

# The clinical effectiveness and cost-effectiveness of management strategies for sciatica: systematic review and economic model

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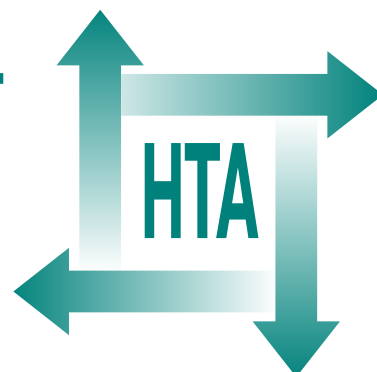


## *Executive summary*

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# Executive summary

## Background

Previous systematic reviews have found evidence for the clinical effectiveness of invasive treatments such as epidural steroid injection, chemonucleolysis and lumbar discectomy in the treatment of sciatica, but found insufficient evidence for less invasive treatments. None of the reviews has made indirect comparisons across separate trials or has examined cost-effectiveness.

## Objectives

To determine the clinical effectiveness and cost-effectiveness of different management strategies for sciatica by undertaking a systematic review and an economic evaluation.

## Review methods

Major electronic databases (for example MEDLINE, EMBASE and the NHS Economic Evaluation Database) and several internet sites including trial registries were searched up to December 2009. No language restrictions were used. Studies examining clinical effectiveness and cost-effectiveness were reviewed separately. Any comparative study or full economic evaluation was considered for inclusion. Studies involving adults who had sciatica or lumbar nerve root pain diagnosed clinically or confirmed by imaging were eligible. The essential clinical criterion was leg pain worse than back pain. Studies that included participants with lower back pain were included only if the findings for patients with sciatica were reported separately. Any intervention or comparator used to treat sciatica was included. Data were extracted by one reviewer and checked by a second reviewer. Quality assessment was conducted independently by two reviewers. Disagreements were resolved by discussion and, when necessary, a third reviewer was consulted.

For the review of clinical effectiveness, interventions were grouped into 18 treatment categories. The analyses were limited to three patient-centred outcome domains – global effect (or overall improvement), reduction in pain intensity (on a continuous scale of 0–100) and improvement in condition-specific functional status – and any reported adverse effects. The data were analysed according to three follow-up intervals: short ( $\leq 6$  weeks), medium ( $> 6$  weeks to 6 months) and long term ( $> 6$  months). The global effect was synthesised as binary data using odds ratios (ORs) and pain intensity and a composite condition-specific outcome measure (CSOM) as continuous data using weighted mean difference and standardised mean difference, respectively. Missing study-level outcome data, where feasible, were dealt with by deriving/imputing replacement values.

Mixed treatment comparison (MTC) meta-analyses were carried out to enable the simultaneous comparison of all treatment modalities for sciatica at a single follow-up interval (closest to 6 months). The analyses were conducted for the three main outcome domains, for all study designs and then after excluding observational studies and non-randomised trials.

The economic evaluation was based on a review of cost-effectiveness studies and a descriptive decision-analytic model, based on estimates of global effect (from the MTC analysis) and cost estimates derived from the literature following consultation with clinical experts.

## Results of review

### Searches

The searches identified 33,590 references, of which 270 studies that met the inclusion criteria were identified and 12 of these also included a full economic evaluation. A further 42 ongoing (or not yet reported) studies and 93 publications that could not be translated were identified.

### Review of clinical effectiveness

The number of studies evaluating invasive interventions such as surgery, epidural and chemonucleolysis was greater than the number evaluating non-invasive interventions such as education/advice, alternative therapies, manipulation and opioid medication. The number of studies evaluating each treatment category ranged from two (manipulation and education/advice) to 63 (disc surgery). The proportion of studies that were randomised control trials (RCTs) also varied, with the lowest being for disc surgery (51%), anti-inflammatory biological agents (50%) and chemonucleolysis (47%). The proportion that were deemed good quality ranged from 0% (chemonucleolysis, non-opioids, traction, alternative therapies, passive physical therapies, biological agents and education/advice) to 50% (manipulation, 1 out of 2); 14% of epidural studies and 3% of surgery studies were deemed to be good quality.

All but one study included patients with nerve root pain (or a combination of both nerve root and referred pain). The presence of disc herniation was confirmed by imaging in a greater proportion of studies evaluating invasive treatments than non-invasive interventions, as was the proportion of studies that did not limit inclusion to patients with acute sciatica (duration of symptoms being < 3 months), although this was not reported for many studies. Five treatment categories included a small number of studies that limited inclusion to patients experiencing their first episode (disc surgery, epidural injections, chemonucleolysis, non-opioid medication and biological agents). The proportion of studies that included patients who had received previous treatment were higher for invasive treatments compared with less invasive interventions, but the proportion was also fairly high for opioids and activity restriction and low for biological agents.

Results from the standard pair-wise meta-analyses were in broad agreement with those from the MTC analyses. The MTC provides an estimate of the relative treatment effects of the different management strategies at a single follow-up interval (closest to 6 months). We found a high level of between-study heterogeneity, so the results from the MTC analyses should be interpreted with caution.

Statistically significant findings were found for the following comparisons. Compared with inactive control, disc surgery [odds ratio (OR) 2.8], epidural injections (OR 3.1), chemonucleolysis (OR 2.0), non-opioids (OR 2.6) and alternative therapies (OR 4.7) resulted in greater overall improvement; epidural injections [weighted mean difference (WMD) -12.9], alternative therapies (WMD -26.1) and biological agents (WMD 21.8) resulted in better pain relief; and biological agents (SMD -0.7) resulted in better back specific function. When compared with usual care, disc surgery (OR 3.4), epidural injections (OR 3.8), chemonucleolysis (OR 2.4), non-opioids (OR 3.1) and alternative therapies (OR 5.7) resulted in better overall improvement. When compared with non-opioids, alternative therapies (WMD -22.1) and biological agents (WMD -17.8) were better for pain relief; and biological agents were better for improving functional status (standardised mean difference -0.8). When compared with opioids, epidural injections (WMD -22.2), alternative therapies (WMD -35.5) and biological agents (WMD -31.2) were better for pain relief; and when compared with activity restriction, alternative therapies (WMD -44.1) and biological agents (WMD -39.7) were also better for reducing pain. Biological agents were also better than passive physical therapy (PT) for pain relief (WMD -22.3).

Pair-wise meta-analyses were performed at short-, medium- and long-term follow-up and the statistically significant improvements were found for the following treatment groups. Disc surgery was superior to usual care (global effect, pain and CSOM at short-, medium- and long-term follow-up) and epidural injection (pain short-term follow-up), non-opioids (pain and CSOM at short-term follow-up), passive PT (global effect at medium- and long-term follow-up) and activity restriction (global effect at medium-term follow-up). Chemonucleolysis was superior to inactive control (pain at medium-term follow-up). Biological agents were superior to inactive control and non-opioid medication (global effect and pain at short-term follow-up). Non-opioid medication was superior to opioids (pain at short- and medium-term follow-up). Traction was superior to activity restriction (pain at short-term follow-up). Passive PT was superior to inactive therapy (pain at short-term follow-up). Spinal manipulation was superior to inactive control (global effect at medium-term follow-up).

Pair-wise analyses of adverse effects found that there was a statistically significant greater number of adverse effects in: disc surgery compared with usual care; epidural injection compared with education/advice, passive PT or usual care; non-opioids compared with inactive control; traction compared with activity restriction; manipulation compared with education/advice; and opioids compared with inactive control.

### **Review of economic evaluations**

The full economic evaluations identified in the systematic review were of reasonable to good quality, but were not able to fully address our research question. Although individual studies raised a number of important issues, it was difficult to draw meaningful conclusions across these studies because of their heterogeneity. Although there was some indication of benefit, such as in the case of disc surgery, robust findings could not be reliably drawn. Although an evidence base is emerging, there remains a dearth of well-designed economic evaluations. In particular, there is a lack of published decision models. Furthermore, the relevance to the UK NHS setting of the studies that have been published is unclear.

### **Economic model**

A decision-analytic model from the perspective of the UK NHS was constructed on the assumption that patients presenting with sciatica would be managed through one of three pathways, with alternative treatments within each of the pathways. The first pathway would involve management within primary care and revolve around what might be termed usual care, with the use of analgesics and other medications if considered appropriate, to attempt to secure symptom resolution. The second pathway would involve a stepped-care approach and include the use of intermediate treatments – offered in addition to the initial treatments provided within primary care – and provided in secondary care outpatients by multidisciplinary teams including physiotherapists, musculoskeletal physicians, etc.; the principle is one of ramping up the level of intervention if there is no timely symptom resolution following simpler, less invasive interventions. The third pathway would involve immediate referral for surgery to alleviate symptoms.

Each of the pathways and the treatment variations available were compared with ‘inactive control’ which, according to the findings from the MTC, has a non-zero probability of symptom resolution, but has been assumed to cost £0 in the baseline model.

A series of 100 independent scenarios were considered, with the utilities associated with success used to generate a utility score for each treatment regime and combined with costs to determine relative incremental cost-effectiveness ratios and a series of sensitivity analyses were conducted on the baseline findings.

## Results of economic evaluation

The treatment regimes that were shown to be the most cost-effective were inactive control; non-opioids followed by alternative/non-traditional treatments; non-opioids followed by alternative/non-traditional treatments followed by epidural; non-opioids followed by alternative/non-traditional treatments followed by epidural followed by disc surgery; and non-opioids followed by biological therapies followed by epidural and followed by disc surgery. Although, this last regime would not be regarded as cost-effective when measured in terms of current cost-effectiveness thresholds employed at national level in the UK NHS.

## Conclusions

These findings provide support for the effectiveness of currently used therapies for sciatica, such as non-opioid medication, epidural corticosteroid injections and disc surgery, but also for chemonucleolysis, which is no longer used in the UK NHS. In addition, these findings do not provide support for the clinical effectiveness of opioid analgesia, which is widely used in this patient group. They also suggest that less frequently used treatments, such as acupuncture, and experimental treatments, such as anti-inflammatory biological agents, may be effective.

In terms of cost-effectiveness, the argument for stepped approaches based on an initial treatment with non-opioids, as opposed to direct referral for surgery, was apparent, although there are a number of limitations associated with the economic model.

Further research is needed to evaluate the use of biological agents and acupuncture compared with interventions that are currently being used such as non-opioids and epidural injections. Further research is also needed to compare the use of opioids with drugs used to treat neurogenic nerve pain or other treatments currently in use.

## Recommendations for future research

The following areas are recommended for further investigation:

- RCTs with concurrent economic evaluation of biological agents compared either with placebo or with currently used treatments
- RCTs with concurrent economic evaluation of acupuncture compared with other currently used treatments
- RCTs with concurrent economic evaluation of opioids compared with drugs used to treat neurogenic nerve pain, such as tricyclic antidepressants and gabapentin (Neurontin<sup>®</sup>, Pfizer)
- development of alternative economic modelling approaches to assess relative cost-effectiveness of treatment regimes, based on the above trial data.

## Funding

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## Publication

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 06/79/01. The contractual start date was in March 2008. The draft report began editorial review in July 2010 and was accepted for publication in February 2011. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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