with the potential to provide clinical benefits.

The clinical importance of the magnitude of these biomechanical effects remains controversial. When described as a pooled effect size (Figure 3.2, SMD=0.61), the decrease in the external knee adduction moment is moderate. Some authors argue that the magnitude of the decrease in load on the medial compartment observed with bracing is too small to be of much benefit, while other authors suggest even small changes in knee joint loading may be important given the thousands of steps taken per day[14-19,26,30-31,33,46].

The preponderance of evidence also suggests that valgus knee braces can significantly improve patient-reported pain[14,16,18-19,29,33,35,46,48,51,52,54,60] and function[14,16,19,35,46-50,52,54]. The present meta-analyses (Figures 3.5A and 3.5B) are generally consistent with previous reviews that suggest improvements in clinical outcomes with valgus knee brace use[62-65]. The present pooled effect sizes can be described as small-to-moderate (pain: SMD=0.46; function: SMD=0.39), but are generally encouraging given the relatively low risks and costs associated with these devices. Bracing has been suggested as a low cost approach to managing symptoms for patients with knee OA[13,66-68]. Although the present results generally support this suggestion, whether or not valgus knee bracing can indeed slow the rate of disease progression and/or reduce health care costs remains unknown.

These positive biomechanical and clinical results are tempered substantially by the review of the available complications and compliance data. The reported parameters affecting dosage (i.e. brace angulation and frequency of use) are quite variable and often unclear. However, there are consistent reports of decreased brace use over time[28,32,52,54]. Potential reasons for poor compliance are numerous and may relate to the reported complications/difficulties with brace use (Figure 3.6). In a related matter, biomechanical studies indicate that greater valgus angulations in the brace create greater reductions in the external knee adduction moment, but are also less comfortable and may not be tolerated by the patient for prolonged durations[16,21,27]. We suggest that if bracing is to play a larger role in the treatment of patients with knee OA, further research to determine optimal dosage is required. This may also involve further exploring the effects of different brace angulations and durations of use, and the combined use of different types of orthoses to achieve larger biomechanical effects while maintaining patient comfort[25,31].

Although the present meta-analyses suggest significant changes in both biomechanical and clinical measures, considerable variation in patient responses was consistently observed across the studies. In other words, some patients appear to respond better to valgus braces than others. Previous investigators have suggested that patient characteristics such as disease severity and body size may influence the effectiveness of valgus knee braces, but data were not consistently reported for such subgroups to evaluate those questions in the present review [23-24,32,51,60].

3.5.1 Study Limitations

Only studies that evaluated the effects of valgus knee bracing during level walking were included in this review. Two of the included studies also evaluated the effects of valgus bracing during stair climbing, but those data were not included[17,27]. Another limitation in the present meta-analysis was the pooling of data obtained from studies using somewhat different methods. For example, biomechanical studies varied in study design, disease severity of patients, brace type, and data collection and analysis procedures. This resulted in moderate heterogeneity. Although decreased after conducting sensitivity analyses, heterogeneity remained moderate. Publication bias was also present due to the evaluation of the greatest change in the knee adduction moment during bracing.

3.6 Conclusion

Systematic review and meta-analysis of the published literature suggests that valgus knee braces can alter the medio-lateral load distribution across the joint through a combination of biomechanical mechanisms, and can significantly improve pain and function in patients with medial compartment knee OA. These positive findings are

tempered substantially by consistent reports of discomfort and poor patient compliance with long-term brace use. If bracing is to play a larger role in the treatment of patients with knee OA, the present findings suggest that future research be directed at strategies to maintain the biomechanical effects while improving brace comfort. Further research evaluating dosage, optimal brace angulations and duration of wear, is also encouraged.

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4. Combined Effects of a Valgus Knee Brace and Lateral Wedge Foot Orthotic on the External Knee Adduction Moment in Patients with Varus Gonarthrosis

4.1 Summary

Objective: To test the hypothesis that a custom-fit valgus knee brace and custom-made lateral wedge foot orthotic will have greatest effects on decreasing the external knee adduction moment during gait when used concurrently. Design: Proof of concept, single test session, cross-over trial. Setting: Biomechanics laboratory within a tertiary care center. Participants: Patients (n=16) with varus alignment and knee osteoarthritis (OA) primarily affecting the medial compartment of the tibiofemoral joint (varus gonarthrosis). Interventions: Custom-fit valgus knee brace and custom-made full-length lateral wedge foot orthotic. Amounts of valgus angulation and wedge height were tailored to each patient to ensure comfort. Main Outcome Measures: The external knee adduction moment (%BW*Ht), frontal plane lever arm (cm) and ground reaction force (N/kg), determined from 3-dimensional gait analysis completed under four randomized conditions: (1) control (no knee brace, no foot orthotic), (2) knee brace, (3) foot orthotic, and (4) knee brace and foot orthotic. Results: The reduction in knee adduction moment was greatest when concurrently using the knee brace and foot orthotic (effect sizes ranged from 0.3 to 0.4). The mean decrease (95%CI) in first peak knee adduction moment compared to control was 0.36 %BW*Ht (-0.66, -0.07). This was accompanied by a mean decrease (95%CI) in frontal plane lever arm of 0.59 cm (-0.94, -0.25). Conclusions: These findings suggest that using a custom-fit knee brace and custom-made foot orthotic concurrently can produce a greater overall reduction in the knee adduction moment, through combined effects in decreasing the frontal plane lever arm.

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4.2 Introduction

Knee osteoarthritis (OA) is a leading cause of disability with substantial personal and economic costs[1,2]. The need to develop strategies for controlling long-term pain, impaired physical function and rising costs is paramount[1,2]. Non-pharmaceutical and non-operative interventions with minimal side effects are encouraged as early treatment options for individuals with knee OA[1,3]. Knee braces and foot orthotics are common examples of such treatments.

The medial compartment of the tibiofemoral joint is more commonly affected by OA than the lateral compartment, largely because of the greater loads typically borne by that compartment during walking. Even healthy, asymptomatic individuals without malalignment experience greater load in the medial compartment[4]. However, this imbalance in load distribution is exacerbated with varus alignment, an important risk factor for medial compartment knee OA[5]. Using three-dimensional gait analysis, the calculated external adduction moment about the knee during walking reflects the asymmetric loading of the tibiofemoral joint[4,6]. Indeed, although limitations exist[7], the external knee adduction moment has emerged as a valid[6], reliable[8] proxy for dynamic load on the medial compartment, and a predictor of radiographic and magnetic resonance imaging means of disease progression[9,10].

The knee adduction moment during walking is calculated using principles of inverse dynamics[11] and is influenced primarily by the frontal plane ground reaction force and its lever arm[4,12,13]. The line of action of the ground reaction force passes from the center of pressure of the foot to the area of the center of mass of the body, and typically remains medial to the knee joint throughout stance. The perpendicular distance between the knee joint center and the line of action of the ground reaction force determines the

magnitude of its lever arm in the frontal plane. Increases in varus alignment shift the knee joint laterally with respect to the ground reaction force line of action, thereby increasing the magnitude of the lever arm and external knee adduction moment.

Although their proposed mechanisms are different, valgus knee braces and lateral wedge foot orthotics both aim to decrease the knee adduction moment. Importantly, while there may be a number of contributing factors, both knee braces and foot orthotics are intended to decrease the frontal plane lever arm by acting on the knee and foot respectively[14-16]. Biomechanical studies suggest valgus knee braces can indeed decrease the knee adduction moment, although results vary widely and the effect sizes (i.e. mean change divided by the pooled standard deviation of the control condition) are generally small-to-moderate (Table 4.1)[15,17-23]. Biomechanical studies suggest that lateral wedge foot orthotics can also decrease the knee adduction moment. Similarly, results vary widely and effect sizes are generally small (Table 4.2)[14-16,24-32].

The results of clinical trials evaluating knee braces and foot orthotics for medial compartment knee OA are also inconsistent[33-38]. Although there are some encouraging findings with respect to pain and function[34,36,38-40], the effect sizes for those studies are generally small-to-moderate. Importantly, difficulties with comfort may partially explain why effect sizes are low[33,36-38]. Some biomechanical evidence suggests that knee braces with greater valgus angulation, and foot orthotics with larger lateral wedges, provide greater reductions in the knee adduction moment in a dose response relationship[15,19,25,41,42]. Unfortunately, studies also suggest that larger knee brace angulations and foot orthotic wedge heights (i.e. greater doses) are associated with less comfort[25,27,33].

Table 4.1: Means ± SD and effect sizes for the knee adduction moment from studies examining the effect of unloader knee braces.

Author (Year)	N	Intervention	Knee Adduction Moment without Brace	Knee Adduction Moment with Brace	Effect Size *
Lindenfeld (1997)[17]	11	Off the Shelf Brace	Peak = 4.0 ± 0.75 (%BW*Ht)	Peak = 3.5 ± 0.8 (%BW*Ht)	0.6
Self (2000)[18]	5	Custom Brace	Peak = 0.555 ± 0.163 (Nm/kg)	Peak = 0.49 ± 0.158 (Nm/kg)	0.4
Pollo (2002)[19]	11	Normal Valgus Brace	Peak = 55.3 ± 18.6 (Nm)	Peak = 54.8 ± 17.7 (Nm)	0.02
		4° Valgus Brace		Peak = 52.6 ± 17.9 (Nm)	0.1
		4° Tight Valgus Brace		Peak = 51.1 ± 16.9 (Nm)	0.2
		8° Valgus Brace		Peak = 51.7 ± 16.9 (Nm)	0.2
Draganich (2006)[20]	10	Off the Shelf Brace	Peak = 6.9% ± 1.9% (%BW*Ht)	Peak = 6.6% ± 2.2% (%BW*Ht)	0.2
		Custom Brace		Peak = 5.9% ± 2.0% (%BW*Ht)	0.5
Schmalz (2010)[21] †	16	Custom Brace	Peak = 0.63 (Nm/kg)	Peak = 0.60 (Nm/kg)	-- ‡
Fantini Pagani (2010)[22]	11	4° Valgus Brace	1st Peak = 0.52 ± 0.16 (Nm/kg)	1st Peak = 0.53 ± 0.15 (Nm/kg)	-0.1
			2nd Peak = 0.48 ± 0.17 (Nm/kg)	2nd Peak = 0.40 ± 0.19 (Nm/kg)	0.5
			Impulse = 30.6 ± 10.8 (Nm/kg*%stance)	Impulse = 26.6 ± 12.0 (Nm/kg*%stance)	0.4
		Neutral Flexible		1st Peak = 0.50 ± 0.15 (Nm/kg)	0.1
				2nd Peak = 0.42 ± 0.19 (Nm/kg)	0.4
				Impulse = 26.6 ± 11.7 (Nm/kg*%stance)	0.4
Toriyama (2011)[23]	19	Off the Shelf Brace	1st Peak = 0.54 ± 0.20 (Nm/kg)	1st Peak = 0.48 ± 0.19 (Nm/kg)	0.3
			2nd Peak = 0.48 ± 0.19 (Nm/kg)	2nd Peak = 0.48 ± 0.19 (Nm/kg)	0
Fantini Pagani (2011)[15]	10	4° Valgus Brace	1st Peak = 0.41 ± 0.15 (Nm/kg)	1st Peak = 0.40 ± .16 (Nm/kg)	0.1
			2nd Peak = 0.38 ± 0.16 (Nm/kg)	2nd Peak = 0.31 ± 0.16 (Nm/kg)	0.4
		8° Valgus Brace		1st Peak = 0.38 ± 0.12 (Nm/kg)	0.2
				2nd Peak = 0.30 ± 0.16 (Nm/kg)	0.5

***** Effect size = (mean change between the control and intervention conditions) / (pooled standard deviation)

† Estimated data from figure

‡ Insufficient data reported to calculate effect size

Table 4.2: Means ± SD and effect sizes for the change in knee adduction moment from studies examining the effect of lateral heel wedges, insoles and variable stiffness shoes.

Author (Year)	N	Intervention	Knee Adduction Moment without Orthotic	Knee Adduction Moment with Orthotic	Effect Size *
Maly (2002)[24]	12	5° Heel Wedge	Peak = 0.48 ± 0.13 (Nm/kg)	Peak = 0.47 ± 0.11 (Nm/kg)	0.1
		5° Wedged Orthotic		Peak = 0.50 ± 0.11 (Nm/kg)	-0.2
Kerrigan (2002)[25]	15	5° Wedged Insole	1st Peak = 0.396 ± 0.084 (Nm/kg*m)	1st Peak = 0.375 ± 0.090 (Nm/kg*m)	0.2
			2nd Peak = 0.339 ± 0.078 (Nm/kg*m)	2nd Peak = 0.317 ± 0.076 (Nm/kg*m)	0.3
		10° Wedged Insole		1st Peak = 0.363 ± 0.083 (Nm/kg*m)	0.4
				2nd Peak = 0.312 ± 0.078 (Nm/Kg*m)	0.3
Shimada (2006)[26]	23	10mm Wedged Insole	Peak = 0.90 ± 0.20 (Nm/kg)	Peak = 0.86 ± 0.19 (Nm/kg)	0.2
Butler (2007)[27]	20	Custom Wedged Orthotic	1st Peak = 0.379 ± 0.128 (Nm/kg*m)	1st Peak = 0.346 ± 0.122 (Nm/kg*m)	0.3
			2nd Peak = 0.245 ± 0.078 (Nm/kg*m)	2nd Peak = 0.240 ± 0.071 (Nm/kg*m)	0.1
Kakihana (2007)[28]	51	6° Wedged Insole	Peak = 0.218 ± 0.049 (Nm/kg*m)	Peak = 0.205 ± 0.049 (Nm/kg*m)	0.3
Erhart (2008)[29]	79	Variable Stiffness Shoe	Peak (slow) = 2.73 ± 0.91 (%BW*Ht)	Peak (slow) = 2.67 ± 0.92 (%BW*Ht)	0.1
			Peak (normal) = 2.87 ± 0.99 (%BW*Ht)	Peak (normal) = 2.74 ± 0.95 (%BW*Ht)	0.1
			Peak (fast) = 3.28 ± 1.17 (%BW*Ht)	Peak (fast) = 3.07 ± 1.11 (%BW*Ht)	0.2
Hinman (2008)[30]	13	5° Heel Wedge	1st Peak = 3.60 ± 0.90 (%BW*Ht)	1st Peak = 3.33 ± 0.69 (%BW*Ht)	0.3
			2nd Peak = 1.98 ± 0.82 (%BW*Ht)	2nd Peak = 1.84 ± 0.76 (%BW*Ht)	0.2
		5° Wedge Orthotic		1st Peak = 3.17 ± 0.61 (%BW*Ht)	0.6
				2nd Peak = 1.70 ± 0.76 (%BW*Ht)	0.4
Hinman (2009)[31]	20	5° Wedged Insole	1st Peak = 3.82 ± 0.62 (%BW*Ht)	1st Peak = 3.62 ± 0.59 (%BW*Ht)	0.3
			2nd Peak = 2.45 ± 0.78 (%BW*Ht)	2nd Peak = 2.32 ± 0.84 (%BW*Ht)	0.2
			Impulse = 1.38 ± 0.49 (%BW*Ht s)	Impulse = 1.31 ± 0.48 (%BW*Ht s)	0.1
Jenkyn (2011)[14]	32	Variable Stiffness Shoe	Peak = 2.76 ± 1.07 (%BW*Ht)	Peak = 2.57 ± 1.00 (%BW*Ht)	0.2
Fantini Pagani (2011)[15]	10	4° Wedged Insole	1st Peak = 0.41 ± 0.15 (Nm/kg)	1st Peak = 0.38 ± 0.13 (Nm/kg)	0.2
			2nd Peak = 0.38 ± 0.16 (Nm/kg)	2nd Peak = 0.35 ± 0.16 (Nm/kg)	0.2
Abdallah (2011)[32]	21	6° Wedged Insole	Peak = 0.66 ± 0.16 (Nm/kg)	Peak = 0.60 ± 0.14 (Nm/kg)	0.4
		11° Wedged Insole		Peak = 0.63 ± 0.15 (Nm/kg)	0.2
Hinman (2012)[16]	73	5° Wedge Insole	Peak = 3.82 ± 0.78 (%BW*Ht)	Peak = 3.60 ± 0.75 (%BW*Ht)	0.3
			Impulse = 1.26 ± 0.37 (%BW*Ht s)	Impulse = 1.18 ± 0.38 (%BW*Ht s)	0.2

* Effect size = (mean change between the control and intervention conditions) / (pooled standard deviation)

A novel treatment strategy may be to use a valgus knee brace and lateral wedge foot orthotic concurrently, where both are custom-fit to doses that ensure comfort. Recent studies suggest that when tested separately, valgus knee braces[15], lateral wedge foot orthotics[15,16] and variable stiffness shoes[14] decrease the external knee adduction moment through decreases in its frontal plane lever arm. This could theoretically be achieved by altering the position of the knee joint center medially (for example with the use of a knee brace), or by altering the orientation of the ground reaction force laterally (for example with the use of a foot orthotic). It is therefore possible that there may be additive effects on decreasing the knee adduction moment when these interventions are used together. Accordingly, the primary objective of this proof of concept study was to test the hypothesis that a custom-fit valgus knee brace and custom-made lateral wedge foot orthotic will have greatest effects on decreasing the external knee adduction moment during gait when used concurrently. The secondary objective was to explore changes in the frontal plane ground reaction force and its lever arm.

4.3 Methods

4.3.1 Participants

Sixteen patients with varus alignment, symptomatic medial compartment knee OA, and who were provided with a prescription for a valgus knee brace, were recruited from a tertiary care center specializing in orthopaedics. Standing hip-to-ankle anteroposterior radiographs were used to assess frontal plane alignment[43]. Varus alignment was defined as a mechanical axis angle of ≥1 degree varus. Kellgren and Lawrence grades were also determined from the full-length standing radiographs[44]. All patients had to have clinical and radiographically confirmed knee OA according to the

Altman classification system[45], with greater severity in the medial compartment of the tibiofemoral joint (i.e. varus gonarthrosis). All patients had to have pain localized to the medial side of the tibiofemoral joint, and greater joint space narrowing on the medial side compared to the lateral. Ethics approval was obtained from the Institution's Ethics Review Board and all patients signed informed consent prior to testing.

4.3.2 Valgus Knee Brace Fitting

All patients were provided with a custom-fit valgus knee brace (Össur Corporate, Foothill Ranch, CA) (Figure 4.1A) by a trained technician (RW) at least 6 months prior to gait testing. The brace was designed on a 3-point bending mechanism to apply a medially directed force to the lateral aspect of the knee. A hard shell cuff was located around the thigh and shank with a medially placed hinge and lateral crossover strap. A casted mould was made from the weight-bearing limb for each patient and sent to the brace manufacturer. From the mould, the custom-fit, adjustable brace was fabricated and set to a valgus angle between 4° and 7°. At the Clinic, the patients walked with the brace and the technician adjusted the amount ± 2° to ensure patient comfort. Patients were instructed to wear the brace while they were awake for activities that had been troublesome to them in the past[34].

4.3.3 Lateral Wedge Foot Orthotic Fitting

Full-length custom-made foot orthotics (Sole Science, London, ON, CAN) (Figure 4.1B) were made from an ethyl vinyl acetate with a 55 shore A durometer hardness using a fully weight bearing plaster positive mould of each patient's foot. A pedorthist (CD) fitted the orthotic to each patient during weight-bearing and walking while also wearing

the custom-fit knee brace. The pedorthist initially assessed the subjective effects of the foot orthotics using three prefabricated full-length lateral wedges of 3, 6 and 9mm. The goal was to provide a custom-made foot orthotic with the maximum wedge height while maintaining comfort. The unaffected leg was also fitted for a foot orthotic with no wedge.

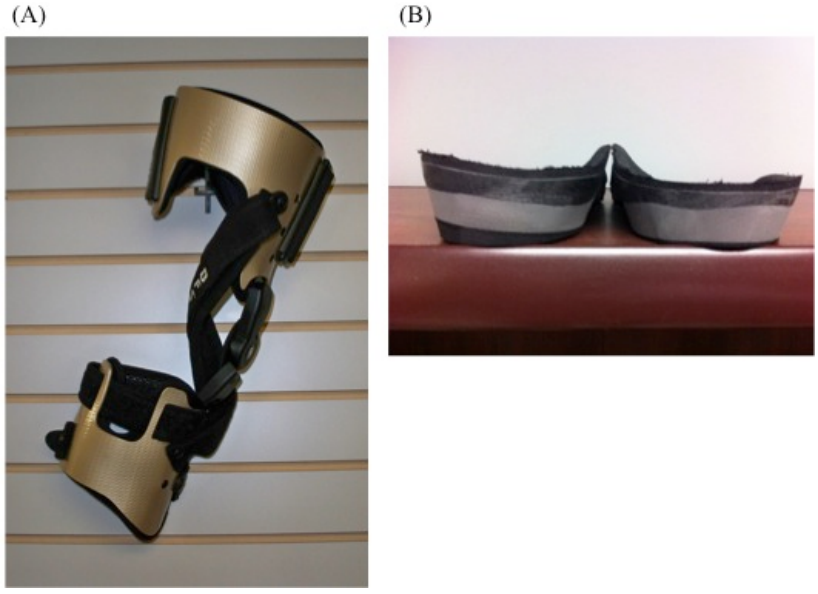

Figure 4.1: Custom-fit (A) valgus knee brace (Össur Unloader XT Lite) and (B) full-length lateral wedge insoles (only the left foot orthotic has a lateral wedge).

4.3.4 Testing Protocol

As patients with prescriptions for valgus knee braces were recruited from this centre, we followed the present clinic's valgus knee bracing practice, which suggests a trial of 6 months use[34]. Afterwards, patients returned to the clinic and were provided with the custom-made full-length lateral wedge foot orthotic. The pedorthic assessment, foot orthotic fabrication and gait testing using both knee brace and foot orthotic took place within a 1 week period. Four different gait conditions were tested during one session: (1) control (no knee brace, no foot orthotic), (2) custom-fit valgus knee brace, (3) custom-

made lateral wedge foot orthotic, and (4) both knee brace and foot orthotic. A balanced latin square design was used to randomize patients to the order of testing conditions[46].

4.3.5 Gait Analysis

All patients underwent 3-dimensional gait analysis using an 8-camera motion capture system (Eagle Cortex; MAC, Santa Rosa, CA) synchronized with a floor mounted force platform (AMTI, Watertown, MA). Twenty-two passive-reflective markers were placed on the patient using a Helen Hayes marker set[47], with modifications illustrated in Figure 4.2. Bilateral markers on the medial aspect of the knee joint line and medial malleolus were used during an initial static trial to identify knee and ankle joint centers, respectively. These four markers were removed prior to gait testing. Patients independently donned and doffed the knee brace according to the manufacturer's instructions. The knee brace did not interfere with markers during walking, or during donning and doffing (Figure 4.3). In each testing condition, the participant walked at a preferred, self-selected pace until five force plate strikes were recorded. Footwear (New Balance, Mississauga, ON, CAN) was standardized for all patients and worn throughout each testing condition.

The frontal plane component of the GRF was calculated as the resultant force vector of the vertical and mediolateral components of the GRF. The frontal plane lever arm was calculated as the perpendicular distance between the frontal plane GRF and knee joint centre of rotation using custom post-processing and data reduction techniques previously described[24,25]. The external adduction moment about the knee was calculated using proprietary software (Orthotrak; MAC, Santa Rosa, CA) from the kinematic (sampled at 60 Hz) and kinetic data (sampled at 1200 Hz) using inverse dynamics. Raw

data were filtered using a 4th order Butterworth low pass filter with a cutoff frequency of 6Hz. Each lower limb segment (foot, shank, and thigh) was modelled as a rigid body with a local coordinate system that coincided with anatomically relevant axes.

(A) (B)

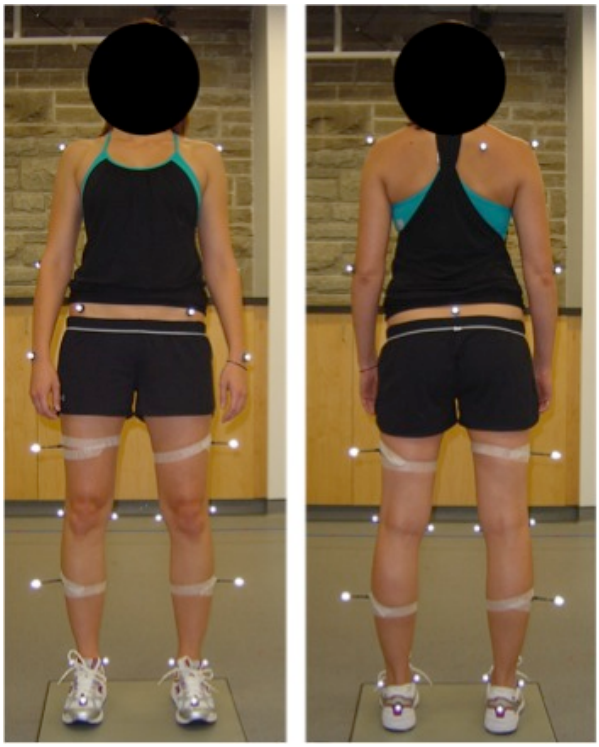

Figure 4.2: Anterior (A) and posterior (B) views of the modified Helen Hayes marker set used for 3-dimensional gait analysis.

Inertial properties of each limb segment were approximated anthropometrically and translations and rotations of each segment were reported relative to neutral positions defined during the initial standing static trial. For each trial, the knee adduction moment waveform was normalized to body weight and height (%BW*Ht), plotted over 100% of stance and inspected visually. The peak magnitudes of the external knee adduction moment in the first and second halves of stance were identified using an algorithm that identified values immediately preceded by a minimum of five continuously ascending

values and followed by a minimum of five continuously descending values. If no identifiable peak occurred in a given half of stance, no knee adduction moment value for that half of stance was recorded. The entire knee adduction moment waveform (not normalized to percent stance) was also summarized as its angular impulse (i.e. the area under the curve in %BW*Ht s). Test retest reliability of these knee adduction moment measures is excellent[8,48].

Given their strong influence on the knee adduction moment, the frontal plane ground reaction force, its lever arm and gait speed were also calculated[4,12,13]. All gait variables were averaged across the five trials. Pain was assessed at rest (i.e. before gait testing began) and after walking in each condition. A numeric rating scale was used, with 0 representing no pain and 10 representing the worst possible pain. Patient preference for condition was also assessed.

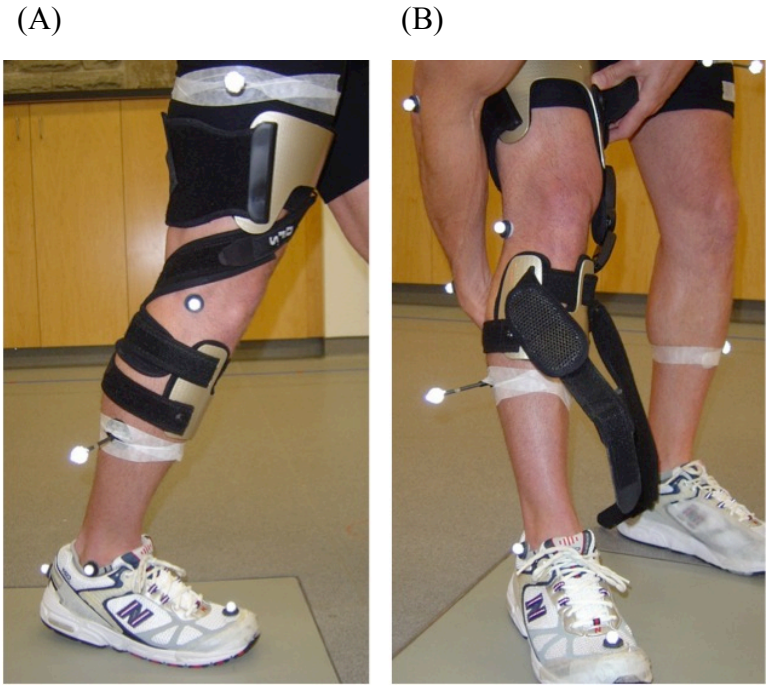

Figure 4.3: Lateral view of the right lower extremity illustrating brace and marker positions during walking (A). Donning and doffing of the knee brace did not interfere with markers (B).

4.3.6 Data Analysis

We first plotted ensemble average (n=16) waveforms throughout stance for the knee adduction moment, frontal plane ground reaction force and lever arm during each test condition. We then calculated means and standard deviations, and mean changes from the control condition with 95% confidence intervals, for each condition. Changes in the knee adduction moment were evaluated statistically using paired t-tests. Given the exploratory nature of this study, we maintained the value for statistical significance at $p<0.05$. The remaining measures were considered secondary outcomes used to help explain the knee adduction moment findings and were not evaluated with statistical testing. The SPSS program version 20.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses.

4.4 Results

Patient demographics and clinical characteristics are presented in Table 4.3. 16 patients (8 men, 8 women) met our inclusion criteria and participated in the study. Eight 9mm lateral wedge foot orthotics, seven 6mm lateral wedge foot orthotics, and one 3mm lateral wedge foot orthotics were custom-made for patients. The final knee brace angles ranged from 2° to 9° of valgus. Ensemble average curves for the external knee adduction moment, frontal plane lever arm and ground reaction force are illustrated in Figure 4.4. Descriptive statistics for all measures during each test condition are presented in Table 4.4. All 16 patients had an identifiable first peak knee adduction moment. Twelve to 15 patients had an identifiable second peak knee adduction moment, depending on the test condition (Table 4.4). Mean changes (95% CI) compared to the control are presented in Table 4.5. A statistically significant reduction in knee adduction moment (first peak and

angular impulse) was only present when concurrently using the knee brace and foot orthotic. Nine patients stated that they preferred wearing the knee brace and foot orthotic concurrently. Five patients preferred the foot orthotic only. One patient preferred the knee brace only. One patient preferred wearing neither device.

Table 4.3: Demographics and clinical characteristics

Characteristic	Mean (SD)
Age	55 (7.0)
BMI (kg/m^2)	32 (6.2)
Mechanical Axis Angle (°) *	6.6 (3.3)
Pain at rest (0-10)	1.2 (1.3)
Kellgren and Lawrence grade (No. of patients) †	
0/1/2/3/4	0/2/5/6/3
KOOS (0-100) ‡	
Pain	49.3 (15.9)
Symptoms	37.5 (11.2)
Activities of Daily Living	54.3 (15.3)
Sport and Recreation	18.8 (14.0)
Quality of Life	23.8 (13.7)

Abbreviations: BMI, body mass index; KOOS, Knee Injury and Osteoarthritis Outcome Score

* A positive value represents varus alignment

† Kellgren and Lawrence grade of OA severity is a radiographic classification system for osteoarthritis. Grade 1, doubtful narrowing of joint space and possible osteophytic lipping; grade 2, definite narrowing of joint space and possible osteophytic lipping; grade 3, moderate multiple osteophytes, definite narrowing of joint space, some sclerosis and possible deformity of bone contour; grade 4, large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour.

‡ The KOOS is a knee specific measure administered by patients to assess opinions of their knees and general health. The score is normalized out of 100 for each subscale (100 represents no symptoms; 0 represents extreme symptoms).

Table 4.4: Descriptive statistics for outcome measures during different testing conditions.

	Mean ± SD			
	Control	Orthotic	Brace	Orthotic and Brace
Primary Outcome Measure				
Knee Adduction Moment (KAM)				
1st Peak (%BW*Ht)	3.08 ± 1.09	2.98 ± 1.05	2.82 ± 0.97	2.72 ± 1.12 ₸
2nd Peak (%BW*Ht) *	2.99 ± 0.81	2.78 ± 1.01	2.61 ± 0.94	2.42 ± 1.24
Impulse (%BW*Ht s)	1.45 ± 0.52	1.44 ± 0.52	1.37 ± 0.46	1.32 ± 0.58 ₸
Secondary Outcome Measures				
Lever Arm (cm)				
Peak value during stance	5.63 ± 1.85	5.45 ± 1.82	5.40 ± 1.84	5.11 ± 2.07
Value at 1st Peak KAM	5.09 ± 1.75	4.79 ± 1.67	4.73 ± 1.73	4.49 ± 1.71
Value at 2nd Peak KAM	5.15 ± 1.95	4.79 ± 1.96	4.44 ± 2.13	4.46 ± 2.37
Resultant Ground Reaction Force (N/kg)				
Peak value during stance	9.98 ± 0.92	10.34 ± 0.78	10.17 ± 0.98	10.43 ± 1.00
Value at 1st Peak KAM	9.80 ± 0.99	9.87 ± 0.88	9.54 ± 1.30	9.96 ± 1.10
Value at 2nd Peak KAM	9.88 ± 0.50	9.73 ± 0.57	9.83 ± 0.54	9.83 ± 0.57
Gait Speed (m/s)	1.15 ± 0.17	1.16 ± 0.17	1.16 ± 0.16	1.17 ± 0.18
NRS Pain (0-10)	3.44 ± 1.86	3.06 ± 2.21	3.31 ± 2.30	3.69 ± 2.06

Abbreviations: KAM, knee adduction moment; NRS, numeric rating scale

* An identified 2nd peak knee adduction moment varied between the control (n=12), orthotic (n=13), brace (n=13) and orthotic and brace (n=15) conditions.

₸ Significant difference compared to control condition; $p<0.05$

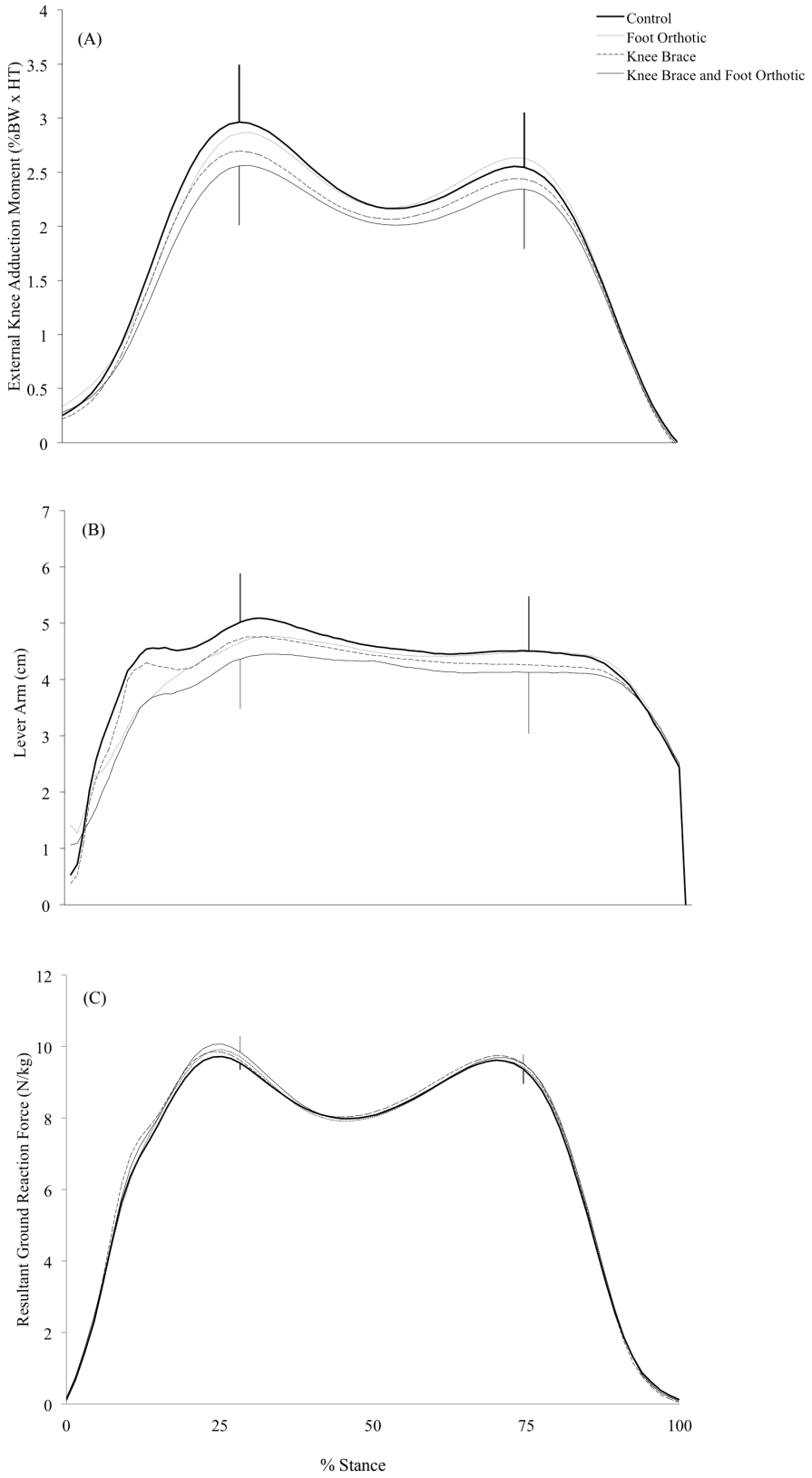

Figure 4.4: Ensemble averages (n=16) of (A) the knee adduction moment, (B) frontal plane lever arm, and (C) resultant ground reaction force throughout stance. Vertical bars represent 95% confidence intervals.

Table 4.5: Change from control for the different testing conditions for each outcome measure.

	Mean Change (95% Confidence Interval)		
	Orthotic	Brace	Orthotic and Brace
Primary Outcome Measures			
Knee Adduction Moment (KAM)			
1st Peak (%BW*Ht)	-0.10 (-0.29, 0.08)	-0.26 (-0.59, 0.07)	-0.36 (-0.66, -0.07)[T]
2nd Peak (%BW*Ht) *	0.08 (-0.24, 0.39)	-0.12 (-0.38, 0.13)	-0.32 (-0.73, 0.07)
Impulse (%BW*Ht s)	-0.003 (-0.11, 0.10)	-0.08 (-0.21, 0.05)	-0.13 (-0.23, -0.02)[T]
Secondary Outcome Measures			
Lever Arm (cm)			
Peak value during stance	-0.18 (-0.44, 0.09)	-0.23 (-0.60, 0.14)	-0.52 (-0.89, -0.15)
Value at 1st Peak KAM	-0.29 (-0.65, 0.06)	-0.36 (-0.74, 0.02)	-0.59 (-0.94, -0.25)
Value at 2nd Peak KAM	-0.03 (-0.37, 0.31)	-0.37 (-0.82, 0.08)	-0.66 (-1.37, 0.04)
Resultant Ground Reaction Force (N/kg)			
Peak value during stance	0.35 (0.10, 0.60)	0.19 (0.02, 0.35)	0.45 (0.29, 0.60)
Value at 1st Peak KAM	0.08 (-0.18, 0.33)	-0.26 (-0.92, 0.40)	0.16 (-0.18, 0.49)
Value at 2nd Peak KAM	-0.07 (-0.19, 0.06)	0.05 (-0.12, 0.21)	0.001 (-0.18, 0.19)
Gait Speed (m/s)	0.01 (-0.02, 0.04)	0.01 (-0.02, 0.04)	0.02 (-0.001, 0.05)
NRS Pain (0-10)	-0.38 (-0.92, 0.17)	-0.13 (-0.82, 0.57)	0.25 (-0.44, 0.94)

Abbreviation: KAM, knee adduction moment; NRS, numeric rating scale
* Note that the change scores at the 2nd peak knee adduction moment do not match the difference between values in table 4 because the sample sizes are different.
[T] Significant difference compared to control condition; $p<0.05$

4.5 Discussion

The present findings support the concept of using a custom-fit knee brace and custom-made foot orthotic concurrently to enhance the magnitude of reduction in the knee adduction moment. We are aware of limited previous research evaluating the combined effects of knee braces and foot orthotics. Schmalz et al. (2006)[49] reported changes in the knee adduction moment during walking with combined use of a heel wedge and rigid ankle-foot-orthosis in healthy participants. In a recent randomized crossover trial, Hunter et al. (2012)[50] reported that the combined use of a valgus knee brace, neutral foot orthotic and motion control shoe significantly improved knee pain more than placebo treatment.

The present results are consistent with the suggestion that patients with knee OA may receive greater load reductions in the medial compartment by using a valgus knee brace and lateral wedge foot orthotic simultaneously. The largest change in the knee adduction moment occurred at its first peak (0.36 %BW*Ht), and represented a 12% reduction. It is presently unclear if this size of a change is clinically important or not. A 12% reduction might be considered disappointing given that two interventions were combined. Alternatively, previous researchers[33,51] have argued that even smaller changes are potentially important given the thousands of steps taken per day and the relationship between high knee adduction moments and future disease progression.

The concurrent use of the valgus knee brace and lateral wedge foot orthotic resulted in effect sizes ranging from 0.3 to 0.4. These are comparable to previously reported effect sizes for these devices when used on their own (Table 4.1 and 4.2). Importantly, the magnitudes of the valgus knee brace angulation and the foot orthotic wedge size were determined in the present study by patient comfort. Therefore, although it is unclear whether or not greater reductions in knee load per individual step taken can be achieved while wearing both devices, maintaining patient comfort with similar effect sizes may improve patient compliance and produce a greater overall, cumulative decrease in load with prolonged use.

Although the secondary outcomes must be interpreted cautiously, the present findings also suggest that decreases in the knee adduction moment observed with both devices are brought about through decreases in the frontal plane lever arm. We are aware of two previous studies[15,16] that quantified changes in the frontal plane lever arm to evaluate mechanisms for decreasing the knee adduction moment with knee brace or lateral wedge foot orthotic use. Fantini Pagani et al.[15] and Hinman et al.[16] reported

decreases in the lever arm at the first peak knee adduction moment of 0.25 cm and 0.29 cm, respectively when patients wore lateral wedge foot orthotics. Those results are very similar to the mean changes in the lever arm observed in the present study (Table 4.5). Of note, the combined effect (using both the foot orthotic and the knee brace) on reducing the frontal plane lever arm appeared to be additive (Table 4.5). Toda et al.[53], Hinman et al.[54], and van Raaij et al.[38] have suggested a variety of ways individual subjects using orthotics experienced decreases in the frontal plane lever arm, including increased hip adduction, a more vertically oriented ground reaction force in the frontal plane and a lateral shift in the center of pressure[15,16]. Future research is required to determine if such mechanisms contribute to the combined effects of knee braces and foot orthotics.

4.5.1 Study Limitations

Valgus knee braces and lateral wedge foot orthotics may affect knee joint loads in ways not evaluated in the present study. For example, the knee brace may absorb external forces[54], and/or may decrease muscle co-contraction[55], and contribute to decreased internal knee joint loads without necessarily being detected by the external knee adduction moment. Also, although the knee adduction moment is strongly correlated to internal contact forces in the medial compartment of the tibiofemoral joint[6], a reduction in the knee adduction moment does not necessarily guarantee a reduction in medial compartment load[7]. The present patients wore the custom-fit knee brace for a longer period than the custom-made foot orthotic, and it is unclear how this may have affected results. We do not have data on the specific final angle of brace adjustment to correlate to observed biomechanical findings, nor do we have data on adherence or adverse events.

Although we speculate that improved comfort may improve compliance and result in greater reductions in overall cumulative knee joint loading, this requires future study.

4.6 Conclusions

The present findings suggest that using a custom-fit valgus knee brace and custom-made lateral wedge foot orthotic concurrently can produce a greater overall reduction in the knee adduction moment, through combined effects in decreasing the frontal plane lever arm. The observed changes were small and the clinical importance is presently unclear; however, given the reported difficulties with compliance with braces and orthotics, these results do lend support to future work investigating potential additive effects of combined interventions tailored to ensure patient comfort.

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5. Summary and General Discussion

The purpose of this chapter is to summarize the main results of the thesis and discuss their implications. Findings from each study are discussed in relation to each other and to the treatment of patients with knee OA. Limitations, implications for future research and recommendations are also provided.

5.1 Summary of Results

The purpose of this thesis was to examine the interaction between lower limb alignment and body mass on dynamic knee joint loading, and to evaluate the effects of knee and foot orthoses, in patients with knee OA.

Chapter 2 (Study 1): This cross-sectional study examined the interaction and relative contributions of frontal plane alignment and body mass on dynamic knee joint loading in patients with knee OA. Using sequential (hierarchical) linear regression, the interaction term (mechanical axis angle × mass) contributed significantly ($P < 0.001$) to a model (total adjusted $R^2 = 0.70$) predicting the external knee adduction moment, that included mechanical axis angle ($R^2 = 0.37$) and mass ($R^2 = 0.06$) while controlling for age, sex, height, Kellgren and Lawrence grade, pain score during walking, gait speed, toe out angle and trunk lean ($R^2 = 0.25$). When the sample was split into tertiles for mass, mechanical axis angle accounted for 32–54% of explained variance in the knee adduction moment. In the tertile with greatest mass, results suggested a 3.2 Nm increase in knee adduction moment for every 1° increase in varus alignment. When split into tertiles for mechanical axis angle, mass accounted for 6–10% of explained variance in the knee adduction moment. In the tertile with the most varus alignment, results suggested a 0.4 Nm increase

in knee adduction moment for every 1 kg increase in mass. These findings describe the interaction between alignment and body mass on dynamic knee joint loading (particularly the distribution of loading across the knee during walking), with the association between alignment and load highest in patients with the highest mass. The findings also emphasize the role of malalignment at all levels of mass, and have implications for better understanding risk factors and intervention strategies for knee OA.

Chapter 3 (Study 2): This systematic review with meta-analyses investigated the biomechanical effects, patient-reported outcomes, complications, and compliance with valgus brace use for medial compartment knee OA. Pooled data from biomechanical studies suggested a significant decrease in the external knee adduction moment during walking while wearing the brace (SMD=0.61; 95%CI: 0.39, 0.83; $p<0.001$). Whether these changes are clinically important remains unclear. However, pooled data from randomized clinical trials suggested significant improvements in pain (SMD=0.46; 95%CI: 0.09, 0.83; p=0.014) and function (SMD=0.39; 95%CI: 0.10, 0.68; p=0.008). The reporting of parameters affecting dosage (i.e. brace angulation and frequency of use) was variable and often unclear. The most common difficulties reported during brace use included slipping, discomfort and poor fit. Complications included skin irritation, swelling, mechanical brace problems, heat and heaviness. Patient-reported brace use varied considerably between studies, but consistently decreased over time. Systematic review with meta-analysis of biomechanical effects and patient-reported outcomes supports the use of valgus knee braces in the management of medial knee OA; however, issues related to their appropriate dosage, patient comfort and compliance remain as substantial challenges to long-term use.

Chapter 4 (Study 3): This proof of concept study tested the hypothesis that a custom-fit valgus knee brace and custom-made lateral wedge foot orthotic would have greatest effects on decreasing the external knee adduction moment during gait when used concurrently. The reduction in knee adduction moment was greatest when concurrently using the knee brace and foot orthotic (effect sizes ranged from 0.3 to 0.4). The mean decrease (95%CI) in first peak knee adduction moment compared to control was 0.36 %BW*Ht (-0.66, -0.07). This was accompanied by a mean decrease (95%CI) in frontal plane lever arm of 0.59 cm (-0.94, -0.25). These findings suggest that using a custom-fit knee brace and custom-made foot orthotic concurrently can produce a greater overall reduction in the knee adduction moment, through combined effects in decreasing the frontal plane lever arm. Although effects were small-to-moderate, maintaining patient comfort may improve compliance with greater cumulative benefits given the thousands of steps taken per day.

5.2 Implications

Knee OA is a multifactorial disease that includes several biomechanical risk factors that likely act independently and together. The findings from Study 1 demonstrate the statistically significant interaction that exists between lower limb alignment and body mass on the external knee adduction moment. More specifically, the results suggest that body mass moderates the relationship between lower limb alignment and the external knee adduction moment. A moderator variable is similar to a confounding variable, affecting the relationship between an independent and dependent variable. However, effect modification influences the relationship depending on the value or level of the moderator variable (Figure 5.1A). As this variable changes, the relationship changes

proportionally. The moderator variable is always present, but how it influences the relationship depends on its value[1,2]. Figure 5.1 illustrates moderation, including the example described in Chapter 2. The strength and direction of the relationship between varus alignment (mechanical axis angle) and the external knee adduction moment is influenced by body mass. The mechanical axis angle explains more variance in the external knee adduction in those patients with higher body mass.

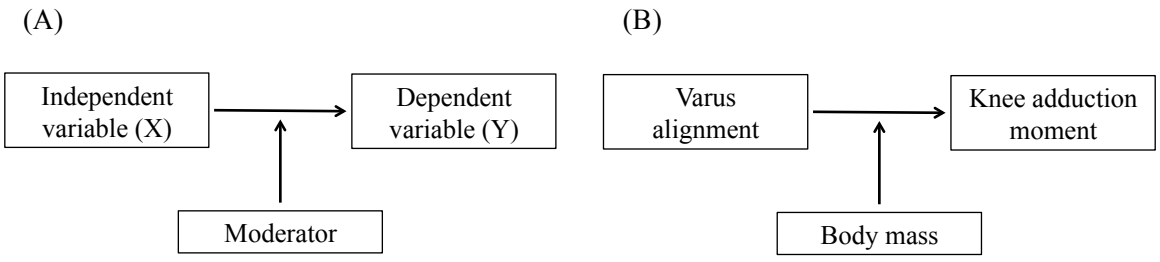

Figure 5.1: (A) A moderator variable influences the relationship between an independent and dependent variable in accordance with the value or level of the moderator. (B) Body mass was identified in Study 1 as a moderator variable influencing the relationship between the mechanical axis angle (lower limb alignment) and the external knee adduction moment (distribution of load across the knee).

Figure 5.2 is similar to Table 2.2 and shows another way of illustrating the interaction between lower limb alignment and body mass on dynamic knee joint loading. In general, as body mass and/or severity of varus alignment increases, the external knee adduction moment also increases. However, note that the increase in knee adduction moment (slope of the line) from the middle to highest tertile of mass is greatest for patients in the highest tertile of alignment. It may also be informative to note that patients with high mass and mild varus alignment (>100kg and >-5°; 37Nm) have lower moments about the knee than patients with low mass and severe varus alignment (<80kg and <-9°; 50Nm). This emphasizes the importance of lower limb alignment on the external knee

adduction moment. The patients with high body mass and severe varus alignment experience the largest imbalance in load distribution across the knee, making them particularly susceptible to OA, and likely candidates for biomechanical interventions.

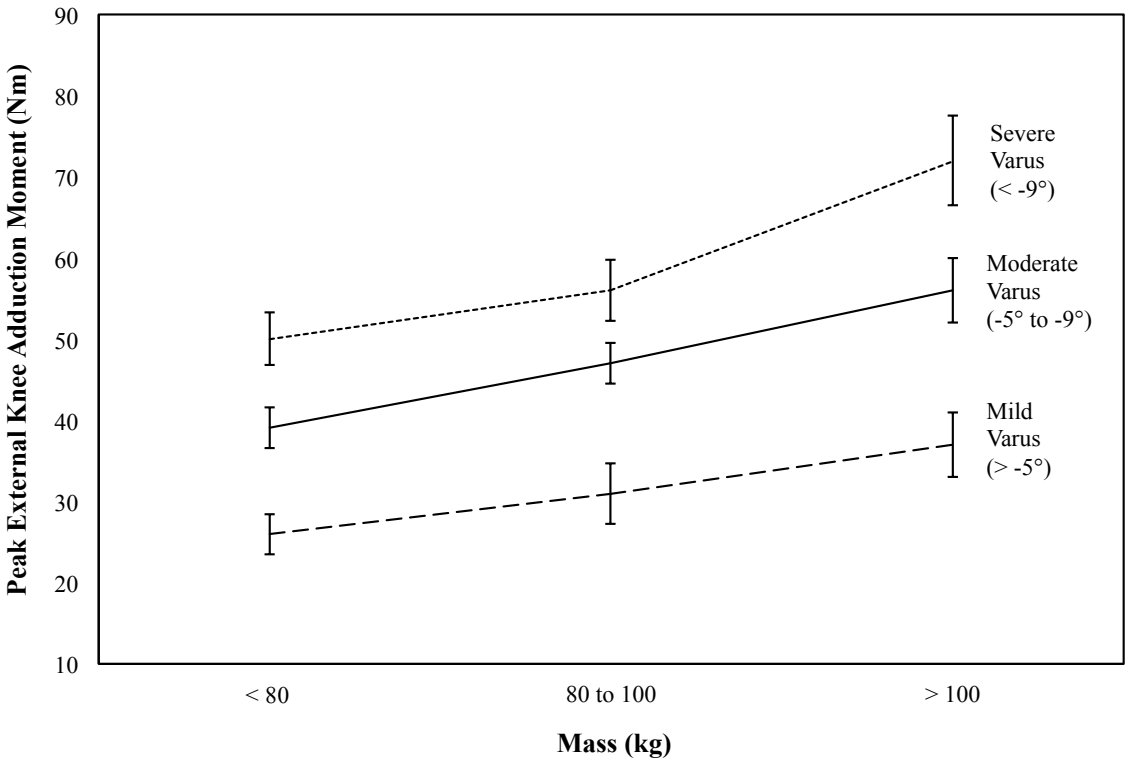

Figure 5.2: Mean and 95% confidence intervals are shown for tertiles based on mass and mechanical axis angle for the sample of patients included in Study 1. A statistical interaction exists between lower limb alignment and body mass on the external knee adduction moment during walking. The relationship between alignment and knee adduction moment is highest in patients with greatest mass. The figure also illustrates that patients with severe varus alignment and low body mass have a higher peak knee adduction moment than patients with high mass and mild varus alignment.

Studies 2 and 3 provide encouraging results regarding the use of orthoses as biomechanical interventions for patients with medial compartment knee OA. The findings described in Chapter 3 suggest moderate effect sizes for the ability of valgus knee bracing to decrease the knee adduction moment during walking. The findings also suggest moderate effect sizes for improvements in pain and function. However, we do not

know whether the change in the distribution of load across the knee correlates with a change in pain and function. Although we might expect a correlation between decreased loads and decreased pain with orthoses use, this is presently unclear. Greater valgus knee brace angulations have been associated with greater reductions in the external knee adduction moment, and therefore may lead to greater reductions in knee pain. However, this relationship is complicated by observations suggesting that greater brace angulations are uncomfortable. Lower limb discomfort may counteract or disguise any improvements in knee pain.

Although patients with greatest body mass and varus alignment may be good candidates for biomechanical interventions, the literature is still unclear whether orthoses are effective in patients who are obese. Some authors have suggested that difficulties exist in applying the off-loading effects in obese patients secondary to increased soft tissue girth and poor brace fixation[3,4]. Conversely, lateral wedge orthotics have been shown to reduce the external knee adduction moment in a sample of obese women with varus alignment, but without a clinical diagnosis of knee OA[5].

In a related matter, patients with knee OA who are capable of participating in low-impact aerobic physical activity should be encouraged to do so[6]. Symptoms associated with knee OA typically limit patients from engaging in exercise and attaining the benefits of weight loss. These patients may benefit from non-surgical, biomechanical interventions that allow them to participate in exercise. Orthoses may improve patient symptoms by enabling higher levels of activity and participation in exercise interventions aimed at weight loss. This sort of "multi-modal therapy" may be required to break the vicious cycle described in Chapter 1. Figure 5.3 illustrates that cycle again while including the interaction described in Chapter 2. Although beyond the scope of the present thesis, it

should be noted that increases in physical activity might also contribute to increased muscular strength and endurance, reduced muscle co-contraction and increased knee stability[7-12].

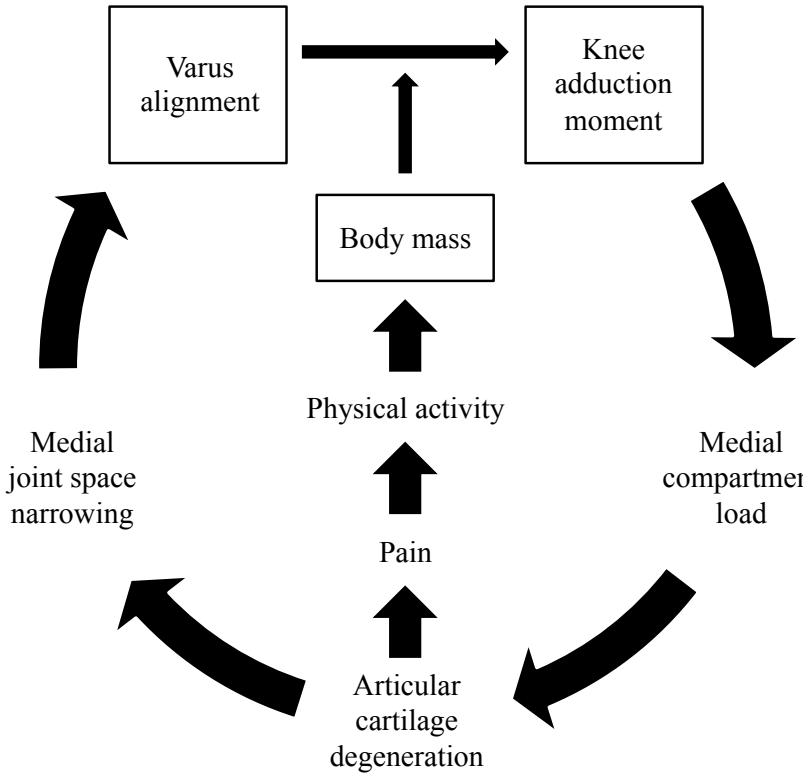

Figure 5.3: A modified vicious cycle of medial compartment knee osteoarthritis incorporating the interaction described in Chapter 2. Varus alignment and body mass create aberrant loads on the medial compartment, lead to structural changes in the joint and decreased medial joint space. Rising pain levels minimize physical activity causing further weight gain and further increased loads at the joint.

5.3 Limitations and Future Research

Limitations in this thesis should be acknowledged. Studies 1 and 3 are largely dependent on the external knee adduction moment as the primary outcome measure. Although this measure is an accepted surrogate for load distribution across the knee, and

there is evidence to suggest that it is correlated to contact force in the medial compartment[13] and OA progression[14-15], limitations in using the knee adduction moment to infer joint loading do exist. Importantly, a change in the knee adduction moment does not necessarily coincide with a change in medial compartment load. Internal contact forces created by muscles and other soft tissue structures also exist at the knee and counteract external moments. More complete calculations of dynamic knee joint loads include internal forces, including those created by muscles. A change in muscular contributions to internal knee joint loading is a likely reason why a reduction in the external knee adduction moment does not necessarily guarantee a reduction in medial compartment load, despite reports of a strong correlation between the knee adduction moment and in vivo contact forces in the medial compartment[13,16-17]. High external knee adduction moments are frequently observed in patients with knee OA, but can also exist in individuals without knee OA, in the absence of injury and in the presence of normal gait patterns[18]. Therefore, a high knee adduction moment represents disproportionate loading across the knee, and is a well-established risk factor for OA progression; however, the differences in the knee adduction moment observed in the subgroups of patients studied in Study 1, and the changes with the use of orthoses observed in Studies 2 and 3, must be interpreted cautiously.

It should also be acknowledged that the combined use of knee and foot orthoses may affect knee joint biomechanics in ways that were not evaluated in Study 3. For example, the valgus moment created by the brace may decrease medial compartment loads, but the moment created by the brace was not quantified. Similarly, a decrease in muscle co-contraction may decrease internal joint loads, but was not evaluated. Future biomechanical studies examining those parameters might provide greater insight into the

combined use of knee and foot orthoses. Similarly, evaluating the effects of knee and foot orthoses during more demanding, functional tasks such as stair climbing is needed.

The effect of orthoses on knee pain is still somewhat unclear. Study 3 included patient-reported levels of knee pain when the orthoses were used together and separately during a single testing session in the lab; however, their prolonged effects on knee pain were not evaluated. Similarly, the potential discomfort in wearing both of these devices for prolonged periods was not evaluated. Results from Study 2 suggested that valgus braces can indeed provide improvements in knee pain, but also suggested that patient discomfort is a substantial barrier to long-term brace use. Future research is required to investigate the appropriate balance between providing enough of a biomechanical effect to decrease knee pain without creating other discomfort.

Although this thesis adds clarity regarding the biomechanical and clinical effects of knee and foot orthoses for patients with knee OA, the potential role of these biomechanical interventions in slowing disease progression requires further research. Study 1 suggested that individuals with greatest body mass and varus alignment may be the most appropriate candidates for these interventions. However, Studies 2 and 3 did not specifically evaluate that subgroup of patients. Few studies have examined the effects of a valgus knee brace and lateral wedge orthotic in obese subjects, despite their high risk for knee OA development and progression[19].

5.4 Recommendations

1. There is an interaction between lower limb alignment and body mass on dynamic knee joint loading. This interaction should be acknowledged and may be particularly relevant when evaluating risk factors for OA progression and potential biomechanical interventions.
2. Systematic review and meta-analysis of the published research supports the clinical use of valgus knee bracing for patients with medial compartment knee OA.
3. Strategies for improving patient compliance must be considered for the prescription of knee and foot orthoses. Research identifying parameters for appropriate dosage (i.e. angulation and duration of use) is needed.
4. There are apparent additive biomechanical effects of using a valgus brace and lateral wedge foot orthotic concurrently. This warrants future investigation and clinical use of multi-modal biomechanical interventions for patients with knee OA.

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6. Appendices

APPENDIX A
MEDLINE DATABASE SEARCH STRATEGY

1. Knee
2. Osteoarthritis.mp. or Osteoarthritis, Knee/
3. 1 and 2
4. (“tibiofemoral” or “tibio-femora” or “tibio femoral”).mp.
5. 2 and 4
6. (“arthritis” OR “arthrosis” OR “osteoarthrosis” or “gonarthrosis” or “degenerative joint disease*” OR “musculoskeletal disease*”).mp.
7. 1 and 6
8. 3 or 5 or 7
9. Brace.mp. or Braces/
10. Knee Brace
11. (“knee device*” or “knee orthotic*” or “knee orthosis”).mp.
12. 1 and 9
13. 10 or 11 or 12
14. (“valgus brace*” or “valgus bracing”).mp.
15. (“unloader brace*” or “unloader bracing” or “un-loader brace*”).mp.
16. (“off loader brace*” or “off-loader brace*” or “off loader bracing”).mp.
17. 13 of 14 or 15 or 16
18. 8 and 17

APPENDIX B
THE PREFERRED REPORTING ITEMS FOR SYSTEMATIC REVIEWS AND META-ANALYSES (PRISMA) 2009 CHECKLIST

Section/topic	#	Checklist item	Page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	40
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	40
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	41-42
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	43
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	43
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	42
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	42, 44
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	109
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	45-46
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	44, 114
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	44
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	44-45
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	45
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	45
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	45

Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	45
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	45-46
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	47-50
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	52-55, 59
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	53-55, 59
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	52-55, 59
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	52-53,55, 59
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	52-53
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	62-65
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	65
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	65-66
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

APPENDIX C
METHODOLOGICAL QUALITY ASSESSMENT FOR NON-RANDOMIZED AND RANDOMIZED TRIALS USING A MODIFIED DOWNS AND BLACK SCALE

Item	16	17	18	19	20	21	22	23	26	/9
n=30 Non-Randomized Studies (Laboratory, Observational Cohorts, Surveys)										
Lindenfed *et al*. (1997)	1	1	1	-	1	1	-	-	1	6
Matsuno *et al*. (1997)	1	1	1	1	1	1	-	-	1	7
Liu *et al*. (1998)	1	-	1	-	-	-	-	-	1	3
Hewett *et al*. (1998)	1	1	1	1	1	-	1	-	1	7
Katsuragawa *et al*. (1999)	1	1	1	-	1	-	-	-	1	5
Komistek *et al*. (1999)	1	1	1	-	1	-	-	-	1	5
Draper *et al*. (2000)	1	1	1	-	1	1	1	-	1	7
Self *et al*. (2000)	1	1	1	-	1	-	-	-	1	5
Finger *et al*. (2002)	1	-	1	1	1	-	-	-	-	4
Pollo *et al*. (2002)	1	1	1	-	1	-	-	-	1	5
Barnes *et al*. (2002)	1	1	1	1	1	1	-	-	1	7
Anderson *et al*. (2003)	1	1	1	-	1	-	-	-	-	4
Giori *et al*. (2004)	1	1	1	1	1	1	1	-	-	7
Nadaud *et al*.(2005)	1	1	1	-	1	1	1	-	1	7
Dennis *et al*. (2006)	1	1	1	-	1	1	-	-	1	6
Gaasbeek *et al*. (2007)	1	1	1	-	1	1	1	-	1	7
Ramsey *et al*. (2007)	1	1	1	-	1	-	-	-	1	5
Schmalz *et al*. (2010)	1	1	1	1	1	-	-	-	1	6
Fantini Pagani *et al*. (2010)	1	1	1	-	1	-	-	1	1	6
Toriyama *et al*. (2011)	1	1	1	-	1	-	-	-	1	5
Fantini Pagani *et al*. (2011)	1	1	1	-	1	1	-	-	1	6
Kutzner *et al*. (2011)	1	1	1	-	1	1	1	-	1	7
Wilson *et al*. (2011)	1	1	1	1	1	1	1	-	-	7
Hurley *et al*. (2012)	1	1	1	1	1	1	1	-	-	7
Esrafilian *et al*. (2012)	1	1	1	-	1	1	1	-	1	7
Fantini Pagani *et al*. (2012)	1	1	1	-	1	1	1	-	1	7
Briggs *et al.* (2012)	1	1	1	1	1	-	-	-	1	6
Moyer *et al*. (2013)	1	1	1	-	1	1	-	1	1	7
Squyer *et al.* (2013)	1	1	1	1	1	1	-	-	1	7
Arazpour *et al*. (2013)	1	1	1	1	1	1	-	1	1	8
n=8 Randomized Studies (Parallel and Crossover)										
Horlick *et al*. (1993)	1	1	1	1	1	1	-	1	1	8
Kirkley *et al*. (1999)	1	1	1	-	1	1	-	1	-	6
Richards *et al*. (2005)	1	1	1	-	1	1	-	1	1	7
Draganich *et al*. (2006)	1	1	1	1	1	1	-	1	1	8
Brouwer *et al*. (2006)	1	1	1	1	1	1	1	1	1	9
van Raaij *et al*. (2010)	1	1	1	1	1	1	-	1	1	8
Hunter *et al*. (2012)	1	1	1	1	1	1	1	1	1	9
Jones *et al*. (2012)	1	1	1	1	1	-	1	1	1	8

APPENDIX D
DATA EXTRACTION FORM

Article Title: _____

_____

Authors: _____

_____

Journal:
Year / Volume / Page Numbers:

Corresponding Author Address: _____

_____

Source of Sponsorship/Funding:
_____

Country: _____
Comments: _____

STUDY DESIGN

RCT: _____ Randomized Crossover: _____ Other (identify): _____
Comments: _____

Intervention: _____
Comments: _____

Number of Groups (including the valgus knee brace group): _____
Comparator Intervention:

- □ Control (no intervention)
- □ Another Brace (specify type if able) _____
- □ Knee Sleeve (specify type if able) _____
- □ Other Treatment (specify if able) _____
- □ Unclear (describe if able) _____

Comments: _____

Duration of Brace Use (i.e. 6 weeks, 3 months, none-single test session): _____
Duration of Other Intervention (describe if needed or indicate same as brace): _____

METHODOLOGY (Modified Downs and Black Scale)

1.	No ____Yes ____	2.	No ____Yes ____	3.	No ____Yes ____
4.	No ____Yes ____	6.	No ____Yes ____	7.	No ____Yes ____
8.	No ____Yes ____	9.	No ____Yes ____	10.	No ____Yes ____
11.	No ____Yes ____	16.	No ____Yes ____	17.	No ____Yes ____
18.	No ____Yes ____	19.	No ____Yes ____	20.	No ____Yes ____
21.	No ____Yes ____	22.	No ____Yes ____	23.	No ____Yes ____
26.	No ____Yes ____	27.	No ____Yes ____		

PARTICIPANTS

Inclusion criteria (general reasons for patient selection):

_____
_____
_____

Exclusion criteria (general reasons for patient exclusion):

_____
_____
_____

Patient Demographics (use 3rd group as needed/add column for 4th group if needed):

	Valgus Brace Group	Control / Comparison Group	Control / Comparison Group
Age:			
Sex (# of males / # of females):			
Height:			
Weight:			
BMI (if given):			
Other:			

Comments:

_____
_____

Number of Participants (use 3rd group as needed/add column for 4th group if needed):

	Valgus Brace Group	Control / Comparison Group	Control / Comparison Group
Start (n) / End (n)	/	/	/

Comments:

_____
_____

Follow Up Time (if the same for all groups, fill out one column; if different between groups, specify):

	Valgus Brace Group	Control / Comparison Group	Control / Comparison Group
Minimum			
Maximum			
Other (frequency of visits):			

Comments:

_____
_____

RESULTS

Only data for the valgus brace is required for the results. The goal of the review is to evaluate the change in outcome measures when patients are not wearing the brace and when they are wearing the brace.

(1) Biomechanical Effects of the Valgus Knee Brace:

A. Indicate General Outcome Measure (KAM, GRF/LOAD, JOINT SPACE, ALIGNMENT, BONE DENSITY, CO-CONTRACTION):

Specific Outcome Measure + Units (I.e. 1st / 2nd peak KAM, HKA, MAA, joint space narrowing, etc.)	Sample Size in the Valgus Brace Group	Indicate the Brace Angle (if given) or Custom v. Off the Shelf	Indicate the Follow Up Time of Measurement (i.e. same day or after 4 weeks of wear, etc.)	Without the Brace Mean (Std. Deviation)	With the Brace Mean (Std. Deviation)	Other (any other info given i.e. mean difference, effect size, % change, p value, 95%CI etc.)

Comments:

_____
_____
_____

B. Indicate General Outcome Measure (KAM, GRF/LOAD, JOINT SPACE, ALIGNMENT, BONE DENSITY, CO-CONTRACTION):

Specific Outcome Measure + Units (I.e. 1st / 2nd peak KAM, HKA, MAA, joint space narrowing, etc.)	Sample Size in the Valgus Brace Group	Indicate the Brace Angle (if given) or Custom v. Off the Shelf	Indicate the Follow Up Time of Measurement (i.e. same day or after 4 weeks of wear, etc.)	Without the Brace Mean (Std. Deviation)	With the Brace Mean (Std. Deviation)	Other (any other info given i.e. mean difference, effect size, % change, p value, 95%CI etc.)

Comments:

_____
_____
_____

(2) Patient-Reported Outcome Measures for Valgus Knee Bracing

A. Indicate General Outcome Measure (Pain, Function):

Specific Outcome Measure + Units (I.e. 1st / 2nd peak KAM, HKA, MAA, joint space narrowing, etc.)	Sample Size in the Valgus Brace Group	Indicate the Brace Angle (if given) or Custom v. Off the Shelf	Indicate the Follow Up Time of Measurement (i.e. same day or after 4 weeks of wear, etc.)	Without the Brace Mean (Std. Deviation)	With the Brace Mean (Std. Deviation)	Other (any other info given i.e. mean difference, effect size, % change, p value, 95%CI etc.)

Comments:

_____
_____
_____

B. Indicate General Outcome Measure (Pain, Function):

Specific Outcome Measure + Units (I.e. 1st / 2nd peak KAM, HKA, MAA, joint space narrowing, etc.)	Sample Size in the Valgus Brace Group	Indicate the Brace Angle (if given) or Custom v. Off the Shelf	Indicate the Follow Up Time of Measurement (i.e. same day or after 4 weeks of wear, etc.)	Without the Brace Mean (Std. Deviation)	With the Brace Mean (Std. Deviation)	Other (any other info given i.e. mean difference, effect size, % change, p value, 95%CI etc.)

Comments:

_____
_____
_____

Repeat the number of tables as needed per biomechanical or patient-reported outcome measure.

Adverse Effects: Some studies report reasons why patients dropped out or stopped wearing the brace. Please describe here. Report the reason, number of patients reporting the adverse effect (I.e. skin irritation, sweating, etc.)

_____
_____
_____

Compliance: If the article describes the frequency of brace use, describe here. (I.e. hours per day, number of participants that wore the brace as instructed and those that stopped wearing the brace, when did they stop wearing the brace, why participants stopped wearing the brace-some of these reasons may also be repeated in the adverse effects section below.)

_____
_____
_____

Overall Findings/Conclusions from the Article that pertain to Valgus Bracing:

(1)

_____

(2)

_____

(3)

_____

APPENDIX E
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Licensed content author	R.F. Moyer,T.B. Birmingham,B.M. Chesworth,C.O. Kean,J.R. Giffin
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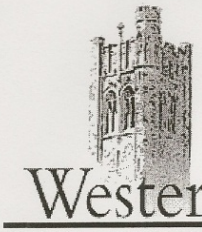
APPENDIX F
ETHICS APPROVAL FORMS



Office of Research Ethics
The University of Western Ontario
Room 4180 Support Services Building, London, ON, Canada N6A 5C1
Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca
Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. T.B. Birmingham
Review Number: 09812E **Revision Number:** 3
Review Date: May 15, 2008 **Review Level:** Expedited
Protocol Title: Medial Opening Wedge High Tibial Osteotomy for the Treatment of Knee Osteoarthritis: Evaluation of Dynamic Joint Loads and Health-Related Quality of Life
Department and Institution: Physical Therapy, University of Western Ontario
Sponsor: CANADIAN INSTITUTES OF HEALTH RESEARCH
Ethics Approval Date: May 15, 2008 **Expiry Date:** April 30, 2012
Documents Reviewed and Approved: Revised co-investigator, study methods, number of study participants. Letter of Information and Consent.
Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

[redacted]

Chair of HSREB: Dr. Joseph Gilbert

[redacted]

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cc: ORE File
LHRI

Western Research

Research Ethics

Use of Human Participants - Ethics Approval Notice

Principal Investigator: Dr. Trevor Birmingham
File Number:8459
Review Level: Delegated
Approved Local Adult Participants:40
Approved Local Minor Participants:0
Protocol Title: The investigation of the combined effects of an unloader brace and a lateral heel wedge on knee joint load in individuals with varus gonarthrosis
Department & Institution: Health Sciences\Physical Therapy,Western University
Sponsor:
Ethics Approval Date: June 11, 2013 **Expiry Date:**September 30, 2013
Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Other	Summary of Changes	
Revised Letter of Information & Consent	Amended Letter of Information	2013/03/01
Revised Western University Protocol	Form 2F002 UWO HSREB Delegated Review (with tracked changes)	

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The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

[redacted]

Ethics Officer to Contact for Further Information

[redacted]

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Rebecca Frances Moyer, PT

Curriculum Vitae
PhD Candidate
Full Time: Yes

EDUCATION

DEGREE	INSTITUTION	FACULTY/DEPARTMENT	DATE
PhD	Western University	Physical Therapy	2008-2013
MPT	Western University	Physical Therapy	2010-2012
BScH	Queen's University	Arts and Science (SSP: Biology)	2003-2008
BPHE	Queen's University	Physical and Health Education	2003-2007

PUBLICATIONS

Career Totals For:	Peer-Reviewed Journal Articles		
		Accepted/In Press:	3
		Under Review:	2
	Peer-Reviewed Abstracts		3
	Presentations at Professional Meetings		12

PEER-REVIEWED JOURNAL ARTICLES

Accepted/In Press

3. Longino PD, Birmingham TB, Shultz WJ, **Moyer RF**, Giffin JR. Combined tibial tubercle osteotomy with medial opening wedge high tibial osteotomy minimizes changes in patellar height. A prospective cohort study with historical controls. *The American Journal of Sports Medicine*. In print.

2. **Moyer R**, Birmingham T, Dombrowski C, Walsh R, Leitch K, Jenkyn T, Giffin JR. (2013) Combined effects of a custom-fit valgus knee brace and lateral wedge orthotic on dynamic knee joint loading in patients with varus gonarthrosis. *Archives of Physical Medicine and Rehabilitation* 94 (1): 103-112

1. **Moyer R**, Birmingham T, Kean C, Chesworth B, Giffin JR. (2010) Alignment, body mass and their interaction on dynamic knee joint load in patients with knee osteoarthritis. *Osteoarthritis and Cartilage* 18 (7): 888-893

Under Review

2. Boulougouris A, Birmingham T, **Moyer R**, Leitch K, Jones I, Giffin JR. Gait Changes in the Non-Surgical Limb Two Years After High Tibial Osteotomy. *Submitted*

1. Fernandes NA, Bryant D, Griffith L, El- Rabbany M, Fernandes N, Kean C, Marsh J, Mathur S, **Moyer R**, Reade CJ, Riva JJ, Somerville L, Bhatnagar N. Are randomized trial participants guinea pigs? Systematic review and meta-analysis. *Submitted*

PEER-REVIEWED ABSTRACTS

3. **Moyer R**, Birmingham T, Dombrowski C, Walsh R, Leitch K, Jenkyn T, Giffin JR. (2011) Combined effects of a custom-fit valgus knee brace and lateral wedge orthotic on dynamic knee joint loading in patients with varus gonarthrosis. *Osteoarthritis and Cartilage 19 (S1): S96*

2. **Moyer R**, Birmingham T, Robbins S, Jones I, Jenkyn T, Giffin JR. (2011) Differences in tibial rotation during walking in patients with anterior cruciate ligament deficiency and knee osteoarthritis. *Osteoarthritis and Cartilage 19 (S1): S85-86*

1. **Moyer R**, Birmingham T, Kean C, Chesworth B, Giffin JR. (2009) Alignment, body mass and their interaction on dynamic knee joint load in patients with knee osteoarthritis. *Osteoarthritis and Cartilage 17 (S1): S82-83*

PRESENTATIONS at PROFESSIONAL MEETINGS

Moyer R, Birmingham T, Jones I, Dombroski C, Walsh R, Jenkyn T, Giffin JR. Combined effects of a valgus knee brace and lateral wedge orthotic on dynamic knee joint load in patients with knee osteoarthritis.
12. *Pedorthist Association of Canada Symposium, Montreal, QC, April 2013;*
11. *Western Sport Medicine Symposium, London, ON, September 2012;*
10. *World Congress on Osteoarthritis, San Diego, CA, September 2011;*
9. *Foot and Lower Extremity Symposium, London ON, May 2011;*
8. *Congress for Scientific Testing of Orthotic Devices, Aix les Bains, France, March 2011*

Boulougouris A., Birmingham T, **Moyer R**, Jones I, Gififn JR. Increased Dynamic Knee Joint Load on the Non-operative Limb after High Tibial Osteotomy.
7. *Western Sport Medicine Symposium, London, ON, September 2011;*
6. *World Congress on Osteoarthritis, San Diego, CA, September 2011*

Moyer R, Birmingham T, Robbins S, Jones I, Jenkyn T, Giffin JR. Differences in tibial rotation during walking in patients with anterior cruciate ligament deficiency and knee osteoarthritis.
5. *World Congress on Osteoarthritis, San Diego, CA, September 2011*

Birmingham T, **Moyer R**, Leitch K, Boulougouris A, Jones I. A Systematic Review of Knee Orthoses.
4. *Congress for Scientific Testing of Orthotic Devices, Aix les Bains, France, March 2011*

Moyer R, Birmingham T, Jones I, Giffin JR. Transverse plane kinematics and under-correction in high tibial osteotomy.
3. *Canadian Society for Biomechanics, Kingston, ON, June 2010;*

Moyer R, Birmingham T, Kean C, Jones I, Chesworth B, Giffin JR. Interaction between mass and alignment on knee adduction moment in patients with knee osteoarthritis.
2. *World Congress on Osteoarthritis, Montreal, QC, September 2009;*
1. *American Society for Biomechanics, State College, PA, August 2009*

FUNDING

1. Moyer RF. 2012-2013. Ontario Graduate Scholarships. Funds awarded: $15,000/1 year
2. Moyer RF. 2011-2012. Ontario Graduate Scholarships. Funds awarded: $15,000/1 year

ONGOING RESEARCH

Moyer R, Birmingham T, Leitch K, Marriot K. Systematic review and meta-analysis of the biomechanical and clinical effects of valgus knee bracing in patients with medial compartment knee osteoarthritis. Manuscript prepared for submission.

Moyer R, Birmingham T, Robbins S, Jones I, Jenkyn T, Giffin JR. Differences in tibial rotation during walking in patients with anterior cruciate ligament deficiency and knee osteoarthritis. Manuscript in preparation.

Moyer R, Birmingham, Jones IC, Gififn JR. Using patient-specific measures of foot rotation to assess lower limb frontal plane alignment. Manuscript in preparation.

RESEARCH HISTORY

2008-Present	Doctorate of Philosophy Wolf Orthopaedic Biomechanics Lab, Western University *Thesis: Alignment, body mass and dynamic knee joint loading in medial compartment knee osteoarthritis: Implications for orthoses use*

2010-2012	Co-Supervisor, Masters of Physical Therapy Research Project School of Physical Therapy, Western University *Title: Systematic Review of Anterior Cruciate Ligament Bracing: Proposed Mechanisms and Clinical Outcomes (2012)* *Title: Systematic Review of Patellofemoral Bracing: Proposed Mechanisms and Clinical Outcomes (2011)*
Jan-Mar 2009	Data Collection and Analysis Wolf Orthopaedic Biomechanics Lab, Western University Fowler Kennedy Sport Medicine Clinic, Western University *Title: Interaction between hip rotation and lower back pain in golfers*
Oct 2007-Mar 2008	Research Assistant Ontario Veterinary College, University of Guelph *Title: A comparison of racing surfaces and the effect on lower extremities in horses*

JOURNAL REVIEWER
Prosthetics and Orthotics International (2013)
Journal of Orthopaedic and Sports Physical Therapy (2012)

COMMENTARIES
Lower Extremity Review Magazine (Oct 2011, Nov 2012)
OARSI Young Investigators (March 2011)

TEACHING

ROLE/POSITION	INSTITUTION	FACULTY/DEPARTMENT	DATE
Guest Lecturer	Western University School of Physical Therapy	PT9512: Integrated Assessment Patient Transfers	2012
Guest Lecturer	Western University School of Physical Therapy	PT9512: Integrated Assessment Gait	2012
Guest Lecturer	Western University School of Physical Therapy	PT9512: Integrated Assessment Vital Signs	2012
Teaching Assistant	Western University Department of Anatomy	HS: 2330 Systemic and Functional Anatomy	2009-2011

CLINICAL EXPERIENCE

RANK/POSITION	INSTITUTION	FACULTY/DEPARTMENT
Physical Therapist	London Health Sciences Centre, UH	Surgical Care Inpatient Orthopaedics
PT Student	Western University	Fowler Kennedy Sport Medicine Clinic, 3M Centre
PT Student	Western University	Parkwood Hospital, Veterans Care Rehabilitation Program
PT Student	Western University	University Hospital, Medical Surgical ICU
PT Student	Western University	St. Joseph's Hospital, Rheumatology
PT Student	Western University	VHA Solutions, Community Home Care

ACADEMIC HONOURS AND AWARDS

AWARD	INSTITUTION/ASSOCIATION	DATE
CPA Student Award	Canadian Physiotherapy Association	2012
Faculty of Health Sciences Travel Award	Western University	2010-Present
Graduate Research Scholarship	Western University	2008-Present
Dean's Entrance Scholarship	Western University	2008
Graduate with Distinction	Queen's University	2007, 2008
Dean's Honour List	Queen's University	2004-2007

CERTIFICATIONS AND ASSOCIATIONS

POSITION/CERTIFICATION	INSTITUTION/ASSOCIATION	DATE
Physiotherapist (Reg. # 15260)	College of Physiotherapists of Ontario	2012-Present
Level I Manual Therapy	Orthopaedic Division, Canadian Physiotherapy Association	2012-Present
Mulligan Concept Introduction	Mulligan Concept	2012-Present
Physiotherapist Member (ID# 2014326)	Canadian Physiotherapy Association Ontario Physiotherapy Association	2010-Present
CPR and First Aid	Divers Alert Network	2010-Present