The effects of various physical non-operative modalities on the pain in osteoarthritis of the knee

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The purpose of this study was to evaluate the effect of various non-operative modalities of treatment (transcutaneous electrical nerve stimulation (TENS); neuromuscular electrical stimulation (NMES); insoles and bracing) on the pain of osteoarthritis (OA) of the knee.

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to identify the therapeutic options which are commonly adopted for the management of osteoarthritis (OA) of the knee.

The outcome measurement tools used in the different studies were the visual analogue scale and The Western Ontario and McMaster Universities Arthritis Index pain index: all pain scores were converted to a 100-point scale.

A total of 30 studies met our inclusion criteria: 13 on insoles, seven on TENS, six on NMES, and four on bracing. The standardised mean difference (SMD) in pain after treatment with TENS was 1.796, which represented a significant reduction in pain. The significant overall effect estimate for NMES on pain was similar to that of TENS, with a SMD of 1.924. The overall effect estimate of insoles on pain was a SMD of 0.992. The overall effect of bracing showed a significant reduction in pain of 1.34.

Overall, all four non-operative modalities of treatment were found to have a significant effect on the reduction of pain in OA of the knee.

This study shows that non-operative physical modalities of treatment are of benefit when treating OA of the knee. However, much of the literature reviewed evaluates studies with follow-up of less than six months: future work should aim to evaluate patients with longer follow-up.

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Arthritis is the most common cause of disability reported by the Centers for Disease Control and Prevention (CDC). One in five adults (22.7% of the population) report a diagnosis of arthritis according to a 2010 to 2012 study from the National Health Interview Survey, while 49.7% of adults aged 65 years or more reported a diagnosis of arthritis.

Osteoarthritis (OA) of the knee is a progressive and debilitating condition, characterised by marked pain and stiffness, which frequently causes physical disability. This affects the patient's ability to function, as manifested by a loss of working days and the ability to perform activities of daily living. OA also places a substantial financial burden on the healthcare system. In 2003, the CDC's Medical Expenditure Panel Survey estimated that the total cost attributed to arthritis and other rheumatic conditions in the United States was $128 billion ($162.5 billion in 2015), an almost two-fold increase from $86.2 billion in 1997. Because of the clear functional and financial impact of this disease, the way in which OA is managed is important. There are various treatment options for OA of the knee depending on the stage of the disease. In its most advanced stage, surgery is the treatment of choice. However, in less advanced cases, there are a number of non-operative alternatives. Among them are invasive techniques such as injections and pharmaceuticals, both of which can carry serious risks and increase costs. More non-operative measures have gained popularity in recent years, the most frequently used being transcutaneous electrical nerve stimulation (TENS), neuromuscular electrical stimulation (NMES), insoles, and bracing.

There have been a number of studies which describe and evaluate the efficacy of these non-operative interventions to control pain, but limited systematic reviews which compare the different modalities of treatment.
The purpose of this study was to assess the efficacy of various non-operative modalities of treatment in relieving the pain caused by OA of the knee. We therefore conducted a comprehensive review of the available literature to examine their efficacy.

Materials and Methods
We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses\(^4\) to conduct a literature search of clinical studies to identify non-operative physical modalities of treatment commonly used for the management of OA of the knee. We used the following search engines: MEDLINE (PubMed), Ovid, and Embase. Two of the co-authors (AL, JJC) evaluated all studies published between January 2000 and December 2014 using a combination of search terms including: “TENS AND Knee osteoarthritis”; “NMES AND Knee osteoarthritis”; “insoles AND Knee osteoarthritis” and “bracing AND Knee osteoarthritis”. A total of 352 papers were identified. The authors read all abstracts to assess the articles for eligibility using the following inclusion criteria: full-text reports; randomised controlled trials (RCTs); cohort studies; randomised crossover studies; studies involving patients with OA of the knee; studies containing one of the non-operative treatments of interest (insoles, bracing, TENS, or NMES); studies that reported pain as an outcome measure; studies that reported mean and standard deviation for both pre- and post-treatment pain scale and studies which reported outcomes for ≥ two weeks. We excluded papers published in languages other than English; studies in which the outcome measures did not include pain; studies that evaluated the use of other non-operative modalities such as pharmaceuticals, patches, creams, and injections; and non-trial papers (i.e. reviews, expert opinions).

The content of each paper was critically analysed to avoid including multiple reports of the same patient population published by the same author. When such a situation was encountered, the study with the larger group of patients and/or the longer follow-up was included in the analysis. The opinion of a third author (JJJ) was sought when a consensus decision could not be reached. This resulted in 16 studies for further analysis, and the references from these were individually searched to find additional studies for the final analysis. This generated an additional four studies bringing the running total to 20. An additional ten papers were added from meta-analyses bringing the overall total to 30.

The quality of all non-randomised articles selected was assessed using the Methodological Index for Non-randomized Studies (MINORS) criteria.\(^5\) The MINORS criteria scoring system was modified to an all-or-nothing scale where studies that adequately reported an index of the MINORS criteria received 1 point. Studies that did not report or inadequately reported one of the criteria received no points, and all studies that had less than nine points were excluded. All studies were analysed by two of the authors (AKL and JJC) for study type; publication year; number of patients; mean age (range); mean follow-up (range) which commonly corresponded to treatment period; mean pre-treatment pain scale; mean post-treatment pain scale; odds ratio (OR) for improvement in pain, and level of evidence. The outcome measurement tools used in the different studies were the visual analogue scale (VAS) for pain and The Western Ontario and McMaster Universities Arthritis Index pain index. In order to standardise the data for statistical analysis, all pain scores were converted to a 100-point scale. The effectiveness of treatment was evaluated using the reported change in outcome score for each study.

Of the studies that met our modified MINORS criteria and inclusion-exclusion criteria, 30 contained the raw data that allowed us to calculate a weighted OR of pain reduction after the use of each modality of treatment. The overall search results and exclusion methods can be seen in Figure 1.

Data analysis. The information from each study was extracted and recorded in an Excel spreadsheet (Excel 2011; Microsoft Corporation, Redmond, Washington). In studies...
which reported raw data for each cohort, MedCalc (MedCalc Software, Osteen, Belgium) was used to calculate a weighted OR, 95% confidence intervals (CIs), and p-values. MedCalc was also used to create multiple forest plots and to calculate the total random effects, which assumed variety in the effects of the selected studies and thereby addresses study heterogeneity. Because the studies used different tools to measure the same outcome, we used standardised mean differences (SMDs) to evaluate any change in pain produced by the intervention. Each study reported an improvement in pain, so it was unnecessary to correct the SMD for differences in the direction of the scale. Study heterogeneity was assessed with the I^2 statistic. Although many of the studies we included were RCTs, we chose to exclude the comparative control data in the meta-analysis in order to be able to include other studies that did not employ a control, and thus expand our pool of data. A p-value < 0.05 was used to determine statistical significance.

### Table I. Characteristics of studies included

<table>
<thead>
<tr>
<th>Source</th>
<th>Number of patients</th>
<th>Intervention</th>
<th>Follow-up</th>
<th>Mean age (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transcutaneous electrical nerve stimulation (TENS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheing et al(^9) 2002</td>
<td>16</td>
<td>TENS (80Hz, 60 mins)</td>
<td>4 wks</td>
<td>55</td>
</tr>
<tr>
<td>Cheing et al(^8) 2003</td>
<td>10</td>
<td>TENS (100 Hz, 40 mins)</td>
<td>2 wks</td>
<td>65</td>
</tr>
<tr>
<td>Itoh et al(^7) 2008</td>
<td>6</td>
<td>TENS (122 Hz, 15 mins)</td>
<td>10 wks</td>
<td>65</td>
</tr>
<tr>
<td>Cetin et al(^6) 2008</td>
<td>20</td>
<td>TENS (60 to 100 Hz) + heat &amp; exercise</td>
<td>8 wk</td>
<td>59</td>
</tr>
<tr>
<td>Atamaz et al(^12) 2012</td>
<td>29</td>
<td>TENS (80 Hz, approx 3 hrs of wearable brace)</td>
<td>6 mths</td>
<td>61</td>
</tr>
<tr>
<td>Cherian et al(^15) 2014</td>
<td>13</td>
<td>(80 HZ)</td>
<td>3 mths</td>
<td>54</td>
</tr>
<tr>
<td>Law and Cheing(^16) 2004</td>
<td>13</td>
<td>TENS (2 Hz, 40 mins)</td>
<td>2 wks</td>
<td>84</td>
</tr>
<tr>
<td><strong>Neuromuscular electrical stimulation (NMES)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imoto et al(^13) 2013</td>
<td>50</td>
<td>NMES + Exercise</td>
<td>8 wks</td>
<td>61</td>
</tr>
<tr>
<td>Elboim-Gabyzon et al(^11) 2013</td>
<td>25</td>
<td>NMES + Exercise</td>
<td>12 wks</td>
<td>68</td>
</tr>
<tr>
<td>Palmieri-Smith et al(^19) 2010</td>
<td>16</td>
<td>NMES (3 x week)</td>
<td>16 wks</td>
<td>57</td>
</tr>
<tr>
<td>Durmu(s) et al(^18) 2007</td>
<td>25</td>
<td>NMES</td>
<td>4 wks</td>
<td>54</td>
</tr>
<tr>
<td>Vaz et al(^14) 2013</td>
<td>12</td>
<td>NMES</td>
<td>8 wks</td>
<td>61</td>
</tr>
<tr>
<td>Gaines et al(^10) 2004</td>
<td>20</td>
<td>NMES + Education</td>
<td>16 wks</td>
<td>70</td>
</tr>
<tr>
<td><strong>Insoles</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hsieh et al(^22) 2014</td>
<td>36</td>
<td>LW insole</td>
<td>6 mths</td>
<td>61</td>
</tr>
<tr>
<td>Barrios et al(^20) 2009</td>
<td>20</td>
<td>LW insole</td>
<td>1 yr</td>
<td>62</td>
</tr>
<tr>
<td>Bennell et al(^21) 2011</td>
<td>103</td>
<td>LW insole</td>
<td>1 yr</td>
<td>64</td>
</tr>
<tr>
<td>Pham et al(^28) 2004</td>
<td>55</td>
<td>LW insole</td>
<td>1 yr</td>
<td>65</td>
</tr>
<tr>
<td>Sattari et al(^25) 2011</td>
<td>20</td>
<td>LW Insole</td>
<td>9 mths</td>
<td>48</td>
</tr>
<tr>
<td>Turpin et al(^20) 2012</td>
<td>16</td>
<td>Shock-absorbing insoles</td>
<td>1 mth</td>
<td>N/A</td>
</tr>
<tr>
<td>Rafiæe et al(^27) 2012</td>
<td>18</td>
<td>7 mm LW insole</td>
<td>2 mths</td>
<td>54</td>
</tr>
<tr>
<td>Jones et al(^24) 2013</td>
<td>28</td>
<td>LW Insoles</td>
<td>2 wks</td>
<td>66</td>
</tr>
<tr>
<td>Arazpour et al(^19) 2012</td>
<td>12</td>
<td>LW insole</td>
<td>6 wks</td>
<td>59</td>
</tr>
<tr>
<td>Hinman et al(^26) 2008</td>
<td>34</td>
<td>LWAS</td>
<td>3 mths</td>
<td>64</td>
</tr>
<tr>
<td>van Raaij et al(^21) 2010</td>
<td>46</td>
<td>10 mm LW insoles</td>
<td>6 mths</td>
<td>54</td>
</tr>
<tr>
<td>Rodrigues et al(^28) 2008</td>
<td>16</td>
<td>Medial insole</td>
<td>8 wks</td>
<td>61</td>
</tr>
<tr>
<td>Fang et al(^25) 2006</td>
<td>28</td>
<td>LW insole</td>
<td>4 wks</td>
<td>67</td>
</tr>
<tr>
<td><strong>Bracing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gaasbeek et al(^23) 2007</td>
<td>15</td>
<td>Unloading brace</td>
<td>6 wks</td>
<td>52</td>
</tr>
<tr>
<td>Haladik et al(^26) 2014</td>
<td>10</td>
<td>Unloading brace</td>
<td>3 wks</td>
<td>60</td>
</tr>
<tr>
<td>Laroche et al(^34) 2014</td>
<td>20</td>
<td>ODRA brace</td>
<td>5 wks</td>
<td>64</td>
</tr>
<tr>
<td>Cherian et al(^12) 2014</td>
<td>26</td>
<td>Unloading brace</td>
<td>3 mths</td>
<td>59</td>
</tr>
</tbody>
</table>

LW, lateral wedge; N/A not applicable

### Results

A total of 30 studies met inclusion criteria: seven on TENS,\(^6-12\) six on NMES,\(^13-18\) 13 on insoles,\(^19-31\) and four on bracing.\(^32-35\) The summary characteristics of each study are displayed in Table I.

**TENS.** A total of seven studies evaluated the use of TENS with a mean follow-up of eight weeks (2 to 24) and a mean patient age of 63 years (55 to 84). The overall effect estimate was a SMD in pain from pre- to post-treatment of 1.702 (95% CI 1.171 to 2.233, p < 0.001), which showed a significant effect from TENS on pain reduction (Fig. 2). The heterogeneity among studies was moderate (I^2 = 62.66%, p = 0.0134).

**NMES.** A total of six studies evaluated the use of NMES with a mean follow-up of 11 weeks (4 to 16) and a mean patient age of 62 years (54 to 70). The overall effect estimate for NMES on pain was similar to TENS, with a SMD improvement of 1.924 (95% CI 0.770 to 3.078, p = 0.001).
This result also indicates that NMES significantly reduces pain in patients who have knee OA (Fig. 3). However, the heterogeneity among NMES studies was substantial ($I^2 = 94.05\%$, $p < 0.0001$), most likely because of the study by Durmus et al,\textsuperscript{18} which showed a considerably greater effect than the other five NMES reports.

**Insoles.** A total of 13 studies evaluated the use of insoles with a mean follow-up of 22 weeks (2 to 52) and a mean patient age of 60 years (54 to 67). The overall effect estimate was a SMD in pain of 0.992 (95% CI 0.606 to 1.378, $p < 0.001$) from pre-treatment to post-treatment, which indicated a significant effect of insoles on pain reduction, yet not as large as that of TENS or NMES (Fig. 4). The heterogeneity among studies was substantial ($I^2 = 85.22\%$, $p < 0.0001$).

**Bracing.** Four studies on bracing involving unloading or distraction of the joint contained raw data to calculate ORs (Fig. 5). The mean follow-up was 22 weeks (3 to 12) and the mean patient age of this group was 59 years (52 to 64). The overall effect estimate was a SMD in pain of 1.34 (95% CI 0.531 to 2.149, $p = 0.001$) from pre-treatment to post-treatment. The heterogeneity among studies was moderate ($I^2 = 78.42\%$, $p = 0.003$).

**Discussion**

OA of the knee causes pain and functional limitation and, if it progresses, patients often enter a cycle of pain, inactivity, and weakness. Various non-operative modalities of treatment are used to decrease pain and improve function. The purpose of this study was to assess these non-operative modalities of treatment.

TENS is a commonly used, inexpensive intervention. It is an effective method of reducing both pain at rest and pain on activity, and may improve function.\textsuperscript{36} All the TENS studies reported an improvement in pain. These results accord with a meta-analysis (n = 184) by Albright et al\textsuperscript{37} which showed that after one month TENS improved pain by about 46% when compared with a control group.

NMES uses electrical stimulation but its purpose is to increase strength by recruiting a greater number of muscle fibres. This is why NMES is frequently used in exercise.
programmes as increasing soft-tissue support to bony structures may decrease knee pain. A recent systematic review showed that NMES alone, or in conjunction with exercise, can improve isometric quadriceps strength in patients with OA of the knee. We found that NMES showed the greatest effect of all the modalities of treatment analysed. This is supported by a 41 patient study by Bruce-Brand et al. who found that six weeks of NMES improved leg muscle strength more than exercise in patients with OA of the knee in terms of functional capacity at week eight ($p \leq 0.001$). The cross-sectional area of the quadriceps femoris muscle increased in both cohorts, but more in the NMES cohort.

Insoles aim to reduce either medial or lateral joint loading with the aim of relieving pain and joint stress. Several studies have examined the biomechanics of insoles and found reduction in lateral knee external movements during gait analyses. However, inconsistent results were found when examining their effect on pain, although some studies have reported an improvement. A RCT of 30 patients compared the use of medial-wedge insoles with neutral insoles. After eight weeks, the medial-wedge insoles had achieved significant reductions in VAS for pain on movement, at rest, and at night with the medial-wedge compared with the neutral insole ($8\text{ vs }4$, $p = 0.001$; $5\text{ vs }3$, $p = 0.002$; and $6\text{ vs }3$ points, $p = 0.001$). Knee braces help protect, stabilise and off-load the joint. There are five main types of brace: prophylactic, which protects the knee from injuries; functional, which give support for the injured knee; rehabilitative, which limit harmful movement during healing after injury or surgery; patella-femoral, which helps the patella move smoothly; and the joint off-loader. Patients with OA of the knee are commonly prescribed off-loaders, which unload varus or valgus knee deformities that have led to unicompartamental OA. This is purported to reduce pain and improve function. Komistek et al. undertook gait analyses on 15 patients using offloader braces to evaluate whether joint space separation was associated with pain relief. Using image intensification, the brace achieved separation of the medial tibial and femoral condyles in 12 of 15 patients, all of whom reported a decrease in pain. Cherian et al. found that offloader bracing significantly improved quadriceps and hamstring muscle strength ($p = 0.022$ and $p = 0.0016$), as well as reducing pain ($p < 0.001$).

Despite our positive results, there were several limitations to this study. Currently, further well-designed studies are needed which compare different brace designs, as well as their use with various degrees of severity of OA of the knee. Furthermore, some modalities of treatment such as topical ointments and assistive devices such as canes and walkers were not included. However, our aim was primarily to assess knee braces. In addition, not all studies were controlled so we were unable to evaluate placebo effects. Patients also had variable lengths of follow-up, from two weeks to a year, most being less than three months. This short follow-up highlights the need for longer-term studies. This limits the potential for definite conclusions and recommendations on the implementation of appropriate treatment. There was also a lack of consistency in implementation which included: hours/day of wear; size of insole/brace; electrode positions for NMES and TENS, and frequency of use. The studies also had small sample sizes, which might limit their reproducibility. Also, OA is a highly individual process, and the degree of impairment it causes depends on multiple factors. Comorbidities can affect the ability of a patient to appreciate any improvement in level of pain, as may occur in diabetes complicated by peripheral neuropathy.

In conclusion, all four non-operative modalities reduced the pain of OA of the knee: NMES and TENS were the most effective. With decreased pain, these patients will improve strength and function. Despite the positive results, further longer-term follow-up studies are needed to assess their effects on quality of life, functional outcome and patient satisfaction as adjuncts to other modalities, as well as for their potential to reduce the need for total knee arthroplasty.

**References**


