The effectiveness of foot orthoses in the treatment of medial knee osteoarthritis: A systematic review

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List of Abbreviations

OA	Osteoarthritis
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
KL	Kellgren Lawrence
KAM	Knee adduction moment
NICE	National Institute of Clinical Excellence guidelines
LWI	Lateral wedge insoles
KAII	Knee adduction angular impulse
QOL	Quality of Life
VAS	Visual Analogue Scale
KOOS	Knee Injury and Osteoarthritis Outcome Score (KOOS)
RCT	Randomised control trial
EULAR	European League Against Rheumatism
EKFS	Edinburgh Knee Function Scale

Abstract

Background: Knee osteoarthritis is a disease of the joint causing decreased function and pain. Currently, treatments range from medication to surgery, with the use of different insoles and footwear recommended. These methods are effective by either correcting the position of the knee or providing shock absorption. However, there is little understanding of the effective characteristics of these devices.

Research question: This paper aims to investigate this question and provide future areas of research to help better define treatment guidelines. Foot orthoses are an example of non-pharmacological conservative treatments mentioned in National Institute for Health and Care Excellence (NICE) guidelines to treat knee osteoarthritis (OA). These include lateral wedge insoles (LWI), developed with the intention of load reduction of the knee. Different footwear has also been shown to affect pain, biomechanical and functional outcomes in knee OA patients.

Methods: To address what features of LWIs and footwear make them effective in the treatment of knee OA, scientific databases were used to search for papers on this topic and then selected to be included based on pre-defined criteria. Data were extracted and analysed from these studies to provide a basis for possible areas for future development of these foot orthoses, and research required to improve clinical treatment guidelines. Databases used were PubMed, Scopus and Web of Science.

Results and Significance: Thirty-four out of 226 papers were included after application of inclusion and exclusion criteria. Regarding LWIs, the characteristics showing the most beneficial effect on either biomechanical, functional or pain outcomes were customisation, full-length, 5° elevation, shock absorption and arch support. For footwear, barefoot mimicking soles produced the most favourable biomechanics. Results also showed that insoles work in correcting the position of the knee, but it may or may not affect patients' pain and function.

1. Introduction

1.1. Background

Knee Osteoarthritis (OA) is a common medical condition seen in primary care affecting 1 in 5 adults over the age of 45 in the UK [1]. It is comprised of varying levels of functional limitations and associated with reduced quality of life (QOL) [2]. OA is a metabolically active process involving all joint tissues, i.e. bone, synovium and muscle [3]. Pathological changes include loss of joint space through the degradation of joint cartilage, and new bone formation at the joint site would cause several malfunctions (osteophytes) [4]. This breakdown and repair process supports the idea that OA is a repair process for synovial joints and trauma may be the trigger. Symptomatic OA occurs when either the repair process is blunted, or the initial trauma is above the repair threshold, resulting in continuing tissue damage [5]. Knee OA has multiple risk factors, usually divided into subgroups: genetic factors [6-9], constitutional factors [10-12], age [13], sex [14, 15], Body Mass Index (BMI) [16-20] and biomechanical factors [21-26] . Heritability for OA is estimated to be around 40-60% [5]. Females, particularly post-menopausal, tend to have a higher incidence of knee OA, and this sex difference is well documented amongst several studies [27-29]. It is also shown that having previous knee trauma increases the risk of knee OA by 3.86 times [30]. Clinically, the most common symptoms of knee OA are persistent knee pain, morning stiffness and reduced function; the triad of symptoms recommended by the European League Against Rheumatism (EULAR) for the diagnosis of knee OA [31]. Pain is the underlying cause of most of the disability seen in knee OA and is usually exacerbated by activity and relieved by rest. It is thus a vital component for disease monitoring by clinicians [30]. Several scoring systems are in place to aid clinicians in monitoring the severity of limitations for knee OA patients [32]. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a physical function subscale widely used as a patient-reported measurement tool for knee OA, covering physical function, pain, stiffness and other symptoms [33]. WOMAC scoring has been well validated and is widely used in medical practice and clinical trials [34]. Radiologically, X-Rays are the initial port of call as they show bony malformations that may exist within the joint. The Kellgren Lawrence (KL) scale is a radiographic classification scheme for OA, which is commonly used both as a research tool for OA studies, and as a potential aid for clinical treatment algorithms. It ranges from grade 0-4, with grade "0" signifying no presence of OA and grade "4" signifying severe OA, based on several radiological findings, i.e. the formation of osteophytes-[35].

The most common form of OA occurs at the medial compartment of the knee and is due to a higher transfer of load to the medial compartment during normal gait compared to the lateral compartment [36]. Pain and functional impairment on the medial side are caused by this asymmetry in loading, resulting in an adduction of the knee moment throughout the stance phase of gait. This often causes a valgus malalignment in patients, causing a greater shift in stress to the medial compartment. It is shown that a high knee adduction moment (KAM) and varus malalignment in load bearing are predictors for disease progression in knee OA [37, 38]. Therefore, reducing loading to the medial side of the knee during daily life should have positive, and sometime long-lasting, effects on patients with medial knee OA. This in fact is a strategy currently employed by several conservative treatment methods.

According to the National Institute for Health and Care Excellence (NICE) guidelines, initial treatment involves the encouragement of patients to undertake -=self-management [39]. This ranges from undergoing weight loss and/or exercising to increase the patient's local muscle strength [40]. Following this, pharmacological treatments, i.e. pain killers and anti-inflammatory medication, are offered that usually involve symptom control [41]. The most severe cases of knee OA have surgical treatments offered; these range from a high tibial osteotomy to full joint replacements [42]. This is currently a massive financial burden on the National Health System (NHS) in the UK, with OA joint replacement surgeries costing £405 million per year [43]. NICE also mentions non-pharmacological conservative treatments in its guidelines. Adjunct treatments include thermotherapy [44], electrotherapy [45] and walking aids [46].

1.2. Description of the intervention

Foot orthoses are an example of non-pharmacological conservative treatments mentioned in NICE guidelines. These include lateral wedge insoles (LWI), which are developed with the intention of load reduction of the knee, in this context of the medial compartment, by creating a valgus effect on the knee. Shock absorbing insoles and different types of footwear have a cushioning effect on the knee [47]. All of these interventions are used to improve function by reducing the symptoms of knee OA, and possibly slow down disease progression [48]. A LWI laterally shifts the centre of pressure, causing a more vertical ground reaction force. This causes a reduced knee ground reaction force lever and a reduced external knee adduction moment [49].

1.3. Rationale

Research is currently split regarding the effectiveness of LWIs. While NICE recommend the possible use of LWIs, European League Against Rheumatism (EULAR) have rejected the recommendation based on evidence showing no clinical effects. However, since the publication of these recommendations in 2012, research has shown positive effects of the use of LWIs. Several review papers have looked at this. Thus, Roodsari et al. concluded that LWIs could provide changes in KAM, pain and function in Knee OA [50]. On the other hand, Cochrane's review concluded that the optimal choice for an orthosis is unclear, with long term effects inconclusive [51]. Regarding footwear, currently EULAR and NICE recommend appropriating footwear to knee OA patients. However, at present no systematic review exists looking at the effect of footwear on knee OA.

Many different types of LWIs and footwear exist within clinical practice. Currently, no review exists looking at specific features of LWIs and footwear that make them effective (and those that maybe ineffective), as well as looking at those that may be superior for the treatment of knee OA. This systematic review aims to be the first to address this issue in the treatment of knee OA and moreover, provide a basis for possible areas for future development of these foot orthoses, and suggest further research that is required to improve clinical treatment guidelines.

2. Material and Methods

2.1. Search methods for identification of studies

The search strategy was based on the Population Intervention Comparison Outcome (PICO) (Table 1).

Table 1: The Population Intervention Comparison Outcome (PICO) used when creating the search strategy

Published research from 2000 to 2019 was searched for on PubMed, Scopus and Web of Science using the following keywords:

1- 'Knee osteoarthritis' (other variations of osteoarthritis used as well i.e. osteoarthrosis, degenerative knee disease)
2- 'Foot Orthoses' (other variations of orthoses used as well i.e. orthotic, orthosis)
3- Insoles
4- Footwear

The following combinations were used:

1 OR 2, 1 OR 3, 1 OR 4,

1 AND 2, 1 AND 3, 1 AND 4,

Relevant articles where then identified and selected for evaluation. No language restrictions were applied. Papers were reviewed following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) method [52]. Titles were then screened to eliminate duplications and then proceeded to abstract screening.

2.2. Inclusion and exclusion criteria

All abstracts were assessed for eligibility using the inclusion criteria found in Tabel 2. Full text articles where then assessed against our exclusion criteria (Table 2) and discarded if any of those criteria were met.

Table 2: Inclusion and exclusion criteria used during the screening process of papers

This situation arose where the same patient population was used for several reports, in this instance this study used the larger group of patients, or the report with the longer follow up period. Figure 1 shows the summarised search process in a PRISMA flowchart.

Figure 1: The flow diagram followed using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) method

2.3. Assessment of study quality

Risk of bias was assessed by looking at the papers' sampling methods, description of dropouts and withdrawals. Journal strength was then assessed through SCImago Journal ratings [53]. Only papers published in journals with ratings in Quartile 2 and above were included in journals that had relevance to the reviews subject area. This would include journals in subject areas such as musculoskeletal problems, orthopaedics, arthritis, rheumatology, gait and posture, physical medicine and rehabilitation etc.

2.4. Data extraction

Data extraction was conducted by extracting data on study design, methods used, sample size, interventions, outcome measures on KAM, pain, function and follow-up periods using a standardised form.

2.5. Data presentation and analysis

Extracted data were then sorted into those relating to either LWIs or shoes and were presented in tables. These allowed comparisons of data that enables a consensus to be reached for the research question.

3. Results

3.1. Search results

The search strategy resulted in 226 articles from the following databases: PubMed, Scopus and Web of Science. Ninety-eight articles were removed due to duplications. One hundred and twenty-eight records' titles and abstracts were then screened against the inclusion criteria, which resulted in removing 35 papers as they did not meet the requirements for study design. The remaining 93 articles were assessed against the exclusion criteria using the full texts, and 59 articles were removed as they satisfied one or more exclusion criteria (the most prevalent being the use of other concurrent treatment, n=22). All reasons for discarding papers along with numbers can be seen in Figure 1. Thirty-four studies remained and were included in this systematic review.

3.2. Study characteristics

The 34 studies chosen to be included in this paper had various characteristics and demographics (Table 3).

Table 3: Study characteristics of the papers included in this systematic review

The publishing year for the papers ranged from 2002 to 2018. Cohort sizes ranged from 8 to 200, with the mean being 57 participants. Fourteen papers were randomised control trials, 18 had a pre-post intervention study design, 1 was a cross-sectional observational study and there was also a single prospective case-control study. Regarding interventions used by the studies, 22 papers looked at LWIs; 12 looking specifically at the effectiveness of LWIs compared to a control (either no insole or a neutral one) [40, 49, 54-63], 2 looked at the effect of insole rigidity [64, 65], 2 at insole customisation [66, 67], 1 at the effect of insole length [68], 2 at the effect of different elevations of LWIs [69, 70], 1 at the correlation between disease severity and LWIs' effectiveness [71], and finally 2 papers investigated the effectiveness of arch support [72, 73]. Eleven papers looked at footwear's effect on knee OA: 1 at the effect of different footwear of knee OA [74], 5 at barefoot mimicking shoes [75-79], 3 at variable sole height shoes [80-82], and 2 at variable stiffness shoes [83, 84]. The remaining 1 paper compared the effectiveness of shoes and insoles on knee OA [85]. Regarding outcome measures, all papers looked at least one of the primary outcome measures we wanted to assess. Eight papers used the WOMAC score to assess and monitor disease function, and 24 papers conducted some biomechanical analysis, i.e. external KAM [86]. Several other outcomes were also looked at, namely, pain medication use, pain on Visual Analogue Scale (VAS) [87] and Knee Injury and Osteoarthritis Outcome Score (KOOS) [88, 89]. Finally, follow-up periods ranged from immediate testing to 2 years follow-up, with the mean study length being 12 weeks.

3.3. Methodological quality

Overall the methodological quality of the studies included in this paper was good (See Table 4).

Table 4: Journal quality for studies included in this systematic review

Twenty-seven out of the 34 papers (79%) were from Q1 SCImago Journal rated papers. Twenty-five out of the 34 published studies (74%) were randomised for either intervention or order of testing condition, reducing selection bias. Twenty-one studies (62%) had no drop-outs by participants, and 2 did not provide any information on drop-out rates. Of the remaining 11 papers, 2 did not provide reasons for patient withdrawal, and the rest presented valid explanations. The highest proportional participant withdrawal was in the study of Pham et al. (2004) with a 17.9% drop-out rate; reasoning ranged from participants undertaking surgery, to participants could not be traced during follow-up. Eighteen papers (53%) mentioned statistical power in the full text, of which 14 reached a statistical power of 80% or above.

3.4. Lateral insoles

Table 5 shows the results for all the papers regarding LWIs. Eleven papers were found evaluating the effectiveness of lateral wedges compared to either control or a neutral wedge.

Table 5: List of studies that evaluated the effect of foot orthoses on pain, functional and biomechanical outcomes on medial compartment knee osteoarthritis patients

Baker et al. compared 5° LWIs to a neutral insole in a randomised control trial (RCT), and found a 13.8% point effect on the WOMAC pain subscale at 6 weeks follow-up ($P=0.13$) [54]. Similar improvements in pain were seen in Hsu et al.'s intervention study [56]. Hinman et al.'s intervention found a reduction of 24% in walking pain, along with a 3-month improvement in WOMAC pain and function subscale ($P = 0.004$) [68]. However, several papers found either no effects on pain or a similar effect on pain in both the intervention and control groups. Bennell et al. showed a pain reduction that was not clinically relevant for both LWIis' and neutral insole groups in a large RCT [57]. Pham et al. (2004) found no statistical difference in disease severity or WOMAC subscales (including pain) after 2 years in another large RCT, but did find that the intervention group had a reduction in the number of days with NSAID intake (71 compared to 127) [59]. This similar reduction in severity of pain for both groups ($P < 0.001$), and reduction in NSAID intake in the intervention group, was also found by Hatef et al. [26] ($P = 0.001$). Moreover, Barrios et al. found a similar reduction in WOMAC score for both the intervention and control groups [60]. Regarding knee mechanics, there was a consensus of findings that LWIs decreased unfavourable knee biomechanics. Hsu et al. found a reduction in KAM at baseline, along with a change in gait at 6 weeks testing without the insoles ($p < 0.05$). The change in gait showed a reduction in KAM [56]. Hinman et al. showed LWIs reduced peak KAM (-5.8%) and angular impulse (-6.3%) in immediate testing ($P<0.001$) [49], and this was similarly replicated by Lewinson et al. [62]. Barrios et al. showed that KAM increased for the control group (subjects with knee OA without LWIs) over a year, whereas LWIs mitigated this increase, and they remained biomechanically active over 1 year of wear [60]. Sawada et al. [61] showed LWIs decreased first peak KAM in a normal foot group (-10%

P, 0.001), but remained unchanged in an abnormal (either everted on inverted) foot group. Alshawabka et al. found that this reduction in KAM due to LWIs was maintained during stair ascent and descent along with KAII (all $P<0.05$) [55]. Finally, Baker et al. assesed 50 feet walking time and chair stand time, finding small improvements in both scores but below clinical relevance [54]. Hatef et al. looked at the Edinburgh Knee Function Scale (EKFS) [90], and found significant improvement in the LWI group ($P < 0.001$) [63].

3.4.1. Size/elevation

Regarding pain, Rafiaee et al. compared 3mm vs 7mm insoles, and found that both wedge heights improved knee joint pain and quality of life (QOL) scores, with the 7mm insole (approximately 6°) having the most significant effect [70]. However, Dessery et al. found no difference in comfort or pain ratings between neutral, 6° and 10° insoles [72]. Biomechanically, Kerrigan et al. report that when compared with no insole, the 5° wedge reduced the peak KAM values by 6%, and the 10° wedge reduced the peaks by 8% [69]. This dose effect of LWI elevation was also found by Allan et al. ($p < 0.001$) [66], but Dessery et al. found no significant difference between 6° and 10 ° insoles; both having a 6% decrease in 2nd peak KAM compared to neutral or no LWI ($p<0.001$) [72]. No studies except Rafiaee et al.'s looked at quality of life measure, as mentioned previously [70].

3.4.2. Insole rigidity

Turpin et al. saw an improvement in the WOMAC pain subscale scores for shock absorbing insoles compared to no wedge ($P<0.05$) [64]. Hseih et al. found significant time×group effect improvements in pain ($P = 0.008$ for the KOOS) for soft LWIs compared to rigid LWIs [65]. Gait analyses for shock absorbing insoles revealed a significant reduction in the late stance peak KAM ($P=0.03$) during follow-up compared with the baseline test session [64].

Functionally, shock absorbing insoles reduced the timed stair climb (P<0.05) [64], and soft LWIs saw improvements in stair ascent time (P = 0.003), daily living function (P = 0.003 for the KOOS), sports and recreation function (P = 0.012 for the KOOS), and quality of life (P = 0.021 for KOOS) [65].

3.4.3. Length

Hinman et al. found full-length LWIs reduced KAM by 12-14% (P < 0.05), whereas rear foot wedging had no effectsf (P < 0.05) [58]. This finding was reciprocated by Allan et al., who showed full-length orthoses provided a greater reduction in first and second (5° forefoot/10° rearfoot wedging) KAM (p = 0.038) and KAM impulse compared to ¾ insoles (p = 0.018) [66].

3.4.4. Arch support

Dessery et al. found no differences in comfort or pain rating between no insoles, insoles with only one medial arch, and LWIs with medial arches at 6° and 10° [72]. However, Jones et al. found a significant reduction in pain in supported wedges (with medial arch) compared to typical wedges (p <0.001) (36). There was a 6% decrease in 2nd peak KAM in LWI conditions compared to others (p<0.001), and a 7% significant increase in KAM during loading response (a phase during walking) in neutral insoles with a medial arch [72]. Jones et al. found that external KAM was reduced in both typical and supported LWIs versus a control shoe (−5.21% and −6.29% respectively) but that there was no difference between the two groups [73]. No functional outcomes were tested in these studies.

3.4.5. Customisation

Skou et al. created custom insoles for participants and found the knee pain due to the OA (as rated on a VAS) after 30 minutes of physical activity, which was significantly reduced after the intervention (P= 0.001). Similar changes were seen for quality of life measurements [67].

3.4.6. Disease severity

Hinman et al. reported that disease severity, along with baseline functioning, the magnitude of immediate change in walking pain and first peak KAM, accounted for 24% of the variance seen in the WOMAC pain score at 3 months [58]. Shimada et al. found that LWIs significantly reduced the peak external KAM in KLre grades I (5.1% P=<0.043), II (6.6%, P=<0.010), III (3.3%, p<0.058) and IV (5.0%, P<0.086) [71]. The first acceleration peak after heel strike was only significantly reduced in KL grades I (P<0.024) and II (P<0.043) [71]. Functional outcomes were not tested in these studies.

3.5. Footwear

Table 6 shows the results for all the papers regarding footwear. Shakoor et al. compared the effect of common footwear on peak knee loads. and found that clogs and stability shoes resulted in a significantly higher peak KAM (p<0.05) compared with that of flat walking shoes, flip-flops and barefoot walking [74].

Table 6: Studies that evaluated the effect of footwear on pain, functional and biomechanical outcomes on medial compartment knee osteoarthritis patients.

There was no difference between flat walking shoes and flip flops compared to barefoot based on the results of this study. This paper did not look at any pain or functional outcomes.

3.5.1. Barefoot mimicking sole

Several papers looked at barefoot mimicking shoes; all apart from one [78] used the Moleca shoe [77]. Trombini-Souza et al. found a reduction in the WOMAC pain subscale by 61.9% ($p=0.003$) [75]. This was replicated again by Trombini-Souza et al., with the intervention group showing improvement in WOMAC subscales for pain and stiffness ($p=0.001$). This paper also showed reduced analgesia intake in the intervention group [77]. Biomechanically, the Moleca shoe has been shown to reduce knee load during midstance by 20.2% ($p=0.003$) and results in a 12.7% decrease ($p=0.034$) in the KAII [78]. In another study, it was shown to reduce the first peak KAM by 12%, the second peak of KAM during terminal stance by 12% compared to heels, with the barefoot condition having similar results to the Moleca shoe. The same study showed that heeled shoes increase 1st and 2nd KAM peaks compared to barefoot [76]. This positive effect has been reproduced in another study, showing a reduction of 21.8% in KAM for the intervention group [77]. Finally, Saco et al. showed that during stair descent, heeled shoes compared to Moleca shoes increased knee loads during early (15.5%) ($P < 0.001$), mid (9.5%) ($P = 0.010$) and late (9.2%) ($P < 0.001$) stance. Shakoor et al. looked at another minimalist shoe, showing an 8% ($P < 0.05$) decrease in peak external KAM with a mobility shoe compared to a self-chosen walking shoe, and a 12% ($P < 0.05$) reduction comparing the mobility shoe to a control [79]. The Moleca shoe showed improvement in WOMAC subscales for function when compared to a control shoe ($p=0.001$) [77].

3.5.2. Rocker soled shoe

Two papers found no significant difference in reduction in pain with rocker soled shoes when compared to control shoes, either at the end the study [81], or while standing or walking ($P = 0.28$) [82]. Madden et al. showed significantly reduced peak KAM between rocker soled vs non-rocker shoes, but 25% of participants showed an increase. No difference was found with KAII; both KAM and KAM impulse were higher in both shoe conditions vs barefoot [81]. Knee flexion moment showed a significant reduction of 16.7% for rocker soled shoes compared to a control ($P<0.01$) [80]. Finally, the only study that reported a functional outcome was conducted by Nigg et al., who showed rocker soled shoes increased static balance [82].

3.5.3. Variable stiffness

Erhart-Hledik et al. found that the variable stiffness types of shoes reduced the peak KAM with the daily activities (−5.5%, $p < 0.001$) [84]. WOMAC pain and total score were also significantly reduced. Reduction in KAM was related to improvement in pain and function ($R2 = 0.11$, $p = 0.04$). Finally, greater efficacy was seen in KAM reduction in the less severe OA group [84]. Paterson et al. (2018) found that KL grade II showed greater pain reduction in conventional shoes compared to unloading shoes. KL grade III+ had greater pain reduction in unloading shoes ($P= 0.02$) [83]. Neither paper looked at functional outcomes.

3.6. Footwear compared to LWIs

Jones et al. looked at several testing conditions, including different types of shoes and wedges [85] (See Table 7).

Table 7: Studies that evaluated the effect of lateral wedge insoles versus footwear on pain and biomechanical outcomes on medial compartment knee osteoarthritis patients.

Compared to a control shoe, typical and supported lateral wedge insoles (−5.9 and −5.6%, $p = 0.001$) and barefoot walking (−7.6% $p < 0.001$) reduced early stance external KAM. Similar improvements were seen for KAII, barefoot condition (−4.3%, $p = 0.023$), typical wedge (−7.95%, $p < 0.001$) and supported wedge (−5.5%, $p < 0.001$) compared to the control. The mobility shoe showed no effect ($p = 0.38$). Significant reduction in latter stance was seen in lateral wedges compared to other conditions ($p < 0.01$). The mobility shoe did show a significant reduction in immediate knee pain and improved scores (<0.001), but did not change medial loading. Lateral wedge insoles showed comparable reductions in medial knee loading [85]. Functional outcomes were not tested.

4. Discussion

4.1. Lateral insoles

This review aimed to look into the effectiveness of foot orthoses and what orthoses features may contribute by looking primarily at the effect on pain, function and KAM. Firstly, looking at the effectiveness of LWIs, regarding pain it seems that the consensus is split as to whether or not LWIs have a positive effect. Although Baker et al. found a positive mean difference in pain on the WOMAC pain scale, it was below the 50-point threshold for minimal perceptible improvement; this paper concluded that LWIs were not clinically relevant. However, the types of shoe worn (the importance of which will be discussed later) and physical activity of patients were not controlled in this study, which may both have affected the results [54]. Bennell et al.'s large RCT found a below minimal clinical importance change in knee pain; however, the pain was only measured at baseline and 12 months follow-up [57], which could cause a type 2 error in findings [91]. Moreover, KL grade 1 and 4 patients were excluded from the study, which may have skewed the results. Two papers saw a reduction in pain medication use while pain scores remained the same [59, 63]. A possible reason may be that patients' pain is reduced by LWIs, resulting in lower pain medication intake, causing higher activity levels, which then causes the same amount of pain as a baseline, however at a higher activity level [59, 63]. In a clinical context, this would reduce the money spent on pharmacological treatments, along with improving the patient's quality of life. Several papers used neutral insoles as their control; these may have the treatment efficacy of LWIs as they may have provided some discomfort relief, along with a placebo effect [54, 57, 59, 60, 63]. However, LWIs' biomechanical efficacy has been well documented. Several papers found that LWIs decreased unfavourable knee loading (either KAM or KAII) during normal walking [49, 62], and stair ascent and descent [55]. The mechanism for reduced KAM/KAII can be seen in Figure 1. Moreover, the biomechanical effectiveness remains after 1 year of use [60]. A longitudinal study demonstrated that a 1-unit increase in the knee adduction moment results in a 6.46-fold increase in the risk of medial disease progression [92]. Bennel et al. did show a positive association between tibial cartilage volume and reduced KAII [57], thus showing that LWIs may have a role to play in slowing down disease progression in the long term. Hsu et al. found that participants developed a specific gait adaptation at follow-up without the insoles. This shows that insoles may be used as a tool for developing a gait with reduced KAM [56].

All this means that while LWIs may not provide symptomatic relief, they may be clinically helpful in reducing unfavourable knee loads and slowing down disease progression, which in the long run would reduce the need for more expensive treatments, i.e. steroid injections or surgery.

4.1.1. Size/elevation

Research is split on the effect of insoles on pain control , with Rafiaee et al. finding a 6° insole to have the most significant effect on pain and function [70], and Dessery et al. finding no effect between their testing conditions. However, this may have been influenced by participants wearing insoles only for 5 trials [72], which may not have been long enough for them to feel a symptomatic effect. Biomechanically, the higher the wedging, the greater the KAM reduction; however, several participants reported pain or discomfort with the higher wedges [66, 69], with 5° being the most comfortable. Overall, 5° wedging seems to be a good compromise between

KAM reductions and discomfort levels for patients, and this is reflected in the studies, with most using 5° as their LWI elevation.

4.1.2. Insole rigidity

Regarding insole rigidity, studies found an overwhelmingly positive influence of either soft or shock absorbing insoles on patients' pain and functional scores [64, 65]. Amongst the healthy population, shock absorbing/softer insoles have been shown to reduce joint loading [64]. However, neither papers could find an underlying biomechanical cause for this. Turpin et al. could not find consistent reductions in KAM; this may have been due to a small study size, which did not allow small reductions in joint loading to be seen. Moreover, there was a lack of a control group, which may have highlighted more differences [64]. Hseih et al. did not include biomechanical analyses in their study [65]. Overall, these findings showed either treatment effect, a placebo effect, or the natural history of the disease, and highlighted the disconnect between pain and functional scores, with joint loading. There may be scope to look into different levels of insole rigidity in larger RCTs to gain a better understanding of possible mechanisms.

4.1.3. Length

Only biomechanical outcomes were tested for; therefore the effect on patient clinical outcomes would be hypothesis-based. Full-length LWIs have a more significant effect on KAM than rear-foot LWIs. Hinman et al. concluded that wedging the whole lateral border of the foot would be a key design feature for an effective reduction in KAM [68]. This is due to a greater lateral shift in the centre of pressure. Moreover, rearfoot wedges only effect 30-40% of the gait cycle [68]. Overall full-length wedging is more effective, and this is reflected in the studies, with most using full-length LWIs.

4.1.4. Arch support

A decrease in pain and increase in comfort has been associated with the use of an arch [73]. This may be due to an arch causing normalisation of step width [66]. Biomechanical outcomes showed no difference between arched and non-arched LWIs [73]. Dessery et al. found no difference in pain scores; this may have been due to the short time participants wore the insole (5 trials). Moreover, painkiller usage was not controlled, which may have blunted the pain response [72]. Clinically, the addition of an arch to an LWI would be done to increase comfort for patients, which may allow for increased adherence to treatment, With adherence being typically poor amongst the Knee OA population [59].

4.1.5. Customisation

Customised insoles showed improvement in pain, function and biomechanical outcomes [66, 67]. Skou et al. concluded that customisation may reduce adverse effects as reported by off the shelf insoles, whilst at the same time optimising the reduction in KAM [67]. However, the downfall in the current literature is that there is no paper comparing customised insoles to non-customised insoles. Therefore, the recommendation of customising insoles for patients would be difficult, as it is not known if the effects are worth the extra cost. Moreover, implementation of a large scale customisation process in current healthcare may be difficult mainly due to the funding requirements, time-based barriers and material limitations.

4.2. Footwear

The literature points toward the fact that the type of footwear affects knee OA patients. Biomechanically, Shakoor et al. picked several common shoes and found variability in KAM [78]. This agrees with the NICE guidelines on giving patients advice on footwear [42].

However, in this study, factors influencing this difference, for example. heel height, were not evaluated. Moreover, participants may have changed the way they walked in different shoes as they were not used to them. Finally, it was not possible to take actual recommendations from this paper, as it would not be practical to prescribe flip flops to the elderly due to the risk of falls.

4.2.1. Barefoot mimicking sole

Studies looking at barefoot mimicking showed overwhelmingly positive results on pain, function and KAM scores. Mechanisms behind this have been postulated in several of these papers, with the ground reaction force being lower due to the flexibility of the shoe allowing for greater force application by the foot [78]. Also, increased sensory input via skin contact would initiate protective reflexes in the foot to minimise joint loads and impact [76]. Further benefits include the barefoot mimicking shoe in the studies (Moleca) being very cheap and sustainable. Overall, these styles of shoe may have a longer lasting effect on disease progression; this is hypothesis-driven, as no paper looked at specific long-term outcomes on knee structure/degradation.

4.2.2. Rocker soled shoes

Papers looking at rocker soled shoes found increased knee joint loads in rocker soled shoes compared to barefoot conditions, as well as no effect on pain [80-82], with the only positive outcome being increased static balance. Moreover, the rocker soled nature of the soles may not be safe for the elderly population. Overall, these styles of shoe do not seem to be of any real benefit to the knee OA population.

4.2.3. Variable stiffness

Studies used variable stiffness shoes [83, 84], which were stiffer in the lateral aspect of the shoe and became softer medially. They found KAM and pain scores to be improved and found that these two were related. Moreover, Paterson et al. highlighted the concept of specific KL grade OA patients responding better to the treatment than others [83]. However, both papers were underpowered. Therefore, a more robust study is needed to draw a reliable conclusion.

4.3. Footwear vs insoles

Jones et al. is currently the only study comparing the efficacy of LWIs to different types of shoe in knee OA. They concluded that supported (with arch) LWIs reduced both knee load and pain, with the mobility shoe being the best at reducing pain scores in patients, but having no effect on KAM. These findings have been backed by other literature. Pain scores were taken immediately after testing, introducing some potential bias in the results. Overall, further research in the comparison of these foot orthoses needs to be done to produce reliable recommendations as to which may be superior.

5. Conclusions and future research

This is the first review to look at what aspects of foot orthoses make them effective in knee OA patients. It is clear that lateral wedges create favourable knee loading conditions, which may affect long-term disease progression; however, their effect on pain and functional outcomes is still debatable. It would seem that the ideal characteristics for an LWI would be customised full-length, 5° elevation, shock absorbing and having arch support. Moreover, KL grade 1 and 2 patients seem to have the most beneficial effects. However further research into the long-term effects on disease progression is needed to make more solid claims for LWIs. Regarding footwear, the outlook seems more positive; barefoot mimicking shoes seem to improve biomechanical outcomes significantly and seem to have the greatest potential for future development. Further research is required to ascertain whether they have any effect on clinical outcomes such as disease severity, pain and function. Finally, a valid conclusion cannot be drawn as to which foot orthoses are superior due to the lack of comparative studies available. This would be another area for future research along with determining whether there is a combined therapeutic effect gained by merging LWIs with barefoot mimicking shoes. Finally, research into which subgroups of knee OA patients respond best to foot orthoses should be conducted, as clearly variance is present in treatment efficacy. Overall, currently, no recommendations can be made to alter clinical guidelines.

Declarations of interest

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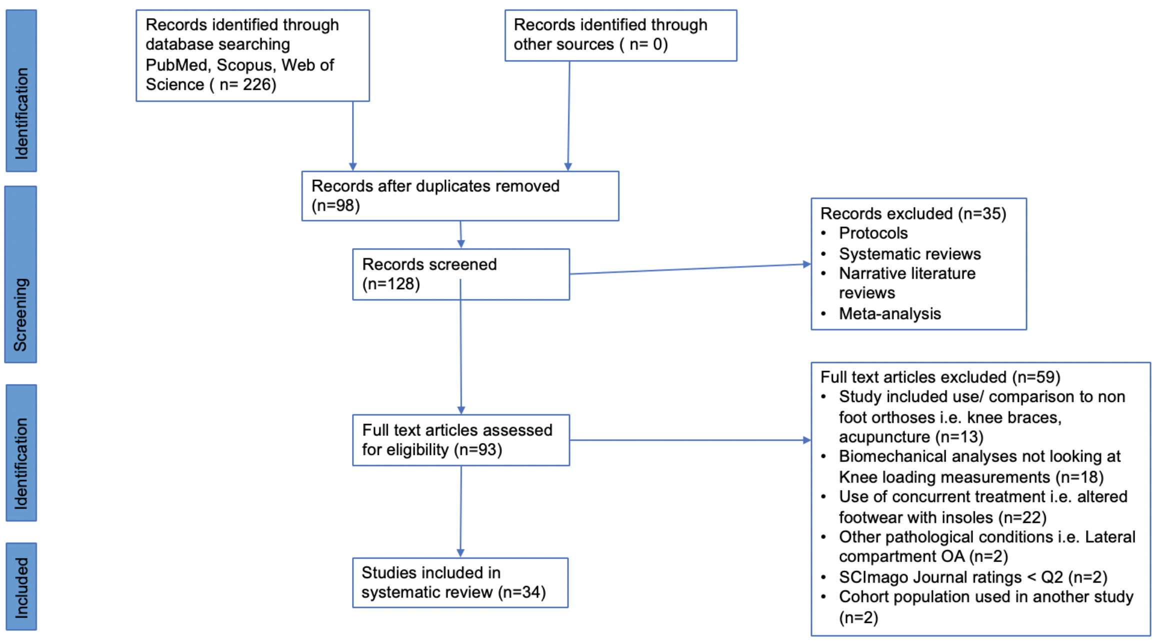

Figure 1: The flow diagram followed using the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) method.

Table 1: The Population Intervention Comparison Outcome (PICO) used when creating the search strategy

Population	**Intervention**	**Comparison**	**Outcome**
Individuals with medial knee osteoarthritis	Lateral wedge insoles (LWI) Footwear	Medial knee osteoarthritis patients without foot orthoses	Pain Function & Knee Adduction Moment

Table 2: Inclusion and exclusion criteria used during the screening process of papers

Inclusion criteria	Exclusion criteria
Types of studies- cohort studies, randomized control trials, randomized crossover trials, clinical intervention trials	Studies included use/ comparison to non-foot orthoses i.e. knee braces, acupuncture
Types of participants- adult patients (>18 years) with medial knee OA. Confirmed upon radiological investigation (KL grade 1-4)	Biomechanical analyses not looking at Knee loading measurements
Types of interventions- All types of LWI's (with or without arch support, customized, varying angles of wedging), and all types of shoes (variable stiffness, varying heel heights etc.)	Use of concurrent treatment i.e. altered footwear with insoles
Types of outcome measures o Major- we considered KAM, WOMAC score, effect on pain (usually on a visual analogue scale (VAS)) and effect on function as our major outcomes o Minor- Knee adduction angular impulse (KAII), Quality of Life (QoL), pain	Other pathological conditions i.e. Lateral compartment OA

medication use, along with other outcomes papers may have looked at	

Table 3: Study characteristics of the papers included in this systematic review

Author	Study design	Sample size	Intervention	Outcome measure	Follow up
[54]	Double- blind crossover RCT	90	5° LWI or a neutral insole .	1°- WOMAC pain scale (VAS). 2°- WOMAC disability, pain medication use, overall knee pain, 50 feet walk time	6 weeks. Then a 4 week washout period then 4 weeks
[64]	Pre-post intervention design with participants exposed to all conditions	16	sulcus length shock-absorbing insoles vs normal footwear	1°- peak, early stance peak, late stance peak external KAM. KAII. 2°- WOMAC pain subscale and total score, timed stair climb	4 weeks
[65]	prospective, double-blind, RCT.	90	Rigid vs soft Lateral wedge arch	KOOS and chronic pain grade questionnaire	1,2 and 3 months
[67]	Pre-post design intervention study	51	custom made insoles with arch support and a 5.08° to 8.78° lateral wedge	1°- VAS before and after the intervention after 30 minutes of physical activity. 2°- Oxford Knee Score and EQ-5D	4 weeks
[68]	Pre-post design intervention study	13	full length wedges vs rear foot wedges	external KAM	Immediate
[84]	blinded RCT	55	variable stiffness footwear vs constant stiffness footwear	1°- WOMAC total score and pain subscale. 2°- peak KAM	12 months
[69]	Pre-post intervention design with participants exposed to all conditions	15	5 ° vs 10 ° LWI	Peak KAM	Immediate
[75]	RCT	56	Flexible non heeled shoes (moleca) vs normal control	1°- WOMAC pain . 2°- Global WOMAC, Joint and stiffness WOMAC. Six minute walk test.	6 months

[74]	Pre-post design with participants exposed to all conditions	31	4 different shoes and barefoot: 1- clogs, 2- stability shoes, 3- flat walking shoes and 4- flip flops	Peak knee loads	immediate
[71]	prospective case control	42	LWI vs no insole	peak external KAM during stance phase and first acceleration peak after heel strike.	immediate
[78]	Pre-post design intervention study	48	Group A- Self chosen walking shoe and mobility shoe. Group B control shoe and mobility shoe	peak external KAM	immediate
[81]	Pre-post intervention design with participants exposed to all conditions	30	rocker soled vs non rocker soled shoes (including barefoot)	1°- peak external KAM. 2°- 11 point scale for knee pain whilst walking	Immediate
[56]	Pre-post design intervention study	10	LWI (7 ° +arch support)	1°- gait analysis after 6 weeks with and wihtout LWI. 2°- WOMAC score	6 weeks
[80]	Pre-post intervention design with participants exposed to all conditions	17	Masai Barefoot Technology (MBT) vs Control shoes	Peak knee loads	immediate
[76]	Pre-post intervention design with participants exposed to all conditions	45	Flexible non heeled shoes (moleca) vs modern heeled shoe vs barefoot	Peak knee loads	immediate
[79]	Pre-post intervention design with participants exposed to all conditions	34	Flexible non heeled shoes (moleca) vs modern heeled shoe vs barefoot in stair descent	Peak knee loads	immediate
[66]	cross sectional observational study	20	custom full and three-quarter- length foot orthoses with lateral posting of 0° 'neutral', 5° rear foot, 10° rear foot and 5° forefoot/ 10° rear foot	Peak knee loads	immediate
[57]	RCT	200	LWI (5°) vs Neutral control insole	1°- past week knee pain on an 11 point scale. Medial tibial cartilage volume. 2°- WOMAC score, progression of medial cartilage defects.	12 months

[72]	blinded RCT	18	no insole vs insole with medial arch vs lWI with 6° and 10°	Peak Knee loads and pain and comfort scores	immediate
[49]	Pre-post design with participants exposed to all conditions	73	LWI (5°) vs no insole	frontal plane parameters, including KAM, KAII, centre of pressure	Immediate
[49]	Pre-post design intervention study	40	LWI (5°) (vs no insole at baseline)	1°- immediate changes in static alignment and KAM. 2°- after 3 months changes in pain and functioning via WOMAC	3 months
[59]	prospective RCT	156	LWI (5°) vs Neutral control insole	1°- WOMAC score and Structural changes on x ray. 2°- medication use	symptomatic outcomes done at month 1,3 and then quarterly. Structural was done once a year.
[68]	Pre-post design intervention study	20	LWI (5°) (vs no insole at testing)	first and second peak KAM, KAII	1 month
[77]	Randomised parallel control trial	56	Flexible non heeled shoes (moleca) vs normal control	1°- WOMAC pain subscale. 2°- other subscales of WOMAC. 6 minute walk test, KAM, Paracetamol intake.	3, 6 months
[60]	Pre-post design intervention study	38	LWI (amount of wedge individualised) vs neutral insole	KAM and frontal plane motion	12 months
[83]	Exploratory analyses from a RCT	164	Unloading shoes vs conventional walking shoes	6 month change in knee pain	6 months
[61]	Pre-post design intervention study	21	LWI (5°)	KAM, KAII, Centre of pressure displacement, knee ground reaction force lever arm	immediate
[62]	RCT	48	LWI (5°) vs no insole	KAMs, KOOS and Physical Activity Scale for the Elderly (PASE) scores were measured at baseline	3 months

[63]	double- blind randomised parallel treatment trial	118	LWI (5°) vs Neutral control insole	Edinburg functional scale (EKFS) was used to evaluate knee function before/after. End measures= severity of knee pain over last 2 days. No. of NSAIDS used for pain relief within last 2 weeks and EKFS were assessed	2 months
[85]	RCT	70	barefoot vs control shoe vs typical wedge vs support wedge vs mobility shoe	EKAM, LAAI, external knee flexion moment, pain and comfort when walking	immediate
[70]	RCT	36	3 vs 7mm insoles	severity of knee pain, tibiofemoral angle, severity of OA and quality of life	2 months
[73]	Pre-post design with participants exposed to all conditions	70	Supported vs typical wedges	external KAM and Knee pain	immediate
[55]	Pre-post design with participants exposed to all conditions	8	LWI vs no insole during eithwer stair ascent or descent	KAM and KAII	immediate
[82]	RCT	123	Masai Barefoot Technology (MBT) vs Control shoes	WOMAC, BMI, OA index, Active range of motion	0,3,6,9,12 weeks

Table 4: Quality of studies included in this systematic review

author	Study design	Sample size	drop out rate/ withdrawal	Journal Strength	sampling method
[54]	Double- blind crossover RCT	90	4 - 3 personal reasons, 1 ineligible	Q1	randomised- stratified to take into account disease severity and whether patient had unilateral or bilateral disease
[64]	Pre-post intervention design with participants exposed to all conditions	16	2- no reasons mentioned	Q1	All participants underwent all testing conditions.
[65]	prospective, double-blind RCT.	90	16- 13 due to personal time reason, 3 due to aggravation of pain	Q2	block randomisation
[67]	Pre-post design intervention study	51	8- 4 due to pain from insole, 4 did not give a reason	Q2	consecutive
[68]	Pre-post design intervention study	13	no drop outs	Q1	consecutive
[84]	blinded RCT	55	5 drop outs- time commitment, back pain, total knee replacement, meniscectomy	Q1	Randomised
[69]	Pre-post intervention design with participants exposed to all conditions	15	no drop outs	Q1	all participants underwent all testing conditions.
[75]	RCT	56	no drop outs	Q1	block randomisation
[74]	Pre-post design with participants exposed to all conditions	31	no drop outs	Q1	all participants underwent all testing conditions.
[71]	prospective case control	42	no drop outs	Q1	all participants underwent all testing conditions.
[78]	Pre-post design intervention study	48	no drop outs	Q1	Groups taken from separate studies
[81]	Pre-post intervention design with participants exposed to all conditions	30	no drop outs	Q1	Randomised for order of condition

[56]	Pre-post design intervention study	10	no drop outs	Q2	all participants underwent all testing conditions.
[80]	Pre-post intervention design with participants exposed to all conditions	17	no drop outs	Q1	Order of conditions not randomised
[76]	Pre-post intervention design with participants exposed to all conditions	45	no drop outs	Q1	Randomised for order of condition
[79]	Pre-post intervention design with participants exposed to all conditions	34	no drop outs	Q1	Randomised for order of condition
[66]	cross sectional observational study	20	no drop outs	Q2	Randomised for order of condition
[57]	RCT	200	21- 10 due to refusal, 2 for knee replacement, 4 lost contact, 2 could not make appointments and 1 moved overseas.	Q1	block randomisation
[72]	blinded RCT	18	no drop outs	Q2	Randomised for order of condition
[49]	Pre-post design with participants exposed to all conditions	73	no drop outs	Q1	N/A
	Pre-post design intervention study	40	6- no reason mentioned	Q1	block randomisation
[59]	prospective RCT	156	28- 2 to surgery, 8 due to personal reasons, 12 lost to follow up, 6 due to 'other'	Q1	Randomised
[68]	Pre-post design intervention study	20	no drop outs	Q1	Randomised for order of condition
[77]	Randomised parallel control trial	56	6- 1 moved away, 2 lost interest, 1 for surgery, 1 developed complications, 1 changed medication	Q1	randomisation to wither intervention or control group
[60]	Pre-post design intervention study	38	no drop outs	Q1	Randomised
[83]	Exploratory analyses from a RCT	164	N/A	Q1	randomised

[61]	Pre-post design intervention study	21	no drop outs	Q1	all participants underwent all testing conditions.
[62]	RCT	48	5- 1 received extra treatment, 3 got pain form insole, 1 changed mind withing 48hrs	Q1	block randomisation
[63]	double- blind randomised parellel treatment trial	118	N/A	Q2	Randomised
[85]	RCT	70	no drop outs	Q1	Randomised for order of condition
[70]	RCT	36	no drop outs	Q2	Randomised by date of birth
[73]	Pre-post design with participants exposed to all conditions	70	no drop outs	Q1	Randomised for order of condition
[55]	Pre-post design with participants exposed to all conditions	8	no drop outs	Q1	Randomised for order of condition
[82]	RCT	123	2- due to pain	Q1	randomised

Table 5: List of studies that evaluated the effect of foot orthoses on pain, functional and biomechanical outcomes on medial compartment knee osteoarthritis patients

[54]	90	5° LWI or a neutral insole	1°- WOMAC pain scale (VAS). 2°- WOMAC disability, pain medication use, overall knee pain, 50 feet walk time	13.8-point effect (95% CI −3.9, 31.4) [P=0.13] on pain. No change in pain medication. Similar small effects seen in 2° outcomes.
[56]	10	LWI (7 ° +arch support)	1°- gait analysis after 6 weeks with and without LWI. 2°- WOMAC score	WOMAC scores decreased after 6 weeks. KAM with insoles was significantly reduced at baseline (p < 0.05). specific gait adaptation with reduced knee loading was revealed when walking without LW insoles
[57]	200	LWI (5°) vs Neutral control insole	1°- past week knee pain on an 11 point scale. Medial tibial cartilage volume. 2°- WOMAC score, progression of medial cartilage defects.	No significant difference for the 1° outcome or the s 2° outcomes.
[49]	73	LWI (5°) vs no insole	frontal plane parameters, including KAM, KAII, centre of pressure	LWI reduced peak KAM (-5.8%) and angular impulse (-6.3%) (P<0.001). Reductions in peak KAM correlated with more lateral Centre of pressure (r=0.25, P<0.05), less Varus misalignment (r values 0.25-0.38, P<0.05), reduced Knee Ground Reaction Force (r=0.69, P<0.01), more vertical frontal plane ground reaction force vector (r=0.67, P<0.001. Only knee-ground reaction force lever arm was significantly predictive in regression analyses P<0.001
[49]	40	LWI (5°) (vs no insole at baseline)	1°- immediate changes in static alignment and KAM. 2°- after 3 months changes in pain and functioning via WOMAC	Reduction in Kam for insoles -0.22% and reduction in walking pain -24%. No mean effect on static alignment. Mean improvements in WOMAC pain and function was observed at 3 months (P = 0.004). Regression analyses demonstrated that disease severity, baseline functioning and magnitude of immediate change in walking pain and first peak KAM was predictive of clinical outcome at 3 months. (24% of the variance in WOMAC pain score)
[59]	156	LWI (5°) vs Neutral control insole	1°- WOMAC score and Structural changes on x ray. 2°- medication use	No statistical significant difference between groups for improvement in WOMAC scores. Number of days NSAIDs taken decreased with LWI group. Joint space narrowing had no difference. LWI group had greater compliance

[60]	38	LWI (amount of wedge individualised) vs neutral insole	KAM and frontal plane motion	Increased KAM and frontal plane motion over 1 year in control group. Mechanical effectiveness did not decrease over time.
[61]	21	LWI (5°)	KAM, KAII, Centre of pressure displacement, knee ground reaction force lever arm	LWI decreased 1st KAM significantly (10%), however no difference in the abnormal foot group. Decreased rear foot eversion strongly correlated with reduction in 1st KAM in normal foot. No significant difference based on K/L grade. Centre of pressure was offset and ankle exhibited significant increased eversion excursion with LWIS.
[62]	48	LWI (5°) vs no insole	KAMs, Knee Injury and Osteoarthritis Outcome Score (KOOS) and Physical Activity Scale for the Elderly (PASE) scores were measured at baseline	No statistical difference in KOOS pain as found in lateral wedge group (p=0.173). No association in KAM reduction and change in KOOS pain
[63]	118	LWI (5°) vs Neutral control insole	Edinburg functional scale (EKFS) was used to evaluate knee function before/after. End measures= severity of knee pain over last 2 days. No. of NSAIDS used for pain relief within last 2 weeks and EKFS were assessed	Severity of pain (VAS) decreased in both groups after intervention (difference being 29.3%, AND 6.25%) (P < 0.001 for both). Significant improvement in EKFS for LWI(P < 0.001). No. of nsaids used during last 2 weeks significantly reduced in wedge group (P = 0.001.
[55]	8	LWI vs no insole during eithwer stair ascent or descent	KAM and KAII	During stair ascent and descent LWI significantly reduced 1st peak EXKAM in early stance, trough in mid stance, 2nd peak in late stance and KAAI compared to control (All P<0.05)
[64]	16	sulcus length shock-absorbing insoles vs normal footwear	1°- peak, early stance peak, late stance peak external KAM. KAII. 2°- WOMAC pain subscale and total score, timed stair climb	Significant reduction in the late stance peak KAM with shock-absorbing insoles (P=0.03) during follow-up compared with the baseline test session. Significant improvements seen in all measures of pain and function (P<0.05)
[65]	90	Rigid vs soft Lateral wedge arch	Knee Injury and Osteoarthritis Outcome Score (KOOS) and chronic pain grade questionnaire	significant time×group effect improvements in pain (P = 0.008 for the KOOS), stair ascent time (P = 0.003), daily living function (P = 0.003 for the KOOS), sports and recreation function (P = 0.012 for the KOOS), and quality of life (P = 0.021 for the KOOS) in the soft LWAS insole group

[67]	51	custom made insoles with arch support and a 5.08° to 8.78° lateral wedge	1°- VAS before and after the intervention after 30 minutes of physical activity. 2°- Oxford Knee Score and EQ-5D	VAS after 30 min of physical activity was significantly reduced after the intervention (P= .001). Similar changes seen for 2°outcomes.
[66]	20	custom full and three-quarter-length foot orthoses with lateral posting of 0° 'neutral', 5° rear foot, 10° rear foot and 5° forefoot/ 10° rear foot	Peak knee loads	showed full length orthoses provided greater reduction in first and second (5° forefoot/10° rear foot wedging) KAM and KAM impulse compared to ¾ insoles (p = 0.038) (p = 0.018). dose effect found for wedge height and reduction on first A, second (p = 0.028) and KAM impulse (p = 0.036) . There was a significant interaction effect of length and wedging condition for second peak knee adduction moment (p = 0.002). There was variability in the response to LWI
[68]	13	full length wedges vs rear foot wedges	external KAM	Full length wedge reduced KAM by 12-14% (P < 0.05). Rear foot had no effect (P < 0.05)
[69]	15	5 ° vs 10 ° LWI	Peak KAM	Compared with no insole, the 5° wedge reduced the peak KAM by about 6% and the 10° wedge reduced the peaks by about 8%. Reduction in KAM compared to neutral insoles. 10° insole was associated with degrees of discomfort.
[70]	36	3 vs 7mm insoles	severity of knee pain, tibiofemoral angle, severity of OA and quality of life	Both wedges improved QOL and decreased knee joint pain, however greater effect with 7mm.
[71]	42	LWI vs no insole	peak external KAM during stance phase and first acceleration peak after heel strike.	LWI significantly reduced the peak external KAM in KL grades I (5.1% P=<0.043) and II (6.6%, P=<0.010) grade III (3.3%, p<0.058), and IV (5.0%, P<0.086) . The first acceleration peak value after heel strike in these patients was relatively high compared with the control. Application of LWI significantly reduced the first acceleration peak in KL grades I (p<0.024) and II (P<0.043) knee OA patients but not III and IV patients.
[72]	18	no insole vs insole with medial arch vs lWI with 6° and 10°	Peak Knee loads and pain and comfort scores	6% decrease in 2nd peak KAM in LWI conditions compared to others (p<0.001). 7% significant increase in in KAM during loading response in neutral insole with medial arch. No difference in comfort or pain rating between conditions.

[73]	70	Supported vs typical wedges	external KAM and Knee pain	significant decrease in pain seen in supported wedges ($p < 0.001$) . EKAM was reduced in both LWIs versus control shoe (−5.21% and −6.29% for typical and supported wedges). 54% where biomechanical responders, but these people did not have more knee pain change than non responders

Table 6: Studies that evaluated the effect of footwear on pain, functional and biomechanical outcomes on medial compartment knee osteoarthritis patients.

author	Sample size	Intervention	outcome measure	results
[74]	31	4 different shoes and barefoot: 1- clogs, 2- stability shoes, 3- flat walking shoes and 4- flip flops	Peak knee loads	clogs and stability shoes, resulted in a significantly higher peak knee adduction moment ($p<0.05$) compared with that of flat walking shoes , flip-flops and barefoot walking. No difference in flat walking shoes and flip flops compared to barefoot.
[75]	56	Flexible non heeled shoes (Moleca) vs normal control	1°- WOMAC pain . 2°- Global WOMAC, Joint and stiffness WOMAC. Six minute walk test.	The 1° outcome (WOMAC subscale pain) decreased 61.9%. increase in WOMAC function subscale (44.9%), and WOMAC total score (49.3%). a 20.2% decrease ($p=0.003$) in the knee load at midstance, and a 12.7% decrease ($p=0.034$) in the KAM angular impulse. Increase in KAM first peak for Control group.
[78]	48	Group A- Self chosen walking shoe and mobility shoe. Group B control shoe and mobility shoe	peak external KAM	Group A showed an 8% ($P < 0.05$) decrease in peak external KAM with mobility shoe compared to self chosen walking shoe. Group B showed a 12% ($P < 0.05$) reduction comparing mobility shoe to control.
[75]	45	Flexible non heeled shoes (Moleca) vs modern heeled shoe vs barefoot	Peak knee loads	Moleca reduced the first peak KAM by 12% and 10.8% for the OAG and CG, second peak of KAM during terminal stance by 12% for the OAG and 15.7% for the CG compared to heels. Barefoot had similar results as the Moleca shoe. Heeled shoes increase first and second KAM peaks compared to barefoot. For OAG the Moleca resulted in a 12% decrease in the first peak of KAM during midstance when compared to the barefoot. Overall Moleca shoes showed a similar KAM to that of barefoot walking, while heeled shoes showed an increase
[79]	34	Flexible non heeled shoes (Moleca) vs modern heeled shoe vs barefoot in stair descent	Peak knee loads	The OA group had similar knee load during early, mid and late stance with the Moleca compared to the barefoot condition. Heeled shoes increase knee loads during early vs Moleca (15.5%) ($P < 0.001$) , in mid vs Moleca (9.5%) ($P = 0.010$) and late vs Moleca (9.2%) ($P < 0.001$).
[77]	56	Flexible non heeled shoes (Moleca) vs normal control	1°- WOMAC pain subscale. 2°- other subscales of WOMAC. 6 minute walk test, KAM, Paracetamol intake.	intervention group showed improvement in WOMAC subscales for pain, function, stiffness ($p=0.001$). Reduction of 21.8% in KAM for intervention group. Analgesia was also decreased

[81]	30	rocker soled vs non rocker soled shoes (including barefoot)	1°- peak external KAM. 2°- 11 point scale for knee pain whilst walking	Peak KAM was significantly reduced between rocker soled vs non rocker shoes. No difference in KAM impulses. Both KAM and KAM impulse was higher in both shoe conditions vs barefoot. No difference in knee pain between conditions.
[80]	17	Masai Barefoot Technology (MBT) vs Control shoes	Peak knee loads	knee flexion moment showed a significant reduction of 16.7% for MBT shoes compared to control $P<0.01$. No change in KAM
[82]	123	Masai Barefoot Technology (MBT) vs Control shoes	WOMAC, BMI, OA index, Active range of motion	MBT shoe showed increased static balance. No difference between groups in the reduction in pain, standing or walking ($P = 0.28$)
[84]	55	variable stiffness footwear vs constant stiffness footwear	1°- WOMAC total score and pain subscale. 2°- peak KAM	variable stiffness shoe reduced within day peak KAM (−5.5%, $p < 0.001$). WOMAC pain and total score was significantly reduced. Reduction in KAM was related to improvement in pain and function ($R2 = 0.11$, $p = 0.04$). Greater efficacy in KAM reduction in less severe OA group
[83]	164	Unloading shoes vs conventional walking shoes	6 month change in knee pain	KL=2 experiences greater pain reductions in conventional shoe compared to unloading. KL=3+ had greater pain reduction in unloading shoes, this maybe due to reduction in peak KAM. ($P = 0.02$)

Table 7: Studies that evaluated the effect of lateral wedge insoles versus footwear on pain and biomechanical outcomes on medial compartment knee osteoarthritis patients.

author	Sample size	Intervention	outcome measure	results
[73]	70	barefoot vs control shoe vs typical wedge and support wedge vs mobility shoe	EKAM, LAAI, external knee flexion moment, pain and comfort when walking	Compared to control shoe, typical and supported lateral wedge insoles (−5.9 and −5.6%, $p = 0.001$) and barefoot walking (−7.6% $p < 0.001$) reduced early stance external KAM . Similar improvements were seen for KAII, barefoot condition (−4.3%, $p = 0.023$), typical wedge (−7.95%, $p < 0.001$), supported wedge (−5.5%, $p < 0.001$) compared to control. Mobility shoe showed no effect ($p = 0.38$). Significant reduction in latter stance EKAM seen in lateral wedge compared to other conditions $p < 0.01$. Mobility shoe did show significant reduction in immediate knee pain and improves scores (<0.001), but did not change medial loading. Lateral wedge insoles shoes comparable reductions in medial knee loading