

Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial

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ABSTRACT

Objective To assess the effect of lateral wedge insoles compared with flat control insoles on improving symptoms and slowing structural disease progression in medial knee osteoarthritis.

Design Randomised controlled trial.

Setting Community in Melbourne, Australia.

Participants 200 people aged 50 or more with clinical and radiographic diagnosis of mild to moderately severe medial knee osteoarthritis.

Interventions Full length 5 degree lateral wedged insoles or flat control insoles worn inside the shoes daily for 12 months.

Main outcome measures Primary symptomatic outcome was change in overall knee pain (past week) measured on an 11 point numerical rating scale. Primary structural outcome was change in volume of medial tibial cartilage from magnetic resonance imaging scans. Secondary clinical outcomes included changes in measures of pain, function, stiffness, and health related quality of life. Secondary structural outcomes included progression of medial cartilage defects and bone marrow lesions.

Results Between group differences did not differ significantly for the primary outcomes of change in overall pain (−0.3 points, 95% confidence intervals −1.0 to 0.3) and change in medial tibial cartilage volume (−0.4 mm³, 95% confidence interval −15.4 to 14.6), and confidence intervals did not include minimal clinically important differences. None of the changes in secondary outcomes showed differences between groups.

Conclusion Lateral wedge insoles worn for 12 months provided no symptomatic or structural benefits compared with flat control insoles.

Trial registration Australian New Zealand Clinical Trials Registry ACTR12605000503628 and ClinicalTrials.gov NCT00415259.

INTRODUCTION

Knee osteoarthritis, which most commonly affects the medial compartment, is a chronic joint disorder that imposes a major healthcare burden.¹ As no cure exists, traditional management aims to reduce pain, improve function, and enhance quality of life while minimising

the adverse effects of therapy. Non-drug conservative interventions are considered the first line approach to osteoarthritis management.² However, given that a substantial proportion of patients with knee osteoarthritis experience progression of structural disease,³ contemporary management also aims to reduce structural deterioration. Research since early 2000 shows that increased medial knee joint loading is an important risk factor for disease progression of medial osteoarthritis.⁴ Thus non-surgical treatments that reduce medial load on the knee warrant investigation.

Lateral wedge shoe insoles are an inexpensive readily available treatment that has been shown to reduce medial knee load.^{5,6} Wedged insoles are recommended by 13 of 14 international guidelines for knee osteoarthritis²; however, the limited research available has failed to show any significant impact of lateral wedge insoles on the symptoms of osteoarthritis. The few randomised controlled trials that have been done are limited by factors such as small sample size, short intervention period, use of suboptimal lateral wedge design, or a heterogeneous cohort with osteoarthritis.^{7–10} Importantly, only one trial has evaluated the effects of lateral wedge insoles on joint structure.⁹ The non-significant finding in this study may be related to the use of radiology to measure structural change, which is less sensitive than magnetic resonance imaging,^{11,12} or to the use of heel wedges, which do not reduce medial load as much as full length wedges.¹³

We carried out a randomised controlled trial to assess the efficacy of lateral wedge insoles compared with control insoles worn daily for 12 months on improving symptoms and slowing structural disease progression in people with medial knee osteoarthritis.

METHODS

We recruited participants from the community through advertisements in local clubs and the print and radio media in metropolitan Melbourne, Australia, between May 2005 and July 2008. Inclusion criteria were age 50 years or more, average knee pain on walking more than 3 on an 11 point scale (0=no pain; 10=worst pain possible) at telephone screening, pain

located over the medial knee compartment, evidence of osteophytes in the medial compartment or medial joint space narrowing on an x ray film,¹⁴ and radiological knee alignment of 185 degrees or less (corresponding to a mechanical axis angle of ≤ 182 degrees and indicating neutral to varus (bow leg) knee alignment on an x ray film of the whole leg).¹⁵ All participants provided written informed consent.

Exclusion criteria were questionable or advanced radiographic knee osteoarthritis (Kellgren and Lawrence grades 1 and 4),¹⁶ predominant patellofemoral joint symptoms on clinical examination (location of pain, pain provoking activities, tenderness on palpation, and pain during mobilisation of the patellar),¹⁷ knee surgery or intra-articular corticosteroid injection within six months, current or past (within four weeks) use of oral corticosteroids, systemic arthritic conditions, history of knee arthroplasty or osteotomy, other musculoskeletal or neurological condition affecting leg function, disease of the ankle or foot precluding the use of insoles, use of foot orthotics within the past six months, usual footwear unable to accommodate insoles, contraindications to magnetic resonance imaging, planning to start other treatment for knee osteoarthritis, and regular use of a gait aid.

Procedures

We carried out a double blind randomised controlled trial over 12 months, the methodology of which has been described previously.¹⁸ Potential participants underwent telephone screening followed by standardised semiflexed standing posteroanterior knee radiology, to assess the severity of knee osteoarthritis and knee joint alignment. A physiotherapist or medical practitioner and a podiatrist then carried out a screening clinical examination. Participants were stratified by disease severity (Kellgren and Lawrence grades 2 and 3¹⁶) and sex and randomly allocated in permuted blocks of 6 to 12 to either the lateral wedge insole or the control insole group. An independent investigator used a computer program to generate the randomisation sequence a priori. Allocation was sealed in opaque and consecutively numbered envelopes held centrally. Envelopes were opened sequentially by an independent person. Participants were informed that two types of insoles were being compared but the insoles and study hypotheses were not described.

Interventions

Participants wore the insoles bilaterally in their own shoes every day. They were provided with two pairs of insoles, which were replaced every four months. The lateral wedge (5 degrees) insoles were made of high density ethyl vinyl acetate (similar to the midsole in a running shoe) and were wedged along the lateral border of the foot (Foot Function, New Zealand, see web extra). We chose a 5 degree wedge because greater wedging is less likely to be tolerated by the wearer⁶ and is difficult to accommodate within a normal shoe. The control insoles were made of easily compressible low

density ethyl vinyl acetate but with no wedging (Foot Function, New Zealand).

Outcome measures

A blinded examiner assessed the participants at baseline and 12 months. In participants with bilateral knee osteoarthritis the most symptomatic eligible knee was assessed. Baseline demographic information was collected and participants rated their expectation of a beneficial effect with insole treatment on an ordinal scale from 1 to 5 (0=no effect at all, 5=complete recovery), with higher scores indicating higher expectations.

Symptomatic measures

The primary symptomatic measure was overall average knee pain (past week) using an 11 point numerical rating scale (0=no pain, 10=worst pain possible).¹⁹ This has well accepted clinimetric properties and is widely used and recommended for clinical trials on knee osteoarthritis.¹⁹⁻²²

Secondary symptomatic measures included pain on walking (measured on the 11 point scale), pain, stiffness, and physical function subscales of the Western Ontario and McMaster Universities osteoarthritis index,²³ assessment of quality of life instrument,²⁴ and patient perceived global change in pain and in physical function (compared with baseline) measured on a 5 point ordinal scale and dichotomised into improvement (slightly better and much better) and no improvement (much worse, slightly worse, and no change). We also measured levels of physical activity using two methods: the physical activity scale for the elderly questionnaire, with higher scores indicating greater physical activity,²⁵ and the average number of steps taken per day, as measured by a pedometer (KH-005; Omron Healthcare, Japan), worn for one week on two occasions. Participants recorded use of and discomfort with insoles daily in a log book (returned on a monthly basis) and using an 11 point numerical rating scale at follow-up. Adverse events and cointerventions were recorded in the log book and by open probe questioning at follow-up.

Structural measures

The primary structural outcome measure was the volume of cartilage in the medial tibial compartment on magnetic resonance imaging. Images of the knee in the sagittal plane were obtained on a T1 weighted whole body unit as previously described.²⁶ We defined the volume of the medial tibial cartilage plate by manually drawing disarticulation contours around the cartilage boundary on each section. Data were resampled by bilinear and cubic interpolation (area of 312 and 312 μm and 1.5 mm thickness, continuous sections) for final three dimensional rendering. We determined the volume of medial tibial cartilage plate by summing the pertinent voxels within the resultant binary volume. Two trained blinded observers independently determined the measurements. The coefficient of variation for the cartilage volume measure was 3.4%.²⁷ To control medial tibial cartilage volume for bone size, we

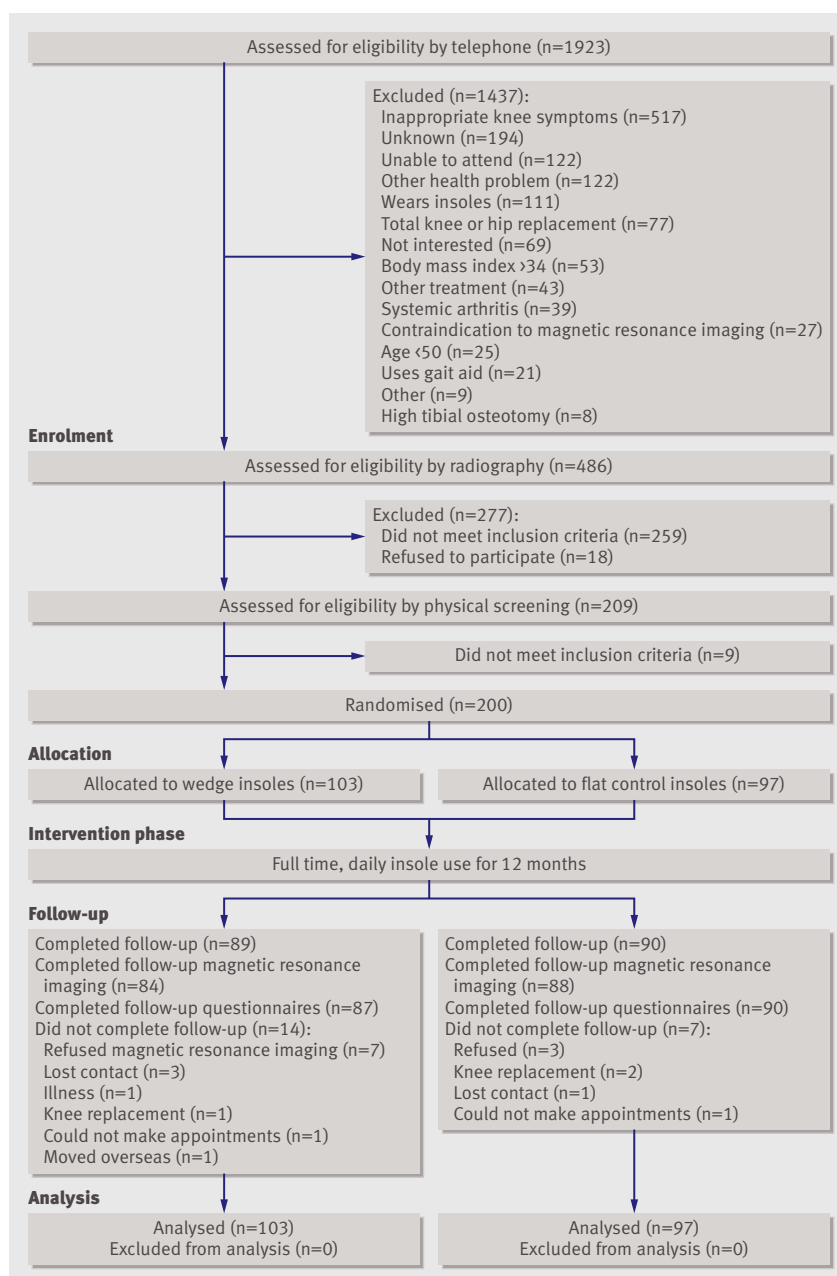


Fig 1 | Flow of participants through trial

determined the cross sectional area of the medial tibial plateau by creating an isotropic volume from the input image, which was reformatted in the axial plane, using the software program Osiris. The area was directly measured from this axial image as described previously.²⁸ By subtracting the follow-up volume from baseline volume and dividing by time between scans we determined the annual change in tibial cartilage volume. This was also expressed as a percentage of initial volume.

Secondary structural outcomes included cartilage defects, graded with a classification system on a 0 to 4 scale, as described previously^{29,30} for medial tibial and femoral compartments: grade 0, normal cartilage; grade 1, focal blistering and intracartilaginous low

signal intensity area with an intact surface and bottom; grade 2, irregularities on the surface or bottom and loss of thickness of less than 50%; grade 3, deep ulceration with loss of thickness of more than 50%; and grade 4, full thickness cartilage wear with exposure of subchondral bone. The measurement was carried out by one trained observer, who measured all images in duplicate on separate occasions. Progression of medial tibiofemoral cartilage defects was determined if the cartilage defect score increased by at least 1 from baseline to follow-up in the medial tibial or medial femoral compartment.

Bone marrow lesions were defined as areas of increased signal intensity adjacent to subcortical bone present in either the medial distal femur or the proximal tibia, and their size was graded on a 0 to 2 scale as described previously from coronal T2 fat saturated images³¹: grade 0, absence of a lesion; grade 1, lesion encompassed up to 25% of the width of the tibial or femoral cartilage being examined from coronal images; and grade 2, lesion encompassed more than 25% of the width of the tibial or femoral cartilage being examined from coronal images. We also recorded the number of slices the bone marrow lesions encompassed. To provide the medial tibiofemoral bone marrow lesion we multiplied the bone marrow lesion grade (0-2) by the number of slices for the medial femoral and medial tibial compartment separately, which was then summed. Progression of bone marrow lesions was defined if there was an increase in bone marrow lesion score of 1 or more over the period—that is, follow-up tibiofemoral bone marrow lesion score minus the baseline lesion score of 1 or more. This scoring system is a valid measure of bone marrow lesions as it has been shown to be sensitive to change and to detect clinically important outcomes.^{32,33}

Magnetic resonance imaging machines

We used two different magnetic resonance imaging machines; initially a Philips machine (Eindhoven, Netherlands) followed by a GE machine (Signa Advantage HiSpeed GE Medical Systems, Milwaukee, WI), owing to decommissioning of the Philips machine. In total, 117 (68%) participants were scanned on the same machine at baseline and follow-up (102 had both scans on the Philips machine and 15 had both scans on the GE machine), whereas 54 (32%) participants were scanned on the Philips machine at baseline and the GE machine at follow-up.

A validity study confirmed no systematic difference with change of machines. Fifteen participants underwent scans of one knee using both machines. The mean medial tibial cartilage volume as measured on the Philips and GE machines was 1706.3 (SD 361.2) mm³ and 1719.3 (SD 394.4) mm³, respectively (P>0.05). The intraclass correlation coefficient from a one way analysis of variance was 0.98 (95% confidence interval 0.95 to 0.99), showing excellent absolute agreement between measures. A Bland-Altman plot of the difference (Philips-GE machine) versus average measurements showed the mean to be -13 mm³, with

Table 1 | Baseline characteristics of participants, by treatment group. Values are numbers (percentages) unless stated otherwise

| Variable | Wedge insoles (n=103) | Control insoles (n=97) |
|--|-----------------------|------------------------|
| Mean (SD) age (years) | 63.3 (8.1) | 65.0 (7.9) |
| Women | 62 (60) | 56 (58) |
| Mean (SD) body mass index | 28.1 (4.2) | 30.4 (5.6) |
| Mean (SD) symptom duration (years) | 7.1 (7.9) | 7.5 (7.7) |
| Duration of symptoms (years): | | |
| <1 | 11 (11) | 5 (5) |
| 1 to <5 | 42 (41) | 40 (41) |
| 5 to <10 | 21 (21) | 23 (24) |
| ≥10 | 28 (28) | 29 (30) |
| Unilateral symptoms | 33 (32) | 37 (38) |
| Radiographic disease severity: | | |
| Grade 2 | 49 (48) | 46 (47) |
| Grade 3 | 54 (52) | 51 (53) |
| Location of osteophytes: | | |
| Medial compartment | 103 (100) | 93 (96) |
| Lateral compartment | 23 (22) | 21 (22) |
| Location of joint space narrowing: | | |
| Medial compartment | 99 (96) | 96 (99) |
| Lateral compartment | 80 (78) | 77 (79) |
| Mean (SD) anatomical alignment (degrees) | 181 (3) | 181 (3) |
| Current drug use: | | |
| Analgesia | 9 (9) | 13 (13) |
| Non-steroidal anti-inflammatory drugs | 15 (15) | 26 (27) |
| Cyclo-oxygenase-2 inhibitors | 2 (2) | 4 (4) |
| Glucosamine products | 34 (33) | 30 (31) |
| Past treatments: | | |
| Arthroscopy | 45 (44) | 43 (44) |
| Physiotherapy | 16 (16) | 11 (11) |
| Exercise | 3 (3) | 2 (2) |
| Cortisone injection | 3 (3) | 3 (3) |

Not all numbers add up to totals owing to missing data.

95% limits of agreement of -152 to 126 mm³. The standard error of measurement was calculated as 49.3 mm³. To compare between machine repeatability with within machine repeatability, 12 of these 15 participants underwent a second measurement on the Philips machine, yielding a standard error of measurement of 33.3 mm³, with 95% limits of agreement of -75.6 to 106.5 mm³. These limits indicate comparable but slightly less reproducibility between machines than within machines.

Sample size

Overall, 126 participants were required to detect a minimal clinically important difference of 1.5 for change in pain between groups,³⁴ assuming a standard deviation of 3 (based on previous data^{35,36}), with 80% power at a 5% significance level. We have shown that the mean rate of tibial cartilage loss is 5.3% (SD 5.2%) per year in knee osteoarthritis.²⁷ Data suggest that a clinically beneficial outcome with lateral wedge insoles would be to reduce the rate of cartilage loss to less than 3% per annum, as this is associated with a reduced risk for arthroplasty within four years.³⁷ Thus we required a minimum of 160 participants to detect a difference of

2.3% between groups, with 80% power at a 5% significance level. We increased the sample size to 200 to account for dropouts and to allow for at least 80% power for both the primary outcomes.

Statistical analysis

A blinded statistician carried out the analysis, which was by intention to treat. All analyses were done using Stata (Version 11), and we considered P values of less than 0.05 to be significant. For continuous outcome measures we used linear regression modelling adjusted for baseline values of the outcome to compare differences in mean change (baseline minus follow-up) between groups. Results are presented as estimated differences with 95% confidence intervals. The analysis of change in medial cartilage volume was repeated with further adjustment for age, sex, body mass index, medial tibial bone size, and magnetic resonance imaging machine. We summarised the total medial bone marrow lesion scores as the median change from baseline (interquartile range) and compared scores between groups using the difference in median change. Using log binomial regression we compared global change in pain and in physical function and progression of cartilage defects between groups. Results are presented as relative risks with 95% confidence intervals. We used bootstrap confidence intervals based on 5000 replications to compare changes in the size of bone marrow lesions.

To account for missing data (31/400 pain measures and 29/400 medial tibial cartilage volume measures, 7% of total baseline and follow-up dataset for each measure) we carried out a sensitivity analysis using single mean imputation of missing baseline measures³⁸ and multiple imputation of missing follow-up measures, assuming data are missing at random and follow a multivariate³⁹ normal distribution. As results were unchanged we present complete case analyses.

We undertook a second sensitivity analysis to estimate the between group difference that would occur if all participants adhered completely to their allocated treatment. For these analyses adherence was measured by the number of days the insoles were worn as reported in the log books. A *t* test was used to compare adherence between the groups. For each of the two primary outcomes we used a two stage least squares instrumental variables approach.⁴⁰ This involved a regression model of the outcome measure adjusted for the baseline value and adherence, and a second regression model of adherence was adjusted for randomised group. The two regression models were fitted simultaneously and we estimated the effect of the lateral wedged insoles under full adherence.

RESULTS

Of the 1923 volunteers, 1437 (74.7%) were ineligible or did not wish to participate (fig 1). In total 200 participants (103 lateral wedge insoles, 97 control insoles) were randomised and 179 (89 lateral wedge insoles, 90 control insoles; 90%) completed the trial. Baseline descriptive characteristics of participants indicated no

Table 2 | Difference in symptomatic and structural changes within and between insole groups from baseline to 12 months' follow-up in participants with medial knee osteoarthritis

| Outcome | Mean (SD) week 0 | | Mean (SD) week 52 | | Mean (SD) difference within groups (week 0–week 52) | | Mean (95% CI) difference between groups (week 0–week 52)* |
|---|-----------------------|------------------------|----------------------|------------------------|---|-----------------|---|
| | Wedge insoles (n=103) | Control insoles (n=97) | Wedge insoles (n=89) | Control insoles (n=90) | Wedge insoles | Control insoles | Wedge insoles – control insoles |
| Secondary measures | | | | | | | |
| Primary outcomes | | | | | | | |
| Average pain† (0-10) | 4.0 (2.1) | 4.3 (1.9) | 3.1 (2.1) | 3.1 (2.3) | 0.9 (2.1) | 1.3 (2.4) | -0.3 (-1.0 to 0.3) |
| Medial tibial cartilage volume (mm ³) | 1550 (452) | 1520 (439) | 1513 (480) | 1483 (432) | 43 (45) | 43 (53) | -0.4 (-15.4 to 14.6) |
| Pain on walking† (0-10) | 4.2 (2.2) | 4.3 (1.9) | 3.2 (2.1) | 3.0 (2.5) | 0.9 (2.2) | 1.4 (2.6) | -0.3 (-1.0 to 0.4) |
| WOMAC‡: | | | | | | | |
| Pain (0-20) | 7.1 (3.0) | 7.2 (2.9) | 6.4 (3.3) | 6.2 (3.2) | 0.7 (2.7) | 1.2 (3.1) | -0.4 (-1.2 to 0.4) |
| Function (0-68) | 23.7 (12.2) | 23.6 (10.9) | 20.8 (12.2) | 20.1 (11.6) | 3.1 (9.0) | 4.0 (11.2) | -0.7 (-3.6 to 2.2) |
| Stiffness (0-8) | 4 (2) | 4 (1) | 3 (2) | 3 (2) | 0.4 (1.4) | 0.6 (1.7) | -0.3 (-0.7 to 0.2) |
| Health related quality of life (-0.04-1.00)§ | 0.7 (0.2) | 0.7 (0.2) | 0.7 (0.2) | 0.7 (0.2) | -0.02 (0.11) | -0.01 (0.13) | -0.01 (-0.05 to 0.02) |
| Physical activity scale for elderly (0-400) | 182 (81) | 162 (68) | 167 (83) | 167 (88) | 16 (77) | 1 (83) | 7.8 (-15.4 to 30.9) |
| No of daily steps | 7908 (3712) | 7562 (3593) | 8059 (4946) | 6688 (4106) | -14 (3189) | 673 (3217) | -797.9 (-1966 to 370.2) |

WOMAC=Western Ontario and McMaster Universities osteoarthritis index.

Differences within and between groups concern only participants with baseline and follow-up data.

*Adjusted for baseline value of variable.

†Assessed using numerical rating scale, with higher scores indicating worse pain.

‡Higher scores indicating worse pain, function, and stiffness.

§Assessed using assessment of quality of life instrument, with higher scores indicating better quality of life.

differences between groups (table 1). Characteristics of the 21 participants lost to follow-up were similar to those completing the study (data not shown). The participants' expectation of treatment outcomes was similar between groups ($P=0.51$), with 54% ($n=97$) of 180 participants who provided these data expecting moderate improvement, 25% ($n=45$) expecting large improvement, and 2% ($n=4$) expecting complete recovery.

Outcome measures

The between group difference for the primary outcome of change in overall average pain did not differ significantly (-0.3 points, 95% confidence interval, -1.0 to 0.3), table 2). Both groups showed small mean reductions in pain over time, but these reductions were smaller than the minimal clinically important difference.³⁴ The between group difference for the primary outcome of change in medial tibial cartilage volume over 12 months did not differ significantly when expressed in absolute terms (-0.4 mm³, 95% confidence interval -15.4 to 14.6 , table 2) or when expressed as the percentage change. Lateral wedge insoles were associated with a mean reduction of 3.0% (SD 3.1%) in cartilage volume compared with 2.8% (3.5%) for control insoles (mean difference 0.2%, 95% confidence interval -0.8% to 1.2%). Further adjustment for covariates (sex, age, body mass index, bone size, and magnetic resonance imaging machine) resulted in an estimate of between group difference in change in medial tibial cartilage volume of -0.7 mm³ (95% confidence interval -16.7 to 15.4).

The primary results did not change under a hypothetical scenario of complete adherence to treatment (allocated insoles worn daily for a year by every patient). In this scenario, the between group difference in mean change in average pain was estimated as -1.6 points (95% confidence interval -5.6 to 2.5 , $P=0.444$), and for change in medial tibial cartilage volume was estimated as -25.5 mg³ (95% confidence interval -130.6 to 80.0 , $P=0.634$).

Lateral wedge insoles had similar effects to control insoles across all secondary outcome measures (tables 2 and 3). Although most participants reported improved pain and function after treatment there was no difference between groups for global change scores (table 3). Changes in secondary structural outcomes were also similar between groups (table 3). A relatively small number of participants showed progression of medial tibial or femoral cartilage defects over 12 months. Changes in the size of bone marrow lesions were also similar between groups, with the median change being 0 (interquartile range -2 -3) for the lateral wedge insole group and 0 (-2 -2) for the control insole group, with an estimated difference in median changes of 0 (95% bootstrap confidence interval -0.31 to 0.31).

Adherence, insole comfort, adverse events, and cointerventions

Log book completion rates were 69% for the lateral wedge insole group and 73% for the control insole group. The mean duration of daily insole use was significantly lower in the lateral wedge insole group than in the control insole group (6.8 (SD 4.3) hours per day *v*

Table 3 | Participants reporting global improvement in symptoms and showing progression of medial tibial and femoral cartilage defects according to insole group. Values are numbers (percentages) unless stated otherwise

| Outcome | Wedge insoles (n=82) | Control insoles (n=85) | Relative risk (95 CI) |
|---|----------------------|------------------------|-----------------------|
| Global improvement in pain* | 57 (70) | 55 (64) | 1.09 (0.88 to 1.35) |
| Global improvement in function* | 46 (56) | 53 (62) | 0.91 (0.71 to 1.17) |
| Progression of medial tibial cartilage defects | 13 (16) | 18 (21) | 0.75 (0.39 to 1.43) |
| Progression of medial femoral cartilage defects | 16 (20) | 18 (21) | 0.92 (0.51 to 1.68) |

*Participants rating themselves as much better or slightly better.

9.1 (3.8) hours per day, $P < 0.01$) and was relatively consistent over the study (fig 2). Self reported adherence with insole use was also lower in the lateral wedge insole group, reflecting log book data (table 4).

More participants reported problems with the lateral wedge insoles (42/89, 47%) than with the control insoles (21/90, 23%, table 4). Lateral wedge insoles were more likely to be associated with back and foot pain and to be difficult to fit into shoes than the control insoles. Lateral wedge insoles were also rated as less comfortable. Around half of the participants stated that the lateral wedge insole was associated with some degree of discomfort compared with 30% of participants in the control group. Severe or very severe discomfort was rated by 7 (10%) in the lateral wedge insole group compared with 1 (1%) in the control insole group.

Use of analgesic, non-steroidal anti-inflammatory drugs and glucosamine preparations was similar between groups (table 4). Cointerventions were reported by 17/89 (19%) participants in the lateral wedge insole group and 14/90 (16%) participants in the control insole group (table 4), with a similar number and type of cointerventions across groups.

DISCUSSION

Our randomised controlled trial showed that lateral wedge insoles compared with flat control insoles worn for 12 months provided no additional benefit in alleviating symptoms or slowing disease progression in older adults (≥ 50 years) with mild to moderately severe medial knee osteoarthritis. Our results do not support the recommendations of clinical guidelines advocating the use of lateral wedge insoles for the management of medial knee osteoarthritis.²

Explanation of results

Most of our participants had varus knee alignment, a factor known to increase the risk of structural disease progression⁴¹ and thus rendering our cohort an osteoarthritis subgroup ideally suited to disease modifying interventions. Our lateral wedge insoles had no significant effect on structural change over time. Similar annual loss of medial tibial cartilage volume was observed in both treatment groups (2.8-3.0%) and this is within the range of annual cartilage loss in knee osteoarthritis reported by longitudinal studies.⁴² Our non-significant findings occurred even though we used lateral wedge insoles known to reduce medial

knee load during walking.⁵ Specifically, we have previously reported a significant reduction of 5.4% (SD 5.2%) in the knee adduction moment during walking (a measure of medial knee joint compartment load) with these particular lateral wedge insoles.⁵ Given the established relation between knee load and risk of structural deterioration over time,⁴ it is unclear why our lateral wedge insoles did not reduce the rate of cartilage loss. It is possible our 12 month intervention period was not long enough to detect a disease modifying effect.

It is also possible that our use of the participant's own non-standardised shoes was a factor. Different shoe types can influence the biomechanical and clinical effectiveness of insoles, and in particular shoes with heels can attenuate their effects.⁴³ Participants were encouraged to wear the insoles in their usual shoes; however, we were unable to assess adherence to this recommendation. This was because of the difficulty in classifying the myriad shoe types in existence and the burden such daily recording would have imposed on participants, with its subsequent impact on adherence and retention in the study.

The amount and type of physical activity could potentially mediate the effect of the insoles, given that physical activity levels will influence cumulative load at the knee. However, given that physical activity levels as measured from either questionnaire or a pedometer did not differ between the groups during the study, this is unlikely to have influenced our results.

We included participants with painful mild to moderate radiographic osteoarthritis of the medial knee compartment and a neutral to varus knee alignment. The participants may have had a heterogeneous response to lateral wedge insoles depending on factors such as radiographic severity of osteoarthritis thereby masking our ability to find a significant treatment effect. Indeed although case series have suggested greater pain relief with wedge insoles in participants with milder radiographic severity,^{5,44} detection of a structural effect in this group may not have been possible in our relatively short follow-up time frame of one year. Conversely, those with moderate disease who show greater rates of structural deterioration⁴⁵ may

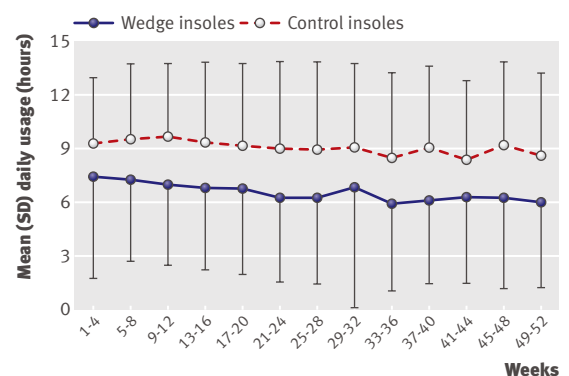


Fig 2 | Mean (standard deviation) daily hours of insole use over 52 weeks

Table 4 | Adverse events, comfort from and compliance with insole use, drug use, and cointerventions according to insole group. Values are numbers (percentages) unless stated otherwise

| Measures | Wedge insoles (n=89) | Control insoles (n=90) |
|--|----------------------|------------------------|
| Self reported problems with insoles: | 42 (47) | 21 (23) |
| Back pain | 9 (10) | 1 (1) |
| Foot pain | 32 (36) | 14 (16) |
| Uncomfortable or difficulty fitting in shoes | 15 (16) | 4 (4) |
| Increased knee pain | 2 (2) | 5 (6) |
| Felt unstable | 0 (0) | 1 (1) |
| Mean (SD) insole comfort rating (0-10)* | 3.7 (3.3) | 2.0 (2.3) |
| Discomfort rating: | (n=76) | (n=87) |
| None | 40 (53) | 64 (74) |
| Mild | 23 (30) | 20 (23) |
| Moderate | 6 (8) | 2 (2) |
| Severe | 5 (7) | 1 (1) |
| Very severe | 2 (3) | 0 (0) |
| Mean (SD) self adherence rating (0-10)† | 6.7 (3.6) | 8.5 (2.4) |
| Drug use | 47 (53) | 47 (52) |
| Drug types: | | |
| Analgesics | 27 (30) | 29 (32) |
| Non-steroidal anti-inflammatory drugs | 18 (20) | 22 (24) |
| Cyclo-oxygenase-2 inhibitors | 5 (6) | 1 (1) |
| Glucosamine | 7 (8) | 7 (8) |
| Unspecified | 6 (7) | 1 (1) |
| Cointerventions | 17 (19) | 14 (16) |
| Cointervention type: | | |
| Physiotherapy | 9 (10) | 7 (8) |
| Exercise | 3 (3) | 0 (0) |
| Cortisone injection | 2 (2) | 1 (1) |
| Chiropractic | 2 (2) | 2 (2) |
| Acupuncture | 2 (2) | 0 (0) |
| Osteopathy | 2 (2) | 0 (0) |
| Hydrotherapy | 1 (1) | 0 (0) |
| Podiatry | 1 (1) | 0 (0) |
| Arthroscopic surgery | 0 (0) | 3 (3) |
| Total knee replacement | 0 (0) | 1 (1) |
| Other | 2 (2) | 2 (2) |

*Based on 11 point numerical rating scale: 0=extremely comfortable and 10=extremely uncomfortable.

†Based on 11 point numerical rating scale: 0=not worn at all and 10=worn as instructed.

not respond to the use of a minor biomechanical intervention such as lateral wedge insoles. However, when we examined our subgroups with mild osteoarthritis (Kellgren and Lawrence grade 2) compared with moderate osteoarthritis (Kellgren and Lawrence grade 3) the direction of treatment effect did not differ, suggesting that the lateral wedge insoles were not having a beneficial effect in either group (data not shown).

Given that lateral wedge insoles reduce knee load, it is often assumed that this will translate to pain relief. Our finding that pain remained unchanged does not support this commonly held belief. Although some studies have shown a positive relation between severity of pain and knee load,⁴⁴⁶⁴⁷ others have found no such relation⁴⁸⁴⁹ or even an inverse one.⁵⁰⁵¹ The multiple mechanisms contributing to the experience of pain with knee osteoarthritis possibly explain our findings

and those of others. For example, pain is influenced by a myriad of psychosocial factors that can vary between people as well as within people over time.⁵² Hence it is not surprising that favourable biomechanical changes do not guarantee pain reduction.

The optimal dosage of insole use needed for beneficial effects on pain and joint structure is not known. It has been reported that 5-10 hours of daily use produces better symptomatic outcomes than less than five hours or more than 10 hours of use.⁵³ Although in our study the mean daily usage of 6.8 (SD 4.3) hours per day reported in the lateral wedge insole group was less than the 9.1 (SD 3.8) hours per day for the control insole group, it still fell within the range of usage recommended by a previous study.⁵³ Furthermore, analysis using a hypothetical scenario with complete adherence to the insoles also showed no significant group differences for symptomatic or structural outcomes, suggesting that adherence was not a factor explaining our results.

Finally, we cannot exclude the possibility that our non-significant results for symptoms could reflect a type II error. Pain was only measured at baseline and at 12 months of follow-up. Knowing that pain fluctuates in patients with osteoarthritis, we may have been able to detect a significant insole effect had we included more measurement time points throughout the 12 months to better estimate the average pain over the duration of the trial.

Comparison with previous studies

Our findings are in agreement with the limited number of other randomised controlled trials that have also failed to show the efficacy of lateral wedge insoles.⁷⁻¹⁰ One study found that customised lateral heel wedge insoles worn for two years were associated with a reduced intake of non-steroidal anti-inflammatory drugs, a secondary outcome, but did not alter pain, stiffness, function, or joint space narrowing on radiography.⁹¹⁰ A crossover trial found no statistical or clinical effect of a lateral wedge insole worn for six weeks.⁸ Similarly, in the most recent study, a customised lateral wedge insole worn in standardised walking shoes had no greater effect on pain over 12 months than a neutral insole.⁷ Using the largest cohort of participants to date, our results concur with these clinical trials and extend their findings by providing novel data relating to the effects of lateral wedge insoles on structural features seen on magnetic resonance imaging.

Strengths and weaknesses of the study

A strength of our randomised controlled trial was its pragmatic nature whereby the intervention was executed in a manner consistent with current clinical practice. Participants were provided with standardised off the shelf wedge insoles and permitted to wear them in their own shoes. Other strengths of our study include the rigorous study design, incorporating blinding of both assessor and participant, adequate statistical power, excellent participant retention, and recruitment of an osteoarthritis subgroup most likely to

WHAT IS ALREADY KNOWN ON THIS TOPIC

Lateral wedge insoles are an inexpensive, easily available conservative treatment for medial knee osteoarthritis

Lateral wedge insoles reduce medial knee load, a risk factor for disease progression, but their effect on knee joint structure is unclear

13 of 14 clinical guidelines currently recommend lateral wedge insoles for symptomatic benefit of knee osteoarthritis

WHAT THIS STUDY ADDS

Lateral wedge insoles used daily for 12 months provided no additional benefit over flat control insoles in alleviating symptoms of medial knee osteoarthritis

The results do not support current clinical guidelines for knee osteoarthritis

Changes in joint structure did not differ between the groups, suggesting a lack of evidence for a disease modifying effect of lateral wedge compared with control insoles

benefit from a lateral wedge insole. Importantly, we tested a lateral wedge insole that had proved effectiveness in reducing knee load and incorporated a sensitive outcome measure (magnetic resonance imaging) to assess change in specific joint structural features. A limitation was the need to use a different magnetic resonance imaging machine for follow-up assessment in about 30% of the participants, which may have increased the error within the measurements. However, our repeatability study showed that differences in measurements between the two machines were essentially comparable to those expected with repeated measurements taken from the same machine. Furthermore, we also recalculated all of the primary and secondary endpoint analyses assessing whether the estimated intervention effect differed for participants who were scanned with one machine compared with those scanned with both machines, but we found no evidence of such differences (all interaction P values >0.15). Our participants were volunteers recruited from the community, which is a common method of recruitment for trials of non-drug conservative interventions in knee osteoarthritis. It is possible that our sample does not reflect fully the patients who seek treatment from general medical practitioners. These patients are likely to exhibit more severe disease and thus could respond differently to treatment with lateral wedge insoles. They may also differ in terms of psychosocial factors that are known to influence symptoms and could affect outcomes from treatment. Our results can only be generalised to other lateral wedge insoles with similar design features. Given that some evidence exists for subtalar strapping enhancing the effectiveness of lateral wedge insoles,^{54,55} this type of insole warrants further investigation.

Conclusions and practice implications

In summary, our findings showed that lateral wedge insoles had no effect on symptoms or disease progression over 12 months in people with mild to moderate medial knee osteoarthritis. These findings have implications for clinical practice. Given that most clinical guidelines currently recommend lateral wedge insoles

for improving pain and function, our results and those of other randomised controlled trials suggest that such insoles are not beneficial for the treatment of symptoms. However, given the clear biomechanical benefits of wedge insoles in reducing medial knee load, further research is needed over a longer time frame to conclusively determine the effects of lateral wedge insoles on joint structure.

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Contributors: KLB and RSH conceived and designed the trial protocol. KLB, RSH, FC, AH, and CP procured the project funding. CP was responsible for the podiatric screening assessment and insole design, acquisition, and fitting. KLB and RSH contributed to clinical screening of participants and graded the x ray films. MD-T and FH analysed the magnetic resonance imaging scans overseen by FC. AF and EW did the statistical analyses. K-AB recruited the participants, measured knee alignment, and carried out the outcome assessments. KLB and RSH drafted the manuscript, and K-AB, AF, EW, CP, FC, FH, AH, and MD-T contributed to the manuscript. All authors read and approved the final manuscript. KLB and RSH accept full responsibility for this work and act as guarantors for the study.

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Data sharing: The statistical code and dataset are available from the corresponding author at k.bennell@unimelb.edu.au.

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