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Braces and orthoses for treating osteoarthritis of the knee (Review)

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[Intervention Review]

Braces and orthoses for treating osteoarthritis of the knee

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ABSTRACT

Background

Individuals with osteoarthritis (OA) of the knee can be treated with a knee brace or a foot/ankle orthosis. The main purpose of these aids is to reduce pain, improve physical function and, possibly, slow disease progression. This is the second update of the original review published in Issue 1, 2005, and first updated in 2007.

Objectives

To assess the benefits and harms of braces and foot/ankle orthoses in the treatment of patients with OA of the knee.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE (current contents, HealthSTAR) up to March 2014. We screened reference lists of identified trials and clinical trial registers for ongoing studies.

Selection criteria

Randomised and controlled clinical trials investigating all types of braces and foot/ankle orthoses for OA of the knee compared with an active control or no treatment.

Data collection and analysis

Two review authors independently selected trials and extracted data. We assessed risk of bias using the 'Risk of bias' tool of The Cochrane Collaboration. We analysed the quality of the results by performing an overall grading of evidence by outcome using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach. As a result of heterogeneity of studies, pooling of outcome data was possible for only three insole studies.

Main results

We included 13 studies (n = 1356): four studies in the first version, three studies in the first update and six additional studies (n = 529 participants) in the second update. We included studies that reported results when study participants with early to severe knee OA (Kellgren & Lawrence grade I-IV) were treated with a knee brace (valgus knee brace, neutral brace or neoprene sleeve) or an orthosis (laterally or medially wedged insole, neutral insole, variable or constant stiffness shoe) or were given no treatment. The main comparisons included (1) brace versus no treatment; (2) foot/ankle orthosis versus no treatment or other treatment; and (3) brace versus foot/ankle orthosis. Seven studies had low risk, two studies had high risk and four studies had unclear risk of selection bias. Five studies had low risk, three studies had high risk and five studies had unclear risk of detection bias. Ten studies had high risk and three studies had low risk of performance bias. Nine studies had low risk and four studies had high risk of reporting bias.

Four studies compared brace versus no treatment, but only one provided useful data for meta-analysis at 12-month follow-up. One study (n = 117, low-quality evidence) showed lack of evidence of an effect on visual analogue scale (VAS) pain scores (absolute percent change 0%, mean difference (MD) 0.0, 95% confidence interval (CI) -0.84 to 0.84), function scores (absolute percent change 1%, MD 1.0, 95% CI -2.98 to 4.98) and health-related quality of life scores (absolute percent change 4%, MD -0.04, 95% CI -0.12 to 0.04) after 12 months. Many participants stopped their initial treatment because of lack of effect (24 of 60 participants in the brace group and 14 of 57 participants in the no treatment group; absolute percent change 15%, risk ratio (RR) 1.63, 95% CI 0.94 to 2.82). The other studies reported some improvement in pain, function and health-related quality of life (P value ≤ 0.001). Stiffness and treatment failure (need for surgery) were not reported in the included studies.

For the comparison of laterally wedged insole versus no insole, one study (n = 40, low-quality evidence) showed a lower VAS pain score in the laterally wedged insole group (absolute percent change 16%, MD -1.60, 95% CI -2.31 to -0.89) after nine months. Function, stiffness, health-related quality of life, treatment failure and adverse events were not reported in the included study.

For the comparison of laterally wedged versus neutral insole after pooling of three studies (n = 358, moderate-quality evidence), little evidence was found of an effect on numerical rating scale (NRS) pain scores (absolute percent change 1.0%, MD 0.1, 95% CI -0.45 to 0.65), Western Ontario-McMaster Osteoarthritis Scale (WOMAC) stiffness scores (absolute percent change 0.1%, MD 0.07, 95% CI -4.96 to 5.1) and WOMAC function scores (absolute percent change 0.9%, MD 0.94, 95% CI - 2.98 to 4.87) after 12 months. Evidence of an effect on health-related quality of life scores (absolute percent change 1.0%, MD 0.01, 95% CI -0.05 to 0.03) was lacking in one study (n = 179, moderate-quality evidence). Treatment failure and adverse events were not studied for this comparison in the included studies.

Data for the comparison of laterally wedged insole versus valgus knee brace could not be pooled. After six months' follow-up, no statistically significant difference was noted in VAS pain scores (absolute percent change -2.0%, MD -0.2, 95% CI -1.15 to 0.75) and WOMAC function scores (absolute percent change 0.1%, MD 0.1, 95% CI -7.26 to 0.75) in one study (n = 91, low-quality evidence); however both groups showed improvement. Stiffness, health-related quality of life, treatment failure and adverse events were not reported in the included studies for this comparison.

Authors' conclusions

Evidence was inconclusive for the benefits of bracing for pain, stiffness, function and quality of life in the treatment of patients with medial compartment knee OA. On the basis of one laterally wedged insole versus no treatment study, we conclude that evidence of an effect on pain in patients with varus knee OA is lacking. Moderate-quality evidence shows lack of an effect on improvement in pain, stiffness and function between patients treated with a laterally wedged insole and those treated with a neutral insole. Low-quality evidence shows lack of an effect on improvement in pain, stiffness and function between patients treated with a valgus knee brace and those treated with a laterally wedged insole. The optimal choice for an orthosis remains unclear, and long-term implications are lacking.

PLAIN LANGUAGE SUMMARY

Braces and orthoses for osteoarthritis of the knee

Research question

This summary of a Cochrane review presents what we know from research about the effects of braces and foot/ankle orthoses in the treatment of patients with osteoarthritis of the knee. We searched for evidence up to March 2014. We found 13 studies (n = 1356) and included in this update six additional studies (n = 529 participants).

Study characteristics

We included studies reporting results in patients with early to severe knee OA (Kellgren & Lawrence grade I-IV) treated with a knee brace (valgus knee brace, neutral brace, neoprene sleeve) or an orthosis (laterally or medially wedged insole, neutral insole, variable or constant stiffness shoe) or given no treatment.

Background: What is osteoarthritis and what are braces and orthoses?

Osteoarthritis is the most common form of arthritis that can affect the hands, hips, shoulders and knees. In osteoarthritis, the cartilage that protects the ends of bones breaks down, causing pain and swelling. Osteoarthritis can occur in different areas of the knee or can affect the whole knee. Depending on the area, osteoarthritis can change the alignment of joints.

Braces and orthoses are devices that you wear to support your knee joint. Orthoses are insoles that fit comfortably inside your shoes. Braces are made of combinations of metal, foam, plastic, elastic material and straps. A knee brace can be fitted specially for the person wearing it.

Key results

This review shows the following in people with osteoarthritis of the knee.

Wearing a knee brace compared with no brace:

• may result in little or no difference in reducing pain and improving knee function and quality of life after 12 months (low-quality evidence); and
• causes many patients to stop their initial treatment because of lack of effect in both groups.

Stiffness and treatment failure (need for surgery) were not reported.

Wearing a laterally wedged insole compared with no insole:

• may result in little or no difference in reducing pain (low-quality evidence).

Function, stiffness, health-related quality of life, treatment failure and side effects were not reported.

Wearing a laterally wedged insole compared with wearing a neutral insole:

• probably results in little or no difference in reducing pain and improving function, stiffness and quality of life after 12 months (moderate-quality evidence).

Treatment failure and side effects were not reported.

Wearing a laterally wedged insole compared with a valgus knee brace:

• may result in little or no difference in reducing pain and improving function after sx months (low-quality evidence).

Stiffness, health-related quality of life, treatment failure and side effects were not reported

We often do not have precise information about side effects and complications. Side effects may include pain in the back of the knee, low back pain, foot sole pain or skin irritation.

Quality of the evidence

• Low-quality evidence suggests that people with OA who use a knee brace may have little or no reduction in pain, improved knee function and improved quality of life.

• Moderate-quality evidence suggests that people with OA of the knee who wear laterally wedged insoles or neutral insoles probably have little or no improvement in pain, function and stiffness.

Summary of findings for the main comparison. Braces and orthoses for varus medial osteoarthritis of the knee

Valgus knee braces and orthoses for varus medial osteoarthritis of the knee

Patient or population: patients with varus medial osteoarthritis of the knee

Settings: general hospital

Intervention: valgus knee brace or lateral wedge insole

Comparison: no brace or neutral insole

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Intervention				
Valgus knee brace compared with no brace						
Pain on walking (VAS) Scale from 0 to 10 Follow-up: 12 months *(Higher score is worse)*	Mean pain score in control groups was **5.2**	Mean pain in intervention groups was **equal** (0.84 lower to 0.84 higher)		115 (1 study)	⊕⊕⊝⊝ **Low** [a,b]	MD = 0.00 (95% CI -0.84 to 0.84) Absolute percent change = 0% (95% CI -8.4 to 8.4) Relative percent change = 0% (95% CI -1.6 to 1.6) NNTB = not statistically significant
Knee function (HSS) Scale from 0 to 100 Follow-up: 12 months *(Higher score is better)*	Mean function score in control groups was **69**	Mean function in intervention groups was **1.00 higher** (2.98 lower to 4.98 higher)		110 (1 study)	⊕⊕⊝⊝ **Low** [a,b]	MD = 1.00 (95% CI -2.98 to 4.98) Absolute percent change = 1.0% (95% CI 3.0 to 5.0) Relative percent change = 0.01% (95% CI 0.05 to 0.07) NNTB = not statistically significant

Quality of life (EQ-5D) Scale from 0 to 100 Follow-up: 12 months *(Higher score is better)*	Mean health-related quality of life score in control groups was **0.6**	Mean health-related quality of life score in intervention groups was **0.04 lower** (0.12 lower to 0.04 higher)		117 (1 study)	⊕⊕⊖⊖ **Low** [a,b]	MD = 0.04 (95% CI -0.12 to 0.04) Absolute percent change = 0.04% (95% CI -0.12 to 0.04) Relative percent change = 0.07% (95% CI -0.2 to 0.07) NNTB = not statistically significant
Total number of adverse events (withdrawals due to lack of effect) [c] Follow-up: 12 months	**Low-risk population**		**RR 1.63** (0.94 to 2.82)	117 (1 study)	⊕⊕⊖⊖ **Low** [a,b]	Absolute percent change = 15% (95% CI -1% to 32%) Relative percent change = 63% (95% CI -6% to 182%) NNTB = not statistically significant
	246 per 1000	**400 per 1000** (239 to 694)				
Lateral-wedge insole compared with neutral insole						
Pain on walking (NRS) Scale from 0 to 10 Follow-up: mean 12 months *(Higher score is worse)*	Mean pain on walking score in control groups was **2.6**	Mean pain on walking in intervention groups was **0.1 higher** (0.45 higher to 0.65 lower)		224 (2 studies)	⊕⊕⊕⊖ **Moderate** [a]	MD = 0.10 (95% CI -0.45 to 0.65) Absolute percent change = 1.0% (95% CI 4.5 to -6.5) Relative percent change = 3.8% (95% CI 1.7 to -25.0) NNTB = not statistically significant
Physical function (WOMAC) - 12 months Scale from 0 to 100 Follow-up: mean 12 months *(Higher score is better)*	Mean function score in control groups was **36.6**	Mean function in intervention groups was **0.94 higher** (2.98 lower to 4.87 higher)		358 (3 studies)	⊕⊕⊕⊖ **Moderate** [a]	MD = 0.94 (95% CI -2.98 to 4.87) Absolute percent change = 0.9% (95% CI -3.0 to 4.9) Relative percent change = 2.6% (95% CI -8.1 to 13.3) NNTB = not statistically significant
Health-related quality of life (HRQoL)	Mean health-related quality of life score in	Mean health-related quality of life score in		179 (1 study)	⊕⊕⊕⊖ **Moderate** [a]	MD = 0.00 (95% CI -0.06 to 0.06)

Scale from 0 to 1.0 Follow-up: 12 months *(Higher score is better)*	control groups was **0.7**	intervention groups was **0.01 lower** (0.05 lower to 0.03 higher)	Absolute percent change = 1.0% (95% CI -5.0 to 3.0) Relative percent change = 1.4% (95% CI -7.1 to 4.3) NNTB = not statistically significant

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **EQ-5D:** EuroQol-5D; **HSS:** Hospital for Special Surgery knee score; **NNTB:** number needed to treat for an additional beneficial outcome; **NRS:** numerical rating scale; **RR:** Risk ratio; **VAS:** Visual analogue scale; **WOMAC:** Western Ontario-McMaster Osteoarthritis Scale.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Limitations in design and implementation of available studies suggest high likelihood of bias.
[b]Imprecision: Results are based on only one study with 117 people.
[c]Many participants stopped their initial treatment because of lack of effect.

Summary of findings 2. Valgus knee brace compared with no brace for varus medial osteoarthritis of the knee

Valgus knee brace compared with no brace for varus medial osteoarthritis of the knee

Patient or population: patients with varus medial osteoarthritis of the knee
Settings: general hospital
Intervention: valgus knee brace
Comparison: no brace

Outcomes	Illustrative comparative risks* (95% CI)		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	No brace	Valgus knee brace			
Pain VAS: scale from 0 to 10 Follow-up: 12 months *(Higher score is worse)*	Mean pain score in control groups was **5.2**	Mean pain on walking in intervention groups was **equal** (0.84 lower to 0.84 higher)	115 (1 study)	⊕⊕⊖⊖ **Low** [a,b]	MD = 0.00 (95% CI -0.84 to 0.84) Absolute percent change = 0% (95% CI -8.4 to 8.4)

					Relative percent change = 0% (95% CI -1.6 to 1.6) NNTB = not statistically significant
Stiffness	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Function HSS: scale from 0 to 100 Follow-up: 12 months *(Higher score is better)*	Mean function score in control groups was **69**	Mean function in intervention groups was **1.00 higher** (2.98 lower to 4.98 higher)	110 (1 study)	⊕⊕⊝⊝ **Low** [a,b]	MD = 1.00 (95% CI -2.98 to 4.98) Absolute percent change = 1.0% (95% CI 3.0 to 5.0) Relative percent change = 0.01% (95% CI 0.05 to 0.07) NNTB = not statistically significant
Health-related quality of life EQ-5S: scale from 0 to 100 Follow-up: 12 months *(Higher score is better)*	Mean health-related quality of life score in control groups was **0.6**	Mean health-related quality of life score in intervention groups was **0.04 lower** (0.12 lower to 0.04 higher)	117 (1 study)	⊕⊕⊝⊝ **Low** [a,b]	MD = 0.04 (95% CI -0.12 to 0.04) Absolute percent change = 0.04% (95% CI -0.12 to 0.04) Relative percent change = 0.07% (95% CI -0.2 to 0.07) NNTB = not statistically significant
Treatment failure	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Serious adverse events	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Total number of adverse events (withdrawals due to lack of effect)[d]	**Study population** 400 per 1000	246 per 1000	117 (1 study)	⊕⊕⊝⊝ **Low** [a,b]	RR = 1.63 (95% CI 0.94 to 2.82) Absolute percent change = 15% (95% CI -1% to 32%) Relative percent change = 63% (95% CI -6% to 182%) NNTB = not statistically significant

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **NNTB:** Number needed to treat for an additional beneficial outcome; **RR:** Risk ratio.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Limitations in design and implementation of available studies suggest high likelihood of bias.
[b]Imprecision: Results are based on only one study with 117 participants.
[c]No useful data were available.
[d]Many participants stopped their initial treatment because of lack of effect.

Summary of findings 3. Lateral wedge insole compared with neutral insole for varus medial osteoarthritis of the knee

Lateral wedge insole compared with neutral insole for varus medial osteoarthritis of the knee

Patient or population: patients with varus medial osteoarthritis of the knee
Settings: general hospital
Intervention: lateral wedge insole
Comparison: neutral insole

Outcomes	Illustrative comparative risks* (95% CI)		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	Neutral insole	Lateral wedge insole			
Pain NRS: scale from 0 to 10 Follow-up: mean 12 months *(Higher score is worse)*	Mean pain on walking score in control groups was **2.6**	Mean pain on walking in intervention groups was **0.1 higher** (0.45 higher to 0.65 lower)	224 (2 studies)	⊕⊕⊕⊖ **Moderate** [a]	MD = 0.10 (95% CI -0.45 to 0.65) Absolute percent change = 1.0% (95% CI 4.5 to -6.5) Relative percent change = 3.8% (95% CI 1.7 to -25.0) NNTB = not statistically significant

Stiffness WOMAC: scale from 0 to 100 Follow-up: mean 12 months *(Higher score is better)*	Mean stiffness score in control groups was **41.6**	Mean stiffness in intervention groups was **0.07 higher** (4.96 lower to 5.1 higher)	358 (3 studies)	⊕⊕⊕⊖ **Moderate** [a]	MD = 0.07 (95% CI -4.96 to 5.10) Absolute percent change = 0.1% (95% CI -5.0 to 5.1) Relative percent change = 0.2% (95% CI -11.9 to 12.3) NNTB = not statistically significant
Function WOMAC: scale from 0 to 100 Follow-up: mean 12 months *(Higher score is better)*	Mean function score in control groups was **36.6**	Mean function in intervention groups was **0.94 higher** (2.98 lower to 4.87 higher)	358 (3 studies)	⊕⊕⊕⊖ **Moderate** [a]	MD = 0.94 (95% CI -2.98 to 4.87) Absolute percent change = 0.9% (95% CI -3.0 to 4.9) Relative percent change = 2.6% (95% CI -8.1 to 13.3) NNTB = not statistically significant
Health-related quality of life HRQoL: scale from 0 to 1.0 Follow-up: 12 months *(Higher score is better)*	Mean health-related quality of life score in control groups was **0.7**	Mean health-related quality of life score in intervention groups was **0.01 lower** (0.05 lower to 0.03 higher)	179 (1 study)	⊕⊕⊕⊖ **Moderate** [b]	MD = 0.00 (95% CI -0.06 to 0.06) Absolute percent change = 1.0% (95% CI -5.0 to 3.0) Relative percent change = 1.4% (95% CI -7.1 to 4.3) NNTB = not statistically significant
Treatment failure	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Serious adverse events	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Total number of adverse events	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **NNTB:** Number needed to treat for an additional beneficial outcome.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded for limitations in design and implementation of available studies suggesting high likelihood of bias.
[b]Downgraded for imprecision: Results were based on only one study with 179 participants.
[c]No useful data were available.

Summary of findings 4. Valgus knee brace compared with lateral wedge insole for varus medial osteoarthritis of the knee

Valgus knee brace compared with lateral wedge insole for varus medial osteoarthritis of the knee

Patient or population: patients with varus medial osteoarthritis of the knee

Settings: general hospital

Intervention: valgus knee brace

Comparison: lateral wedge insole

Outcomes	Illustrative comparative risks* (95% CI)		Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	Lateral wedge insole	Valgus knee brace			
Pain VAS: scale from 0 to 10 Follow-up: 6 months *(Higher score is worse)*	Mean pain score in control groups was **4.8**	Mean pain score in intervention groups was **0.2 lower** (1.15 lower to 0.75 higher)	91 (1 study)	⊕⊕⊖⊖ **Low** [a,b]	MD = -0.20 (95% CI -1.15 to 0.75) Absolute percent change = -2.0% (95% CI -11.5 to 7.5) Relative percent change = -4.2% (95% CI -24.0 to 15.6)

					NNTB = not statistically significant
Stiffness	See comment	See comment	Not estimable	See comment	Outcome not reported in included studies
Function WOMAC: scale from 0 to 100 Follow-up: 6 months *(Higher score is better)*	Mean function score in control groups was **50.7**	Mean function score in intervention groups was **0.1 higher** (7.26 lower to 0.75 higher)	91 (1 study)	⊕⊕⊖⊖ **Low** [a,b]	MD = 0.10 (95% CI -7.26 to 7.46) Absolute percent change = 0.1% (95% CI -7.26 to 0.75) Relative percent change = 0.2% (95% CI -14.3 to 1.5) NNTB = not statistically significant
Health-related quality of life	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Treatment failure	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Serious adverse events	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies
Total number of adverse events	See comment	See comment	Not estimable[c]	See comment	Outcome not reported in included studies

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **NNTB:** number needed to treat for an additional beneficial outcome; **RR:** Risk ratio.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Downgraded for imprecision: Results were based on only one study with 91 participants.
[b]Downgraded for limitations in design and implementation of available studies suggesting high likelihood of bias.
[c]No useful data were available.

BACKGROUND

Description of the condition

Osteoarthritis (OA) of the knee is a common medical condition that is often seen in general practice and causes considerable pain and immobility. In the United States, approximately 9% of individuals aged 60 years and older suffer from knee OA (Losina 2013). The prevalence of symptomatic knee OA has increased substantially over the past 20 years. Aging, obesity and increased awareness of knee pain have accounted for this trend (Nguyen 2011). Risks for a poor functional outcome in individuals with knee OA involve collateral and cruciate ligament laxity, age, body mass index (BMI) and degree of pain (Sharma 2003). In addition to consequences for the patient, OA presents a considerable burden for society because of its chronic course, high costs of interventions and related productivity costs (Healy 2002; Hermans 2012).

Osteoarthritis of the entire knee is distinguished from OA of one compartment (Grelsamer 1995), which generally is caused by a mechanical problem (Brouwer GM 2007; Tetsworth 1994). Individuals with OA of the medial compartment often have a varus alignment, and the mechanical axis and load bearing pass through the medial compartment. Those with OA of the lateral compartment generally have a valgus alignment, and the mechanical axis and load bearing pass through the lateral compartment. Malalignment increases risk and progression of knee OA and predicts decline in physical function (Brouwer GM 2007; Sharma 2001; Tanamas 2009).

Initial treatment for patients with OA of the knee is conservative, consisting of restricted activity, decreased body mass index (BMI), patient education and physical therapy (Foley 2003; Fransen 2001; Fransen 2008; Garner 2005; Goorman 2000; Hoffmann 2001; Huang 2000; Hurley 1998; Zhang 2010). Pharmacological treatments tend to only modify symptoms (e.g. analgesics, anti-inflammatory drugs); however some are intended to be curative (hyaluronic acids, chondroitin sulphate) (Bellamy 2006; Cepeda 2006; Gibofsky 2003; Karlsson 2002; Leopold 2003; Nuesch 2009; Towheed 2006; Uebelhart 2004; Whittle 2011).

Electro-acupuncture, transcutaneous electrical nerve stimulation (TENS), braces, foot/ankle orthoses and leech therapy are not standard treatments (Rutjes 2009) but can be effective in symptom reduction (Deshaies 2002; Michalsen 2003; Ng 2003). If symptoms persist, surgical therapy such as high tibial osteotomy or knee arthroplasty can be considered (Brouwer RW 2007; Fletcher 2006; Stukenborg 2001) .

Description of the intervention

A knee brace or a foot/ankle orthosis is defined as "any medical device added to a person's body to support, align, position, immobilize, prevent or correct deformity, assist weak muscles, or improve function" (Deshaies 2002). The general purpose of braces and orthoses is to decrease pain, improve physical function and possibly slow disease progression. Proprioception/stability is a hypothesised but unproven underlying explanatory factor. Lateral wedge insoles and special valgus braces are designed to reduce load in the medial compartment (Hewett 1998; Katsuragawa 1999; Kirkley 1999; Komistek 1999; Lindenfeld 1997; Maillefert 2001; Reeves 2011).

Several types of orthoses are available to treat patients with medial knee OA non-operatively. This review includes studies comparing the laterally wedged insole, the valgus knee brace, the neutral knee brace, the neoprene sleeve and variable shoe stiffness versus each other or versus no treatment. The valgus knee brace and the laterally wedged insole are used most commonly in the non-operative treatment of varus medial knee OA.

How the intervention might work

The goal of the interventions is to improve function, reduce symptoms and possibly slow disease progression. The valgus knee brace and the laterally wedged insole are used with the goal of unloading the diseased medial compartment by creating a valgus effect on the knee. Neutral braces and neoprene sleeves are thought to immobilise and stabilise the knee. Neutral insoles, shoes of variable stiffness and lateral wedged insoles could have a cushioning effect (Reeves 2011).

Why it is important to do this review

The literature suggests that patients with varus medial knee OA may benefit from braces and foot/ankle orthoses. However many different types of braces and foot/ankle orthoses are available. It remains unclear which brace or foot/ankle orthosis will provide the greatest benefit or harm to patients treated for varus medial knee OA (Parkes 2013; Reeves 2011; Zhang 2010).

OBJECTIVES

To assess the benefits and harms of braces and foot/ankle orthoses in the treatment of patients with OA of the knee.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and controlled clinical trials investigating all types of braces and foot/ankle orthoses for OA of the knee compared with no treatment or other treatment such as restricted activity, patient education, physiotherapy, pharmacological treatment and orthoses or surgical treatment.

Types of participants

Adult patients (> 18 years) with OA of the knee confirmed by radiological investigation (Kellgren & Lawrence (K&L) grade I-IV).

Types of interventions

All types of braces (rigid knee braces intended to reduce load, knee sleeves/supporters) and foot/ankle orthoses (laterally or medially wedged insoles with or without an ankle support or variable stiffness shoes) for individuals with OA of the knee. The main comparisons were (1) brace versus no treatment; (2) foot/ankle orthosis versus no treatment or other treatment; and (3) brace versus foot/ankle orthosis.

Types of outcome measures

Major outcomes

We considered major outcomes such as pain, function, stiffness, quality of life, treatment failure (need to undergo surgery), serious adverse events and total number of adverse events.

Minor outcomes

We also considered other outcomes such as radiographic scores, compliance and walking distance.

We considered all major outcomes and presented them in the 'Summary of findings' table.

Search methods for identification of studies

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE (current contents, HealthSTAR) until October 2002 in the original review, until May 2007 in the first update and until March 2014 in the second update to identify clinical trials investigating braces and foot/ankle orthoses for OA of the knee. We performed MEDLINE searches for clinical trials using the strategy of The Cochrane Collaboration (Appendix 1, completed March 2014). We applied no language restriction. Moreover we checked the reference lists of included studies and clinical trial registers for ongoing studies.

Data collection and analysis

Selection of studies

Two review authors initially selected trials on the basis of title and abstract. We assessed title, keywords and abstract to establish whether the study met the inclusion criteria regarding diagnosis, design and intervention. For each selected study, we retrieved the full article for final assessment. Next, two review authors independently performed a final selection of trials to be included in the review, using a pretested standardised form. We resolved disagreements on inclusion by discussion.

Data extraction and management

Three review authors independently extracted data on the intervention, types of outcome measures, follow-up, loss to follow-up and outcomes using a standardised form. We have presented the various outcome measures separately. We resolved disagreements or discrepancies on data extraction by discussion.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias of included studies. We resolved disagreements in a consensus meeting and when necessary consulted an independent third person. The Cochrane Collaboration recommends a specific tool for assessing risk of bias in each included study. This comprises a description and a judgement for each entry in a 'Risk of bias' table, wherein each entry addresses a specific feature of the study. The judgement for each entry involves providing a response of 'low risk of bias', 'high risk of bias' or 'unclear risk of bias', indicating lack of information or uncertainty about the potential for bias.

Entries used to assess risk of bias include the following (see also 'Risk of bias' table).

- Random sequence generation (selection bias).
  - Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
- Allocation concealment (selection bias).
  - Selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment.
- Blinding (performance bias and detection bias).
  - Performance bias or detection bias due to knowledge of allocated interventions after assignment.
- Blinding of participants and personnel (performance bias).
  - Performance bias due to knowledge of allocated interventions by participants and personnel during the study.
- Blinding of outcome assessment (detection bias).
  - Detection bias due to knowledge of allocated interventions by outcome assessors.
- Incomplete outcome data (attrition bias).
  - Attrition bias due to quantity, nature or handling of incomplete outcome data.
- Selective reporting (reporting bias).
  - Selection of a subset of original variables recorded on the basis of results.

Measures of treatment effect

For dichotomous outcomes, we calculated risk ratios (RRs) with corresponding 95 per cent confidence intervals (95% CIs). For continuous outcomes, we calculated mean differences (MDs) with 95% CIs.

Unit of analysis issues

Not applicable.

Dealing with missing data

It is unclear to us whether we missed outcome data. Many studies have not published a research protocol. Therefore, we analysed only available data.

Data synthesis

We used RevMan 5 software to analyse the data and have presented the various outcomes in analysis graphs. We used both fixed-effect and random-effects models. In cases of substantial between-trial heterogeneity, we used random-effects analysis instead of a fixed-effect approach. Pooling of outcomes was possible only for the comparison of lateral wedged insole versus neutral insole. We considered the rest of the trials to be clinically heterogeneous in terms of study population and intervention.

'Summary of findings' table

We created a 'Summary of findings' table for the major outcomes of pain, function, stiffness, health-related quality of life, treatment failure, serious adverse events and total adverse events.

We analysed the quality of the presenting results by performing an overall grading of evidence by outcome using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach (Guyatt 2008a; Guyatt 2008b; Schünemann 2008). We assigned the highest quality rating to randomised trial evidence.

The GRADE approach specifies the following levels of quality.

- High quality: Further research is very unlikely to change our confidence in the estimate of effect.
- Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

- Very low quality: We are very uncertain about the estimate.

Trial evidence can be downgraded to moderate, low or very low quality depending on the presence of the following factors.

- Limitations in design and implementation of available studies suggesting high likelihood of bias.
- Indirectness of evidence (indirect population, intervention, control, outcomes).
- Unexplained heterogeneity or inconsistency of results (including problems with subgroup analyses).
- Imprecision of results (wide confidence intervals).
- High probability of publication bias.

Quality will fall by one level for each factor, up to a maximum of three levels for all factors. If very severe problems are noted for any one factor (e.g. when assessing limitations in design and implementation, all studies were unconcealed and unblinded and lost more than 50% of participants to follow-up), the quality of randomised trial evidence may fall by two levels on the basis of that factor alone.

If pooling of study results is not possible, then a single study is included and by definition low-quality evidence, which can be downgraded according to risk of bias items.

RESULTS

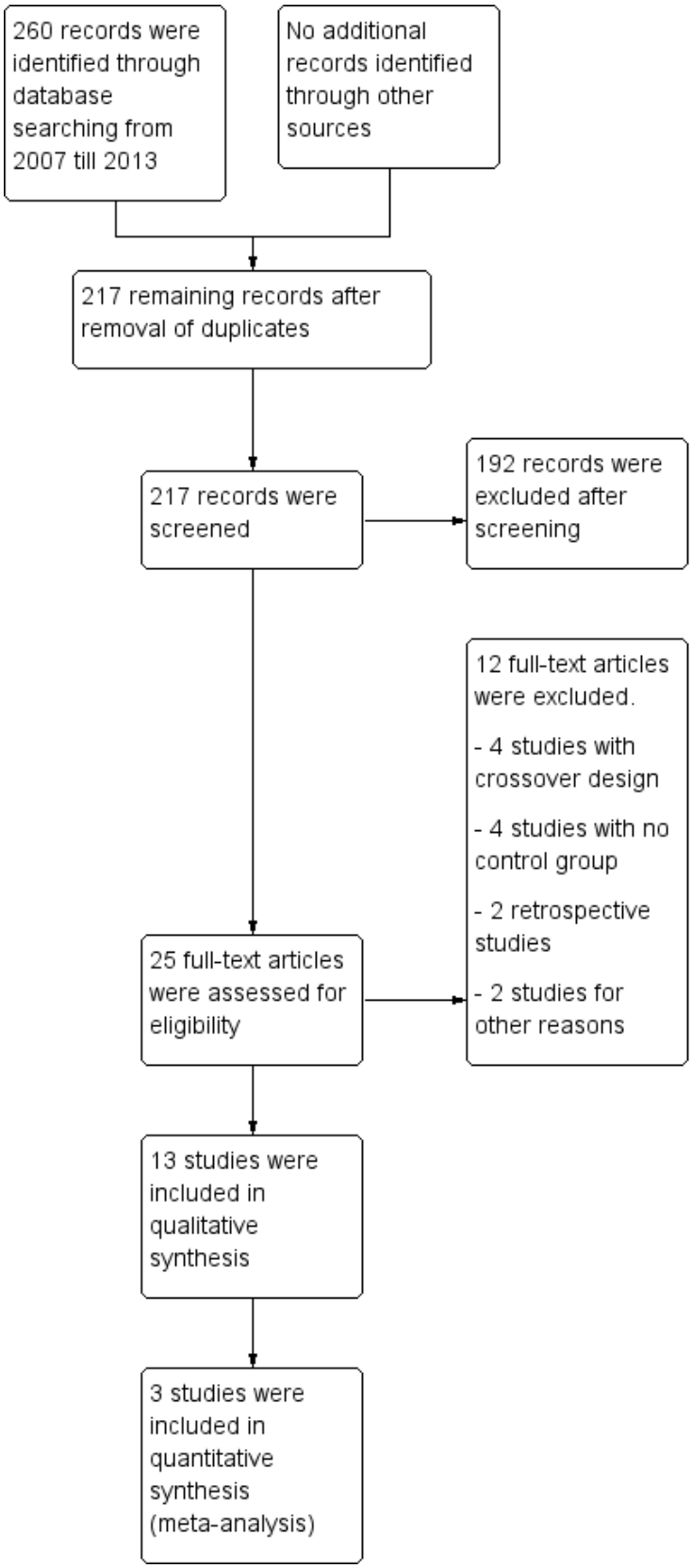
Description of studies

Results of the search

The search strategy (Appendix 1, completed May 2014) yielded a total of 217 records from the following databases: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE (current contents, HealthSTAR). The search resulted in identification of the citations of 25 reports of potentially eligible studies, for which (where possible) full reports were obtained. We included a total of 13 studies in the review. We needed the opinion of a third review author once (Shakoor 2008) before we could come to a final decision.

Overall, this review consists of 13 included studies, 12 excluded studies, no ongoing studies and no studies awaiting classification (Figure 1). We checked the reference lists of the included studies but identified no further studies.

Figure 1. Figure 1 Flow diagram of the study according to the PRISMA statement.



Included studies

We included 13 studies described in 17 publications involving 1356 participants; we included four studies in the first version, added three studies in the first update and added six more studies in this second update. We have described these studies in detail in the Characteristics of included studies table.

One group (Maillefert 2001) published separately six-month and two-year results, another group presented separately six-month and one-year results (Erhart-Hledik 2012) and another group (Toda 2001) published separately eight-week, six-month and two-year results. We have described the 13 selected studies in detail in the Characteristics of included studies table. Four studies (Brouwer 2006; Kirkley 1999; Müller-Rath 2011; Sattari 2011) investigated knee braces, and eight studies (Barrios 2009; Bennell 2011; Erhart-Hledik 2012; Maillefert 2001; Sattari 2011; Toda 2001; Toda 2002; Toda 2008) examined foot/ankle orthoses for medial compartment OA of the knee. Two studies (Raaij van 2010; Sattari 2011) compared a knee brace with a foot orthosis. Only two studies (Brouwer 2006; Rodriques 2008) also assessed the benefits of a brace or a foot/ankle orthosis for treating lateral compartment osteoarthritis. No studies assessed the benefits of a brace or an insole for general OA of the knee. In 12 studies the degree of OA was scored according to Kellgren & Lawrence (K&L) (Kellgren 1957), and in one study (Brouwer 2006) according to Ahlback (Ahlback 1968). In two studies osteoarthritic changes were also checked on magnetic resonance imaging (MRI) (Bennell 2011; Erhart-Hledik 2012). The mean number of participants in the 13 studies was 103 (range 30-207). Mean participant age was 62 years (range 48-65 years). In two trials, all participants were females (Toda 2001; Toda 2002). (See also Characteristics of included studies.)

Barrios 2009 published an RCT of 66 participants with symptomatic medial knee OA (K&L grade II-IV). In this RCT, a treatment group - a full-length (9.1 degrees (standard deviation (SD) 3.9 degrees)) laterally wedged insole into the shoe (n = 35) - had been compared with a control group - a non-custom neutral insole into the shoe (n = 31). Block randomisation was performed based on OA grade, gender and age (older or younger than 55 years). Allocation was done by an administrative assistant who was unaware of the methods used. The study included 29 males and 37 females with medial tibiofemoral OA (scored according to K&L), mean age of 62.4 years and mean BMI of 33.0 kg/m^2. Baseline characteristics (gender, BMI, OA grade) did not differ between groups. A total of 20/35 (57%) participants remained in the treatment group and 25/31 (81%) in the control group at final one-year follow-up. The primary outcome measure was mean Western Ontario-McMaster Osteoarthritis Scale (WOMAC) subscore (100-0); secondary outcomes included a six-minute walking test and a stair negotiation test. Mean and P values were presented, but SD values were missing.

Bennell 2011 reported a double-blinded RCT of 200 participants with mild to moderately severe medial knee OA and radiological evidence of osteophytes in the medial compartment or medial joint space narrowing on an x-ray film. In this RCT, a treatment group - a full-length five-degree laterally wedged insole (n = 103) - was compared with a control group - a flat insole (n = 97). The randomisation procedure consisted of a computer-generated block method using sealed envelopes. Participants included 82 men and 118 women; mean age was 64 years. Mean BMI was 29.2. The degree of radiological OA was scored according to K&L on posteroanterior radiographs and on MRI. Mean varus alignment was 181 degrees. Follow-up was 12 months. Eleven participants in the intervention group and ten in the control group were lost to follow-up.

Brouwer 2006 published a multi-centre RCT of 117 participants with symptomatic unicompartmental knee OA (Ahlback > 0). In this RCT, investigators studied the additive effect of a brace intended to reduce load in the conservative treatment of unicompartmental (medial or lateral) knee OA. A total of 60 participants were included in the intervention group (brace and standard conservative treatment) and 57 in the control group (standard conservative treatment alone). The brace is available for right and left knees in four sizes. The brace consists of a thigh shell and a calf shell (both of carbon fibre) connected by titanium hinges on the medial and lateral sides. The adjustable side bar on the medial side of the brace provides valgus (1-12.5 degrees) with medial unloading, or varus (1-10 degrees) with lateral unloading. The randomisation procedure consisted of a computer-generated block method using sealed envelopes. Participants included 59 men and 58 women. Mean age was 59 years. Mean BMI was 29. The degree of OA was scored according to Ahlback. Patients with an Ahlback score of I or II were included. Mean varus alignment was nine degrees. Mean valgus alignment was six degrees (hip-knee-ankle (HKA) angle). Follow-up was 12 months. Four participants in the control group were lost to follow-up.

Erhart-Hledik 2012 reported an RCT of 79 participants with symptomatic medial knee OA and osteoarthritic changes on MRI. In this study a treatment group - variable-stiffness shoe (n = 40) - was compared with a control group - constant stiffness shoe (n = 39). The randomisation procedure was not described. Participants included 42 men and 37 women. Mean age was 60 years. Mean BMI was 27.7. The degree of radiological OA was scored on MRI at baseline. Follow-up was 12 months. Eight participants in the intervention group and 13 in the control group were lost to follow-up.

Kirkley 1999 reported an RCT comparing (1) a valgus brace with medical treatment (n = 41); (2) a neoprene sleeve with medical treatment (n = 36); and (3) a control (i.e. medical treatment only) (n = 33). Individuals with OA of the knee and pain localised to the medial compartment were included in this trial. The valgus brace was custom made and consisted of a polyethylene thigh shell connected to a polyethylene calf shell through a polyaxial hinge on the medial side, which allowed application of four degrees valgus. The randomisation procedure consisted of a computer-generated block method using sealed envelopes. Follow-up was six months. Nine participants were lost to follow-up (neoprene sleeve - two/control - seven). Participants included 79 men and 31 women. Mean age was 59 years. Mean varus alignment was nine degrees. Degree of OA of the knee was described only in the unloader brace group. Outcome data were presented as means and P values but without standard deviations; this made pooling impossible. Additional information was obtained from The Kirkley Research Group, but this information was not sufficient for analysis.

Maillefert 2001 presented an RCT of 156 participants with symptomatic medial knee OA (K&L > I). Laterally wedged insoles (n = 82) were compared with neutral insoles (n = 74). Both insoles were made of Ledos material, which consists of pure rubber with cork powder. The laterally elevated insoles were individually modelled, with elevation depending on static pedometer evaluation. The randomisation procedure was not described. Participants included 41 men and 108 women. Mean age was 65 years. Mean BMI was 29. Degree of varus alignment was not measured. After six months'

follow-up, nine participants (four from the wedged insole group) were lost to follow-up. Two-year follow-up results were provided in 2004 (Pham 2004). A total of 106 participants completed the two-year follow-up: neutrally wedged insole (n = 51) versus laterally wedged insole (n = 55).

Müller-Rath 2011 reported a non-blinded RCT of 33 participants with symptomatic medial knee OA with a minimum of grade II according to the radiographic classification of K&L. Two treatment groups were included: a valgus knee brace (n = 13) and an elastic knee bandage (n = 10). The control group consisted of untreated individuals (n = 10). The randomisation procedure was not described. Participants included 24 men and nine women; mean age was 53.2 years. Mean BMI was 27.2. Mean alignment was 189 degrees of varus femoro-tibial angle (FTA). The number of participants lost to follow-up was not reported.

Raaij van 2010 reported a non-blinded RCT of 91 participants with symptomatic medial knee OA (K&L ≥ I). Participants were block-randomised to treatment with a 10-mm laterally full-length wedged insole (index group, n = 45) or a valgus brace (control group, n = 46). Baseline characteristics were similar regarding mean age (55 years), mean BMI (29 kg/m^2), medial and lateral OA grades, analgesic use, mean VAS pain score (5.6 (0-10 scale)) and mean WOMAC function (47 (0-100 scale)). Gender differed statistically significantly (index group 65% female vs control group 35% female). At six months, a non-blinded investigator assessed VAS and WOMAC scores as well as varus alignment correction in the frontal plane using the HKA angle on standardised whole leg films.

Rodriques 2008 randomly assigned 30 consecutive women with bilateral valgus deformity knee OA to two groups: medial insole (insoles with 8-mm medial elevation at the rearfoot (n = 16)) and neutral insoles (similar insoles without elevation (n = 14)). Both groups also wore ankle supports. The demographic features of both groups were similar regarding mean age (62 years), mean BMI (30 kg/m^2), mean disease duration (five years), radiographic osteoarthritis severity (K&L), race distribution and sedentary habits. A blinded examiner assessed VAS, Lequesne and WOMAC scores, along with femorotibial, talocalcaneal and talar tilt angles at baseline and after eight weeks.

Sattari 2011 reported an RCT of 60 participants with knee pain, genu varum and moderate to severe medial knee OA (K&L grade III or IV). Investigators included two treatment groups: a custom-molded valgus stress knee support (n = 20) and a 1/4-inch laterally wedged insole (n = 20). The control group (n = 20) received only general management that was universally applied to all three groups, consisting of activity modification, heating agents, straight leg raising, isometric quadriceps home exercises and analgesic use, when needed. The randomisation procedure was computer-generated. Participants included 22 men and 38 women. Mean age was 48 years. Mean VAS pain score was 6.9. The degree of radiological OA was scored according to K&L. Follow-up was nine months. Five participants were lost to follow-up.

Toda 2001 published a prospective trial comparing an elastic subtalar strapped insole (n = 46) versus a traditional lateral wedge insole (n = 44). This study included individuals with symptomatic medial knee OA (K&L II-IV). The wedge of the strapped insole was made from urethane with elevation of 6.35 mm strapped to an ankle sprain supporter. The traditional insole was a lateral rubber heel wedge with elevation of 6.35 mm. Quasi-randomisation was performed according to birth date. All participants were female. Mean age was 65 and mean BMI was 25. Follow-up was eight weeks, and no participant was lost to follow-up. Standing radiographs of participants with and without their respective insoles were taken before entry into the eight-week study. Degree of varus was 181 degrees FTA. Six-month results were published in 2004. A total of 61 participants completed the six-month follow-up: subtalar strapped insole (n = 29) versus traditional laterally wedged insole (n = 32). Two-year results were published in 2006. Only 42 participants completed the two-year follow-up: subtalar strapped insole (n = 21) versus traditional laterally wedged insole (n = 21). Analysis was performed without an intention-to-treat approach. All results were presented in the original articles as pre/post analysis, not as between-group differences (Toda 2001). However, for both the original review and the updated review, the study author was contacted for more information; he sent the missing information on between-group analysis of FTA, VAS and Lequesne index scores.

Toda 2002 published a second trial comparing a subtalar strapped insole (n = 42) with a sock-type ankle supporter (n = 46). Individuals with symptomatic medial knee OA were included in this trial (K&L II-IV). The wedge of the strapped insole was made from urethane with elevation of 6.35 mm strapped to an ankle sprain supporter. The sock-type ankle support extended from malleoli to metatarsals and consisted of a lateral wedged heel insole with elevation of 6.35 mm. The trial took place in the same year (2000) as the first study. The quasi-randomisation procedure was performed according to birth date. All participants were female. Mean age was 65 and mean BMI was 25. Degree of varus was 181 degrees (FTA). Follow-up was eight weeks, and no participant was lost to follow-up. Results were presented as pre/post analysis, not as between-group differences. Second, the Lequesne index was presented graphically and no exact numbers were given. However, the study author was contacted for more information again, and he provided the missing information on between-group analysis of the Lequesne index.

Toda 2008 published a third RCT of 227 participants with symptomatic medial knee OA (K&L I-IV). In this study a placebo - a neutral wedged insole into shoes (n = 45) - was compared with four interventions - a wedged insole with shoes (n = 45), a sock-type ankle supporter with a wedged insole without shoes (n = 46), a subtalar strapped insole with shoes (n = 45) and a subtalar strapped insole without shoes (n = 46). The randomisation procedure consisted of a computer-generated block method using sealed envelopes. Baseline characteristics and outcomes were presented only for the 207 participants who completed the 12-week follow-up. A total of 20 of 227 participants did not complete the study, which included 24 men and 183 women. Mean age was 65 years. Mean BMI was 25. Degree of OA was scored according to K&L. Degree of varus was 181 degrees (FTA). Most results were presented as pre/post analysis, and only intake of non-steroidal anti-inflammatory drugs (NSAIDs) was compared between placebo and different interventions.

Outcome measures included function scores, VAS scores (pain), analgesic/NSAID intake, walking distance, WOMAC scores (pain, function and stiffness), Hospital for Special Surgery knee scores (HSS; function), McMaster Toronto Arthritis score (MACTAR; function), Lequesne index (pain and function), degree of OA (Ahlback and K&L), global patient assessment, quality of life (EQ-5D; a measure of health status), leg alignment (HKA angle; FTA), compliance and side effects.

Excluded studies

After retrieving the full text for final assessment, the review authors excluded 12 studies (Baker 2007; Birmingham 2001; Horlick 1993; Hunter 2012; Katsuragawa 1999; Kuroyanagi 2007; Matsuno 1997; Rooser 1988; Sasaki 1987; Shakoor 2008; Toda 2002b; Tohyama 1991): two studies (Sasaki 1987; Tohyama 1991) because of a retrospective design, four studies because of a cross-over design (Baker 2007; Hunter 2012; Kuroyanagi 2007; Shakoor 2008), four studies because of lack of a control group (Birmingham 2001; Horlick 1993; Katsuragawa 1999; Matsuno 1997) and two studies (Rooser 1988; Toda 2002b) because investigators did not report the targeted outcome measure.

Risk of bias in included studies

Further details on risk of bias of each study are available in Figure 2, Figure 3 and the 'Risk of bias' tables (Characteristics of included studies).

Figure 2. Figure 2 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

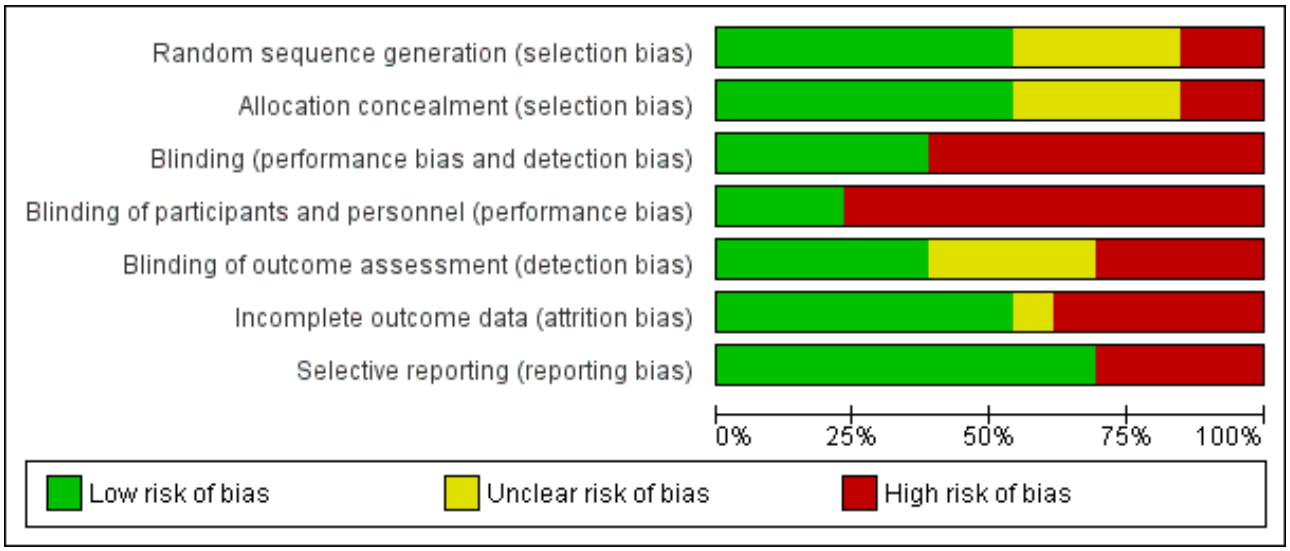
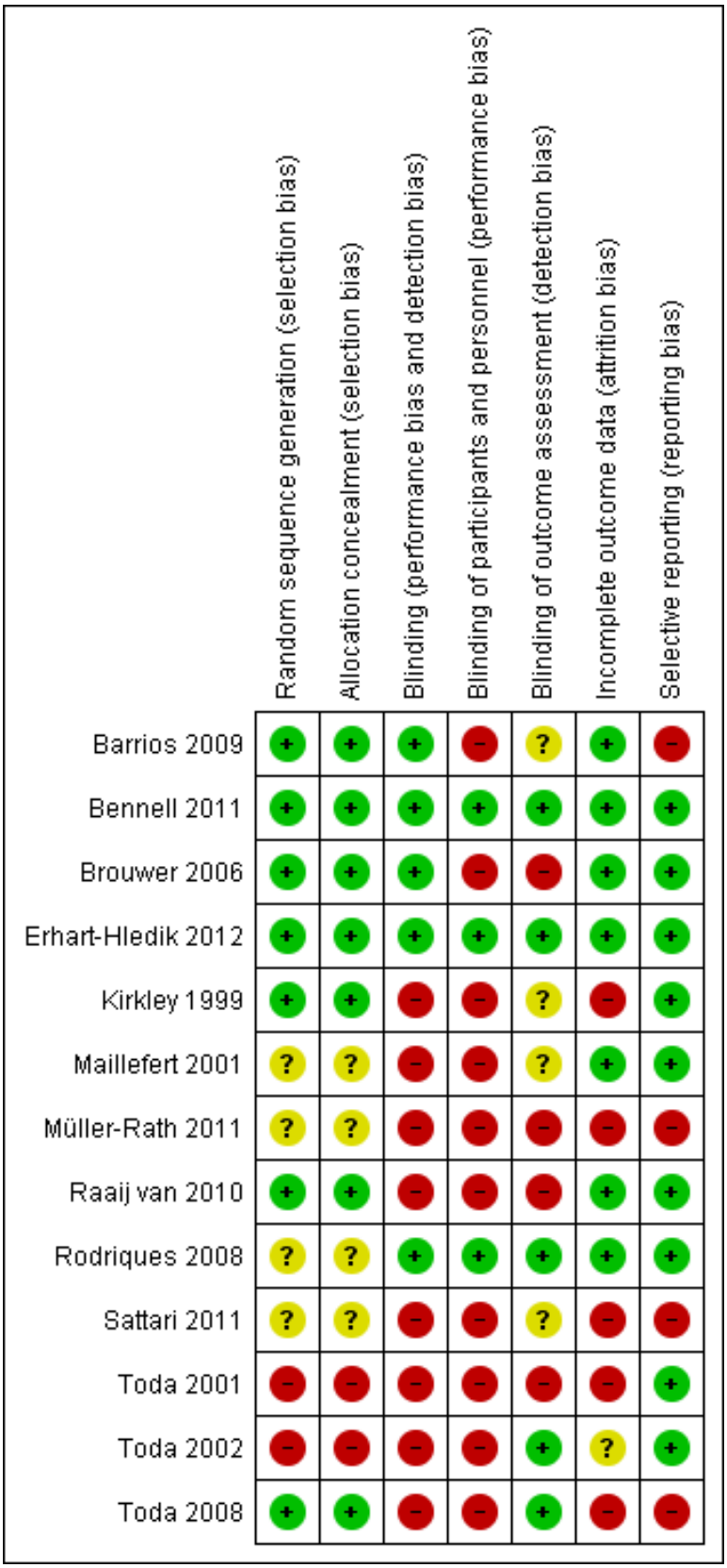


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Randomisation was performed in all studies. However in four studies, the procedure was not clearly described (Maillefert 2001; Müller-Rath 2011; Rodriques 2008; Sattari 2011). In the other nine studies, the randomised sequence was adequately generated and clearly described (Barrios 2009; Bennell 2011; Brouwer 2006; Erhart-Hledik 2012; Kirkley 1999; Raaij van 2010; Toda 2001; Toda 2002; Toda 2008). In seven studies, randomisation and concealment of allocations before assignment were adequately generated (Barrios 2009; Bennell 2011; Brouwer 2006; Erhart-Hledik 2012; Kirkley 1999; Raaij van 2010; Toda 2008).

Blinding

In many studies, blinding procedures for treatment providers, participants and outcome assessors were insufficient. In most trials, blinding procedures for outcome assessors, treatment providers and participants were scored as 'high risk'. In five studies at least one of the outcome assessors was blinded (Bennell 2011; Erhart-Hledik 2012; Rodriques 2008; Toda 2002; Toda 2008), and in only three of these studies, care providers and participants were also blinded (Bennell 2011; Erhart-Hledik 2012; Rodriques 2008).

Incomplete outcome data

In six studies, incomplete outcome data were not adequately addressed. These studies with drop-outs did not include an intention-to-treat analysis (Kirkley 1999; Müller-Rath 2011; Sattari 2011; Toda 2001; Toda 2002; Toda 2008).

Selective reporting

In most studies, the selective outcome reporting item was unclear because no study protocol was provided (Kirkley 1999; Müller-Rath 2011; Sattari 2011; Toda 2001; Toda 2002; Toda 2008).

Effects of interventions

See: **Summary of findings for the main comparison** Braces and orthoses for varus medial osteoarthritis of the knee; **Summary of findings 2** Valgus knee brace compared with no brace for varus medial osteoarthritis of the knee; **Summary of findings 3** Lateral wedge insole compared with neutral insole for varus medial osteoarthritis of the knee; **Summary of findings 4** Valgus knee brace compared with lateral wedge insole for varus medial osteoarthritis of the knee

We have described comparisons of three main groups, namely, knee brace, foot/ankle orthosis and knee brace versus laterally wedged insole. Below we present the effects of interventions for the main comparisons, and we present the quality of evidence scored by the GRADE approach for each outcome. A 'Summary of findings' table was created using GRADEpro (http://ims.cochrane.org/revman/gradepro) for the three main comparisons, namely, valgus knee brace versus no brace (see Summary of findings for the main comparison; Summary of findings 2), laterally wedged insole versus neutral insole (see Summary of findings for the main comparison; Summary of findings 3) and valgus knee brace versus laterally wedged insole (see Summary of findings 4). We have included in our 'Summary of findings' tables the outcomes of pain, stiffness, physical functioning, health-related quality of life, treatment failure, serious adverse events and total adverse events. Pooling of outcomes was possible only for the comparison of laterally wedged insole versus neutral insole. Data on other comparisons could not be pooled. Almost all studies used different interventions and comparison treatments with a wide variety of outcome measures, often with different follow-up times.

Valgus knee brace versus no treatment

Four studies described the results of knee braces versus no treatment in OA of the knee (Brouwer 2006; Kirkley 1999; Müller-Rath 2011; Sattari 2011).

Pain scores

We found four studies that reported pain scores. Brouwer 2006 reported improved VAS pain score after 12 months' follow-up; however no statistically significant difference was found with no treatment (MD 0, 95% CI -0.8 to 0.8). Kirkley 1999 reported significantly better WOMAC pain scores in the brace group compared with the no brace group (P value < 0.001) after six months. Müller-Rath 2011 reported statistically significantly improved VAS score in a valgus knee brace group after 16 weeks but no improvement in the control group (no treatment). Müller-Rath 2011 provided no between-group comparison. In Sattari 2011 the severity of pain decreased statistically significantly more in the knee brace group compared with the no treatment group (MD -2.8, 95% CI -3.6 to -2.0) after nine months (see also Analysis 1.1).

Function

We found three studies that reported function scores. Brouwer 2006 reported statistically non-significant results or lack of evidence of effect of HSS knee function for patients with a valgus knee brace and no brace after 12 months of follow-up (MD 1.0, 95% CI -3.0 to 5.0). Kirkley 1999 found after six months' follow-up better WOMAC physical function scores in the brace group than in the no brace group (P value ≤ 0.001). Müller-Rath 2011 reported improved Tegner, Insal, Lequesne and WOMAC scores in a valgus knee brace group but no improvement in the control group (no treatment). Müller-Rath 2011 provided no between-group comparisons (see also Analysis 1.2).

Stiffness

Stiffness was not reported in the included studies.

Health-related quality of life

We found two studies that reported health-related quality of life. Brouwer 2006 found no statistically significant differences in EuroQol score after 12 months between participants with and without a knee brace (MD -0.04, 95% CI -0.12 to 0.04). Kirkley 1999 found after six months' follow-up statistically significant improvement in disease-specific quality of life (P value 0.001) in favour of the brace group (see also Analysis 1.4).

Treatment failure

Treatment failure was not reported in the included studies.

Serious adverse events

Serious adverse events were not reported in the included studies.

Total adverse events

In total, 24 of 60 participants in the brace group and 14 of 57 participants in the control group in Brouwer 2006 stopped their initial treatment, most often because of lack of effect (RR 1.63, 95%

CI 0.94 to 2.82) (see also Analysis 1.5). Other reasons for stopping were skin irritation (n = 2) and poor fit (n= 2). Sattari 2011 and Müller-Rath 2011 reported no side effects in either group.

Radiographic scores

Radiographic scores were not reported in the included studies.

Compliance

Compliance was not reported in the included studies.

Walking distance

We found two studies that reported walking distance. Brouwer 2006 reported no statistically significant difference in walking distance after 12 months in a brace group compared with a no brace group (MD 0.4, 95% CI -0.9 to 1.7). Sattari 2011 reported statistically significantly increased walking distance in the brace group after nine months in contrast to the control group, which received no treatment (MD 1.2, 95% CI 1.0 to 1.5) (see also Analysis 1.3).

According to the GRADE approach

Low-quality inconclusive evidence suggests that patients with varus medial knee OA benefit more from brace treatment than from no treatment for the outcomes of pain, function and health-related quality of life (Guyatt 2008a; Guyatt 2008b; Schünemann 2008).

Foot/Ankle orthosis

Four studies (Barrios 2009; Bennell 2011; Maillefert 2001; Sattari 2011) described the results of a foot/ankle orthosis for medial compartment OA of the knee (foot/ankle orthosis vs no treatment or a neutral insole) (see also Summary of findings 3).

Laterally wedged insole versus no treatment

One study (Sattari 2011) described the effects of a laterally wedged insole versus no treatment.

Pain scores

In Sattari 2011, a statistically significantly decreased pain score is described in the insole group compared with the no treatment group (MD -1.6, 95% CI -2.3 to -0.9) (see also Analysis 3.1).

Function

Function was not reported in the included study.

Stiffness

Stiffness was not reported in the included study.

Health-related quality of life

Health-related quality of life was not reported in the included study.

Treatment failure

Treatment failure was not reported in the included study.

Serious adverse events

Serious adverse events were not reported in the included study.

Total adverse events

Adverse events were not reported in the included study.

Radiographic scores

Radiographic scores were not reported in the included study.

Compliance

Compliance was not reported in the included study.

Walking distance

Sattari 2011 described no statistically significant differences in walking distance after nine months between laterally wedged insole versus no treatment (MD 0.7, 95% CI 0.5 to 0.9) (see also Analysis 3.2).

Laterally wedged insole versus neutral insole

Three studies (Barrios 2009; Bennell 2011; Maillefert 2001) described the effects of a laterally wedged insole versus a neutral insole.

Pain scores

In Barrios 2009, the WOMAC pain subscale improved statistically significantly in both study groups (neutral insole and laterally wedged insole) compared with baseline at one-year follow-up. Between-group comparisons showed no statistically significant differences (MD -2.5, 95% CI -13.5 to 8.5). Bennell 2011 showed small mean reductions in pain scores over time in a neutral insole group and in a laterally wedged insole group; however these reductions were smaller than the minimal clinically important difference. Between-group comparisons did not show a statistically significant difference (MD 1.0, 95% CI -3.8 to 5.8). At six months' follow-up, Maillefert 2001 described a statistically significantly increased WOMAC pain score in a neutral group compared with a laterally wedged insole group (MD 6.4, 95% CI 0.0 to 12.9) (see also Analysis 4.1 and Analysis 4.2).

Function

We found three studies that reported function. In Barrios 2009, the WOMAC function subscale score improved statistically significantly in both study groups (neutral insole and laterally wedged insole) compared with baseline at one-year follow-up. Between-group comparisons showed no statistically significant differences (MD 1.4, 95% CI -9.2 to 12.0). Bennell 2011 showed in both neutral insole and laterally wedged insole groups small mean reductions in WOMAC function scores over time; however these reductions were smaller than the minimal clinically important difference. Between-group comparisons did not show a statistically significant difference (MD 1.0, 95% CI -4.1 to 6.1). Maillefert 2001 described a non-statistically significant difference in WOMAC function score after six months in a laterally wedged insole group compared with a neutral insole group (MD 0.6, 95% CI -6.9 to 8.1) (see also Analysis 4.4).

Stiffness

We found three studies that reported stiffness. In Barrios 2009, the WOMAC stiffness subscale score improved statistically significantly in both study groups (neutral insole and laterally wedged insole) compared with baseline at one-year follow-up. Between-group comparisons showed no statistically significant differences (MD 4.1, 95% CI -10.1 to 18.3). Bennell 2011 showed in both neutral insole and laterally wedged insole groups small mean reductions in WOMAC stiffness scores over time; however these reductions were smaller than the minimal clinically important difference. Between-group comparisons did not show a statistically significant

difference (MD 0.0, 95% CI -7.3 to 7.3). Maillefert 2001 found at six months' follow-up no statistically significant difference in WOMAC stiffness in a neutral compared with a wedged insole group (MD -1.1, 95% CI -9.0 to 6.8) (see also Analysis 4.3).

Health-related quality of life

Health-related quality of life was not reported in the included studies.

Treatment failure

During 12-month follow-up, 43% of participants in the lateral wedge group versus 19% of those in the neutral insole group changed their initial treatment in Barrios 2009. Mean duration of insole use in Bennell 2011 was statistically significantly less in the laterally wedged insole group than in the neutral insole group.

Serious adverse events

Serious adverse events were not reported in the included studies.

Total adverse events

Adverse events were not reported in the included studies.

Radiographic scores

Radiographic scores were not reported in the included studies.

Compliance

Maillefert 2001 found statistically significantly better compliance with the laterally wedged insole (87.8%) than with the neutral insole (74.3%).

Walking distance

Walking distance was not reported in the included studies.

According to the GRADE approach

Evidence is lacking to suggest that a laterally wedged insole is more effective than no treatment. Moderate evidence suggests that a laterally wedged insole is as effective as a neutral insole for the outcomes of pain, function and stiffness (Guyatt 2008a; Guyatt 2008b; Schünemann 2008).

Knee brace versus laterally wedged insole

Two studies (Raaij van 2010; Sattari 2011) described the results when a valgus knee brace versus a laterally wedged insole was used for medial compartment OA of the knee (see also Summary of findings 4).

Pain scores

We found two studies that reported pain scores. In Raaij van 2010 after six months' follow-up, VAS pain scores statistically significantly improved in both the insole group and the brace group compared with baseline measurements, but no statistically significant differences were observed between the two study groups for this outcome (MD 0.2, 95% CI -1.15 to 0.75). In Sattari 2011, severity of pain decreased statistically significantly in the knee brace group and in the laterally wedged insole group. Investigators reported less pain in the brace group (MD -2.8, 95% CI -3.6 to -2.0) after nine months (see also Analysis 2.3).

Function

We found one study that reported function scores. Raaij van 2010 reported statistically significantly improved WOMAC function scores in both the insole group and the brace group compared with baseline measurements but noted no statistically significant differences between the two study groups for this outcome (MD 0.1, 95% CI -7.26 to 0.75) (see also Analysis 2.2).

Stiffness

None of the studies reported a specific stiffness score.

Health-related quality of life

Health-related quality of life was not reported in the included studies.

Treatment failure

Treatment failure was not reported in the included studies.

Serious adverse events

Serious adverse events were not reported in the included studies.

Total adverse events

Adverse events were not reported in the included studies.

Radiographic scores

Radiographic scores were not reported in the included studies.

Compliance

Compliance was not reported in the included studies.

Walking distance

We found one study that reported walking distance. Sattari 2011 reported an MD of 0.5 km (95% CI 0.23 to 0.77) in favour of the brace group (see also Analysis 2.1).

According to the GRADE approach

Low-quality evidence suggests no statistically significant differences in clinical effect between the laterally wedged insole group and the valgus knee brace group for the outcomes of pain and function (Guyatt 2008a; Guyatt 2008b; Schünemann 2008).

DISCUSSION

Summary of main results

We conducted this review to assess the benefits and harms of braces and orthoses for treatment of patients with osteoarthritis (OA) of the knee. We included a total of 13 studies (n = 1356). These studies have reported results for patients with early to severe knee OA (Kellgren & Lawrence (K&L) I-IV) treated with a valgus knee brace, a laterally wedged insole, a neutral insole or a variable or constant stiffness shoe, or given no treatment.

We found inconclusive evidence for the benefits of a valgus knee brace: Only four controlled trials were published. Kirkley 1999 concluded that in patients with varus knee OA, a brace provides additional beneficial effects in terms of pain and function compared with medical treatment alone. However, baseline characteristics were different between study groups, and the

quality of the study was low. Brouwer 2006 concluded that a brace offers little or no additional effect compared with conservative treatment alone in patients with unicompartmental OA. However, many patients do not adhere in the long run to this kind of treatment because the positive effects are too small or because the side effects are too large. Müller-Rath 2011 reported improved Tegner, Insal, Lequesne, Western Ontario-McMaster Osteoarthritis Scale (WOMAC) and visual analogue scale (VAS) scores in the knee brace group after 16 weeks of treatment. They reported no improvement in the control group (no treatment) and described no side effects of treatment; however this study was sponsored, and study authors were not able to provide their data because of a server breakdown. Sattari 2011 reported a statistically significantly decreased pain score in the knee brace group compared with the no treatment group after nine months. Walking distance was increased statistically significantly in the brace group in contrast to the no treatment group after nine months. Investigators described no side effects of the brace. All four studies showed some clinical effect; however the methodological quality of these studies was low.

Moderate-quality evidence shows the benefits of a laterally wedged insole (vs no treatment or a neutral insole) for medial compartment OA: We included seven controlled trials in this review with conflicting evidence. Barrios 2009, Maillefert 2001, Sattari 2011, Toda 2002 and Toda 2008 reported statistically significantly improved patient-reported outcomes after a laterally wedged insole was worn; however Bennell 2011 and Toda 2001 reported reductions smaller than the minimal clinically important difference.

Conflicting evidence was found for preference of a neutral or a laterally wedged insole. Results reported by Barrios 2009 favoured the laterally wedged insole, Maillefert 2001 favoured the neutral insole and Bennell 2011 reported no statistically significant differences between the two insoles. Pooling of results of three studies comparing laterally wedged and neutral insoles resulted in lack of evidence of an effect on WOMAC pain scores, WOMAC stiffness scores and WOMAC function scores at one month and at 12 months (see also Summary of findings 3).

Data for the comparison of laterally wedged insole versus valgus knee brace could not be pooled. After six months' follow-up, VAS pain scores and WOMAC function scores were improved and did not differ statistically significantly in the two groups (see also Summary of findings 4).

Overall completeness and applicability of evidence

Four trials investigated a knee brace and eight studies examined foot/ankle orthoses for medial compartment OA of the knee. It is important to note that the findings of these studies may lack generalisability: In the studies of Toda and Rodriques (Toda 2001; Toda 2002; Rodriques 2008), all participants were female, and in Kirkley 1999 and Sattari 2011, most participants were male. In all studies the age of participants was relatively high (mean 63 years). In the Kirkley 1999 trial, baseline characteristics differed between participants. It is important to present full data: Kirkley 1999 presented change scores without baseline scores and without a standard deviation. Toda 2001 and Toda 2002 presented pre-analysis and post-analysis results but did not report between-group differences. Müller-Rath 2011 presented their scores only graphically and could not provide their data because of a server breakdown.

Particularly, researchers studied the effects of braces and orthoses for medial compartment OA. Compared with lateral compartment OA of the knee, medial compartment OA has a much higher prevalence because lateral compartment OA is associated with trauma and is less clinically frequent. This is probably why only one randomised controlled trial (RCT) (Brouwer 2006) examined the effect of a brace or an orthosis for lateral compartment or general OA of the knee. Furthermore, varus bracing for lateral OA is probably less effective; the adduction moment at the knee during the stance phase of walking causes mainly medial loading (Johnson 1980). In general OA of the knee, there is no compartment to unload, and perhaps a sleeve or a neutral brace will benefit. No studies compared a brace or an orthosis with operative treatment such as high tibial osteotomy or unicompartmental knee arthroplasty.

Quality of the evidence

Two studies in this review had low risk of any type of bias, six studies had moderate risk and five studies had high risk. The randomisation procedure frequently was not described or was insufficient. Except for the trials of Bennell 2011, Brouwer 2006, Kirkley 1999, Raaij van 2010 and Toda 2008, the randomisation procedure was not described or was inadequate. In most studies, blinding procedures were insufficient, although we realise that when braces are used, blinding is not always possible; for footwear inserts, it is generally less difficult. Results were based on small studies, leading to imprecision.

Potential biases in the review process

One study did not report the number of participants lost to follow-up. This study was funded by Medi, provider of orthoses. Outcomes were presented only graphically in this publication. Study authors were not able to provide their data on request because of a "server breakdown" (Müller-Rath 2011).

Agreements and disagreements with other studies or reviews

Other meta-analyses or systematic reviews were not available for comparison of our results.

AUTHORS' CONCLUSIONS

Implications for practice

We conclude that in cases of varus medial compartment knee OA, low-quality inconclusive evidence shows benefits of bracing for pain, stiffness, function and quality of life in the treatment of medial compartment knee OA. Moderate-quality evidence suggests that a laterally wedged insole is as effective as a neutral insole. Evidence is lacking to suggest that a laterally wedged insole is more effective than no treatment. Also evidence of low quality suggests no statistically significant difference in clinical effect between the laterally wedged insole and the valgus knee brace.

The optimal choice for an orthosis remains unclear, and long-term implications are lacking.

Implications for research

The methodological quality of studies investigating the benefits of braces and orthoses has to be improved, particularly the randomisation procedure and blinding measures. Moreover to

improve the generalisability of results, studies should not be limited to female participants.

Short-term benefit must be established first to justify the considerable resources required by and the ethical implications involved in a lengthy study. Subsequently, a follow-up period of at least five years is needed because OA is a chronic disease. One general knee score would allow pooling of results. We recommend using the WOMAC because this has been shown to be a valid instrument for measurement of OA (Bellamy 1997). Between-groups analysis is necessary to show relevant differences. Future studies should provide complete data on outcome measures, including means and standard deviations or 95% confidence intervals.

It is important to score side effects because they influence the patient's compliance with the intervention. This especially concerns braces, which can be obtrusive in many cases. For insoles, bigger and less stylish shoes are needed. New trials should investigate the long-term benefits of braces and orthoses compared with standard conservative care. More studies are needed to identify predictive factors for the success of brace and insole treatment. If feasible, braces should be compared with ankle/foot orthoses. If braces and orthoses are effective, they should be compared with operative treatment such as high tibial osteotomy or knee arthroplasty for medial compartment OA. It will be interesting to learn for how long surgery can be delayed by this kind of conservative treatment (Gossec 2007).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barrios 2009

Methods	RCT; block randomisation
Participants	Medial tibiofemoral OA: n = 66 Male/female: 29/37 Mean age (years): 62 Mean BMI (kg/m^2): 33 Grade of OA according to Kellgren & Lawrence: II = 27, III = 24, IV = 15
Interventions	I = full-length (9°) wedged insole into shoe (n = 35) vs C = non-custom neutral insole into shoe (n = 31) Follow-up: 12 months
Outcomes	WOMAC, 6-minute walking test, stair negotiation test
Notes	Mean and P values are presented, but SD values are missing

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a block-randomization was performed based on OA grade, gender, and age (greater or less than 55 years)"
Allocation concealment (selection bias)	Low risk	Quote: "the allocation was done by an administrative assistant unaware of the methodologies used"
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "the subjects were blinded from group assignment"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants assigned to the treatment group were tested to determine the amount of wedging Quote: "subjects who had no pain relieve (after wedging) were excluded from the study"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of assessors was not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat
Selective reporting (reporting bias)	High risk	Quote: "subjects who had no pain relieve (after wedging) were excluded from the study"

Bennell 2011

Methods	RCT; computer-generated block randomisation
Participants	Painful medial knee osteoarthritis: n = 200 Male/ female: 82/118 Mean age (years): 64 Mean BMI (kg/m^2): 29.2 Mean varus (degrees): 181 Grade of medial OA according to Kellgren & Lawrence: II = 95, III = 105
Interventions	I = full-length (5^o) wedged insole into shoe (n = 103) vs C = neutral insole into shoe (n = 97) Follow-up: 12 months
Outcomes	NRS scale (pain), WOMAC scale, physical activity scale for the elderly, average number of steps taken per day
Notes	No competing interests

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were stratified by disease severity (Kellgren and Lawrence grades 2 and 3) and sex and randomly allocated in permuted blocks of 6 to 12"
Allocation concealment (selection bias)	Low risk	Quote: "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"
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "a double blind randomised controlled trial"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants were informed that two types of insoles were being compared but the insoles and study hypotheses were not described"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A blinded examiner assessed the participants at baseline and 12 months" according to patient-reported outcome measures; participants were blinded as well
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat
Selective reporting (reporting bias)	Low risk	Complete data were reported

Brouwer 2006

Methods	RCT; computer-generated block randomisation

Brouwer 2006 *(Continued)*

Participants	Unicompartmental knee OA: n = 117 Male/ female: 69/48 Mean age (years): 59 Mean BMI (kg/m^2): 28.5 Varus: n = 95/valgus: n = 22 Mean varus (degrees) = 188 Mean valgus (degrees) = 173
Interventions	I = Brace intended to reduce load (n = 60) vs C = standard conservative treatment (n = 57) Follow-up: 12 months
Outcomes	VAS, HSS knee score, walking distance, EuroQol
Notes	No competing interests

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomised according to a computer-generated procedure in blocks of 24"
Allocation concealment (selection bias)	Low risk	Quote: "the allocation of treatment was concealed until after the patient was included and baseline measurements were executed; sealed envelopes contained the group assignment"
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcome assessor of the HSS knee was blinded for allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded; outcome assessor of the HSS knee was blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study used patient-reported outcome measures; participants were not blinded. Functional outcome (HSS knee score) was measured blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat
Selective reporting (reporting bias)	Low risk	Complete data were reported

Erhart-Hledik 2012

Methods	RCT; randomisation procedure not described; outcome assessment partially blinded
Participants	Medial compartment knee OA: n = 79 Male/female: 42/37 Mean age (years): 60 Mean BMI (kg/m^2): 27.7
Interventions	I = Variable-stifness shoe (n = 40) vs C = constant stiffness shoe (n = 39)

Erhart-Hledik 2012 *(Continued)*

	Follow-up = 6 and 12 months
Outcomes	WOMAC
Notes	6-Month results were presented earlier. Patients were included on the basis of MRI. Anteroposterior radiograph was used during follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a random number generator"
Allocation concealment (selection bias)	Low risk	Quote: "The randomization code was revealed to the study coordinator in charge of subject recruitment and in contact with the subjects regarding WOMAC scores, once recruitment, data collection, and analyses were completed"
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: "Subjects were blinded to their shoe type"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Subjects were blinded to their shoe type (The researcher performing the gait analysis was not blinded to the shoe type)"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Subjects were blinded to their shoe type"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat
Selective reporting (reporting bias)	Low risk	Complete data were reported; study author provided additional data for this review

Kirkley 1999

Methods	RCT; computer-generated blocked randomisation scheme with use of sealed envelopes; blinding of outcome assessment not described
Participants	Varus arthrosis: n = 119 Male/female: 79/31 Mean age (years): 59 Mean varus (degrees): 189
Interventions	I = unloader brace (n = 41) vs C1 = neoprene brace (n = 36) vs C2 = medical treatment only (n = 33) Follow-up: 6 months
Outcomes	WOMAC and MACTAR scores Function assessed with use of the 6-minute walking and the 30-second stair climbing test
Notes	No competing interests

Kirkley 1999 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a computer-generated blocked randomisation scheme"
Allocation concealment (selection bias)	Low risk	Quote: "with use of sealed envelopes"
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded to the intervention
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Study used patient-reported outcomes. Outcome assessor of patient-reported outcome measures was not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	No intention-to-treat analysis
Selective reporting (reporting bias)	Low risk	Complete data were reported

Maillefert 2001

Methods	RCT; randomisation procedure not described; outcome assessment partially blinded
Participants	Painful medial knee osteoarthritis: n = 156 Male/female: 41/108 Mean age (years): 65 Mean BMI (kg/m^2): 29 Grade of OA according to Kellgren & Lawrence: II = 69, III = 60, IV = 18
Interventions	I = laterally wedged insole (n = 78) vs C = neutrally wedged insole (n = 69); follow-up: 1, 3, 6 months
Outcomes	WOMAC, concomitant treatment, compliance
Notes	No competing interests

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation sequence generation procedure was not described

Maillefert 2001 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation concealment procedure was not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were blinded to randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The practitioner nor the patient was blinded to the randomization"; however the research nurse was blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Any missing data were collected by a research nurse, unaware of the randomisation by telephone"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Analysis was made using an intention-to-treat approach"
Selective reporting (reporting bias)	Low risk	Complete data were reported

Müller-Rath 2011

Methods	RCT; randomisation procedure and blinding of outcome assessment not described
Participants	Symptomatic varus knee OA: n = 33 Male/female: 24/9 Mean age (years): 53 Mean BMI (kg/m^2): 27.2
Interventions	I = valgus knee brace or elastic knee bandage vs C = no treatment Follow-up: 16 weeks
Outcomes	Tegner, Insall, Lequesne, WOMAC, HSS, VAS
Notes	Number of participants lost to follow-up is not reported. Study is funded by Medi, provider of orthoses. Study authors could not provide their data because of a "server breakdown"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded

Müller-Rath 2011 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	No lost participants were reported; study authors could not provide their data because of a "server breakdown"
Selective reporting (reporting bias)	High risk	No intention-to-treat

Raaij van 2010

Methods	RCT; computer-generated blocked randomisation
Participants	Medial knee OA: n = 91 Male/female: 46/45 Mean age (years): 55 Mean BMI (kg/m^2): 29 Mean varus (degrees) = 187 Degree of medial OA according to Kellgren & Lawrence (n): I = 37, II = 17, III = 35, IV = 2 Degree of lateral OA according to Kellgren & Lawrence (n): 0 = 67, I = 22, II = 2
Interventions	I = 10-mm laterally full-length wedged insole (n = 45) vs C = valgus brace (n = 46)
Outcomes	VAS (pain), WOMAC, degree of varus (hip-knee-ankle angle)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "participants were randomised according to a computer-generated procedure (block randomisation, with variable sizes of the blocks)"
Allocation concealment (selection bias)	Low risk	Quote: "the randomizations codes were held by an independent observer to ensure masked blocking"
Blinding (performance bias and detection bias) All outcomes	High risk	Unblinded trial
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "completely unblinded"

Raaij van 2010 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "one non-blinded investigator, a trained orthopedic surgeon, assessed the follow-up measurements"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "by intention-to-treat"
Selective reporting (reporting bias)	Low risk	Complete data were reported

Rodriques 2008

Methods	RCT; randomisation procedure not described; outcome assessment blinded
Participants	Bilateral valgus deformity knee OA: N = 30 All female Mean age (years): 62 Mean BMI (kg/m^2): 30 Degree of OA lateral compartment according to Kellgren & Lawrence: II = 16, III = 8, IV = 6
Interventions	I = medially wedged insole (n = 16) vs C = neutral insole (n = 14) Follow-up: 2 months
Outcomes	VAS pain (night, rest, movement), Lequesne index score, WOMAC
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomisation sequence procedure is not described
Allocation concealment (selection bias)	Unclear risk	Allocation concealment procedure is not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blind trial
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients of both groups received the same new shoe and were blind to insole use"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "outcomes were administered at baseline and after 8 weeks by a blinded examiner"

Rodriques 2008 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete data were reported
Selective reporting (reporting bias)	Low risk	Complete data were reported

Sattari 2011

Methods	RCT; computer-generated randomisation
Participants	Varus knee OA: n = 60 Male/female: 22/38 Mean age (years): 48 Mean BMI (kg/m^2): not reported Degree of OA medial compartment according to Kellgren & Lawrence: III = 39, IV = 21
Interventions	I = custom-molded valgus stress knee support (n = 20) or 1/4-inch lateral wedged insole (n = 20) vs C = no intervention Follow-up: 9 months
Outcomes	VAS (pain), Lequesne index (walking distance)
Notes	Conflicts of interest are not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation sequence procedure is not described
Allocation concealment (selection bias)	Unclear risk	Allocation concealment procedure is not described
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded; outcome assessors were blinded; study used patient-reported outcome measures
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "5 patients were removed from the study because of absence from follow-up. They were substituted with new patients, to maintain 20 patients in each group"

Sattari 2011 *(Continued)*

Selective reporting (reporting bias)	High risk	No intention-to-treat

Toda 2001

Methods	RCT; randomisation performed by date of birth. Blinded assessments of level of pain according to VAS, Lequesne index, radiographic outcome
Participants	American College of Rheumatology criteria for knee osteoarthritis (n = 90) All female Mean age (years): 65 Mean varus (FTA; degrees): 181 Degree of OA according to Kellgren & Lawrence: II = 55, III = 27, IV = 8
Interventions	I = strapped insole (n = 46) vs C = lateral wedge insole (n = 44) Follow-up: 8 weeks, 6 months and 2 years
Outcomes	VAS, Lequesne (pain) index score, radiographic changes
Notes	In Table 3 of the first publication, median value of final VAS score in strapped insole group is incorrect No between-groups analysis was performed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Randomisation was performed by date of birth"
Allocation concealment (selection bias)	High risk	Quote: "Randomisation was performed by date of birth"
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded; outcome assessors were blinded; study used patient-reported outcome measures; radiographic changes were measured blinded
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to the intervention. Research nurse was blinded to objectives of the study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study used patient-reported outcome measures (PROMs). Outcome assessor of PROMS, namely, the participant, was not blinded in this study. However participant and research nurse were blinded to objectives of the study
Incomplete outcome data (attrition bias) All outcomes	High risk	No intention-to-treat analysis
Selective reporting (reporting bias)	Low risk	Complete data were reported

Toda 2002

Methods	RCT; randomisation performed by date of birth
Participants	American College of Rheumatology criteria for knee OA: n = 88 All female Mean age (years): 65 Mean BMI (kg/m^2): 25 Degree of varus (FTA; degrees): 181
Interventions	I = subtalar strapped support (n = 44) vs C = sock-type support (n = 46) Follow-up: 8 weeks
Outcomes	Lequesne (pain) index, radiographic changes
Notes	Scores were shown in figures; no exact numbers were given No between-groups analysis was performed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Randomisation was performed by date of birth"
Allocation concealment (selection bias)	High risk	Quote: "Randomisation was performed by date of birth"
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded; outcome assessment was blinded; study used patient-reported outcome measures. Radiographic changes were measured blinded
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "in this study, participants were not blinded to the treatment. However, participants were not told whether the method of fixation at ankle joint, belt or sock-type, was thought to be important"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All other items were assessed by physical therapists who were unin-formed of the objective of the study when patients presented the OOC" "The radiographic assessment was completed by 3 orthopedic surgeons prior to being informed of the category of the patients"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Scores were shown in figures; no exact numbers were given
Selective reporting (reporting bias)	Low risk	Complete data were reported

Toda 2008

Methods	RCT; computer-generated blocked randomisation
Participants	Patients with medial compartment OA of the knee according to American College of Rheumatology criteria and a criterion stipulating standing femorotibial angle greater than 176 degrees: n = 207 Male/female: 24/183

Toda 2008 *(Continued)*

	Mean age (years): 65 Mean BMI (kg/m^2): 25 Grade of OA according to Kellgren & Lawrence: I = 17, II = 133, III = 35, IV = 22 Varus: 181 degrees (FTA)
Interventions	I = wedged insole with shoes (n = 45), sock-type ankle supporter with wedged insole without shoes (n = 46), subtalar strapped insole with shoes (n = 45) and subtalar strapped insole without shoes (n = 46) vs C = neutral wedged insole into shoes (n = 45)
Outcomes	Lequesne index VAS pain NSAID intake
Notes	Baseline characteristics and outcomes (differences compared with baseline) were presented only for the 207 participants who completed 12-week follow-up Most results were presented as pre/post analysis, and only NSAID intake was compared between placebo and the different interventions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomisation procedure for the allocation was a computer-generated block method using sealed envelopes"
Allocation concealment (selection bias)	Low risk	Quote: "In the initial visit, clinicians were given randomly generated treatment allocations with sealed opaque envelopes in a series of blocks of 10"
Blinding (performance bias and detection bias) All outcomes	High risk	Participants were not blinded to the intervention; study used patient-reported outcome measures
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to the intervention; research nurse was blinded to objectives of the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a research nurse who was blind to the objectives of the study asked the participants to assess the Lequesne index and the VAS for subjective knee pain at baseline and 12-weeks assessments"; however participants were not blinded to the intervention, and patient-reported outcome measures were used
Incomplete outcome data (attrition bias) All outcomes	High risk	Intention-to-treat analysis
Selective reporting (reporting bias)	High risk	Baseline characteristics and outcomes (differences compared with baseline) were presented for only the 207 participants who completed 12-week follow-up

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Baker 2007	Cross-over design
Birmingham 2001	No control group
Horlick 1993	Participants are their own controls
Hunter 2012	Cross-over design
Katsuragawa 1999	No control group
Kuroyanagi 2007	Cross-over design
Matsuno 1997	No control group
Rooser 1988	Rheumatoid arthritis after total knee arthroplasty Healthy controls
Sasaki 1987	Retrospective trial
Shakoor 2008	Cross-over design
Toda 2002b	Correlation study
Tohyama 1991	Retrospective study

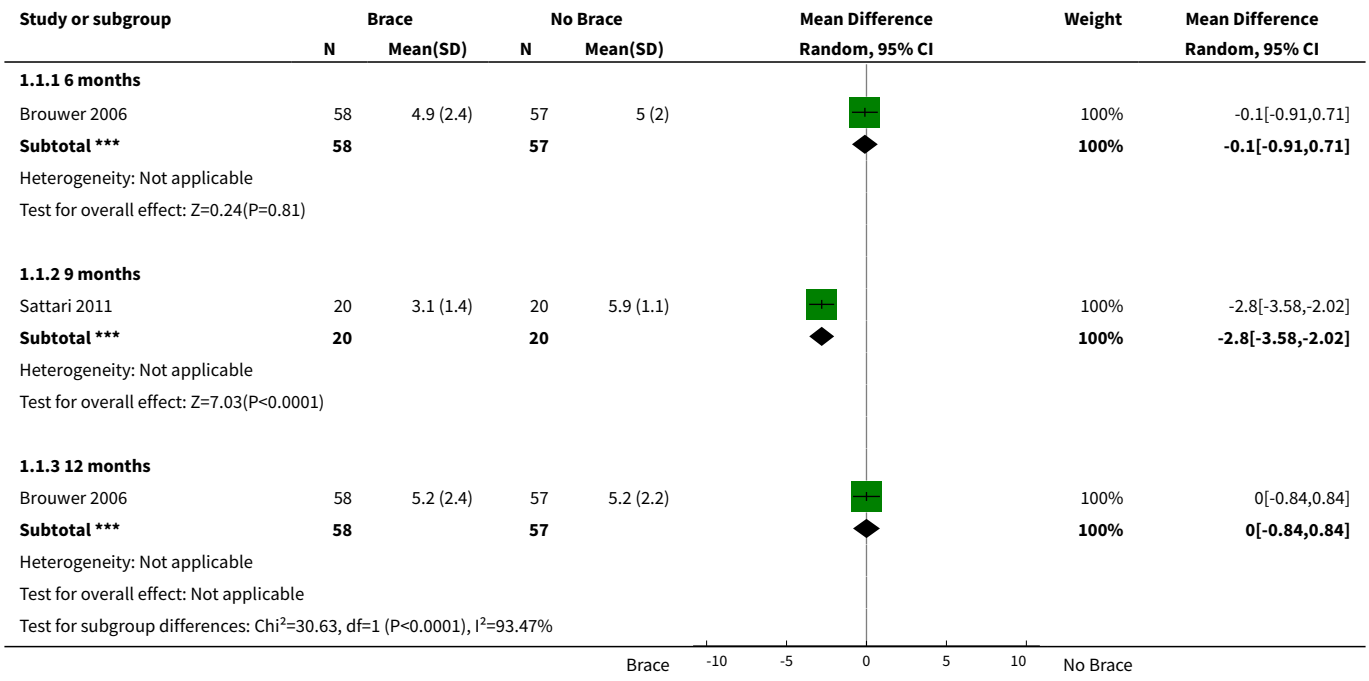
DATA AND ANALYSES

Comparison 1. Brace versus no treatment

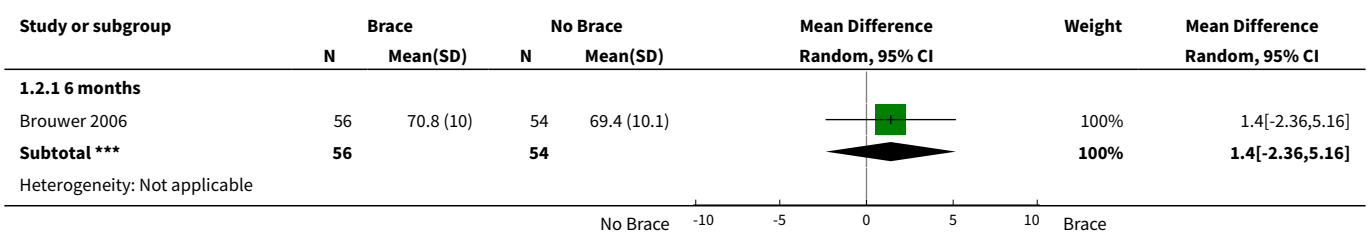
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Pain (VAS)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 6 months	1	115	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.91, 0.71]
1.2 9 months	1	40	Mean Difference (IV, Random, 95% CI)	-2.80 [-3.58, -2.02]
1.3 12 months	1	115	Mean Difference (IV, Random, 95% CI)	0.0 [-0.84, 0.84]
2 Knee function (HSS)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 6 months	1	110	Mean Difference (IV, Random, 95% CI)	1.40 [-2.36, 5.16]
2.2 12 months	1	110	Mean Difference (IV, Random, 95% CI)	1.0 [-2.98, 4.98]
3 Walking distance (km)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 6 months	1	116	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.32, 1.12]

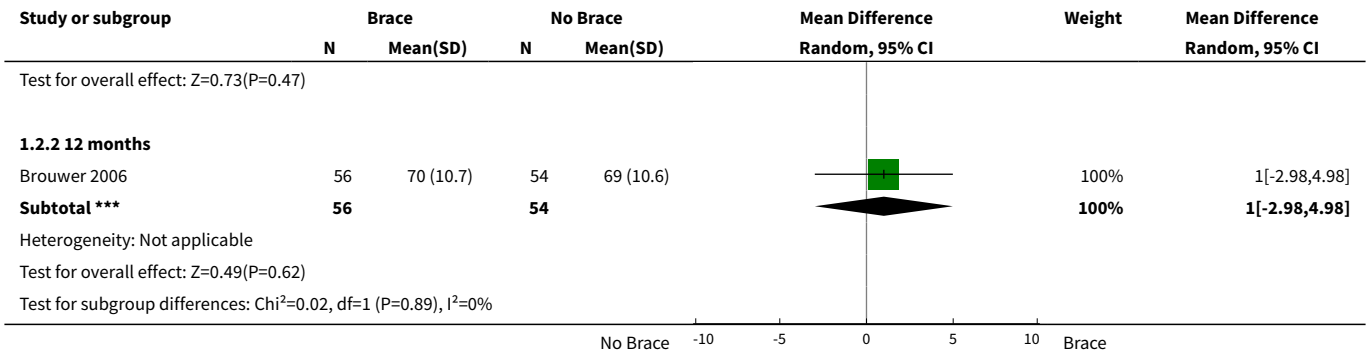
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.2 9 months	1	40	Mean Difference (IV, Random, 95% CI)	1.20 [0.95, 1.45]
3.3 12 months	1	117	Mean Difference (IV, Random, 95% CI)	0.40 [-0.87, 1.67]
4 Quality of life (EQ-5D)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 6 months	1	117	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.14, 0.04]
4.2 12 months	1	117	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.12, 0.04]
5 Total adverse events	1	117	Risk Ratio (M-H, Random, 95% CI)	1.63 [0.94, 2.82]

Analysis 1.1. Comparison 1 Brace versus no treatment, Outcome 1 Pain (VAS).

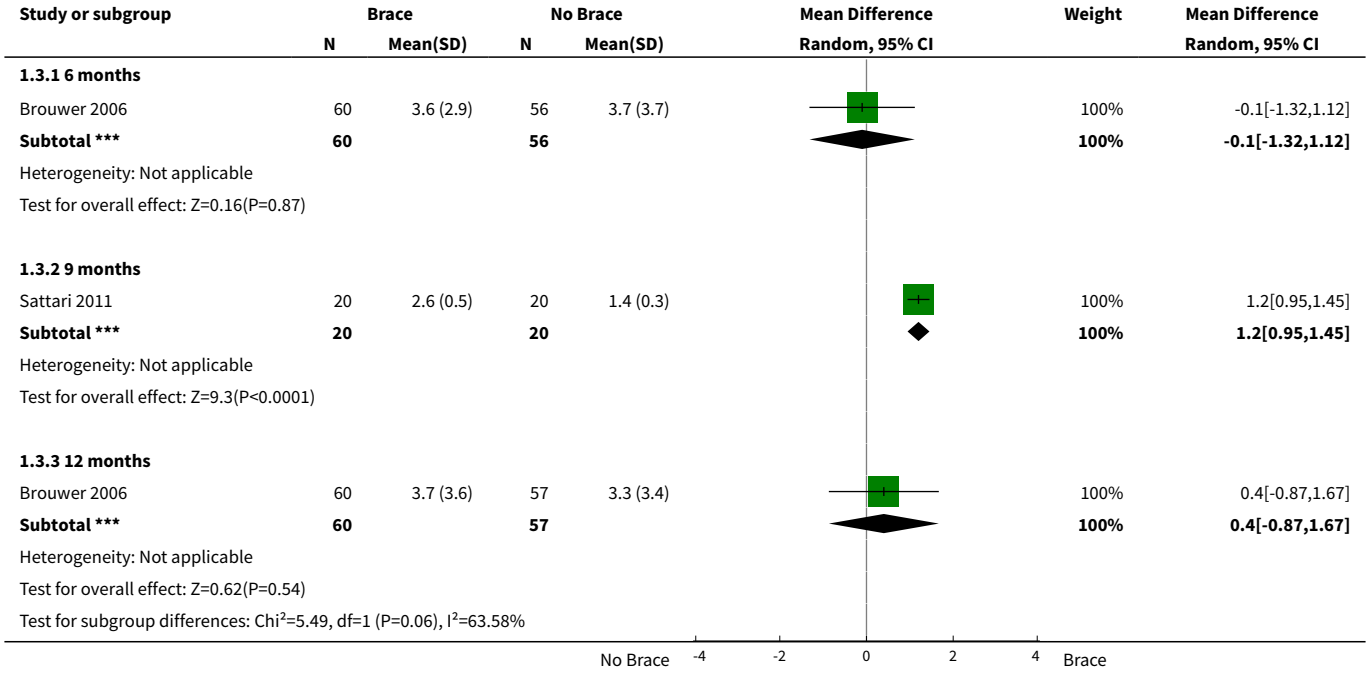


Analysis 1.2. Comparison 1 Brace versus no treatment, Outcome 2 Knee function (HSS).

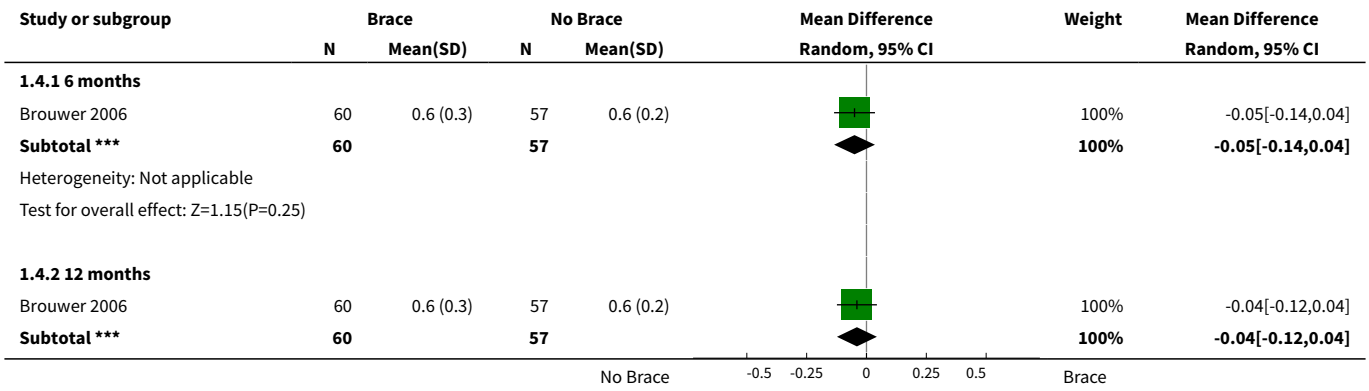


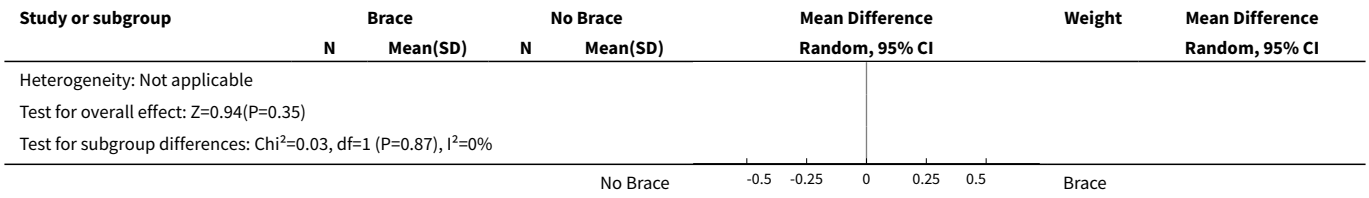


Analysis 1.3. Comparison 1 Brace versus no treatment, Outcome 3 Walking distance (km).

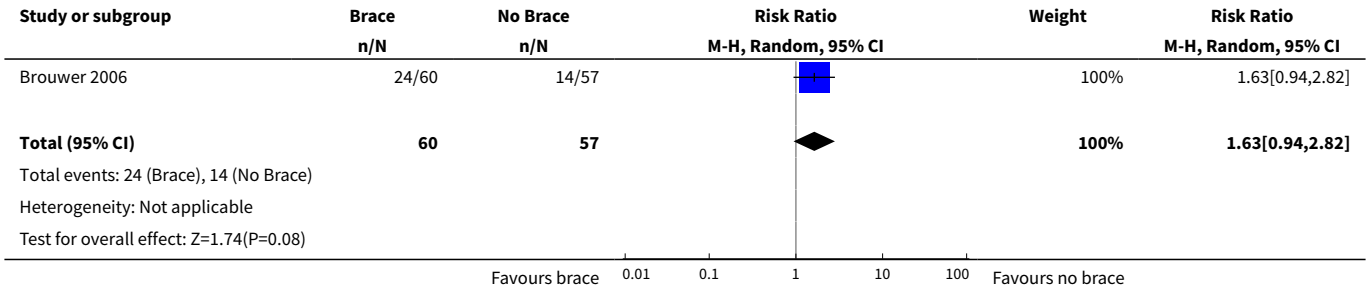


Analysis 1.4. Comparison 1 Brace versus no treatment, Outcome 4 Quality of life (EQ-5D).





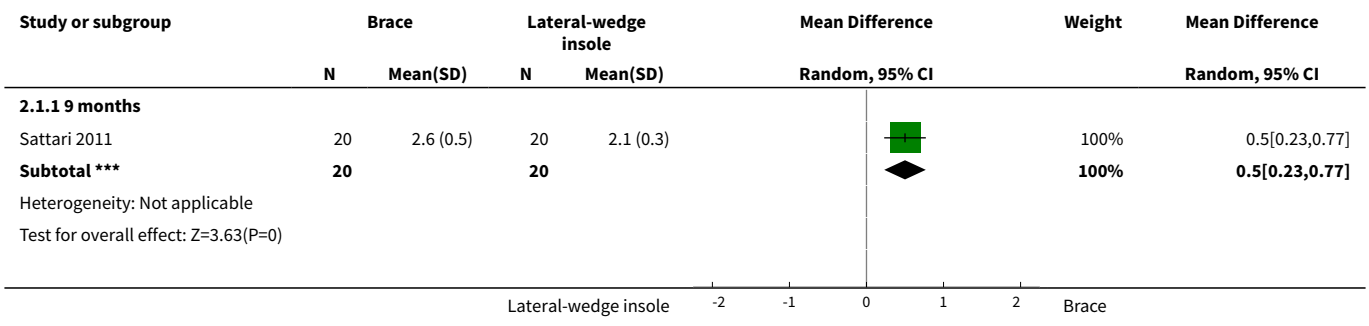
Analysis 1.5. Comparison 1 Brace versus no treatment, Outcome 5 Total adverse events.

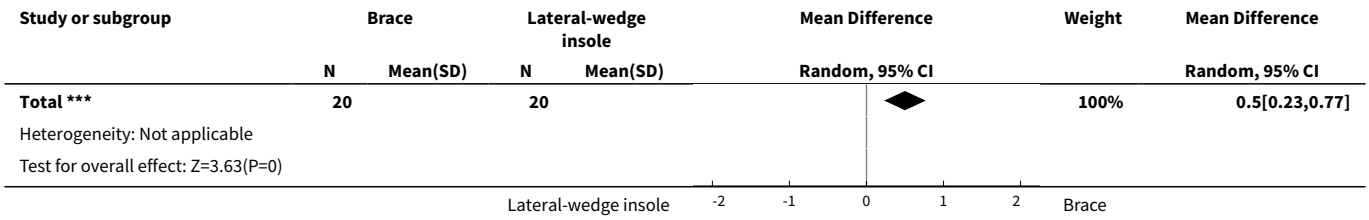


Comparison 2. Brace versus lateral wedge insole

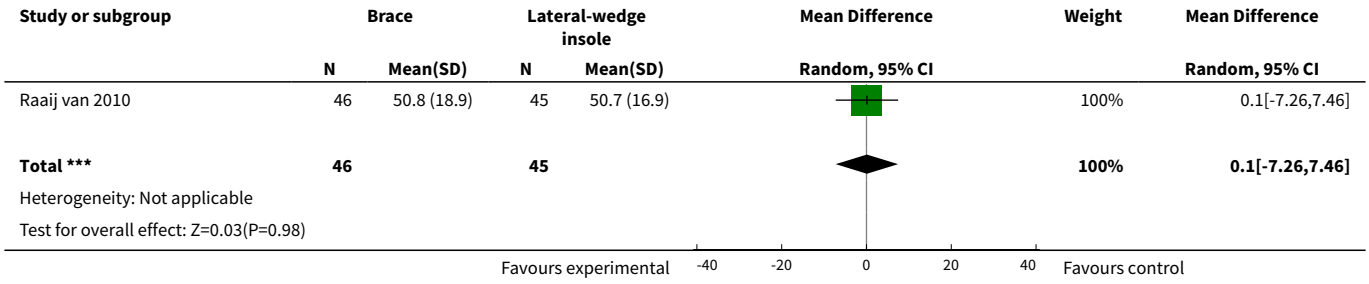
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Walking distance	1	40	Mean Difference (IV, Random, 95% CI)	0.5 [0.23, 0.77]
1.1 9 months	1	40	Mean Difference (IV, Random, 95% CI)	0.5 [0.23, 0.77]
2 WOMAC 6 months	1	91	Mean Difference (IV, Random, 95% CI)	0.10 [-7.26, 7.46]
3 Pain (VAS)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 6 months	1	91	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.15, 0.75]
3.2 9 months	1	40	Mean Difference (IV, Random, 95% CI)	-2.80 [-3.58, -2.02]

Analysis 2.1. Comparison 2 Brace versus lateral wedge insole, Outcome 1 Walking distance.

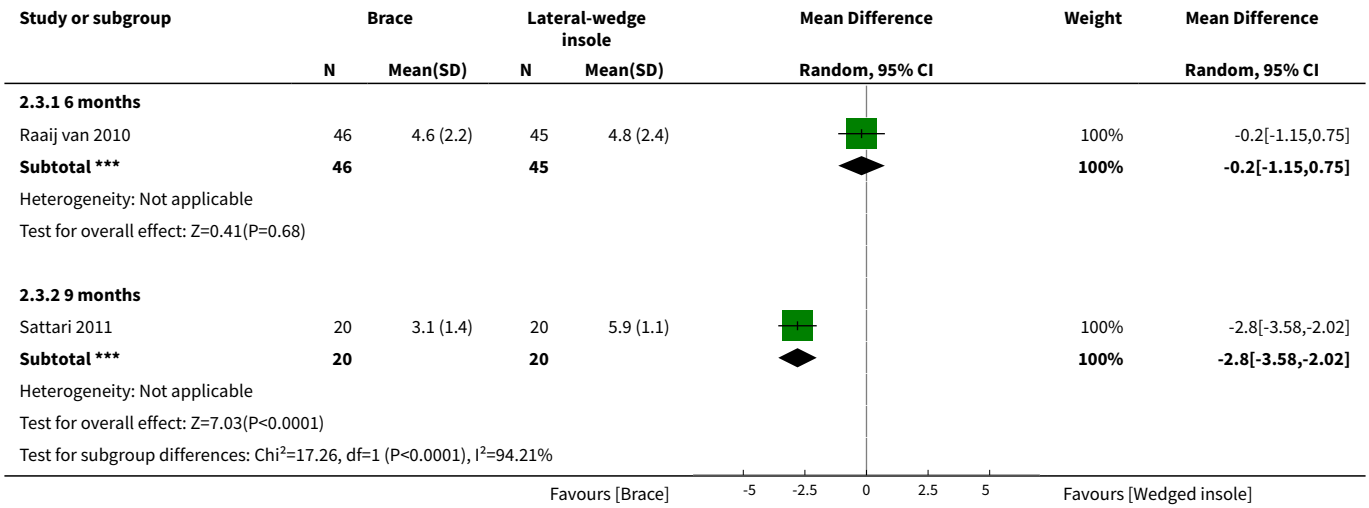




Analysis 2.2. Comparison 2 Brace versus lateral wedge insole, Outcome 2 WOMAC 6 months.



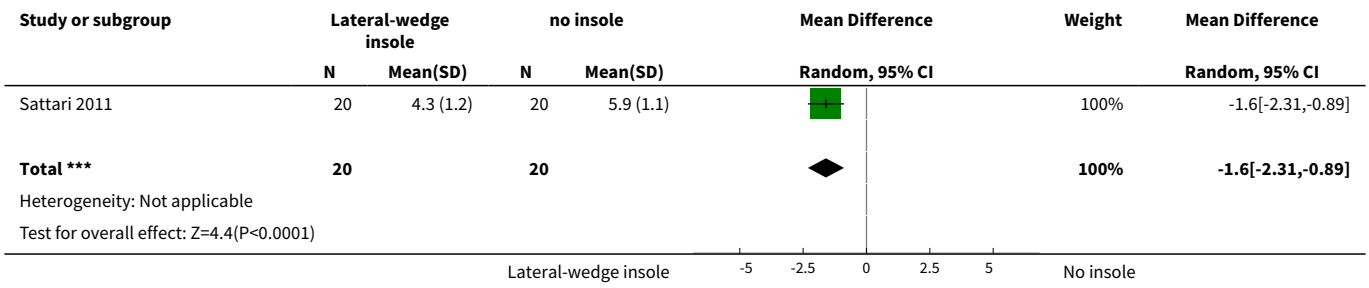
Analysis 2.3. Comparison 2 Brace versus lateral wedge insole, Outcome 3 Pain (VAS).



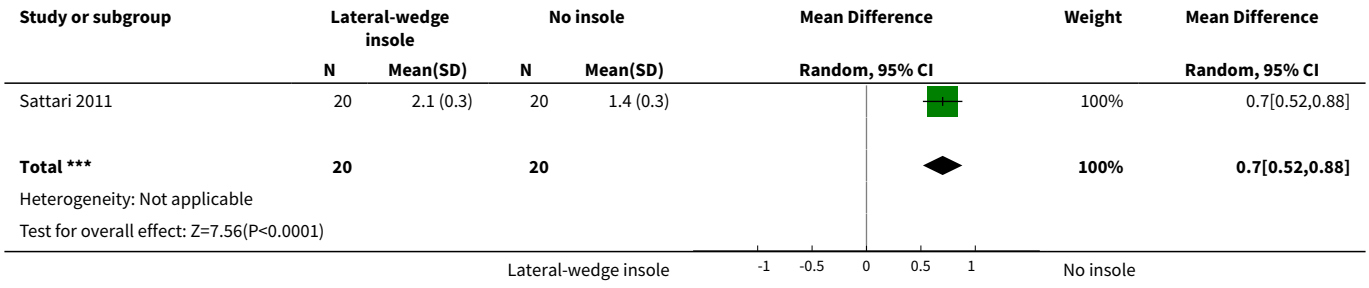
Comparison 3. Lateral wedge insole versus no insole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain (VAS)	1	40	Mean Difference (IV, Random, 95% CI)	-1.60 [-2.31, -0.89]
2 Walking distance (km)	1	40	Mean Difference (IV, Random, 95% CI)	0.70 [0.52, 0.88]

Analysis 3.1. Comparison 3 Lateral wedge insole versus no insole, Outcome 1 Pain (VAS).



Analysis 3.2. Comparison 3 Lateral wedge insole versus no insole, Outcome 2 Walking distance (km).



Comparison 4. Lateral wedge insole versus neutral insole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain (NRS)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Pain on walking 1 month	1	59	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.97, 0.77]
1.2 Maximum pain change with stairs 1 month	1	59	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Average pain at rest 12 months	1	179	Mean Difference (IV, Random, 95% CI)	-0.4 [-1.06, 0.26]
1.4 Pain on walking 12 months	2	224	Mean Difference (IV, Random, 95% CI)	0.10 [-0.45, 0.65]
1.5 Maximum pain change with stairs 12 months	1	45	Mean Difference (IV, Random, 95% CI)	0.0 [-0.58, 0.58]
2 Pain (WOMAC)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 1 month	2	206	Mean Difference (IV, Random, 95% CI)	1.17 [-7.69, 10.03]
2.2 3 months	1	147	Mean Difference (IV, Random, 95% CI)	5.5 [-1.95, 12.95]
2.3 6 months	1	147	Mean Difference (IV, Random, 95% CI)	6.40 [-0.07, 12.87]
2.4 12 months	3	358	Mean Difference (IV, Random, 95% CI)	0.89 [-2.89, 4.67]
2.5 24 months	1	106	Mean Difference (IV, Random, 95% CI)	2.80 [-6.12, 11.72]
3 Stiffness (WOMAC)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 1 month	2	206	Mean Difference (IV, Random, 95% CI)	5.74 [-0.49, 11.97]
3.2 3 months	1	147	Mean Difference (IV, Random, 95% CI)	4.20 [-2.61, 11.01]
3.3 6 months	1	147	Mean Difference (IV, Random, 95% CI)	6.0 [-0.48, 12.48]
3.4 12 months	3	358	Mean Difference (IV, Random, 95% CI)	0.07 [-4.96, 5.10]
3.5 24 months	1	106	Mean Difference (IV, Random, 95% CI)	1.80 [-7.22, 10.82]
4 Physical function (WOMAC)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.1 1 month	2	206	Mean Difference (IV, Random, 95% CI)	2.47 [-2.49, 7.44]
4.2 3 months	1	147	Mean Difference (IV, Random, 95% CI)	5.20 [-0.94, 11.34]
4.3 6 months	1	147	Mean Difference (IV, Random, 95% CI)	6.0 [-0.48, 12.48]
4.4 12 months	3	358	Mean Difference (IV, Random, 95% CI)	0.94 [-2.98, 4.87]
4.5 24 months	1	106	Mean Difference (IV, Random, 95% CI)	-0.40 [-9.47, 8.67]
5 Health-related quality of life	1	179	Mean Difference (IV, Random, 95% CI)	0.0 [-0.06, 0.06]
6 Physical activity scale for the elderly	1	179	Mean Difference (IV, Random, 95% CI)	15.0 [-8.45, 38.45]
7 Number of steps taken per day	1	179	Mean Difference (IV, Random, 95% CI)	1371.0 [38.53, 2703.47]
8 Global patient assessment at 24 months	1	106	Mean Difference (IV, Random, 95% CI)	1.60 [-7.41, 10.61]
9 Compliance at 6 months	1	156	Risk Ratio (M-H, Random, 95% CI)	1.18 [1.01, 1.38]
10 Time for negotiation of stairs	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.1 1 month	1	59	Mean Difference (IV, Random, 95% CI)	1.10 [-1.18, 3.38]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.2 12 months	1	45	Mean Difference (IV, Random, 95% CI)	-0.30 [-3.06, 2.46]
11 6-Minute walk distance	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 1 month	1	59	Mean Difference (IV, Random, 95% CI)	23.00 [-18.61, 64.61]
11.2 12 months	1	45	Mean Difference (IV, Random, 95% CI)	-25.20 [-77.37, 26.97]

Analysis 4.1. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 1 Pain (NRS).

Study or subgroup	Laterally wedged N	Laterally wedged Mean(SD)	Neutrally wedged N	Neutrally wedged Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
4.1.1 Pain on walking 1 month							
Barrios 2009	29	1.1 (1.8)	30	1.2 (1.6)		100%	-0.1[-0.97,0.77]
Subtotal ***	**29**		**30**			**100%**	**-0.1[-0.97,0.77]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.23(P=0.82)							
4.1.2 Maximum pain change with stairs 1 month							
Barrios 2009	29	0.6 (1)	30	0.5 (0)			Not estimable
Subtotal ***	**29**		**30**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
4.1.3 Average pain at rest 12 months							
Bennell 2011	89	0.9 (2.1)	90	1.3 (2.4)		100%	-0.4[-1.06,0.26]
Subtotal ***	**89**		**90**			**100%**	**-0.4[-1.06,0.26]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.19(P=0.24)							
4.1.4 Pain on walking 12 months							
Barrios 2009	20	1 (1.8)	25	1.1 (1.4)		33.11%	-0.1[-1.06,0.86]
Bennell 2011	89	3.2 (2.1)	90	3 (2.5)		66.89%	0.2[-0.48,0.88]
Subtotal ***	**109**		**115**			**100%**	**0.1[-0.45,0.65]**
Heterogeneity: Tau^2=0; Chi^2=0.25, df=1(P=0.62); I^2=0%							
Test for overall effect: Z=0.36(P=0.72)							
4.1.5 Maximum pain change with stairs 12 months							
Barrios 2009	20	0.5 (0.9)	25	0.5 (1.1)		100%	0[-0.58,0.58]
Subtotal ***	**20**		**25**			**100%**	**0[-0.58,0.58]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Chi^2=1.38, df=1 (P=0.71), I^2=0%							

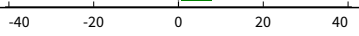
Laterally wedged Neutrally wedged

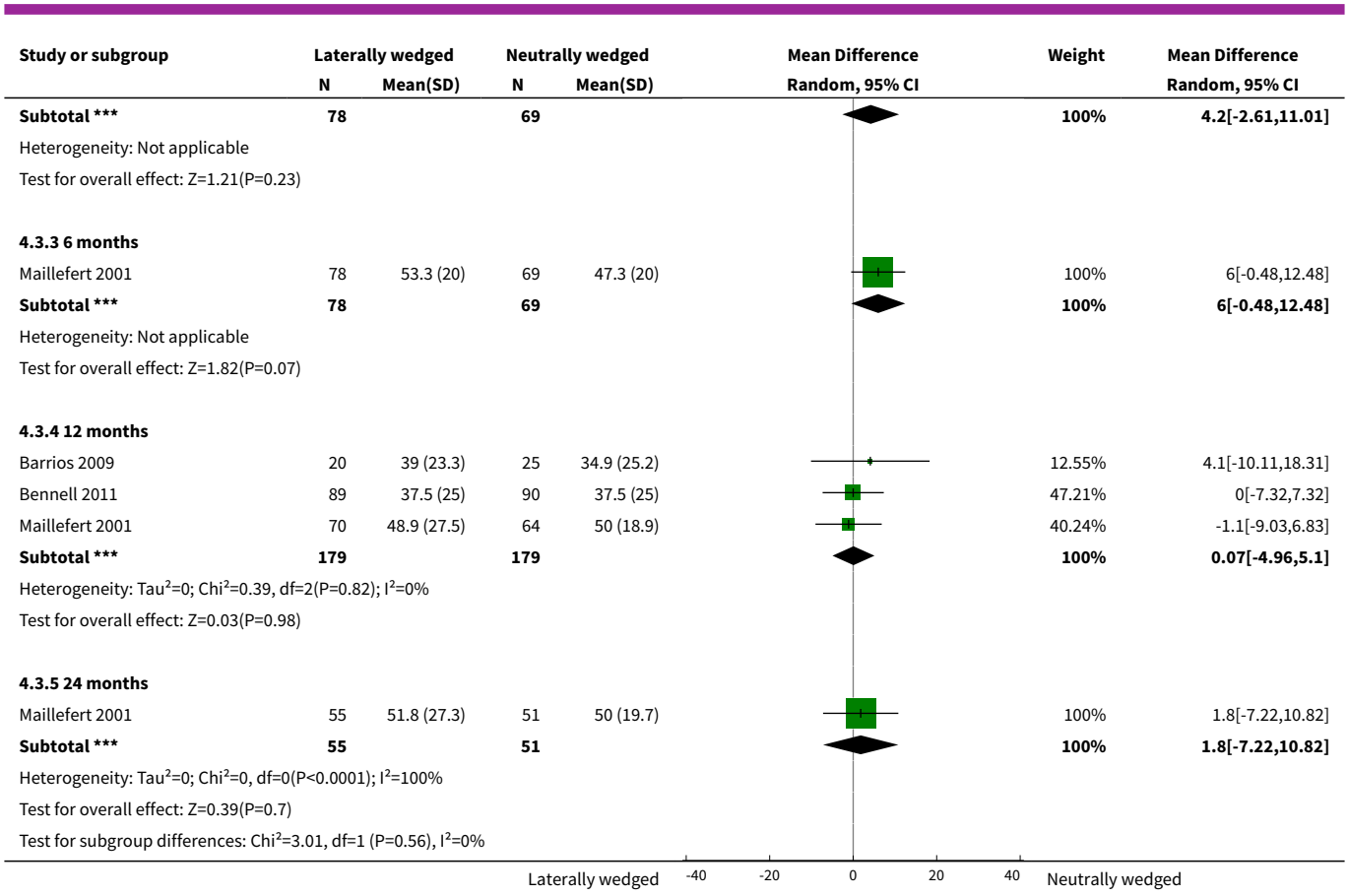
Analysis 4.2. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 2 Pain (WOMAC).

Study or subgroup	Laterally wedged N	Laterally wedged Mean(SD)	Neutrally wedged N	Neutrally wedged Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
4.2.1 1 month							
Barrios 2009	29	31.4 (17.6)	30	35.3 (15.6)		44.28%	-3.9[-12.4,4.6]
Maillefert 2001	78	54.1 (19)	69	48.9 (18)		55.72%	5.2[-0.78,11.18]
Subtotal ***	**107**		**99**			**100%**	**1.17[-7.69,10.03]**
Heterogeneity: Tau^2=27.35; Chi^2=2.95, df=1(P=0.09); I^2=66.05%							
Test for overall effect: Z=0.26(P=0.8)							
4.2.2 3 months							
Maillefert 2001	78	54 (23)	69	48.5 (23)		100%	5.5[-1.95,12.95]
Subtotal ***	**78**		**69**			**100%**	**5.5[-1.95,12.95]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.45(P=0.15)							
4.2.3 6 months							
Maillefert 2001	78	52.8 (22)	69	46.4 (18)		100%	6.4[-0.07,12.87]
Subtotal ***	**78**		**69**			**100%**	**6.4[-0.07,12.87]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=1.94(P=0.05)							
4.2.4 12 months							
Barrios 2009	20	30.2 (21)	25	32.7 (15.3)		11.82%	-2.5[-13.49,8.49]
Bennell 2011	89	32 (16.5)	90	31 (16)		62.88%	1[-3.76,5.76]
Maillefert 2001	70	50.1 (24.8)	64	47.9 (19.4)		25.31%	2.2[-5.31,9.71]
Subtotal ***	**179**		**179**			**100%**	**0.89[-2.89,4.67]**
Heterogeneity: Tau^2=0; Chi^2=0.48, df=2(P=0.78); I^2=0%							
Test for overall effect: Z=0.46(P=0.64)							
4.2.5 24 months							
Maillefert 2001	55	51 (26.7)	51	48.2 (19.9)		100%	2.8[-6.12,11.72]
Subtotal ***	**55**		**51**			**100%**	**2.8[-6.12,11.72]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.62(P=0.54)							
Test for subgroup differences: Chi^2=2.79, df=1 (P=0.59), I^2=0%							

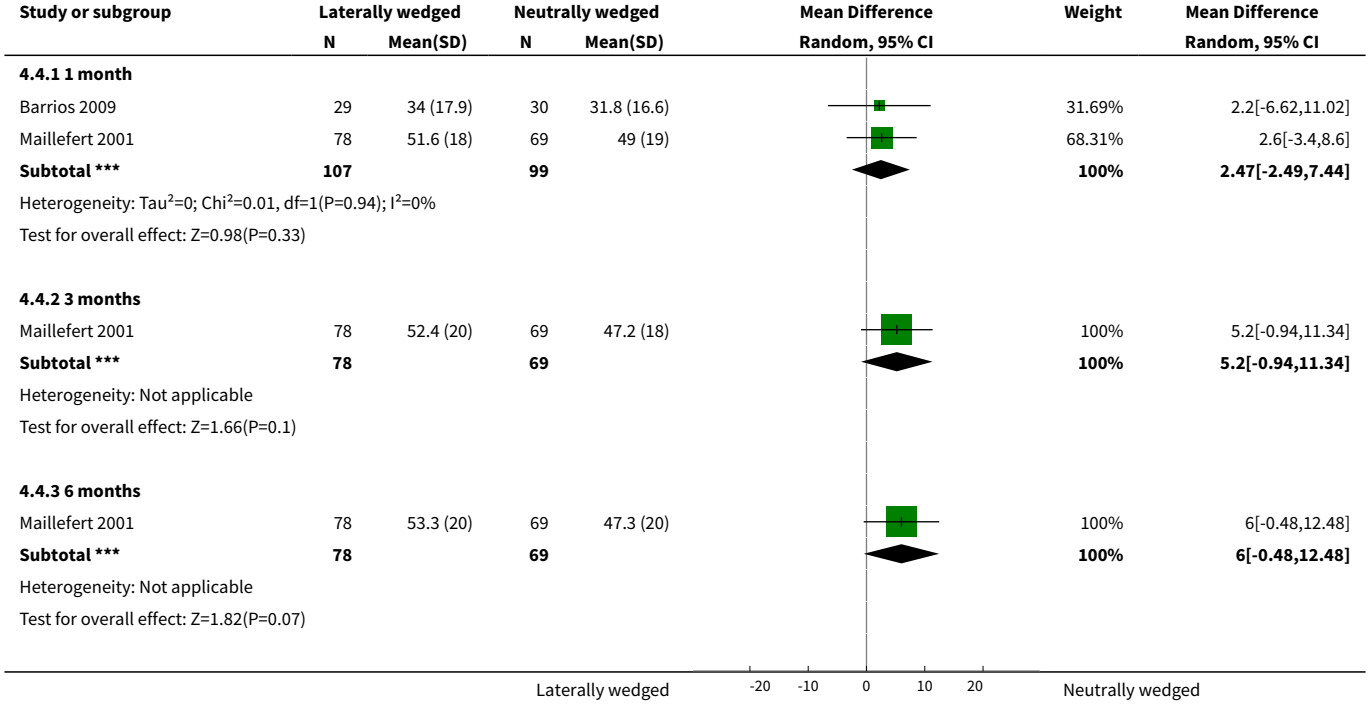
Analysis 4.3. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 3 Stiffness (WOMAC).

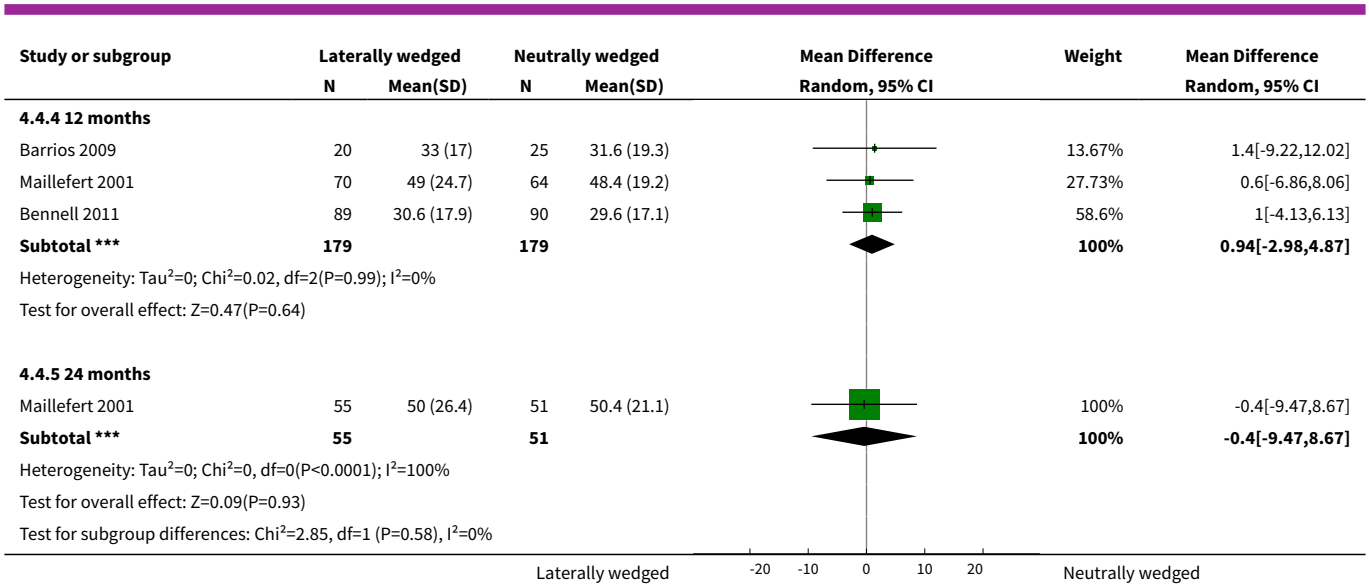
Study or subgroup	Laterally wedged N	Laterally wedged Mean(SD)	Neutrally wedged N	Neutrally wedged Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
4.3.1 1 month							
Barrios 2009	29	43.5 (22.5)	30	37.2 (22.1)		29.99%	6.3[-5.08,17.68]
Maillefert 2001	78	54 (23)	69	48.5 (23)		70.01%	5.5[-1.95,12.95]
Subtotal ***	**107**		**99**			**100%**	**5.74[-0.49,11.97]**
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.91); I^2=0%							
Test for overall effect: Z=1.8(P=0.07)							
4.3.2 3 months							
Maillefert 2001	78	53 (24)	69	48.8 (18)		100%	4.2[-2.61,11.01]



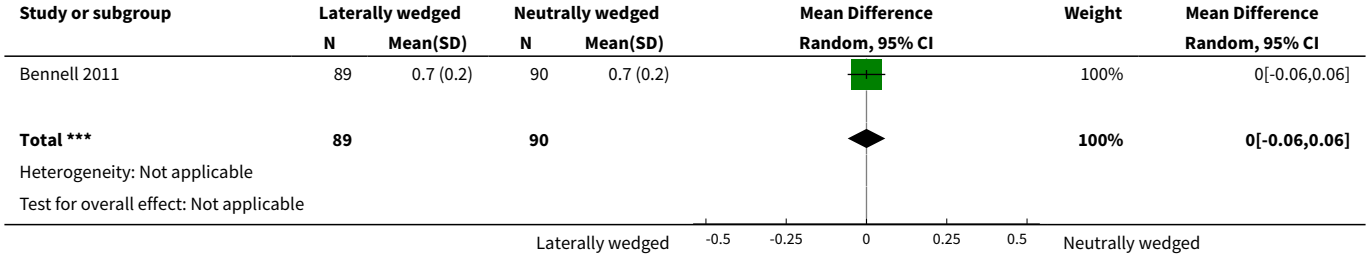


Analysis 4.4. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 4 Physical function (WOMAC).

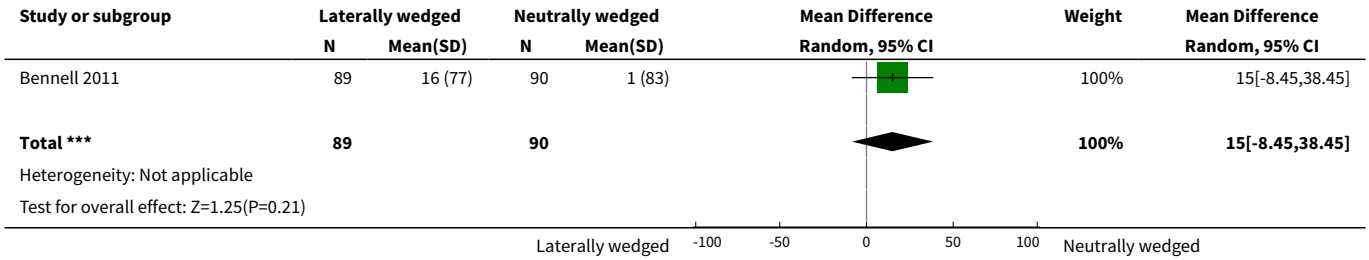




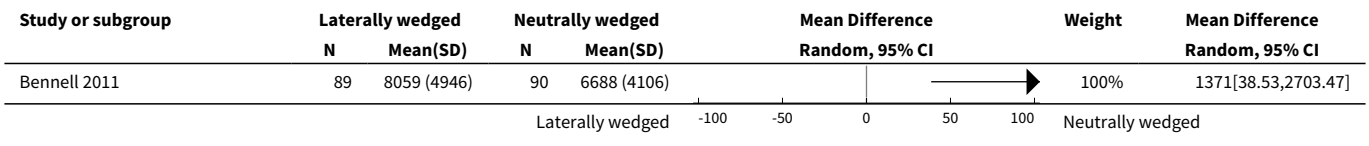
Analysis 4.5. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 5 Health-related quality of life.

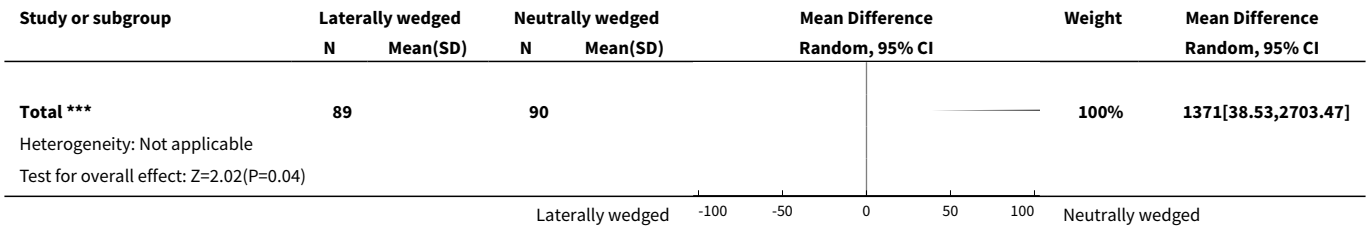


Analysis 4.6. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 6 Physical activity scale for the elderly.

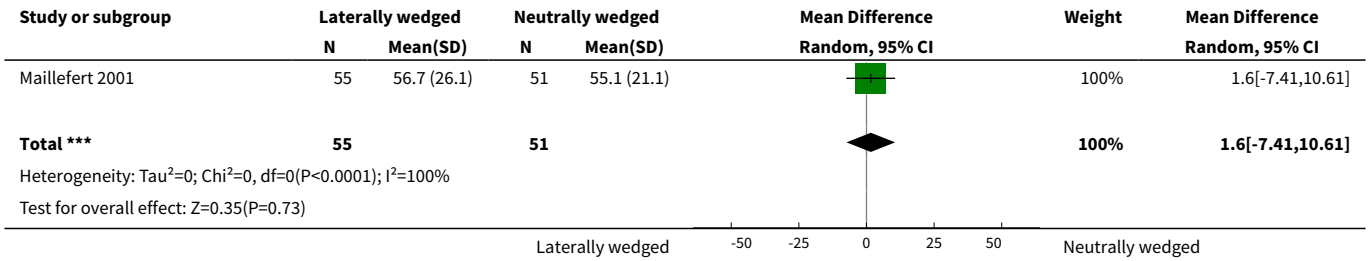


Analysis 4.7. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 7 Number of steps taken per day.

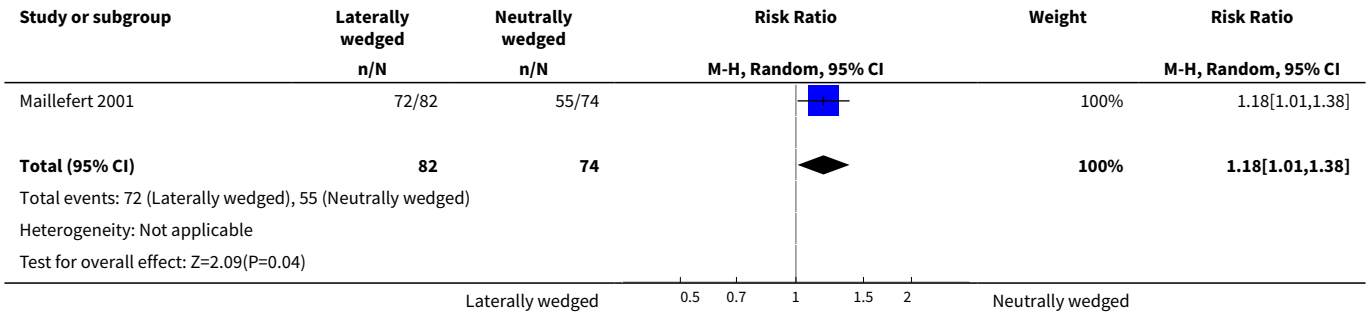




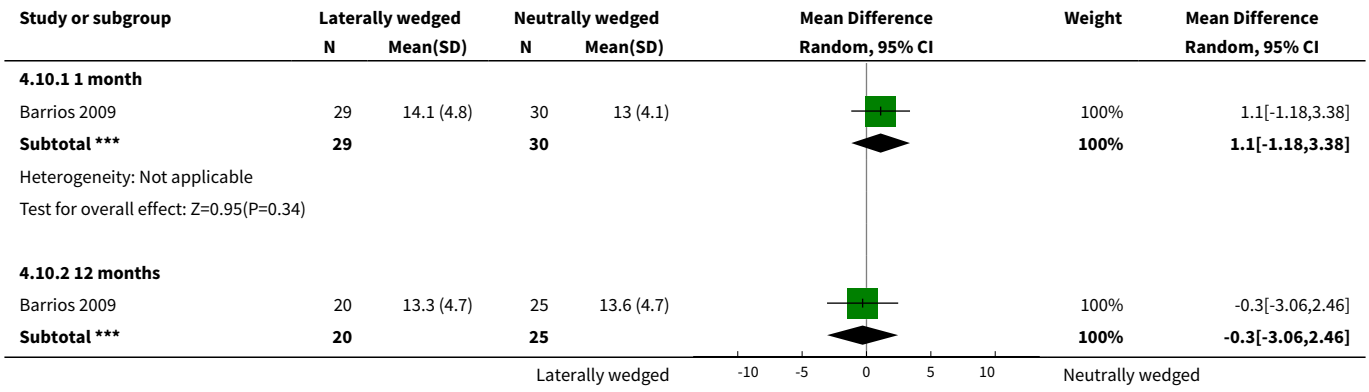
Analysis 4.8. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 8 Global patient assessment at 24 months.

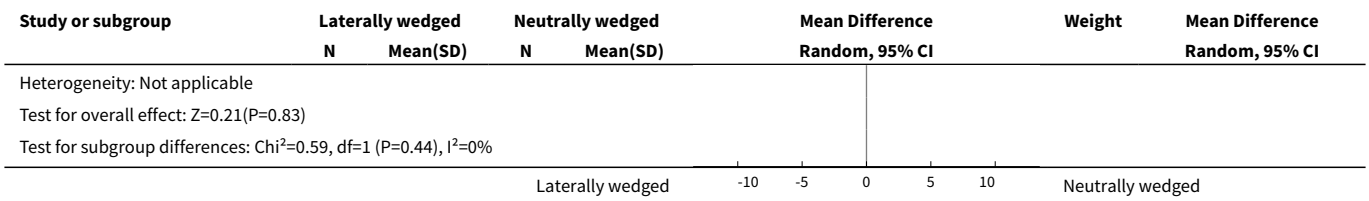


Analysis 4.9. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 9 Compliance at 6 months.

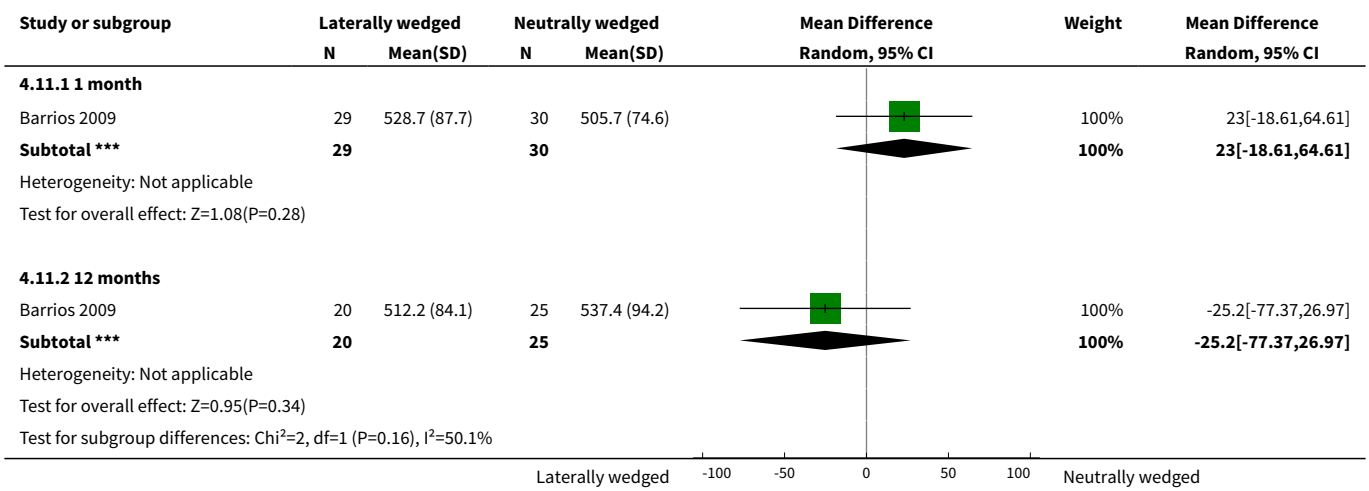


Analysis 4.10. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 10 Time for negotiation of stairs.





Analysis 4.11. Comparison 4 Lateral wedge insole versus neutral insole, Outcome 11 6-Minute walk distance.



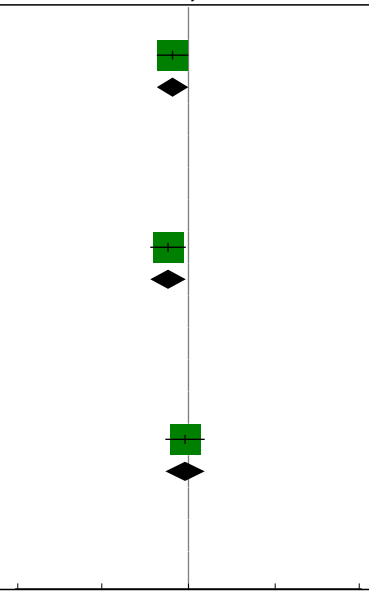
Comparison 5. Subtalar strapped insole versus inserted lateral wedge insole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain (VAS)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 8 weeks	1	90	Mean Difference (IV, Random, 95% CI)	-9.20 [-18.28, -0.12]
1.2 6 months	1	61	Mean Difference (IV, Random, 95% CI)	-11.80 [-22.04, -1.56]
1.3 24 months	1	42	Mean Difference (IV, Random, 95% CI)	-2.0 [-13.34, 9.34]
2 Lequesne index	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 8 weeks	1	90	Mean Difference (IV, Random, 95% CI)	-0.60 [-2.81, 1.61]
2.2 6 months	1	61	Mean Difference (IV, Random, 95% CI)	-1.5 [-4.23, 1.23]
2.3 24 months	1	42	Mean Difference (IV, Random, 95% CI)	-2.3 [-5.45, 0.85]
3 FTA - angle	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 8 weeks	1	90	Mean Difference (IV, Random, 95% CI)	-1.30 [-3.45, 0.85]
3.2 6 months	1	61	Mean Difference (IV, Random, 95% CI)	-1.00 [-5.84, -0.16]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.3 24 months	1	42	Mean Difference (IV, Random, 95% CI)	-2.70 [-5.13, -0.27]
4 Side effects at 8 weeks	1	90	Risk Ratio (M-H, Fixed, 95% CI)	5.74 [0.72, 45.77]

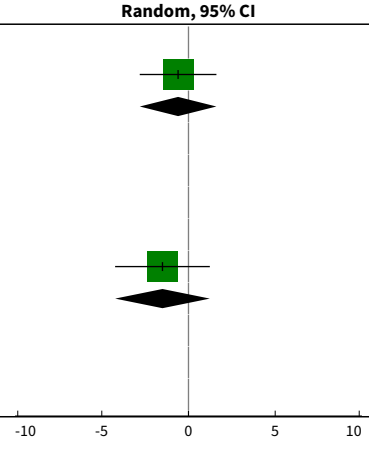
Analysis 5.1. Comparison 5 Subtalar strapped insole versus inserted lateral wedge insole, Outcome 1 Pain (VAS).

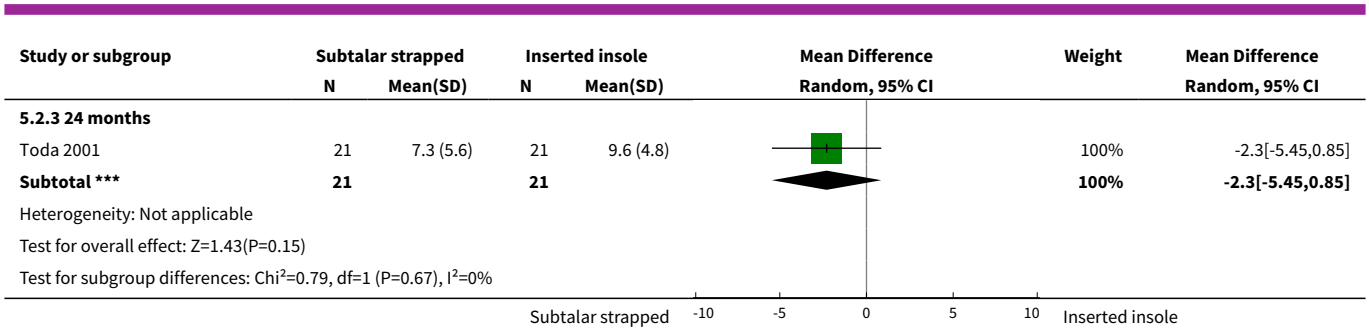
Study or subgroup	Subtalar strapped N	Subtalar strapped Mean(SD)	Inserted insole N	Inserted insole Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.1.1 8 weeks							
Toda 2001	46	34.6 (21.3)	44	43.8 (22.6)		100%	-9.2[-18.28,-0.12]
Subtotal ***	**46**		**44**			**100%**	**-9.2[-18.28,-0.12]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.99(P=0.05)							
5.1.2 6 months							
Toda 2001	29	32.7 (20.7)	32	44.5 (20)		100%	-11.8[-22.04,-1.56]
Subtotal ***	**29**		**32**			**100%**	**-11.8[-22.04,-1.56]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.26(P=0.02)							
5.1.3 24 months							
Toda 2001	21	39.6 (18.7)	21	41.6 (18.8)		100%	-2[-13.34,9.34]
Subtotal ***	**21**		**21**			**100%**	**-2[-13.34,9.34]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.35(P=0.73)							
Test for subgroup differences: Chi^2=1.67, df=1 (P=0.43), I^2=0%							



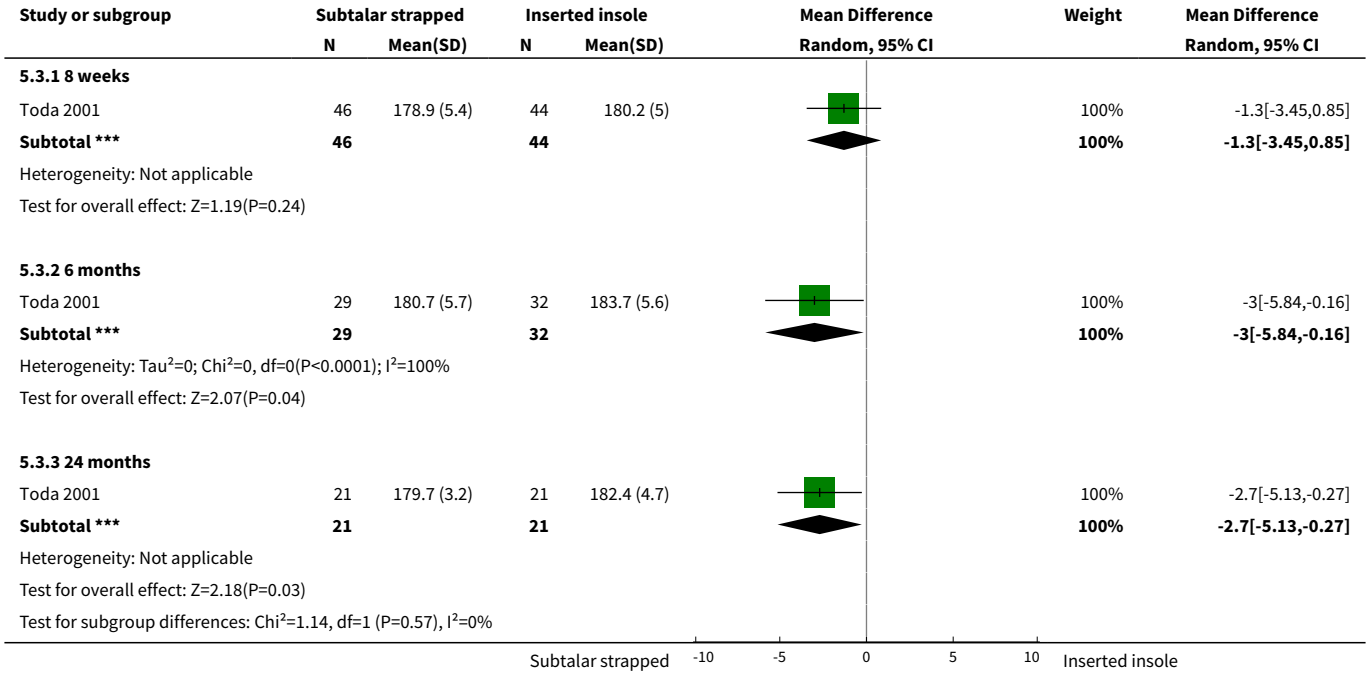
Analysis 5.2. Comparison 5 Subtalar strapped insole versus inserted lateral wedge insole, Outcome 2 Lequesne index.

Study or subgroup	Subtalar strapped N	Subtalar strapped Mean(SD)	Inserted insole N	Inserted insole Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.2.1 8 weeks							
Toda 2001	46	8.2 (5.4)	44	8.8 (5.3)		100%	-0.6[-2.81,1.61]
Subtotal ***	**46**		**44**			**100%**	**-0.6[-2.81,1.61]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.53(P=0.59)							
5.2.2 6 months							
Toda 2001	29	7.5 (5.8)	32	9 (5)		100%	-1.5[-4.23,1.23]
Subtotal ***	**29**		**32**			**100%**	**-1.5[-4.23,1.23]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.08(P=0.28)							

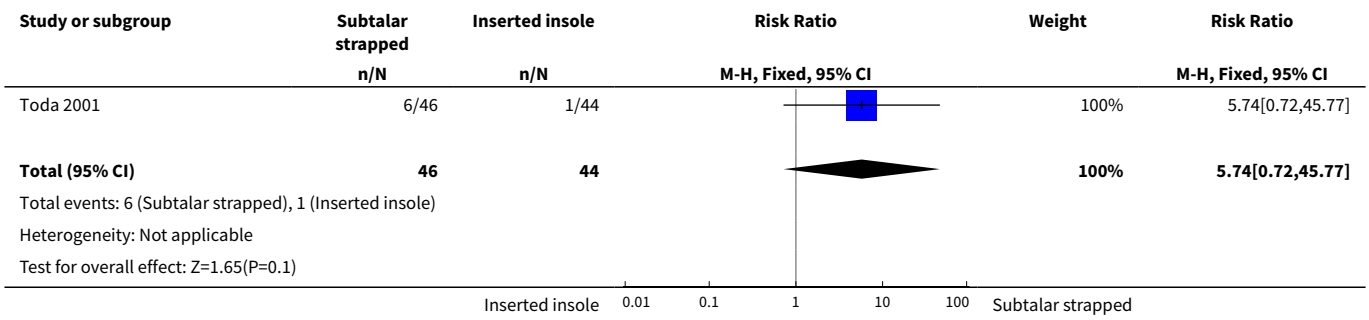




Analysis 5.3. Comparison 5 Subtalar strapped insole versus inserted lateral wedge insole, Outcome 3 FTA - angle.



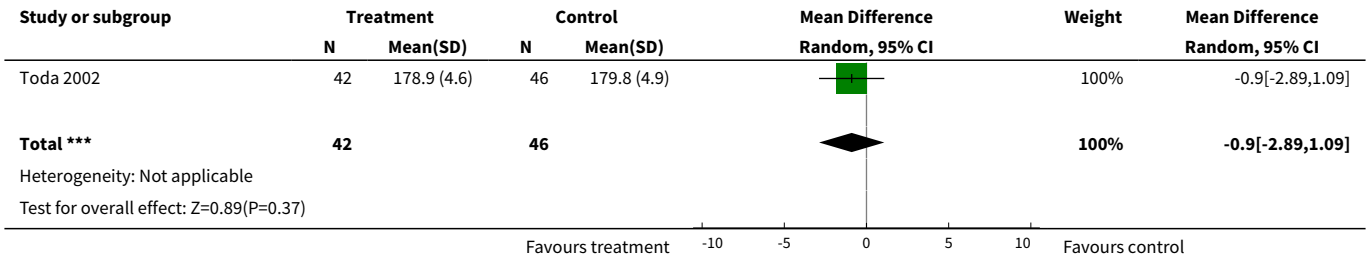
Analysis 5.4. Comparison 5 Subtalar strapped insole versus inserted lateral wedge insole, Outcome 4 Side effects at 8 weeks.



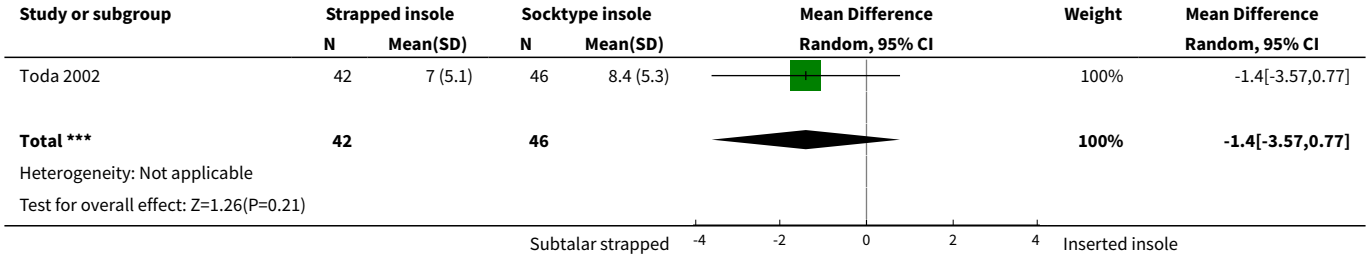
Comparison 6. Subtalar strapped insole versus sock-type insole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 FTA angle	1	88	Mean Difference (IV, Random, 95% CI)	-0.90 [-2.89, 1.09]
2 Aggregate score	1	88	Mean Difference (IV, Random, 95% CI)	-1.40 [-3.57, 0.77]

Analysis 6.1. Comparison 6 Subtalar strapped insole versus sock-type insole, Outcome 1 FTA angle.



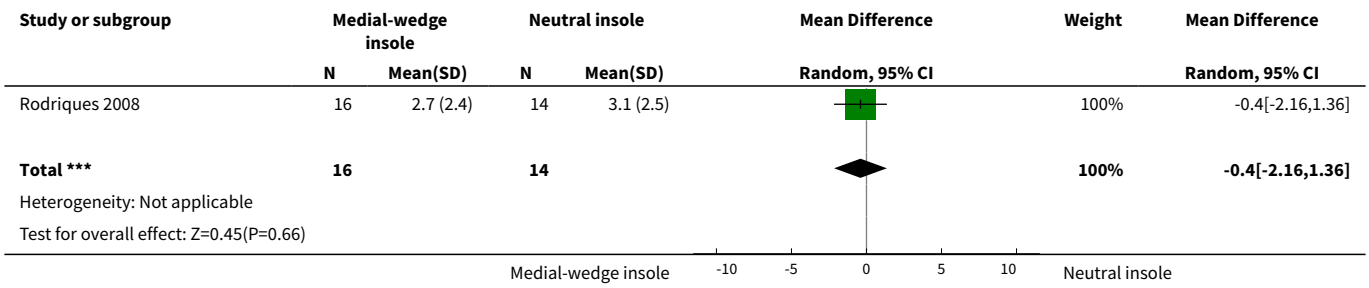
Analysis 6.2. Comparison 6 Subtalar strapped insole versus sock-type insole, Outcome 2 Aggregate score.



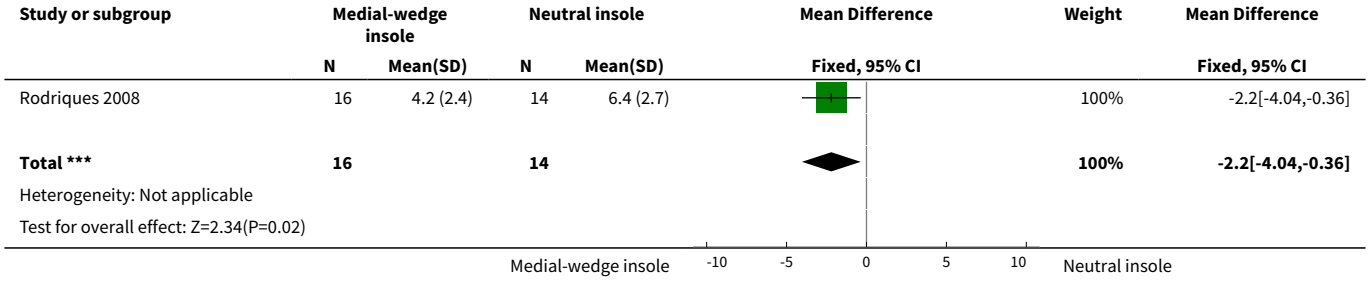
Comparison 7. Medial wedge insole versus neutral insole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 VAS rest	1	30	Mean Difference (IV, Random, 95% CI)	-0.40 [-2.16, 1.36]
2 VAS movement	1	30	Mean Difference (IV, Fixed, 95% CI)	-2.2 [-4.04, -0.36]
3 VAS night	1	30	Mean Difference (IV, Fixed, 95% CI)	-1.50 [-3.12, 0.12]
4 WOMAC	1	30	Mean Difference (IV, Fixed, 95% CI)	-6.70 [-17.09, 3.69]
5 Lequesne	1	30	Mean Difference (IV, Fixed, 95% CI)	-2.40 [-5.28, 0.48]

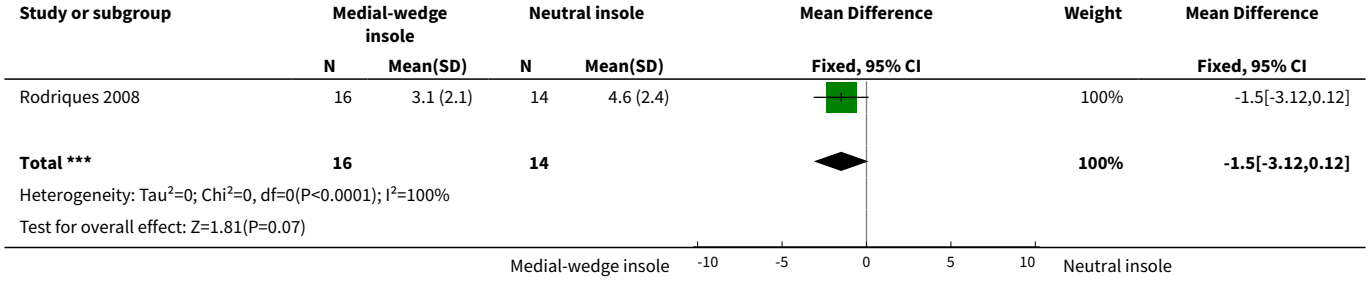
Analysis 7.1. Comparison 7 Medial wedge insole versus neutral insole, Outcome 1 VAS rest.



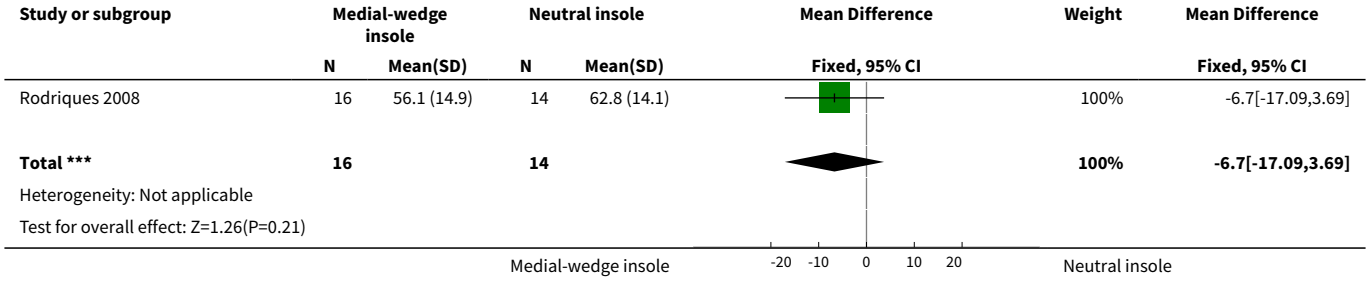
Analysis 7.2. Comparison 7 Medial wedge insole versus neutral insole, Outcome 2 VAS movement.



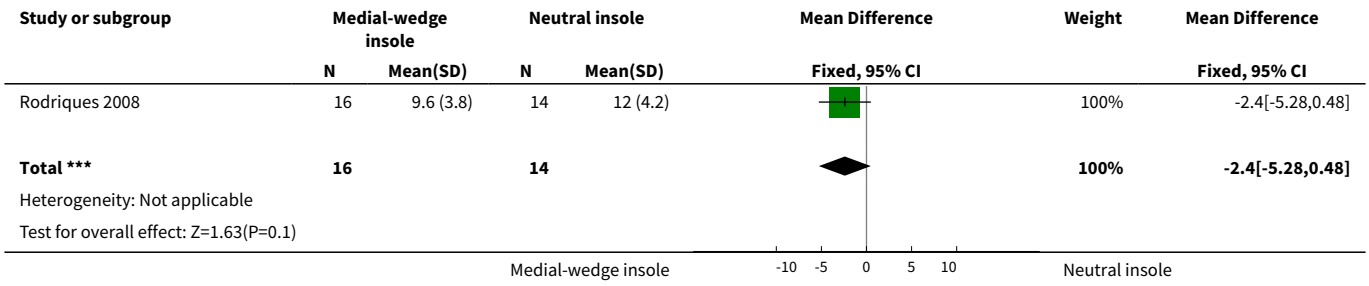
Analysis 7.3. Comparison 7 Medial wedge insole versus neutral insole, Outcome 3 VAS night.



Analysis 7.4. Comparison 7 Medial wedge insole versus neutral insole, Outcome 4 WOMAC.



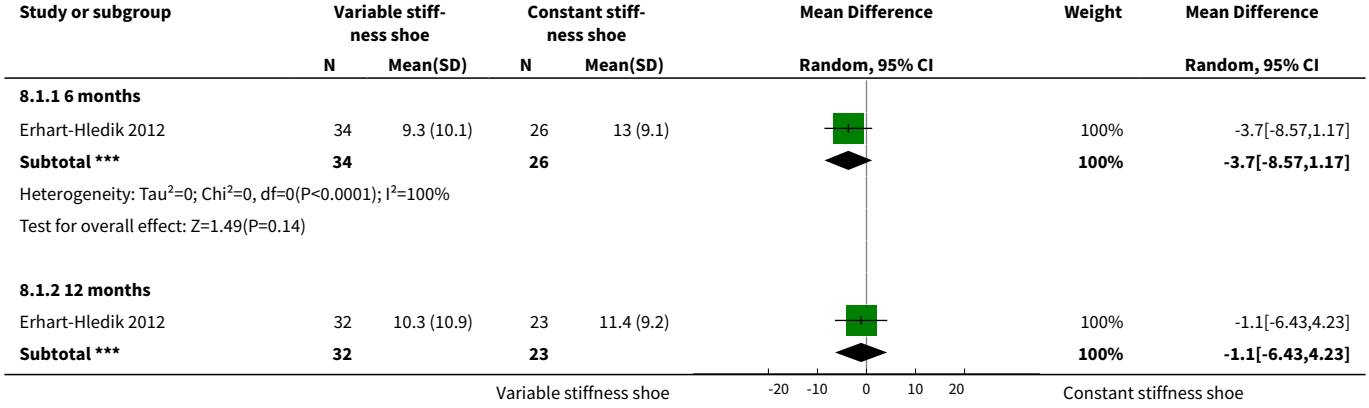
Analysis 7.5. Comparison 7 Medial wedge insole versus neutral insole, Outcome 5 Lequesne.

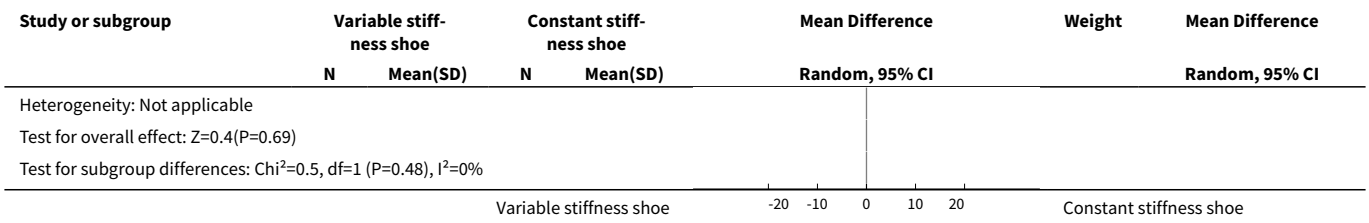


Comparison 8. Variable stiffness shoe versus constant stiffness shoe

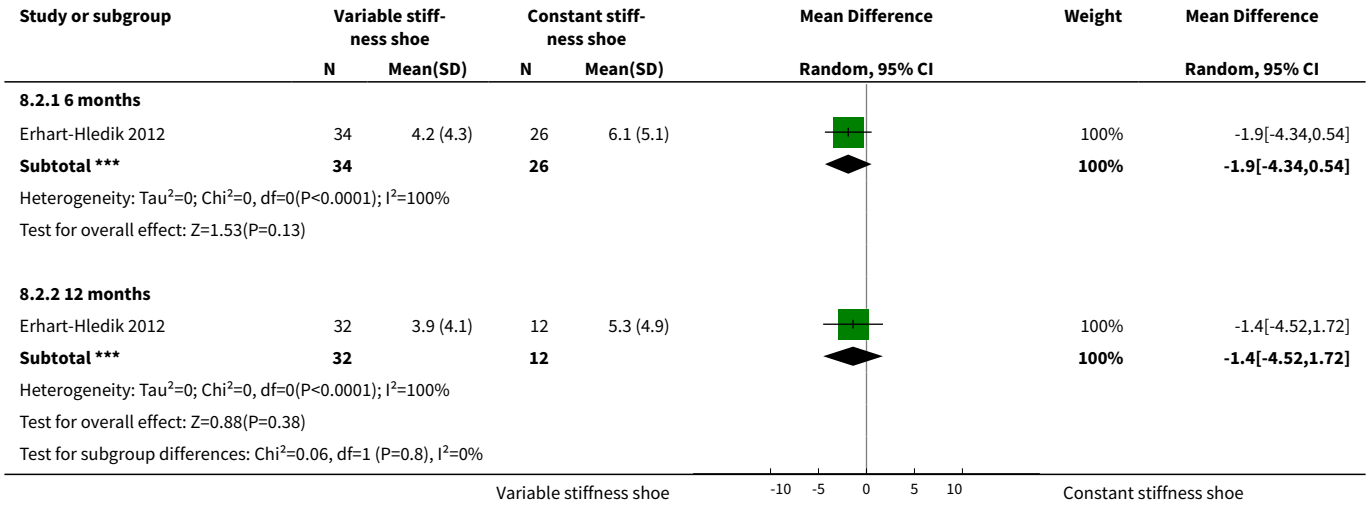
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Pain (WOMAC)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 6 months	1	60	Mean Difference (IV, Random, 95% CI)	-3.70 [-8.57, 1.17]
1.2 12 months	1	55	Mean Difference (IV, Random, 95% CI)	-1.10 [-6.43, 4.23]
2 Stiffness (WOMAC)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 6 months	1	60	Mean Difference (IV, Random, 95% CI)	-1.90 [-4.34, 0.54]
2.2 12 months	1	44	Mean Difference (IV, Random, 95% CI)	-1.40 [-4.52, 1.72]
3 Physical function (WOMAC)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 6 months	1	60	Mean Difference (IV, Random, 95% CI)	-6.90 [-24.14, 10.34]
3.2 12 months	1	55	Mean Difference (IV, Random, 95% CI)	-4.90 [-24.54, 14.74]

Analysis 8.1. Comparison 8 Variable stiffness shoe versus constant stiffness shoe, Outcome 1 Pain (WOMAC).

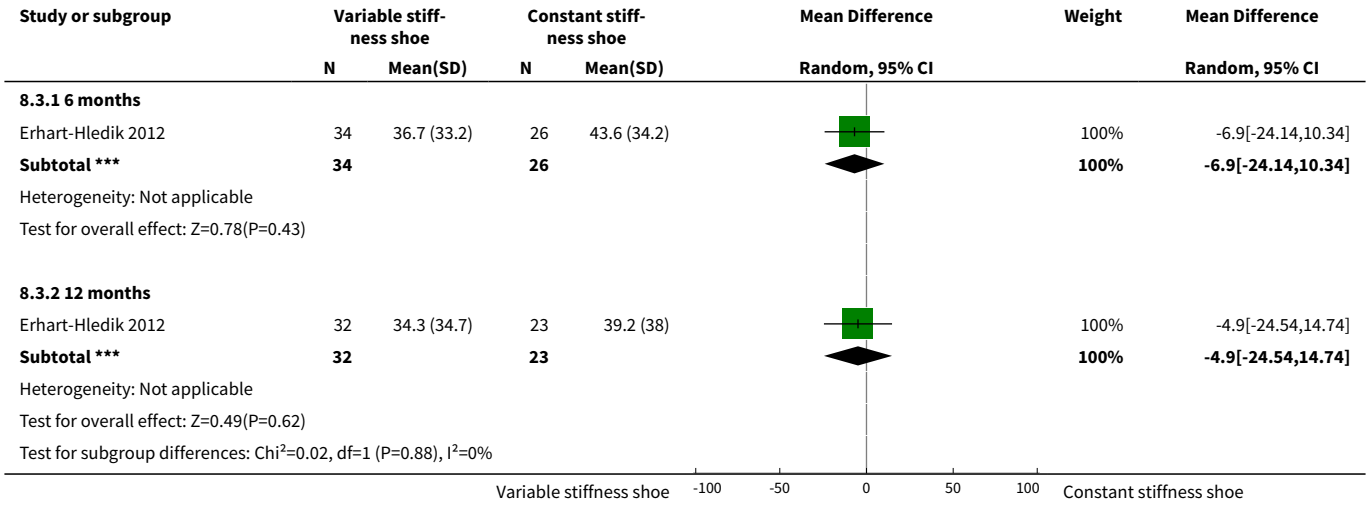




Analysis 8.2. Comparison 8 Variable stiffness shoe versus constant stiffness shoe, Outcome 2 Stiffness (WOMAC).



Analysis 8.3. Comparison 8 Variable stiffness shoe versus constant stiffness shoe, Outcome 3 Physical function (WOMAC).



APPENDICES

Appendix 1. Search strategy and summary of results

Database: MEDLINE Ovid SP

Search strategy:

("osteoarthritis, knee"/ OR ((osteoarthritis/ OR (osteoarthritis OR osteoarthrosis OR "degenerative joint disease" OR "osteo arthritis" OR "osteo arthrosis" OR "degenerative arthritis").ab,ti.) AND ("knee joint"/ OR (knee*).ab,ti.))) AND (exp "Orthotic Devices"/ OR (brace* OR bracing OR orthotic* OR orthoses OR orthosis).ab,ti.)

Database: EMBASE

Search strategy:

('knee osteoarthritis'/de OR ((osteoarthritis/de OR (osteoarthritis OR osteoarthrosis OR 'degenerative joint disease' OR 'osteo arthritis' OR 'osteo arthrosis' OR 'degenerative arthritis'):ab,ti) AND (knee/de OR (knee*):ab,ti))) AND (orthosis/de OR (brace* OR bracing OR orthotic* OR orthoses OR orthosis):ab,ti) AND [01-05-2007]/sd

Database: *The Cochrane Library*

Search strategy

((((osteoarthritis OR osteoarthrosis OR 'degenerative joint disease' OR 'osteo arthritis' OR 'osteo arthrosis' OR 'degenerative arthritis'):ab,ti) AND ((knee*):ab,ti))) AND ((brace* OR bracing OR orthotic* OR orthoses OR orthosis):ab,ti)

Database and coverage	Search date	Number of references retrieved	Number of references after de-duplication
MEDLINE Ovid SP 2007-2013	March 1, 2014	82	56
EMBASE 2007-2013	March 1, 2014	167	161
The Cochrane Library	March 1, 2014	23	11
	Totals	**272**	**228**

WHAT'S NEW

Date	Event	Description
1 March 2014	New search has been performed	New search with 6 new studies
1 March 2014	New citation required but conclusions have not changed	Change in authorship

HISTORY

Protocol first published: Issue 1, 2003

Review first published: Issue 1, 2005

Date	Event	Description
2 May 2011	Amended	Converted to new review format. CMSG ID C102-R
21 August 2007	New search has been performed	Minor update approved: 8/20/07 New studies found and included or excluded: 5/31/07 See published notes for additional details
17 November 2004	New citation required and conclusions have changed	Substantive amendments made

CONTRIBUTIONS OF AUTHORS

Reinoud Brouwer (RB) proposed the review. RB, Sita Bierma-Zeinstra (SB) and Arianne Verhagen (AV) wrote the protocol. RB, Tom van Raaij (TR) and Tijs Duivenvoorden (TD) selected the studies following review of the abstracts. RB, TD and TR made the final selection after reading the full articles. RB, TD, SB and Jan Verhaar (JV) assessed methodological quality. RB, TD and AV performed data extraction. With contributions from all co-authors, RB wrote the review.

DECLARATIONS OF INTEREST

Conflict of interest is possible because two included studies (Brouwer 2006; Raaij van 2010) were conducted by four of the authors (RB, TR, SB, JV) of this systematic review.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

No major differences exist between the protocol and the review.

NOTES

This is an update of the original review, which was published in Issue 1, 2005. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE for controlled clinical trials until May 2007. As a result of the search, we have included six new studies in this updated review. The conclusions of this update are consistent with those provided in the original review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Orthotic Devices; Braces; Osteoarthritis, Knee [*therapy]; Quality of Life; Randomized Controlled Trials as Topic; Shoes

MeSH check words

Humans