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R Lewis,[1]* N Williams,[1] HE Matar,[1] N Din,[1]
D Fitzsimmons,[2] C Phillips,[2] M Jones,[1] A Sutton,[3]
K Burton,[4] S Nafees,[1] M Hendry,[1] I Rickard,[5]
R Chakraverty[6] and C Wilkinson[1]

[1]Department of Primary Care and Public Health, Cardiff University, School of Medicine, North Wales Clinical School, Wrexham, UK
[2]School of Human and Health Sciences, Swansea University, Swansea, UK
[3]Department of Health Sciences, University of Leicester, Leicester, UK
[4]Spinal Research Institute, University of Huddersfield, Huddersfield, UK
[5]Patient representative, Betws-y-coed, UK
[6]The Spinal Unit, Royal Orthopaedic Hospital NHS Trust, Birmingham, UK

*Corresponding author

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Abstract

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

R Lewis,[1]* N Williams,[1] HE Matar,[1] N Din,[1] D Fitzsimmons,[2] C Phillips,[2] M Jones,[1] A Sutton,[3] K Burton,[4] S Nafees,[1] M Hendry,[1] I Rickard,[5] R Chakraverty[6] and C Wilkinson[1]

[1]Department of Primary Care and Public Health, Cardiff University, School of Medicine, North Wales Clinical School, Wrexham, UK
[2]School of Human and Health Sciences, Swansea University, Swansea, UK
[3]Department of Health Sciences, University of Leicester, Leicester, UK
[4]Spinal Research Institute, University of Huddersfield, Huddersfield, UK
[5]Patient representative, Betws-y-coed, UK
[6]The Spinal Unit, Royal Orthopaedic Hospital NHS Trust, Birmingham, UK

*Corresponding author

Background: Sciatica is a symptom characterised by well-localised leg pain with a sharp, shooting or burning quality that radiates down the back of the leg and normally to the foot or ankle. It is often associated with numbness or altered sensation in the leg.
Objectives: To determine the clinical effectiveness and cost-effectiveness of different management strategies for sciatica.
Data sources: Major electronic databases (e.g. MEDLINE, EMBASE and NHS Economic Evaluation Database) and several internet sites including trial registries were searched up to December 2009.
Review methods: Systematic reviews were undertaken of the clinical effectiveness and cost-effectiveness of different treatment strategies for sciatica. Effectiveness data were synthesised using both conventional meta-analyses and mixed treatment comparison (MTC) methods. An economic model was then developed to estimate costs per quality-adjusted life-year gained for each treatment strategy.
Results: The searches identified 33,590 references, of which 270 studies met the inclusion criteria and 12 included a full economic evaluation. A further 42 ongoing studies and 93 publications that could not be translated were identified. The interventions were grouped into 18 treatment categories. A larger number of studies evaluated invasive interventions and non-opioids than other non-invasive interventions. The proportion of good-quality studies for each treatment category ranged from 0% to 50%. Compared with studies of less invasive interventions, studies of invasive treatments were more likely to confirm disc herniation by imaging, to limit patients included to those with acute sciatica (<3 months' duration) and to include patients who had received previous treatment. The MTC analyses gave an indication of relative therapeutic effect. The statistically significant odds ratios of global effect compared with inactive control were as follows: disc surgery 2.8, epidural injection 3.1, chemonucleolysis 2.0 and non-opioids 2.6. Disc surgery and epidural injections were associated with more adverse effects than the inactive control. There was

some evidence for the effectiveness of biological agents and acupuncture. Opioid medication and activity restriction were found to be less effective than the comparator interventions and opioids were associated with more adverse effects than the inactive control. The full economic evaluations 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 studies because of their heterogeneity. The economic model demonstrated that stepped-care approaches to patient management were likely to be cost-effective, relative to strategies that involved direct referral to disc surgery.

Limitations: The limited number of studies for some comparisons, the high level of heterogeneity (within treatment comparisons) and the potential inconsistency (between treatment comparisons) weaken the interpretation of the MTC analyses.

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. These findings do not provide support for the effectiveness of opioid analgesia, which is widely used in this patient group, or activity restriction. They also suggest that less frequently used treatments, such as acupuncture, and experimental treatments, such as anti-inflammatory biological agents, may be effective. Stepped-care approaches to treatment for patients with sciatica are cost-effective relative to direct referral for surgery. Future research should include randomised controlled trials with concurrent economic evaluation of biological agents and acupuncture compared with placebo or with currently used treatments. Development of alternative economic modelling approaches to assess relative cost-effectiveness of treatment regimes, based on the above trial data, would also be beneficial.

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Contents

List of abbreviations

ANCOVA	analysis of covariance
AUC	area under the curve
CCS	concurrent cohort study
CEA	cost-effectiveness analysis
CI	confidence interval
CSOM	condition-specific outcome measure
CUA	cost–utility analysis
DRG	diagnostic-related group
EPHPP	Effective Public Health Practice Project
EQ-5D	European Quality of Life-5 Dimensions
ESI	epidural steroid injection
GP	general practitioner
GPE	global perceived effect
HCS	historical cohort study
HMO	health maintenance organisation
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio (e.g. incremental cost per QALY gained)
IQR	interquartile range
ITT	intention to treat
LRS	lumbar radicular syndrome
MANOVA	multivariate analysis of variance
MRI	magnetic resonance imaging
MTC	mixed treatment comparison
NICE	National Institute for Health and Clinical Excellence
NNT	number needed to treat
NSAID	non-steroidal anti-inflammatory drug
ODI	Oswestry Disability Index
OR	odds ratio
OTC	over the counter
PENS	percutaneous electrical nerve stimulation
PT	physical therapy
QALY	quality-adjusted life-year
QDS	Quebec Back Pain Disability Scale
QoL	quality of life
Q-RCT	quasi-randomised controlled trial
RCT	randomised controlled trial
RMDQ	Roland–Morris Disability Questionnaire
SD	standard deviation
SE	standard error
SF-36	Short Form questionnaire-36 items
SG	standard gamble
SLR	straight leg raise
SMD	standardised mean difference
SPORT	Spine Patient Outcomes Research Trial
TENS	transcutaneous electrical nerve stimulation
TNF-α	tumour necrosis factor-alpha
TTO	time trade-off
VAS	visual analogue scale

WHO	World Health Organization
WMD	weighted mean difference

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

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 (≤ 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®, Pfizer)
- development of alternative economic modelling approaches to assess relative cost-effectiveness of treatment regimes, based on the above trial data.

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Chapter 1

Introduction

Research is needed to identify the most clinically effective and cost-effective management strategies for sciatica. Many treatment modalities for sciatica have been evaluated in placebo-controlled trials (or usual care used as the comparator), and the evidence relating to the direct comparison of numerous treatment modalities is missing. Previous systematic reviews have found evidence for the clinical effectiveness of invasive treatments such as epidural steroid injection (ESI), chemonucleolysis and lumbar discectomy, but found insufficient evidence to advise bed rest, keeping active, analgesia, intramuscular steroid injection or traction. None of the reviews made indirect comparisons across separate trials or examined cost-effectiveness. Previous economic evaluations that have been conducted vary quite considerably, and their value is limited to the perspective and setting for which they were undertaken. We undertook a systematic review of the clinical effectiveness and cost-effectiveness of the different management strategies for sciatica, which tries to address some of these issues. We have also developed a decision-analytic model to assess the cost-effectiveness of different treatment modalities from the UK NHS perspective.

Chapter 2

Research objectives

- To undertake a systematic review of the clinical effectiveness and cost-effectiveness of different management strategies for sciatica.
- To synthesise the results using meta-analyses and a mixed treatment comparison (MTC) method.
- To construct an appropriate decision-analytic model to estimate costs per quality-adjusted life-year (QALY) gained for each treatment strategy.

Chapter 3

Background

Definition of sciatica

Sciatica is a symptom defined as unilateral, well-localised leg pain with a sharp, shooting or burning quality that approximates to the dermatomal distribution of the sciatic nerve down the posterior lateral aspect of the leg, and normally radiates to the foot or ankle. It is often associated with numbness or paraesthesia in the same distribution.[1,2] The symptom of sciatica is used by clinicians in different ways. Some refer to any leg pain referred from the back as sciatica, others prefer to restrict its use to pain originating from the lumbar nerve root. Some authors prefer to use the term 'lumbar nerve root pain' to distinguish it from referred leg pain.[3]

Epidemiology of sciatica

The lack of clarity in the definition of sciatica persists in the epidemiological literature. In the UK, the prevalence of 'sciatica suggesting a herniated lumbar disc' has been reported as 3.1% in men and 1.3% in women.[4] However, like most surveys, this study did not use strict criteria to diagnose sciatica. A large population survey in Finland which did found a lifetime prevalence of 5.3% in men and 3.7% in women.[5] Sciatica accounts for < 5% of the cases of lower back pain presenting to primary care.[3] Some cohort studies have found that most cases resolve spontaneously, with 30% of patients experiencing persistent troublesome symptoms at 1 year, 20% out of work and 5–15% requiring surgery.[6,7] However, another cohort found that 55% still had symptoms of sciatica 2 years later, and 53% after 4 years (which included 25% who had recovered after 2 years, but had relapsed again by 4 years).[8] As the sciatica becomes more chronic (> 12 weeks), or with recurrent episodes, it becomes less responsive to treatment.[9] Effective treatment for patients with acute or subacute sciatica is therefore important in order to prevent patients developing a more chronic condition that is resistant to treatment and likely to incur high health-care and socioeconomic costs. The cost of sciatica to society in the Netherlands in 1991 was estimated at US$128M for hospital care, US$730M for absenteeism and US$708M for disablement.[10]

Pathological mechanism

Sciatica caused by lumbar nerve root pain usually arises from a prolapsed intervertebral disc, but also from spinal stenosis, or surgical scarring as well as other aetiologies such as trauma and tumours.[6] It was initially thought to occur predominantly as a result of compression of the nerve root,[11] leading to neural ischaemia, oedema (which would, in turn, lead to chronic inflammation), scarring and perineural fibrosis. However, it is now known that symptoms can occur in the absence of direct nerve root compression, possibly as a result of release of proinflammatory factors from the damaged disc. Pain occurs because of chronic, repetitive firing of the inflamed nerve root.[12,13] Referred leg pain occurs because pain fibres from paraspinal structures and from the leg converge on interneurons in the spinal cord and brain, so that nociceptive input from painful paraspinal tissues is perceived as leg pain.

Clinical diagnosis

It has been claimed that nerve root pain can be distinguished from referred leg pain because it is unilateral, radiates below the knee, results in leg pain that is worse than the back pain, can be aggravated by coughing or sneezing and has a segmental distribution. Important clinical signs include provocation tests for dural irritation, such as a limited straight leg raise (SLR) reproducing the leg pain, and compromised nerve root function leading to reduced power, sensation or reflexes in one nerve root.[3] A systematic review of the diagnostic value of history and physical examination in nerve root pain found that pain distribution was the only useful item in the history. The SLR test was the only sensitive sign in the physical examination, but had poor specificity; the crossed SLR test was the only specific sign, but had poor sensitivity.[14] However, another review found that there was no standard SLR procedure, no consensus on interpretation of results, no evidence of intra- and inter-observer reliability and its predictive value in lumbar intervertebral disc surgery was unknown.[15]

Treatments

A variety of surgical and non-surgical treatments have been used to treat sciatica and have been the subject of previous systematic reviews, the findings of which are summarised below. However, none of the reviews examined the cost-effectiveness of the various treatment modalities.

Bed rest and advice to stay active

Most cases resolve spontaneously and, traditionally, bed rest has been advised. A Cochrane systematic review of bed rest[16] found that there was high-quality evidence of little or no difference in pain or functional status between bed rest and staying active; moderate-quality evidence of little or no difference in pain intensity between bed rest and physiotherapy, but small improvements in functional status with physiotherapy; and moderate-quality evidence of little or no difference in pain intensity or functional status between 2–3 and 7 days' bed rest. A Cochrane systematic review of advice to keep active reviewed the same trials comparing bed rest with activity and came to the same conclusions. Although there is no evidence to advise bed rest for sciatica, there is also very little evidence of any benefit of keeping active.[16]

Analgesia

Most patients will obtain analgesic medication either on prescription or purchased 'over the counter' from their pharmacist. A systematic review of the conservative treatment for sciatica identified three randomised controlled trials (RCTs) that compared non-steroidal anti-inflammatory drugs (NSAIDs) with a placebo tablet and found no evidence of efficacy.[17]

Intramuscular steroids

Part of the mechanism of production of nerve root pain is the release of proinflammatory factors from damaged discs, so administration of intramuscular corticosteroid steroid injections to reduce inflammation of the nerve root has a theoretical basis. The systematic review of conservative treatment for sciatica identified two RCTs comparing steroid injections with a placebo injection and found no evidence of efficacy.[17]

Traction

Traction is used relatively frequently to treat sciatica in North America, but less frequently in the UK, Ireland and the Netherlands.[18,19] A Cochrane systematic review found strong evidence that there was no significant difference between either continuous or intermittent traction versus placebo, sham or other treatments.[20]

Epidural steroids

Introduction of corticosteroids into the epidural space is a commonly used treatment for lumbar nerve root pain, with the rationale of reducing nerve root inflammation. It was performed on 47,665 occasions in the NHS in England in 2005–6.[21] Systematic reviews of ESIs have reached conflicting conclusions with regard to their efficacy compared with placebo and their effectiveness compared with other treatments.[17,22–24]

Spinal manipulation

The systematic review of conservative treatment for sciatica identified two RCTs of spinal manipulation. One found that manipulation was more effective than placebo, and another found no difference compared with manual traction, exercises or corset.[17]

Chemonucleolysis

Chemonucleolysis is a technique that is now rarely used. It attempts to decrease the volume of a disc herniation by reducing the amount of material contained within the nucleus pulposus by injecting the enzyme chymopapain. A systematic review of lumbar discectomy and percutaneous treatments identified three RCTs that compared chymopapain with placebo injection, and reported that symptom relief was greater in the group that received chymopapain.[25]

Lumbar discectomy

Between 5% and 15% of patients with lumbar nerve root pain are treated with surgery,[6,7] usually involving a lumbar discectomy. In 2005–6, 8683 lumbar discectomies were performed in the NHS in England.[21] A Cochrane systematic review of surgery for lumbar disc prolapse[26] found 40 RCTs and two quasi-randomised controlled trials (Q-RCTs), but only four RCTs comparing discectomy with conservative management, which suggested a temporary benefit in clinical outcomes at 1 year, but no difference at longer-term follow-up. Meta-analyses showed that surgical discectomy produced better clinical outcomes than chemonucleolysis, which was better than placebo. The review concluded that there was considerable evidence of the clinical effectiveness of discectomy for carefully selected patients with sciatica caused by lumbar disc prolapse that fails to resolve with conservative management. Serious complications from lumbar disc surgery are uncommon, with one study[25] reporting a mortality rate of 0.3% an infection rate of 3% and 4% requiring an intraoperative transfusion. Surgery failed to relieve symptoms in 10–20% of the cases.[25]

Other treatments

A number of other treatments that have not been included in previous systematic reviews, for example complementary therapies such as acupuncture, will be included in this review.

Pattern of treatments

Overall, there is no close correlation between symptom severity and pathology in sciatica. Increasing distance between onset and effective treatment has an unfavourable influence on symptoms and disability. Although there is reason to suppose that a stepped-care approach to sciatica could be helpful, the application of the various available treatments depends more on availability, clinician preference and socioeconomic variables than on patient needs. In practice, some patients will recover under an analgesic cocktail while on a waiting list, some will be offered surgery as a first-line intervention, and yet others will receive a combination of treatments in no particular order. With few exceptions, it would appear that the patients receiving differing treatments are clinically indistinguishable.

Chapter 4

Evidence synthesis: methods

Methods for reviewing clinical effectiveness and cost-effectiveness

The review was undertaken according to the methodology reported in the Centre for Reviews and Dissemination (CRD) report *Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews*[27] and the *Cochrane handbook for systematic reviews of interventions*.[28] Studies examining clinical effectiveness and those evaluating cost-effectiveness were reviewed separately. (The review protocol is presented in the appendices.)

Literature search

The following databases were searched for published, semi-published and grey literature. Full details of the search strategies are reported in *Appendix 1*. Initial searches took place in June 2008 and were then updated in December 2009, with databases searched from inception to the date of the search:

- MEDLINE
- MEDLINE In-Process & Other Non-Indexed Citations
- OLDMEDLINE
- EMBASE
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Allied and Complimentary Medicine Database (AMED)
- British Nursing Index
- Health Management Information Consortium (HMIC)
- PsychINFO
- Inspec
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Database of Systematic Reviews (CDSR)
- Health Technology Assessment (HTA) Database
- NHS Economic Evaluation Database (NHS EED)
- System for Information on Grey Literature In Europe (SIGLE)
- Science Citation Index
- Social Science Citation Index (SSCI)
- Index to Scientific & Technical Proceedings (ISTP)
- Physiotherapy Evidence Database (PEDro)
- BIOSIS
- National Research Register (NRR)
- National Institute for Health's ClinicalTrials.gov database
- CenterWatch Clinical Trials Listing Service
- Current Controlled Trials (CCT)
- World Health Organization's (WHO) International Clinical Trials Registry Platform (ICTRP) this collects weekly data from:

  - Australian New Zealand Clinical Trials Registry
  - ClinicalTrials.gov
  - International Standard Randomised Controlled Trial Number Register (ISRCTN)

  and monthly data from:
  - Chinese Clinical Trial Registry
  - Clinical Trials Registry – India
  - German Clinical Trials Register
  - Iranian Registry of Clinical Trials
  - Japan Primary Registries Network
  - Sri Lanka Clinical Trials Registry
  - The Netherlands National Trial Register
- Australian New Zealand Clinical Trials Registry
- Clinical Trials Search.

The bibliographies of previous systematic reviews and included studies were screened to identify further relevant studies.

Management of references

The results of the searches were entered onto the reference management software Endnote (Thomson Reuters, CA, USA) and duplicate records removed. Articles written in a language other than English were translated whenever possible. Multiple publications arising from the same study were identified, grouped together and represented by a single reference.

Inclusion and exclusion of studies

Selection criteria

Study design

Studies using any of the following study designs were considered for inclusion: RCTs, Q-RCTs, non-RCTs, cohort studies (with concurrent or historical controls), case–control studies, before and after studies and full economic evaluations as defined by Drummond *et al.*[29] and The Cochrane handbook.[28]

Patient population

Studies involving adults with 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. Other clinical criteria which support the diagnosis include unilateral leg pain, pain radiation below the knee, pain aggravated by coughs/sneezes, segmental distribution of pain, pain induced by provocation tests (e.g. impaired SLR) and reduced power, sensation or reflexes in one nerve root. Studies that included participants with low back pain were included only if the findings for patients with sciatica were reported separately; studies in which the results were not reported separately for sciatica were excluded. Studies of sciatica caused by specific conditions such as spinal stenosis or discogenic pain were only included if it was documented that leg pain was worse than back pain. If imaging was used it had to demonstrate evidence of nerve root irritation. Studies of sciatica caused by a tumour were excluded.

Interventions

Any intervention or comparator used to treat sciatica was included. Treatments were categorised using the system reported in *Table 1*. Inactive control represents placebo or sham treatment used within the study setting and could include sham traction or placebo epidural.

TABLE 1 Treatment categorisation

Level 1	Level 2		Level 3
Invasiveness	**Treatment category**	**Category code[a]**	**Type of treatment**
Inactive control	Inactive control	A	Placebo
			Sham treatment
			No treatment
Non-invasive	Usual/conventional care	B	Usual care
			Conventional care
			Non-surgical treatment
			GP care
Invasive – surgical	Disc surgery	C	Discectomy
			Microdiscectomy
			Automated percutaneous discectomy
			Nucleoplasty
			Laser discectomy
			Disc sequestrectomy
			Laminectomy
			Surgical decompression
Invasive – non-surgical	Epidural/intradiscal injections (includes spinal nerve block)	D	Caudal epidural
			Segmental epidural
			Intradiscal injections
			Facet joints injections
			Intraforaminal injections
			Spinal nerve root block
Invasive – non-surgical	Chemonucleolysis	E	Chymopapain
			Collagenase
			Ozone
Non-invasive	Non-opioids	F	Oral, i.v. or intramuscular
			Steroids
			COX-2 inhibitors
			NSAIDs
			Paracetamol
			Muscle relaxants
			Neuropathic pain treatment
Invasive – surgical	Intraoperative interventions	G	
Non-invasive	Traction	H	Mechanical traction
Non-invasive	Manipulation	I	Manipulation
			Chiropractic
			Osteopathic
			McKenzie
Non-invasive	Alternative	J	Acupuncture
			Feldenkrais
			Muscle energy
			Reiki therapy
			Energy work
			Magnets

continued

TABLE 1 Treatment categorisation *(continued)*

Level 1	Level 2		Level 3
Invasiveness	**Treatment category**	**Category code[a]**	**Type of treatment**
Non-invasive	Active PT/exercise therapy	K	Flexibility
			Strengthening
			Conditioning
			Stabilisation
Non-invasive	Passive PT	L	Ultrasound/phonophoresis
			Iontophoresis
			Heat/ice
			Massage
			Therapeutic touch
			Interferential
			Electrical stimulation techniques (TENS/PENS)
			Laser
Non-invasive	Biological agents	M	Anti-TNFs (and other antibody related interventions)
Non-invasive	Activity restriction	N	Bed rest
Non-invasive	Opioids	O	Oral, i.v. or intramuscular opioids
Non-invasive	Education/advice	P	Back school
			Home exercise instruction
			Coping skills training
			Vocational counselling
			Activities of daily living (ALD)
Invasive + non-invasive	Mixed treatments	Q	Combination of different physical therapies and advice, etc.
Invasive – non-surgical	Others	R	Peripheral nerve block
			Spinal cord stimulation (level 2, code Q)
			Radiofrequency lesioning (level 2, code S)

COX-2, cyclo-oxygenase-2; GP, general practitioner; i.v., intravenous; PENS, percutaneous electrical nerve stimulation; PT, physical therapy; TENS, transcutaneous electrical nerve stimulation; TNF, tumour necrosis factor.
a Interventions are summarised using these codes for displaying the results of the MTC analyses in *Appendix 9*.

Outcome measures

All relevant patient-based outcome measures such as pain, disability, functional status, adverse effects, health status, quality of life (QoL), analgesic use, operation rates, health utility, return to work, health-service use and costs were considered for inclusion in the review. Biochemical outcomes and biomechanical measurements (e.g. change in disc space) were excluded. Although all relevant outcome measures were extracted, because of the high volume of studies and time constraints, only those covered by the following important patient-centred outcome[9] domains were included in the analysis of clinical effectiveness: global effect, pain intensity, condition-specific outcome measures (CSOMs) (*Table 2*) and adverse event data. This means that the outcomes health status, QoL, analgesic use, operation rates, health utility, return to work, health-service use and costs have not been analysed in the clinical effectiveness section of the review.

Assessing relevancy of included studies

Two reviewers independently screened the titles and abstracts identified by the electronic searches for relevance. Potentially relevant studies were ordered and assessed for inclusion, using the criteria reported above, by two independent reviewers. Disagreements during both stages were resolved by discussion or if necessary taken to a third reviewer.

TABLE 2 Sciatica outcome measures

Measure	Interpretation
Global effect	
MacNab criteria	Excellent, good, fair, poor
Global perceived effect (GPE)	Complete recovery to vastly worse
Patient perceived overall improvement	Various ordinal or dichotomous scales
Physician perceived overall improvement	Various ordinal or dichotomous scales
Proportion of patients below a threshold on a specific scale	
Proportion of patients free of pain	
Sciatica bothersomeness	Higher score indicates greater bothersomeness
Pain intensity outcomes	
Visual analogue scale (VAS)	Higher score indicates greater pain
Bergquist-Ullman and Larson, pain index (B-U&LPI)	Higher score indicates greater pain
Numerical rating scale (NRS)	Higher score indicates greater pain
Likert scale	Higher score indicates greater pain
Low back pain rating scale (LBRS) (pain subscale)	Higher score indicates greater pain
McGill Pain Questionnaire (subscales: VAS, present pain inventory)	Higher score indicates greater pain
Japanese Orthopaedic Association (JOA) score (pain subscale)	Lower score indicates greater pain
Roland–Morris annotated thermometer	Higher score indicates greater pain
Von Korff pain intensity	Higher score indicates greater pain
Pain diagram	Higher score indicates greater pain
CSOMs	
Roland–Morris Disability Questionnaire (RMDQ) (including modified versions)	Higher score indicates greater disability
Revised RMDQ	Lower score indicates greater disability
Oswestry Disability Index (ODI, also referred to as Oswestry Low Back Pain Disability Questionnaire) [including modified versions, e.g. Modified Oswestry Disability Index (MODEMS)]	Higher score indicates greater disability
Japanese Orthopaedic Association (JOA) score	Lower score indicates greater disability
Low back outcome score (LBOS)	Lower score indicates greater disability
Dallas Pain Questionnaire (subscales: daily activities, work and leisure activities, anxiety-depression and sociability)	Higher score indicates greater disability
Low back pain rating scale (LBRS) (subscales: pain, activity of daily living and physical function)	Higher score indicates greater disability
North American Spine Society (NASS) instrument score (subscales: neurogenic symptoms score and pain and disability score)	Lower score indicates greater disability
Symptom scoring system	Higher score indicates greater disability
Waddell Disability Index	Higher score indicates greater disability
Sciatica index	Higher score indicates greater disability
Funktionsfragebogen Hannover (FFbH)	Lower score indicates greater disability
Core Outcome Measures Index (COMI)	Higher score indicates greater disability
Quebec Back Pain Disability Scale (QDS)	Higher score indicates greater disability

Data extraction

Data were extracted using predefined forms developed on a Microsoft Access database (Microsoft Corporation, Redmond, WA, USA). Separate forms were used for clinical effectiveness and cost-effectiveness studies. Data were extracted by one reviewer and checked for accuracy, against the original paper, by a second independent reviewer. Any disagreements were resolved by discussion or by a third reviewer if necessary.

Data extracted for clinical effectiveness studies included study location and setting, description of study population (including method of diagnosis and previous treatment), type of intervention and control used, how allocation was performed, outcome measures used and results (such as final means, change scores and proportions) with sufficient information, such as standard errors (SEs), significance levels and confidence intervals (CIs), in order to estimate missing standard deviations (SDs) wherever possible. When necessary, the results and the measures of dispersion were approximated from figures in the reports. Data for both continuous and binary outcomes were extracted based on the number of patients included in the analysis. Where possible, reported findings based on intention-to-treat (ITT) analysis were used. However, we did not recalculate findings based on the ITT principle, e.g. using worst- or best-case scenario for missing variables, as we believed we would be unlikely to have data on crossovers. For studies in which arm-level data were not available, but the mean difference between arms and associated SE had been reported, these were extracted and used in the synthesis instead. Additionally, if studies reported the mean difference between arms adjusted for baseline values, e.g. using analyses of covariates (ANCOVA), these were also extracted.

Data extraction for cost-effectiveness studies included the following: type of economic evaluation, specific details about the interventions being compared, study population, time period, measures of effectiveness, direct costs (medical and non-medical), productivity costs, resource use, currency, results and details of any decision modelling and sensitivity analysis.

Quality assessment

Quality assessment was undertaken by two independent reviewers with differences being resolved by consensus or by a third reviewer if necessary. Data relating to quality assessment were recorded in an Access database.

For clinical effectiveness studies, the quality of both trials and observational studies was assessed using the same checklist based on the one used by the 'Back Review Group' of the Cochrane Collaboration for RCTs[30] and the one developed by the Hamilton Effective Public Health Practice Project (EPHPP) team for quantitative studies (which includes both comparative observational studies and RCTs).[31] The checklist is presented in *Appendix 2*. The criteria cover selection bias and confounding, detection bias, performance bias and attrition bias. Criteria relating to external validity have also been added.

The quality of the economic evaluations was assessed according to an updated version of the checklist developed by Drummond *et al.*[29] (see *Appendix 2*). The checklist reflects the criteria for economic evaluation detailed in the methodological guidance developed by the National Institute for Health and Clinical Excellence (NICE). For studies based on decision models, the critical appraisal was based on the checklist developed by Weinstein *et al.*[32] (see *Appendix 2*).

Methods of analysis/synthesis

Treatments were categorised according to the system reported in *Table 1*. Pair-wise (standard) meta-analyses were initially conducted followed by MTC analysis. These were based on the three main outcome domains: global improvement (including absence of pain), reduction in pain intensity (measured using a continuous scale) and improvement in function based on a composite CSOM. Where feasible, the data were analysed according to chronicity of sciatica (acute ≤ 3 months; chronic > 3 months). The global effect was synthesised as binary data, pain intensity and the composite CSOM as continuous data.

Missing study-level outcome data, where feasible, were dealt with by deriving/imputing replacement values. Where mean values were unavailable but the medians were reported, the latter were used instead (i.e. medians were assumed to be equal to means). Where possible, SDs were estimated from SEs, 95% CIs or *p*-values, using methods reported in The Cochrane handbook,[33] and for median values,using the interquartile range (IQR). If SDs for baseline values were available, then these were substituted for missing SDs. Finally, for studies that did not report sufficient data to derive the SDs, these were imputed using the weighted mean,[34] which was calculated separately for each intervention category.

Global effect (including the absence of pain)

When this outcome was reported in an ordinal format, this was converted into binary data (e.g. improved, not improved, absence of pain, presence of pain). For studies that used ordinal scales, where little improvement (or similar terms) was a central category or grouped with unchanged, the data for patients in this group were classified as not improved. Where both treatment success and failure were reported, treatment success was used. Where treatment failure was reported on its own, the data were converted to treatment success. Where studies reported both overall improvement (sometimes based on a number of scales) and improvement in pain (categorical data), the data on overall improvement were used. For studies that reported both physician- and patient-perceived global effect, the data for patients' perceived effect were used, as this is considered to be the most useful; if the study reported only physician's assessment, then this was used.

Pain intensity (based on a continuous scale)

Most of the studies reporting pain intensity used a visual analogue scale (VAS) to measure pain, with a mixture of both final mean and change scores reported. Studies were pooled using weighted mean difference (WMD). Studies that measured pain intensity on a similar continuous scale were also included, with the data converted to a scale of 0–100. Other types of pain measures were excluded as their inclusion would have necessitated using standardised mean differences (SMDs), where both final and change scores could not be used. Multiple and different locations of the pain were assessed across the studies. We included a pain assessment from only one site from each study using the following preference hierarchy: leg pain (preferred), then overall pain, and then back pain.

Condition-specific outcome measures

The included studies used a number of different scales to measure condition-specific functional status. The Roland–Morris Disability Questionnaire (RMDQ)[35] and the Oswestry Disability Index (ODI)[36] are the most widely used CSOMs for sciatica studies,[37] and an expert panel has recommended the use of either in lower back pain research.[35] The RMDQ was designed, and is more widely used, in primary care settings; the ODI was designed, and is more widely used, in secondary care. Both show some evidence of criterion and construct validity. The RMDQ is the more frequently cited and is more responsive than the ODI, which in turn has better test–retest reliability.[36] The RMDQ has undergone Rasch analysis to examine item separation, which found that all but four of the items contributed to a single underlying construct, but several items in the middle of the disability hierarchy were too similar and there were insufficient items at the upper and lower extremes.[38] The ODI has not undergone Rasch analysis, but like the RMDQ shows evidence of ceiling and floor effects. There are also different versions of the ODI following its adaptation by different groups.[39]

To enable synthesis, the data were combined using a SMD. We had initially intended using change scores. In order to impute change from baseline SDs for studies that report only baseline and final means, it is necessary to include an estimate of the correlation between baseline and follow-up values for individuals. This entails estimating the correlation coefficient from (other)

studies in the synthesis that reported SDs for baseline, final and change from baseline.[40] However, when doing this we found the average correlation to be ≤ 0.5 for most treatment categories, which means that there is little advantage over using final means. Some studies report findings for more than one CSOM scale, but results from only one scale from each study were used in the analyses, based on the following preference hierarchy: RMDQ,[41] ODI,[42] Quebec Back Pain Disability Scale (QDS), others.

Standard pair-wise meta-analyses

Data were analysed according to three follow-up periods: short (≤ 6 weeks), medium (6 weeks to 6 months) and long (> 6 months). Where studies reported findings for multiple follow-up intervals within a single follow-up period, the data relating to the duration closest to the upper limit were used.

Results are presented in structured tables and forest plots, grouped according to the treatment category being evaluated (see *Table 1*). Studies were pooled using the random effects model[43] in Stata (StataCorp LP, College Station, TX, USA), with between-study heterogeneity examined using I^2 and chi-squared statistics. [There were insufficient studies to use individual treatments (level 3) as separate meta-analyses.]

Although studies comparing different interventions that fell into the same category were included in the review, their findings are not reported here, e.g. studies comparing different types of surgery or different types of epidural injections.

Mixed treatment comparison meta-analyses

Prior to performing the MTC we checked whether or not the included studies formed a closed network using level 2 treatment categorisations (see *Table 1*) [there were insufficient data to use individual (level 3) treatments as nodes]. Studies evaluating mixed treatments (or combination therapy) were excluded, because of the uncertainty regarding the extent of interaction between the combined interventions. For the MTC, only one time point was considered, with the findings from individual studies closest to 6 months' follow-up used in the analyses. Analyses were conducted for global effect, pain intensity and CSOMs, for all study designs and after excluding observational studies and non-RCTs.

The analyses were performed by the Multi-parameter Evidence Synthesis Research Group in the Bayesian framework and the modelling computed with Markov chain Monte Carlo stimulation methods using WinBUGS (MRC Biostatistics Unit, Cambridge, UK). The codes that were used are presented in the *Appendix 3* and are based on those used elsewhere.[44] An inactive control was used as the reference treatment. In all cases, an initial burn-in of at least 50,000 stimulations was discarded and all the results presented are based on a further sample of at least 50,000 stimulations. Convergence was assessed using the Brooks–Gelman–Rubin diagnostic tool in WinBUGS and the inspection of the auto-correlation and history plots. The model fit was checked by the global goodness of fit statistic, residual deviance. If the model is an adequate fit, it is expected that the residual deviance would be roughly equal to the number of unconditional data points.

The main parameters of interest in an MTC are the estimates of effects of treatments B, C, D, etc. relative to a baseline 'treatment' A (which is considered as a 'nuisance' variable). In our review, 'usual care' was a treatment category that we were interested in, and we therefore considered

inactive control to be the most appropriate 'baseline' comparator. We also included treatment categories such as non-opioids, which could similarly be used as a baseline comparator if considering the use of usual care.

Analysis of covariates

Where 10 or more studies were included in the pair-wise meta-analyses described in *Chapter 6*, it had been our intention to evaluate the effect of study-level covariates (e.g. symptom duration used and study quality criteria such as adequate randomisation procedure, adequate allocation concealment, > 80% followed up and blind outcome assessment) on between-study heterogeneity using metaregression, but only one comparison (disc surgery vs chemonucleolysis for global effect at long-term follow-up) included sufficient studies. The possible effect of covariates such as study design, study quality and duration of symptoms on pooled results has been discussed when summarising the findings.

Publication bias

For all comparisons for which there were more than eight studies, funnel plots together with associated statistical tests were used to assess the potential publication bias.

Economic evaluations

Given the nature and lack of homogeneity between included economic evaluations, we performed a narrative review of the included studies and made overall conclusions. Details of each published economic evaluation, together with a critical appraisal of its quality, are presented in structured tables with a narrative summary. Where appropriate and where the data permitted, indications of the uncertainty underlying the estimation of the differential cost and effects of the alternative treatment options were summarised.

Economic model

The methods and results of the economic model are reported separately in *Chapter 9*.

Chapter 5

Results of searches

The electronic searches identified 33,560 references and a further 30 references were identified by hand searching. Of these, 777 references were ordered and, after collating multiple publications, 270 studies that met the inclusion criteria were identified. These included 12 economic evaluations performed as part of the clinical effectiveness studies, but reported separately.

A flow diagram showing the number of references identified, retrieved and included in the review is presented in *Figure 1*.

Forty-two ongoing or unpublished studies were identified while searching trial registries and are summarised in *Appendix 4*.

Seventeen (18%) out of 96 studies that reported data on CSOMs used more than one condition-specific outcome scale, five (5%) of which reported data on both RMDQ and ODI.

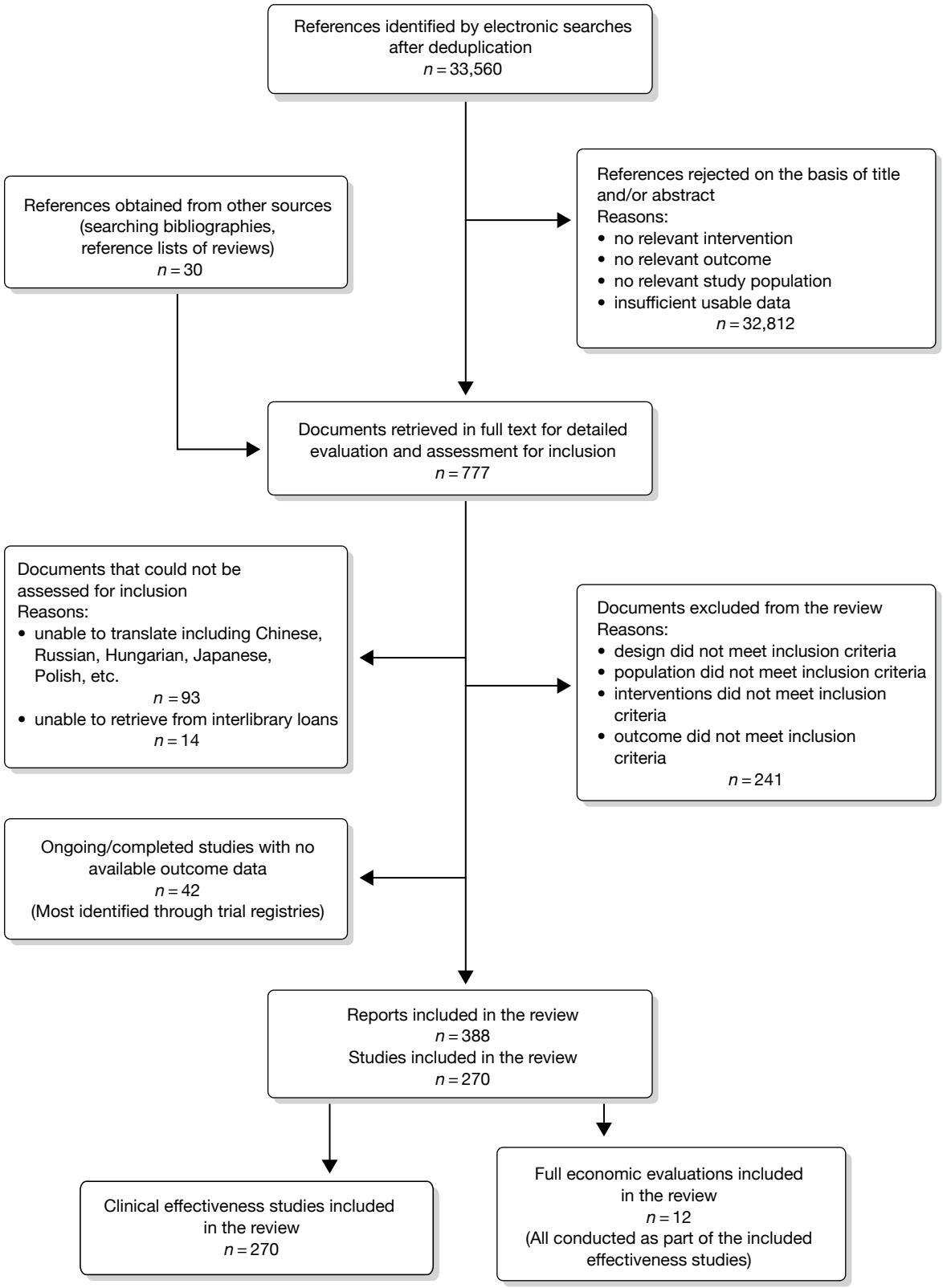

FIGURE 1 Flow diagram showing the number of references identified, documents/studies retrieved for assessment and included in the review.

Chapter 6

Review of clinical effectiveness: results

The results of clinical effectiveness are presented for each intervention category separately, according to the order that interventions are listed in *Table 1*. Findings relating to usual care and inactive control are not reported separately (only as comparators for other interventions). Studies that evaluated mixed treatments are also not reported separately. Studies that compared interventions that fell under the same treatment category were included in the review as a whole, but their findings are not presented here. However, information on the type of interventions that they examined is presented (see *Chapter 4, Standard pair-wise meta-analysis*).

The results are presented for overall recovery (global effect), pain intensity and back-specific functional status (CSOMs) at short-, medium- and long-term follow-up. The findings for any adverse effects that occurred during the study (overall follow-up) are also reported.

Details of the quality assessment of individual studies are presented in *Appendix 5*.

Disc surgery (including intraoperative interventions)

Intraoperative interventions have been considered as a separate intervention category to disc surgery in the MTC and are therefore treated the same here. Intraoperative interventions are supplemental procedures undertaken during surgery, such as the application of steroids or free fat grafts.

Description of disc surgery studies

Summary of interventions

A total of 97 studies evaluated disc surgery for sciatica.[45–141] Sixty-three of these studies compared disc surgery with an alternative type of intervention (including intraoperative).[45–107] The type of interventions being compared are listed in *Table 3a*. One of theses studies,[46] which compared disc surgery with chemonucleolysis, did not include useable comparative data and reported only descriptive results for change from baseline for each group separately. One further study[61] did not report any data on global effect, pain intensity or CSOMs.

Thirty-eight studies compared different types of disc surgery[64,65,69,82,108–141] and five compared different intraoperative interventions[64,65,69,82,141] (four of these studies were three-arm studies that also compared intraoperative interventions with disc surgery[64,65,69,82]). The types of surgical procedures being compared are listed in *Table 3b*, but the findings of these studies are not considered any further than this.

One further study[142] compared disc surgery plus epidural (mixed treatments) with conventional care given while waiting for surgery. However, the study only reported health-care utilisation and employment-related outcomes.

Summary of study participants for disc surgery

Summary data for included participants are presented in *Table 4*. The number of participants included in the 61 studies that reported outcome data for global effect, pain or CSOMs ranged from 10 to 2749 (median 103). A similar number of studies included patients with

TABLE 3a Summary of the interventions used when comparing disc surgery with alternative interventions (ordered by control group then author)

ID no.	Author, year	Study design	Treatment description	Control description
Disc surgery vs chemonucleolysis				
884	Alexander, 1989[103]	CCS	Disc surgery (removal of protruding disc fragment only + free fat graft)	Chemonucleolysis with chymopapain (2000 U)
43	van Alphen, 1989[47]	RCT	Discectomy with emptying of disc space	Chemonucleolysis with chymopapain (4000 U)
441	Bonafe, 1993[75] (French language)	CCS	Percutaneous automated nucleotomy	Chemonucleolysis with chymopapain (4000 U)
183	Bouillet, 1983[61]	CCS	Conventional lumbar disc surgery	Chemonucleolysis with chymopapain injections
453	Brown, 1989[76]	CCS	Disc surgery	Chemonucleolysis with chymopapain
453	Brown, 1989[76]	CCS	Disc surgery	Collagenase chemonucleolysis
454	Buric, 2005[77]	Non-RCT	Standard microdiscectomy	Chemonucleolysis with ozone–oxygen mixture
166	Crawshaw, 1984[60]	RCT	Disc surgery	Chemonucleolysis with chymopapain (4000 U)
48	Dabezies, 1978[51]	CCS	Laminectomy with or without fusion	Chemonucleolysis with chymopapain (2 ml)
471	Dei-Anang, 1990[79] (German language)	CCS	Percutaneous nucleotomy	Chemonucleolysis with chymopapain (4000 U) or collagenase (600 U)
727	Ejeskar, 1983[96]	RCT	Discectomy with unilateral laminotomy and removal of disc hernia only	Chemonucleolysis with chymopapain (400 IU)
132	Hoogmartens, 1976[56]	HCS	Discectomy	Chemonucleolysis with chymopapain
44	Javid, 1995[48]	CCS	Partial hemilaminectomy using magnification and fat graft	Chemonucleolysis with chymopapain (3000 IU)
35	Krugluger, 2000[46]	RCT	Automated percutaneous discectomy	Chemonucleolysis with chymodiactin (4000 U)
117	Lagarrigue, 1991[54] (French language)	CCS	Discectomy with minimal bony resection	Chemonucleolysis with chymopapain (2000–5000 U)
129	Lavignolle, 1987[55] (French language)	RCT	Microscopic discectomy Unilateral limited interlaminar	Chemonucleolysis with chymopapain (4000 U)
889	Lee, 1996[104] (German language)	CCS	Automated percutaneous lumbar discectomy	Chemonucleolysis with chymopapain
889	Lee, 1996[104] (German language)	CCS	Percutaneous manual and laser discectomy	Chemonucleolysis with chymopapain
593	Muralikuttan, 1992[85]	RCT	Standard discectomy with fenestration, disc space cleared	Chemonucleolysis with chymopapain (2000 U)
47	Norton, 1986[50]	CCS	Conventional surgical discectomy	Chemonucleolysis with chymopapain
45	Postacchini, 1987[49]	Non-RCT	Disc excision using unilateral laminotomy	Chemonucleolysis with chymopapain (2 ml)
617	Revel, 1993[88]	RCT	Automated percutaneous lumbar discectomy	Chemonucleolysis
641	Steffen, 1999[90] (German language)	RCT	Laser disc decompression	Chemonucleolysis with chymodiactin (2 ml)
49	Stula, 1990[52] (German language)	RCT	Conventional disc surgery	Chemonucleolysis with chymopapain (500 U)
61	Tregonning, 1991[53]	CCS	Fenestration or partial laminectomy removing extruded disc material	Chemonucleolysis with chymopapain
893	Watters,1988[105]	Non-RCT	Microdiscectomy with free fat graft over exposed dura	Chemonucleolysis with chymopapain (4000 U)
160	Watts, 1975[59]	CCS	Discectomy with laminotomy and foraminotomy	Chemonucleolysis with chymopapain (4 mg)
672	Weinstein, 1986[92]	CCS	Discectomy	Chemonucleolysis with chymopapain
150	Zeiger, 1987[58]	CCS	Microdiscectomy with intraoperative injection into intervertebral space with steroid 125 mg methylprednisolone + morphine 4 mg used to reduce postoperative pain and morbidity	Chemonucleolysis with chymodiactin (2.5 ml)

TABLE 3a Summary of the interventions used when comparing disc surgery with alternative interventions (ordered by control group then author) *(continued)*

ID no.	Author, year	Study design	Treatment description	Control description
Disc surgery vs epidural/intradiscal injection				
725	Buttermann, 2004[95]	RCT	Discectomy	Epidural injection of steroid betamethasone 10–15 mg up to three injections
Disc surgery vs exercise therapy				
300	Osterman, 2006[68]	RCT	Microdiscectomy and exercise therapy	Exercise therapy
Disc surgery vs intraoperative interventions				
268	Aminmansour, 2006[64]	Q-RCT	Discectomy with fenestration + distilled water injection	Discectomy with fenestration + 40 mg intravenous dexamethasone
268	Aminmansour, 2006[64]	Q-RCT	Discectomy with fenestration + distilled water injection	Discectomy with fenestration + 80 mg intravenous dexamethasone
436	Bernsmann, 2001[74]	RCT	Microdiscectomy with partial hemi-laminectomy, but no free fat graft	Microdiscectomy with partial hemi-laminectomy and free fat graft
470	Debi, 2002[78]	RCT	Lumbar discectomy with saline applied to exposed nerve route on a collagen sponge	Lumbar discectomy with steroid methylprednisolone 80 mg applied to exposed nerve route on a collagen sponge
492	Gerszten, 2003[81]	RCT	Sham irradiation prior to repeat surgical decompression (control group)	Irradiation prior to repeat surgical decompression (treatment group)
497	Glasser, 1993[82]	RCT	Microdiscectomy with partial hemilaminectomy and emptying of disc space only (group 3)	Microdiscectomy with partial hemilaminectomy, emptying of disc space and intraoperative steroid methylprednisolone 490 mg + local anaesthetic 30 ml bupivacaine (group 1)
497	Glasser, 1993[82]	RCT	Microdiscectomy with partial hemilaminectomy and emptying of disc space only (group 3)	Microdiscectomy with partial hemilaminectomy, emptying of disc space and intraoperative local anaesthetic 30 ml bupivacaine (group 2)
520	Jensen, 1996[83]	RCT	Flavectomy, partial laminectomy without free fat transplantation (group B)	Flavectomy, partial laminectomy with free fat transplantation (group A)
909	Jirarattanaphochai, 2007[106]	RCT	Disc surgery + saline administered to nerve root + intramuscularly (placebo group)	Disc surgery + corticosteroid administration (80 mg of methylprednisolone sodium succinate) to nerve root + bupivacaine (30 ml 0.375%) intramuscularly (steroid group)
400	Kim, 2003[73]	RCT	Discectomy without Oxiplex®/SP Gel (FzioMed, CA, USA)	Discectomy with anti-adhesion barrier Oxiplex®/SP Gel
551	Langmayr, 1995[84]	RCT	Microdiscectomy plus intrathecal saline injection (placebo group)	Microdiscectomy with intrathecal steroid injection betamethasone (2 ml) (steroid group)
366	Lavyne, 1992[70]	Q-RCT	Microdiscectomy followed with epidural irrigation of saline	Microdiscectomy followed with epidural irrigation of steroid methylprednisolone 40 mg
276	Lundin, 2003[66]	RCT	Discectomy + saline (control group)	Discectomy + intramuscular, intravenous and fat graft soaked in steroids methylprednisolone 490 mg
270	MacKay, 1995[65]	RCT	Standard hemilaminotomy, limited discectomy, dura left uncovered	Standard hemilaminotomy, limited discectomy, dura covered with free fat graft
270	MacKay, 1995[65]	RCT	Standard hemilaminotomy, limited discectomy, dura left uncovered	Standard hemilaminotomy, limited discectomy, dura covered with gelfoam interposion membrane
854	Rasmussen, 2008[101]	RCT	Patients received disc surgery only	Local application of 40 mg methylprednisolone following disc excision
618	Richter, 2001[89]	RCT	Microdiscectomy unilateral interlaminar without applying any gel	Microdiscectomy unilateral interlaminar with the application of ADCON-L gel (Gliatech Inc., OH, USA)

continued

TABLE 3a Summary of the interventions used when comparing disc surgery with alternative interventions (ordered by control group then author) *(continued)*

ID no.	Author, year	Study design	Treatment description	Control description
856	Ronnberg, 2008[102]	RCT	Partial discectomy with no gel applied prior to closure of the wound	Partial discectomy and ADCON-L gel applied around the nerve root, thecal sac and posterior longitudinal ligament
316	Cengiz, 2007[69]	RCT	Disc surgery + no adhesion barrier	Disc surgery + anti-adhesion barrier ADCON-L
316	Cengiz, 2007[69]	RCT	Disc surgery + no adhesion barrier	Disc surgery + anti-adhesion barrier Healon GV
915	de Tribolet, 1998[107]	RCT	Decompression of the affected nerve root. Type of surgery: laminectomy 4, laminotomy 25, hemilaminectomy 53, hemilaminotomy 58, foraminotomy 1. Incision was closed in a routine fashion. No gel applied	Decompression of the affected nerve root. Type of surgery: laminectomy 2, laminotomy 22, hemilaminectomy 49, hemilaminotomy 55, foraminotomy 0. Before closure 3–5 g of ADCON-L gel applied to nerve root
Disc surgery vs mixed treatments				
734	Hoogland, 2006[97]	Q-RCT	Endoscopic discectomy	(Surgery + chemonucleolysis) Endoscopic discectomy and chemonucleolysis with chymopapain (1000 U)
379	Prestar, 1995[71] (German language)	RCT	Discectomy without preoperative, intraoperative or postoperative steroid	(Surgery + non-opioids) Discectomy with preoperative, intraoperative and postoperative steroid dexamethasone 4–40 mg for 7 days
705	Starkweather, 2006[93]	RCT	Microdiscectomy and placebo medication	(Surgery + non-opioids) Microdiscectomy and antidepressant medication – amitriptyline 75 mg for 7 days prior
705	Starkweather, 2006[93]	Non-RCT	*(An additional non-randomised group)* Microdiscectomy with no intervention	(Surgery + non-opioids) Microdiscectomy and antidepressant medication – amitriptyline 75 mg for 7 days prior
263	Wang, 2000[63]	RCT	Placebo acupuncture before and after surgery	(Surgery + alternative) Classical acupuncture before or after surgery
Disc surgery vs non-opioids				
475	Dubourg, 2002[80]	CCS	Disc surgery (operative group) (various surgical techniques)	Non-operative intervention group. Some received steroids
144	Rossi, 1993[57] (Italian language)	Non-RCT	Percutaneous discectomy (groups Ia and IIa)	Oral dexamethasone 8 mg for 9 days, naproxen 500–1000 mg for 5 days (group Ib)
144	Rossi, 1993[57] (Italian language)	Non-RCT	Microdiscectomy (group 2b)	Oral dexamethasone 8 mg for 9 days, naproxen 500–1000 mg for 5 days (group Ib)
Disc surgery vs others				
600	North, 2005[86]	RCT	Re-operation with laminectomy, discectomy with our without fusion	Spinal cord stimulation group
Disc surgery vs usual/conventional care				
716	Alaranta, 1990[94]	CCS	Discectomy with partial laminectomy	Conservative treatment
386	Atlas, 1996[72]	CCS	Surgery most had open discectomy	Various non-surgical treatments
772	Hansson, 2007[100]	CCS	Surgical treatment	Conservative non-surgical treatment. No further details
294	Koranda, 1995[67] (Czech language)	Q-RCT	Disc surgery	Conservative therapy
606	Peul, 2007[87]	RCT	Microdiscectomy	Conventional care control
211	Shvartzman, 1992[62]	HCS	Standard lumbar discectomy	Physical therapy at a local rehabilitation centre. No further details

TABLE 3a Summary of the interventions used when comparing disc surgery with alternative interventions (ordered by control group then author) *(continued)*

ID no.	Author, year	Study design	Treatment description	Control description
2	Thomas, 2007[45]	CCS	Lumbar microdiscectomy with hemilaminotomy	Non-operative multidisciplinary care, no injections
664	Weber, 1983[91]	RCT	Discectomy	Bed rest, physiotherapy, analgesia
750	Weinstein, 2006[98]	CCS	Open or microdiscectomy (group S)	Non-operative treatment (usual care)
751	Weinstein, 2006[99]	RCT	Standard open or microdiscectomy (group S)	Non-operative treatment (usual care)

CCS, concurrent cohort study; HCS, historical cohort study; IU, international units; U, units.

TABLE 3b Summary of the interventions used when comparing alternative forms of disc surgery (ordered by control group then author)

ID no.	Author, year	Study design	Intervention type	Treatment description	Control type	Control description
Bilateral vs unilateral						
21	Barlocher, 2000[108]	CCS	Unilateral (microscope)	Unilateral fenestration with microdiscectomy	Bilateral (microscope)	Bilateral fenestration with microdiscectomy
502	Hagen, 1977[128]	CCS	Bilateral	Discectomy with bilateral laminectomy and emptying of disc space (group1)	Unilateral	Discectomy with unilateral laminectomy and emptying of disc space (group 2)
Day case vs inpatient						
219	Gonzalez-Castro, 2002[117]	Q-RCT	Day-case	Conventional discectomy (fenestration) day-case surgery – disc space cleared, no microscope	Inpatient	Conventional discectomy (fenestration) inpatient stay – disc space cleared, no microscope
Disc surgery + fusion vs disc surgery alone						
66	Takeshima, 2000[109]	HCS	Disc surgery + fusion	Disc excision with posterolateral fusion (fusion group)	Disc surgery alone	Disc excision without fusion (non-fusion group)
653	Tria, 1987[136]	HCS	Disc surgery + fusion	Laminectomy combined with spinal fusion	Disc surgery alone	Simple laminectomy
673	White, 1987[138]	Non-RCT	Disc surgery + fusion	Discectomy with laminectomy plus fusion with internal fixation	Disc surgery alone	Simple laminectomy with no fusion
Discectomy + endplate curettage vs disc surgery alone						
430	Balderston, 1991[124]	CCS	Discectomy + endplate curettage	Lumbar discectomy combined with vertebral endplate curettage	Discectomy alone	Lumbar discectomy with laminectomy, but no endplate curettage
Endoscopic discectomy vs endoscopic discectomy						
680	Yang, 2005[140]	HCS	Endoscopic discectomy (without laser)	Automated percutaneous lumbar discectomy	Endoscopic discectomy (laser decompression)	Percutaneous laser disc decompression
164	Righesso, 2007[114]	RCT	Open discectomy (no microscope)	Open discectomy using magnification	Endoscopic discectomy (microscope)	Microendoscopic discectomy

continued

TABLE 3b Summary of the interventions used when comparing alternative forms of disc surgery (ordered by control group then author) *(continued)*

ID no.	Author, year	Study design	Intervention type	Treatment description	Control type	Control description
402	Ruetten, 2008[121]	Q-RCT	Open discectomy (microscope)	Conventional microsurgical discectomy	Endoscopic discectomy (no microscope)	Full endoscopic interlaminar or transforaminal discectomy
403	Ryang, 2008[122]	RCT	Open discectomy (microscope)	Standard open microdiscectomy	Endoscopic discectomy (microscope)	Minimal access trocar microdiscectomy
651	Toyone, 2004[135]	Non-RCT	Open discectomy (no microscope)	Standard open microdiscectomy with removal of herniated material only	Endoscopic discectomy (microscope)	Microendoscopic discectomy
Endoscopic discectomy vs open discectomy						
460	Chatterjee, 1995[127]	RCT	Endoscopic discectomy	Automated percutaneous lumbar discectomy	Open discectomy	Microdiscectomy
536	Kim, 2007[130]	CCS	Endoscopic discectomy (no microscope)	Targeted percutaneous transforaminal endoscopic discectomy	Open discectomy (no microscope)	Microscopic discectomy
582	Mayer, 1993[131]	RCT	Endoscopic discectomy (no microscope)	Percutaneous endoscopic discectomy	Open discectomy (no microscope)	Microdiscectomy
632	Schizas, 2005[132]	Non-RCT	Endoscopic discectomy (no microscope)	Microendoscopic discectomy	Open discectomy (no microscope)	Microdiscectomy
327	Shin, 2008[119]	RCT	Endoscopic discectomy (microscope)	Microendoscopic discectomy with partial hemilaminectomy	Open discectomy (microscope)	Microscopic discectomy with partial hemilaminectomy
409	Wu, 2006[123]	CCS	Endoscopic discectomy (microscope)	Microendoscopic discectomy	Open discectomy (no microscope)	Standard open posterior lumbar discectomy
459	Zhang, 2007[126]	Non-RCT	Endoscopic discectomy (microscope)	Microendoscopic discectomy	Open discectomy (no microscope)	Open lumbar discectomy
Extensive disc surgery vs limited disc surgery						
391	Carragee, 2006[120]	HCS	Open discectomy	Subtotal discectomy with removal of extruded fragments and emptying of disc space	Limited discectomy	Limited discectomy with removal of extruded fragments only
525	Kahanovitz, 1989[129]	CCS	Extensive disc surgery (microscope)	Microdiscectomy (with an operating microscope)	Limited disc surgery (no microscope)	Limited unilateral discectomy without magnification
643	Striffeler, 1991[133]	CCS	Limited discectomy (microscope)	Conservative microdiscectomy with removal of prolapsed disc, disc space irrigated	Extensive discectomy (microscope)	Standard microdiscectomy with emptying of disc space
647	Thome, 2005[134]	RCT	Extensive discectomy (microscope)	Microdiscectomy with emptying of disc space	Limited discectomy (microscope)	Sequestrectomy with removal of herniated material only
Laser discectomy vs open discectomy						
116	Lee, 2006[111]	CCS	Endoscopic discectomy (no microscope) Laser decompression	Percutaneous endoscopic lumbar discectomy	Open dicectomy (microscope) No laser	Open lumbar microdiscectomy with partial hemilaminectomy
165	Tassi, 2006[115]	HCS	Laser decompression	Percutaneous laser disc decompression	(Microscope)	Standard surgical microdiscectomy

TABLE 3b Summary of the interventions used when comparing alternative forms of disc surgery (ordered by control group then author) *(continued)*

ID no.	Author, year	Study design	Intervention type	Treatment description	Control type	Control description
Ligamentum flavum preservation vs ligamentum flavum excision						
69	Aydin, 2002[110]	HCS	Ligamentum flavum preservation (microscope)	Microdiscectomy with preservation of ligamentum flavum (group 1)	Ligamentum flavum excision (microscope)	Standard microdiscectomy with fenestration, foraminotomy, partial or total excision of ligamentum flavum (group 2)
Microscope vs no microscope						
432	Barrios, 1990[125]	CCS	Microscope	Standard discectomy with partial hemilaminectomy	No microscope	Microdiscectomy
167	Katayama, 2006[116]	RCT	Microscope	Microdiscectomy without laminectomy, disc space emptied (group B)	No microscope	Macrodiscectomy with partial laminectomy, no microscope, disc space emptied (group A)
143	Kho, 1986[113] (German language)	HCS	Microscope	Microdiscectomy	No microscope	Lumbar discectomy without microscope
126	Lagarrigue, 1994[112] (French language)	RCT	Microscope	Microscopic lumbar discectomy	No microscope	Normal lumbar discectomy (without microscope)
232	Tullberg, 1993[118]	RCT	Microscope	Microscopic surgery (micro-group) – disc space cleared	No microscope	Standard macrodiscectomy (without microscope) – disc space cleared
654	Tureyen, 2003[137]	RCT	Microscope	Microdiscectomy with emptying of disc space (group A)	No microscope	Macrodiscectomy with laminectomy and emptying of disc space, no microscope (group B)
674	Wilson, 1981[139]	HCS	Microscope	Microdiscectomy with evacuation of disc space, but no curettage of end plates	No microscope	Standard open discectomy with evacuation of disc space, but no curettage of end plates

CCS, concurrent cohort study; HCS, historical cohort study.

chronic sciatica, or either chronic or acute sciatica, or did not report this information. Four studies[62,68,80,87] included patients with acute sciatica, with a mean duration of symptoms ranging from 25.7 days[80] to 68.5 days.[68] Four studies[54,67,69,83] included some patients with spinal stenosis and 10[68,74,83,95,97,98,99,101,103,107] included patients with sequestered or extruded discs. The diagnosis of sciatica, or the presence of herniated disc, was confirmed by imaging in 52 (85%) studies. Six studies[49,66,74,92,95,105] included patients who had sciatica for the first time and seven studies[50,57,63,72,80,81,83,86] included only patients with recurrent sciatica. The remaining studies included patients with either first-episode or recurrent sciatica, or did not report this information. The majority of studies ($n = 40$) included patients who had received previous treatment for their current episode of sciatica. Ten studies[45,56,59,63,71,80,81,86,88,95] included patients who had received previous disc surgery and 32 studies included patients who had not.

TABLE 4 Summary of sciatica type and study population details for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Mean age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis? [a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Disc surgery vs chemonucleolysis													
884	Alexander, 1989[103]	CCS	100	33.5 (range 18–65)	90 (90)	Mean 5.5 months	Nerve root pain	Yes	NR	No	Yes	Yes	No
43	van Alphen, 1989[47]	RCT	151	34 (range 18–45)	99 (66)	55% <6 months; 45% >6 months	Nerve root pain	Yes	NR	No	No	Yes	No
441	Bonafe, 1993[75] (French language)	CCS	40	46 (range 27–68)	28 (70)	Mean 3 months (range several days to 15 months)	Nerve root pain	Yes	NR	No	No	Yes	NR
183	Bouillet, 1983[61]	CCS	2749	NR	NR	Ranged from weeks to months	Nerve root pain	Yes	NR	No	No	Yes	NR
453	Brown, 1989[76]	CCS	85	37.6	59 (69)	At least 3 months	Nerve root pain	Yes	NR	No	No	Yes	No
454	Buric, 2005[77]	Non-RCT	45	45 (SD 14.2; range 19–77)	23 (51)	Mean 203.9 days (SD 129.6; range 21 to >365 days)	Nerve root pain	Yes	NR	No	No	Yes	No
166	Crawshaw, 1984[60]	RCT	52	37	NR	NR	Nerve root pain	Yes	NR	No	No	Yes	No
48	Dabezies, 1978[51]	CCS	200	39	132 (66)	NR	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	Yes	NR
471	Dei-Anang, 1990[79] (German language)	CCS	201	NR	NR	NR	Nerve root pain	NR	NR	No	No	NR	NR
727	Ejeskar, 1983[96]	RCT	29	39.3	21 (72)	Mean 4.5 months (SD 3 months)	Nerve root pain	Yes	NR	No	No	NR	No
132	Hoogmartens, 1976[56]	HCS	97	35.5	48 (49)	25–35 months	Nerve root pain	NR	Recurrent and first episode	No	No	Yes	Yes
44	Javid, 1995[48]	CCS	200	39 (range 17–81)	134 (67)	Mean 7.2 months	Nerve root pain	Yes	NR	No	No	Yes	No

ID no.	Author, year	Study design	No. of patients	Mean age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis? [a]	Included patients with sequestered disc (or extruded)? [a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
35	Krugluger, 2000[46]	RCT	22	40 (range 24–60)	16 (73)	Mean 7 months	Nerve root pain	Yes	NR	No	No	Yes	NR
117	Lagarrigue, 1991[54] (French language)	CCS	1085	42 (range 14–83)	682 (63)	Mean 13.4 months	Nerve root pain	No	NR	Yes	No	Yes	NR
129	Lavignolle, 1987[55] (French language)	RCT	358	41 (SD 12.03)	225 (63)	NR	Nerve root pain	NR	NR	No	No	NR	NR
889	Lee, 1996[104] (German language)	CCS	300	50% < 30; 25% > 40	213 (71)	NR	Nerve root pain	Yes	NR	No	No	Yes	NR
593	Muralikuttan, 1992[85]	RCT	92	35 (range 19–60)	55 (60)	Mean 24 weeks	Nerve root pain	Yes	NR	No	No	Yes	NR
47	Norton, 1986[50]	CCS	105	40 (range 20–67)	86 (82)	Mean 18.5 months (range 5 days–128 months)	Nerve root pain	Yes	Recurrent	No	No	Yes	No
45	Postacchini, 1987[49]	Non-RCT	161	NR	NR	Mean 8.75 months (range 1.2–36.0 months)	Nerve root pain and referred pain	Yes	First episode	No	No	Yes	NR
617	Revel, 1993[88]	RCT	165	39 (SD 9; range 21–65)	96 (68)	NR	Nerve root pain	Yes	NR	No	No	Yes	Yes
641	Steffen, 1999[90] (German language)	RCT	69	NR	NR	10.6 months	Nerve root pain	Yes	NR	No	No	Yes	NR
49	Stula, 1990[52] (German language)	RCT	69	Range 22–54	57 (83)	< 1 year	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	No
61	Tregonning, 1991[53]	CCS	268	40.4 (range 20–65)	135 (68)	NR	Nerve root pain	Yes	NR	No	No	Yes	No
893	Watters,1988[105]	Non-RCT	100	36.5	59 (59)	Mean 13 weeks	Nerve root pain	Yes	First episode	No	No	NR	NR
160	Watts, 1975[59]	CCS	274	Range 24–62	55 (55)	NR	Nerve root pain and referred pain	Yes	Recurrent and first episode	No	No	Yes	Yes

continued

TABLE 4 Summary of sciatica type and study population details for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Mean age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis? [a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
672	Weinstein, 1986[92]	CCS	159	41 (range 28–57)	64 (41)	Minimum period of 3 months	Nerve root pain	Yes	First episode	No	No	Yes	No
150	Zeiger, 1987[58]	CCS	126	NR	NR	4 weeks or more	Nerve root pain	Yes	NR	No	No	Yes	No
Disc surgery vs epidural													
725	Buttermann, 2004[95]	RCT	100	40.5 (SD 12)		Mean 3.55 months (SD 2.75 months)	Nerve root pain	Yes	First episode	No	Yes	Yes	Yes
Disc surgery vs exercise therapy													
300	Osterman, 2006[68]	RCT	57	38 (SD 7)	34 (61)	Mean 68.5 days (SD 27 days)	Nerve root pain	Yes	Recurrent and first episode	No	Yes	NR	No
Disc surgery vs intraoperative interventions													
268	Aminmansour, 2006[64]	Q-RCT	61	38.5 (SD 10.4)	35 (57)	NR	Nerve root pain	Yes	NR	No	No	NR	NR
436	Bernsmann, 2001[74]	RCT	200	43 (range 22–75)	97 (52)	NR	Nerve root pain	Yes	First episode	No	Yes	NR	NR
470	Debi, 2002[78]	RCT	70	41 (range 18–60)	43 (70)	Mean 56 days (range 12–135 days)	Nerve root pain	NR	NR	No	No	Yes	No
492	Gerszten, 2003[81]	RCT	10	42	5 (50)	Mean 3.5 years (range 1.5–10.0 years)	Nerve root pain	Yes	Recurrent	No	No	Yes	Yes
497	Glasser, 1993[82]	RCT	32	46.1 (SD 3.66)		Within 6 months	Nerve root pain	Yes	NR	No	No	Yes	No
520	Jensen, 1996[83]	RCT	118	Median 46 (range 19–75)	53 (45)	NR	Nerve root pain	Yes	Recurrent	No central stenosis but some had lateral stenosis	Yes	NR	No

ID no.	Author, year	Study design	No. of patients	Mean age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis? [a]	Included patients with sequestered disc (or extruded)? [a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
909	Jirarattanaphochai, 2007[106]	RCT	103	52 (SD 11; range 21–79)	48 (47)	NR	Nerve root pain	NR	NR	No	No	NR	NR
400	Kim, 2003[73]	RCT	35	43.5 (range 28–65)	11 (31)	NR	Nerve root pain	Yes	NR	No	No	NR	No
551	Langmayr, 1995[84]	RCT	26	42	20 (77)	Median 35 days (range 14–150 days)	Nerve root pain	Yes	NR	No	No	Yes	No
366	Lavyne, 1992[70]	Q-RCT	84	40 (range 17–70)	57 (73)	Few days to several months	Nerve root pain	Yes	NR	No	No	Yes	NR
276	Lundin, 2003[66]	RCT	80	41.7	44 (55)	Mean 4.5 months	Nerve root pain	Yes	First episode	No	No	NR	No
270	MacKay, 1995[65]	RCT	190	39 (range 14–79)	106 (69)	NR	Nerve root pain	Yes	NR	No	No	Yes	NR
854	Rasmussen, 2008[101]	RCT	200	42.5 (range 18–66)	122 (61)	NR	Nerve root pain	Yes	NR	No	Yes	Yes	NR
618	Richter, 2001[89]	RCT	398	43 (range 30–65)	221 (62)	NR	Nerve root pain	Yes	NR	No	No	NR	No
856	Ronnberg, 2008[102]	RCT	128	39 (range 18–66)	68 (53)	NR	Nerve root pain	Yes	NR	No	No	Yes	No
316	Cengiz, 2007[69]	RCT	60	44.2 (SD 10.2)	35 (58)	Mean 12.3 years (SD 9.2 years)	Nerve root pain	Yes	Recurrent and first episode	Yes	No	NR	No
915	de Tribolet, 1998[107]	RCT	298	39.1 (SD 9.5)	167 (56)	Not stated	Nerve root pain	Yes	Recurrent and first episode	No	Yes extruded and sequestered discs	Yes	No
Disc surgery vs mixed treatments													
734	Hoogland, 2006[97]	Q-RCT	280	40.5 (range 18–60)	186 (66)	NR	Nerve root pain	Yes	NR	No	Yes	Yes	No
379	Prestar, 1995[71] (German language)	RCT	100	44.7 (range 26–76)	NR	NR	Nerve root pain	Yes	NR	No	No	Yes	Yes

continued

TABLE 4 Summary of sciatica type and study population details for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Mean age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis? [a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
705	Starkweather, 2006[93]	RCT	70	45.5 (SD 11; range 21–65)	40 (57)	61% <1 year; 39% >1 year	Nerve root pain	Yes	NR	No	No	NR	NR
263	Wang, 2000[63]	RCT	145	21–80	78 (59)	At least 6 months	Nerve root pain	Yes	Recurrent	No	No	Yes	Yes
Disc surgery vs non-opioids													
475	Dubourg, 2002[80]	CCS	67	48.8 (SD 13.9; range 28–81)	42 (63)	Mean 25.7 days (SD 28.7 days)	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	Yes
144	Rossi, 1993[57] (Italian language)	Non-RCT	40	42.5 (SD 10.5; range 20–65)	NR	<6 months	Nerve root pain	Yes	Recurrent	No	No	NR	NR
Disc surgery vs others													
600	North, 2005[86]	RCT	60	50.2 (SD 13.3; range 26–76)	30 (50)	NR	Nerve root pain	Yes	Recurrent	No	No	Yes	Yes
Disc surgery vs usual/conventional care													
716	Alaranta, 1990[94]	CCS	357 (322 partial rhizography)	39.6	179 (50)	Mean 3.6 months	Nerve root pain	No	NR	No	No extrusion	NR	No
386	Atlas, 1996[72]	CCS	507	42 (range 18–85)	322 (64)	41% <1 year; 1–24% 5 years; 35% >5 years	Nerve root pain	No	Recurrent	No	No	Yes	No
772	Hansson, 2007[100]	CCS	184	43 (range 22–59)	87 (47)	20% <1 week; 39% 1 week to 1 year; 42% >1 year	Nerve root pain	Yes	NR	No	No	NR	No
294	Koranda, 1995[67] (Czech language)	Q-RCT	100	NR	NR	NR	Nerve root pain	Yes	Recurrent and first episode	Yes	No	Yes	NR

ID no.	Author, year	Study design	No. of patients	Mean age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis? [a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
211	Shvartzman, 1992[62]	HCS	55	42.3 (SD 11.1; range 23–59)	55 (100)	Patients presented with acute episode of sciatica, actual duration NR	Nerve root pain	Yes	NR	No	No	Yes	No
2	Thomas, 2007[45]	CCS	623	42.9	291 (59)	Mean 191.5 days (SD 195 days)	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	Yes
664	Weber, 1983[91]	RCT	126	41 (range 25–55)	68 (54)	At least 14 days	Nerve root pain	Yes	NR	No	No	NR	No
751	Weinstein, 2006[99]	RCT	501	42 (SD 11.6)	278 (59)	79% <6 months	Nerve root pain	Yes	Recurrent and first episode	No	Yes	Yes	No
606	Peul, 2007[87]	RCT	283	42.6 (SD 9.8)	186 (66)	Mean 9.5 weeks (range 6–12 weeks)	Nerve root pain	Yes	NR	No	No	NR	No
750	Weinstein, 2006[98]	CCS	743	41.4 (SD 11.2)	406 (56)	77% <6 months	Nerve root pain	Yes	Recurrent and first episode	No	Yes	Yes	No

CCS, concurrent cohort study; HCS, historical cohort study; NR, not reported; SD, standard deviation.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise, reported as no.

TABLE 5 Summary of the study details for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Disc surgery vs chemonucleolysis										
884	Alexander, 1989[103]	100	Mean 14 months; range 6–35 months	CCS	No	No	80–100	Unclear	Weak	Weak
43	van Alphen, 1989[47]	151	12 months	RCT	Partial	Unclear	80–100	No	Moderate	Strong
441	Bonafe, 1993[75] (French language)	40	Mean 15 months; range 3–36 months	CCS	No	No	80–100	Unclear	Weak	Weak
453	Brown, 1989[76]	85	3 months	CCS	No	No	80–100	Yes	Weak	Weak
454	Buric, 2005[77]	45	18 months	Non-RCT	No	No	80–100	NA	Weak	Weak
166	Crawshaw, 1984[60]	52	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Moderate
48	Dabezies, 1978[51]	200	2 years	CCS	No	No	Can't tell	No	Weak	Moderate
471	Dei-Anang, 1990[79] (German language)	201	1 year	CCS	No	No	NA	Unclear	Weak	Weak
727	Ejeskar, 1983[96]	29	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Moderate
132	Hoogmartens, 1976[56]	97	58 months for discectomy and 38 months for chemonucleolysis	HCS	No	No	NA	NA	Weak	Moderate
44	Javid, 1995[48]	200	1 year	CCS	No	No	80–100	No	Weak	Moderate
35	Krugluger, 2000[46]	22	2 years	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
117	Lagarrigue, 1991[54] (French language)	1085	Mean 17.2 months; range 12–4 months	CCS	No	No	80–100	Unclear	Weak	Moderate
129	Lavignolle, 1987[55] (French language)	358	Mean 25 months for surgery and 22 months for chemonucleolysis	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
889	Lee, 1996[104] (German language)	300	1 year	CCS	No	No	Can't tell	Unclear	Weak	Weak
593	Muralikuttan, 1992[85]	92	1 year	RCT	Yes	Unclear	80–100	Unclear	Moderate	Moderate
47	Norton, 1986[50]	105	At least 1 year	CCS	No	No	NA	Unclear	Weak	Weak
45	Postacchini, 1987[49]	161	Mean 2.9 years; range 20–38 months in chemonucleolysis. Mean 2.8 years; range 21–42 months in surgery	Non-RCT	No	No	80–100	No	Weak	Moderate

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ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
617	Revel, 1993[88]	165	1 year	RCT	Yes	Unclear	80–100	Unclear	Moderate	Weak
641	Steffen, 1999[90] (German language)	69	1 year	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
49	Stula, 1990[52] (German language)	69	Postoperative	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
61	Tregonning, 1991[53]	268	10 years	CCS	No	No	80–100	No	Weak	Moderate
893	Watters,1988[105]	100	3 years	Non-RCT	No	No	80–100	No	Weak	Weak
160	Watts, 1975[59]	274	2 years	CCS	No	No	80–100	Unclear	Weak	Weak
672	Weinstein, 1986[92]	159	Mean 10.3 years; range 10.0–13.5 years	CCS	No	No	80–100	NA	Weak	Weak
150	Zeiger, 1987[58]	126	Range 6–46 months; average time from treatment to follow-up 18 months	CCS	No	No	NA	Yes	Weak	Weak
Disc surgery vs epidural										
725	Buttermann, 2004[95]	100	2–3 years	RCT	Unclear	Unclear	80–100	No	Moderate	Moderate
Disc surgery vs exercise therapy										
300	Osterman, 2006[68]	57	2 years	RCT	Yes	Yes	80–100	NA	Moderate	Weak
Disc surgery vs intraoperative interventions										
268	Aminmansour, 2006[64]	61	2 months	Q-RCT	No	No	80–100	Yes	Weak	Moderate
436	Bernsmann, 2001[74]	200	Median of 24.2 months after surgery	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
470	Debi, 2002[78]	70	1 year	RCT	Unclear	Partial	80–100	No	Weak	Weak
492	Gerszten, 2003[81]	10	1 year	RCT	Yes	Unclear	80–100	NA	Moderate	Weak
497	Glasser, 1993[82]	32	1 month	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
520	Jensen, 1996[83]	118	Median 376 days; range 276–501 days	RCT	Unclear	Unclear	80–100	Yes	Moderate	Moderate
909	Jirarattanaphochai, 2007[106]	103	3 months	RCT	Yes	Partial	80–100	Yes	Moderate	Moderate
400	Kim, 2003[73]	35	6 months	RCT	Yes	Yes	80–100	NA	Moderate	Weak
551	Langmayr, 1995[84]	26	6 months	RCT	Unclear	Unclear	80–100	Yes	Moderate	Moderate

continued

TABLE 5 Summary of the study details for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
366	Lavyne, 1992[70]	84	6 weeks	Q-RCT	No	No	80–100	Unclear	Weak	Weak
276	Lundin, 2003[66]	80	2 years	RCT	Unclear	Unclear	80–100	Yes	Moderate	Moderate
270	MacKay, 1995[65]	190	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
854	Rasmussen, 2008[101]	200	2 years	RCT	Yes	Unclear	80–100	Yes	Moderate	Weak
618	Richter, 2001[89]	398	6 months	RCT	Yes	Yes	80–100	Yes	Moderate	Weak
856	Ronnberg, 2008[102]	128	2 years	RCT	Unclear	Partial	80–100	Yes	Weak	Weak
316	Cengiz, 2007[69]	60	12 months	RCT	Unclear	Yes	80–100	Unclear	Moderate	Weak
915	de Tribolet, 1998[107]	298	6 months	RCT	Yes	Unclear	80–100	Yes	Moderate	Moderate
Disc surgery vs mixed treatments										
734	Hoogland, 2006[97]	280	2 years	Q-RCT	No	No	80–100	Unclear	Weak	Weak
379	Prestar, 1995[71] (German language)	100	1 year	RCT	Unclear	Unclear	60–79	Unclear	Weak	Moderate
705	Starkweather, 2006[93]	70	6 weeks	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
263	Wang, 2000[63]	145	3 days	RCT	Unclear	Unclear	80–100	Unclear	Moderate	Moderate
Disc surgery vs non-opioids										
475	Dubourg, 2002[80]	67	6 months	CCS	No	No	80–100	No	Weak	Weak
144	Rossi, 1993[57] (Italian language)	40	6 months	Non-RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
Disc surgery vs others										
600	North, 2005[86]	60	2 years	RCT	Yes	Partial	60–79	No	Weak	Moderate
Disc surgery vs usual/conventional care										
716	Alaranta, 1990[94]	357 (322 with partial rhizography)	1 year	CCS	No	No	80–100	No	Weak	Moderate
386	Atlas, 1996[72]	507	10 years	CCS	No	No	60–79	NA	Moderate	Moderate
772	Hansson, 2007[100]	184	2 years	CCS	No	No	80–100	NA	Weak	Moderate
294	Koranda, 1995[67] (Czech language)	100	3 months	Q-RCT	No	No	80–100	Unclear	Weak	Moderate

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
606	Peul, 2007[87]	283	1 year (main follow-up visits at 8 weeks, 6 months and 1 year). 2 years' data reported later	RCT	Yes	Partial	80–100	NA	Strong	Strong
211	Shvartzman, 1992[62]	55	2 years	HCS	No	No	NA	NA	Weak	Weak
2	Thomas, 2007[45]	623	12 months	CCS	No	No	80–100	NA	Moderate	Strong
664	Weber, 1983[91]	126	10 years	RCT	Unclear	Partial	60–79	No	Weak	Moderate
751	Weinstein, 2006[99]	501	2 years	RCT	Yes	Yes	80–100	NA	Strong	Weak
750	Weinstein, 2006[98]	743	2 years	CCS	No	No	80–100	NA	Moderate	Weak

CCS, concurrent cohort study; HCS, historical cohort study; NA, not applicable.

Summary of study design and quality for disc surgery studies

Summary information on study details are presented in *Table 5*. The full results of the quality assessment are presented in the *Appendix 5*. Just over half (33/62, 53%) of the disc surgery studies were RCTs, of which only two[87,99] were good quality overall (comparing disc surgery with usual care). Four RCTs[68,73,89,99] had used both adequate randomisation and allocation concealment (comparators included exercise therapy, intraoperative interventions and usual care). A further eight studies[81,85–88,101,106,107] used adequate randomisation, but not allocation concealment (although two studies[87,106] used sealed envelopes), and one study[69] used adequate allocation concealment, but not randomisation. Two studies[91,93] used sealed envelopes, but gave no further details on method of randomisation. Three studies[45,47,87] had strong external validity.

Disc surgery results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 6* and the accompanying forest plot (*Figure 2*). Disc surgery was compared with exercise therapy, chemonucleolysis (which is not widely used in the UK NHS) and intraoperative interventions. Most studies included patients with chronic sciatica.

One well-conducted RCT[68] compared disc surgery plus exercise therapy with exercise therapy alone for patients with acute sciatica owing to an intervertebral disc extrusion or sequester. Disc surgery plus exercise therapy was found to be superior to exercise therapy alone, but the findings were not statistically significant, probably owing to a lack of power as a result of the analysis of a small sample size ($n = 57$).

Six studies[48,49,52,79,92,104] compared disc surgery with chemonucleolysis, for which there was no overall difference between the groups. Only one of these studies was an RCT,[52] which was poorly reported with method of randomisation and allocation concealment not stated. Forty-four patients were randomised to each group, but 19 in the chemonucleolysis group received surgery and were analysed as surgery group patients. The results and methods of the remaining studies were also poorly reported.

Two RCTs[71,82] compared surgery with intraoperative interventions and found no overall statistically significant difference.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 7* and the accompanying forest plot (*Figure 3*). Disc surgery was compared with usual care, intraoperative interventions, exercise therapy, mixed treatments and chemonucleolysis. Most studies included patients with chronic sciatica.

One study based in the Netherlands[87] compared early surgical intervention with usual care in patients with severe sciatica for 6–12 weeks. The study was well conducted with good external validity. Patients in the disc surgery group experienced a significantly greater reduction in pain intensity than those who received conventional care (WMD −15.70; 95% CI −20.98 to −10.42). Conventional care included rehabilitation at home supervised by a physiotherapist using a standardised exercise protocol, advice to resume work as soon as possible, pain medication and conservative treatment provided by general practitioners (GPs) (or neurologist where necessary). Microdiscectomy was offered if sciatica persisted for more than 6 months after randomisation. Patients with increasing leg pain not responsive to medication or progressive neurological deficits were offered surgery sooner.

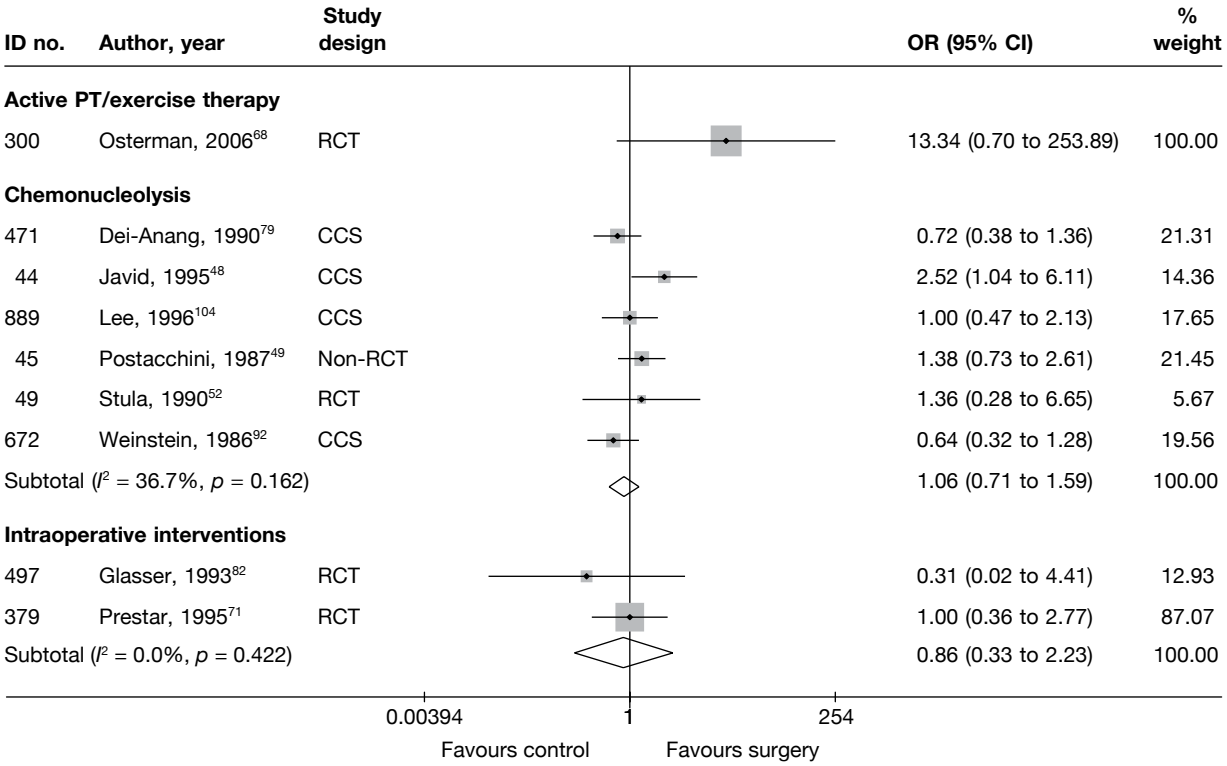

FIGURE 2 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing disc surgery with alternative interventions. CCS, concurrent cohort study; PT, physical therapy. Note: weights are from random effects analysis.

As with global effect, one well-conducted RCT[68] found disc surgery plus exercise therapy to be superior to exercise therapy alone for acute sciatica due to an intervertebral disc extrusion or sequestration, but the findings were not statistically significant.

Two studies,[63,93] compared disc surgery with mixed treatments: acupuncture plus surgery[63] and disc surgery plus non-opioids.[93] Both found that the added intervention was significantly more effective than disc surgery alone for chronic sciatica. Both were poorly reported RCTs. For one study,[63] patients in the intervention group were divided into two non-random groups, with half receiving preoperative acupuncture and the other half postoperative acupuncture. The results were reported separately for preoperative and postoperative patients; thus, only those who had preoperative acupuncture are included in the meta-analysis.

Six RCTs[66,73,78,84,89,106] compared surgery with intraoperative interventions and found no overall significant difference between treatment groups. Two studies[78,84] included patients with either chronic or acute sciatica and one[66] included patients who had had sciatica for longer than 3 months; the chronicity of sciatica was not reported in three studies.[73,89,106] Three studies[73,89,106] were of moderate to good quality, with adequate randomisation in all three and allocation concealment in two.[73,89]

Three studies compared disc surgery with chemonucleolysis: two were RCTs[85,88] and one was a concurrent cohort study (CCS).[76] Overall, there was no statistically significant difference between the intervention groups. However, the results were heterogeneous, with the CCS favouring disc surgery and one of the RCTs[88] showing statistically significant findings in favour of chemonucleolysis. One study[76] included patients who had not received previous disc surgery,

TABLE 6 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Disc surgery vs chemonucleolysis														
471	Dei-Anang, 1990[79] (German language)	NR	CCS	42 days	Reported absence of pain	Patient	100	72	0	101	79	0	0.72 (0.38 to 1.36)	Data inferred from graphs, presented as percentages
44	Javid, 1995[48]	C	CCS	6 weeks	Successful outcome: good or excellent (vs unsuccessful: slight or no improvement)	Patient	100	92	0	100	82	0	2.52 (1.04 to 6.11)	
889	Lee, 1996[104] (German language) (i)[a] (APLD)	NR	CCS	6 weeks	Disappearance of back pain		100	16	?	100	16	?	1.00 (0.47 to 2.13)	Number randomised not stated, 300 included in analysis Excluded 29% chemonucleolysis and 14% surgery
889	Lee, 1996[104] (German language) (ii)[a] (PELD)	NR	CCS	6 weeks	Disappearance of back pain		100	29	?	100	16	?	2.14 (4.08 to 4.26)	Number randomised not stated, 300 included in analysis Excluded 29% chemonucleolysis and 29% surgery
45	Postacchini, 1987[49]	A+C	Non-RCT	1 month	Satisfactory outcome: good or excellent (vs unsuccessful: fair or poor)		84	52	0.03	72	39	0.03	1.38 (0.73 to 2.61)	Data inferred from graphs. Five patients lost to follow-up were excluded. Patients who had surgery in chemonucleolysis group regarded as failure

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
49	Stula, 1990[52] (German language)	C	RCT	Postoperative	Successful outcome: good (vs unsuccessful: unsatisfactory)	Physician	44	40	0.76	25	22	0.43	1.36 (0.28 to 6.65)	Nineteen patients in chemonucleolysis group received surgery and analysed as surgery group
672	Weinstein, 1986[92]	C	CCS	< 6 weeks	Recovered within 2–6 weeks or immediate (vs no recovery, > 12 weeks or 6–12 weeks)		63	39	0.11	85	61	0.03	0.64 (0.32 to 1.28)	Data presented as percentages
Disc surgery vs exercise therapy														
300	Osterman, 2006[68]	A	RCT	6 weeks	Reported full recovery	Patient	28	5	0.03	28	0	0	13.34 (0.70 to 253.89)	
Disc surgery vs intraoperative interventions														
497	Glasser, 1993[82] (i)[b]	C	RCT	1 month	Radicular pain: complete relief (vs partial or no relief)		7	5	0.3	9	8	0.25	0.31 (0.02 to 4.41)	
497	Glasser, 1993[82] (ii)[b]	C	RCT	1 month	Radicular pain: complete relief (vs partial or no relief)		7	5	0.3	7	6	0.3	0.42 (0.03 to 6.06)	
379	Prestar, 1995[71] (German language)	NR	RCT	At discharge	Success: pain free, slight lumbar pain, slight radicular pain (vs failure: radicular pain considerably improved, complaint unchanged)		50	41	0.0	50	41	0.0	1.00 (0.36 to 2.77)	

?, unclear; A, acute; APLD, automated percutaneous lumbar discectomy; C, chronic; A + C, acute and chronic; NR, not reported; OR, odds ratio; PEDL, percutaneous manual and laser discectomy.

a Lee *et al.*[104] included three treatment groups: APLD (i), PELD (ii) and chemonucleolysis (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 2*).

b Glasser *et al.*[82] included three treatment groups: surgery + corticosteroid and bupivicaine (i), surgery + bupivicaine (ii) and surgery + no corticosteroid or bupivicaine (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 2*).

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TABLE 7 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs chemonucleolysis																
453	Brown, 1989[76] (i)[d] (chymopapain)	C	CCS	6 weeks	Leg	VAS (0–100)	19	51	70	60	3 (20.87)	22 (25.48)			−19.00 (−30.70 to −7.30)	SD imputed from weighted average
453	Brown, 1989[76] (ii)[d] (collagenase)	C	CCS	6 weeks	Leg	VAS (0–100)	19	15	70	58	3 (20.87)	46 (25.48)			−43.00 (−58.95 to −27.05)	SD imputed from weighted average
593	Muralikuttan, 1992[85]	A+C	RCT	6 weeks	Leg	VAS (0–100)	46	46	72	64	19 (20.87)	19 (25.48)			0.0 (−3.52 to 9.52)	SD imputed from weighted average
617	Revel, 1993[88]	NR	RCT	1 month	Leg	VAS (0–100)	62	68	68.1 (21.6)	63.4 (24.6)	39.4 (32.28)	28.3 (27.21)			11.10 (0.79 to 21.41)	SD estimated from SE ITT not used Dropouts: 24/165 (15%), group allocation not stated plus further 11/141 (8%); intervention = 7/69, control = 4/72
Disc surgery vs exercise therapy																
300	Osterman, 2006[68]	A	RCT	6 weeks	Leg	VAS (0–100)	28	28	61 (20)	57 (21)	12 (20)	25 (27)			−13.00 (−25.45 to −0.55)	
Disc surgery vs intraoperative interventions																
470	Debi, 2002[78]	A+C	RCT	14 days	Leg	VAS (0–10)	35	26	71	58	22 (20.87)	18 (37.61)			4.00 (−12.03 to 20.03)	SD imputed from weighted average Data inferred from graphs

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
909	Jirarattanaphochai, 2007[106]	NR	RCT	1 month	Leg	NRS (0–10)	52	51	80	80	0 (20.87)	0 (37.61)			0.00 (–11.78 to 11.78)	Median used as mean SD imputed from weighted average ITT using LOCF Dropouts 2/52 (4%): intraoperative 1/51, surgery 2/52
400	Kim, 2003[73]	NR	RCT	30 days	Leg	Composite score (0–100)	12	23	65.8 (16.7)	57.8 (18.4)	25 (28.2)	13.2 (18.8)	–40.8 (30)	–44.60 (29.7)	3.80 (–17.07 to 24.67)	Pain scale 1–6 (also taking into account when patients had pain); six scores per patient combined into a single score (0–100) Dropouts 2/35 (6%): intervention = 1/23, control = 1/12
551	Langmayr, 1995[84]	A + C	RCT	8 days	Overall	VAS (0–100)	12	12	55 (11.54)	54 (21.27)	10 (13.86)	5 (4.5)			5.00 (–3.24 to 13.24) *Repeated measures analysis: between subjects – use of steroids* p = *0.014; within subjects – time preoperative to 8 days postoperative* p < *0.001; interaction between time and steroids* p = *0.04*	Data imputed from graph SD estimated from SE Small sample size ITT not used Dropouts 8%: intervention = 1/13, control = 1/13

continued

TABLE 7 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)			
ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Mean difference (95% CI)[b]	Comment/conversion[c]
276	Lundin, 2003[66]	C	RCT	6 weeks	Overall	VAS (0–100)	42	38	48	54	14 (20.87)	9 (37.61)			5.00 (–8.52 to 18.52)	SD imputed from weighted average Mean inferred from graphs
618	Richter, 2001[89]	NR	RCT	1 month	Leg	VAS (0–10)	142	147	75 (14.8)	78 (14.8)	20 (22.2)	22 (22)			–2.00 (–7.10 to 3.10)	SD estimated from IQR Dropouts 109 (27%): intervention = 57/199, control = 52/199
Disc surgery vs mixed treatments																
705	Starkweather, 2006[93] (surgery + non-opioids)	C	RCT	6 weeks	Overall	VAS (0–100)	20	10	70 (13.42)	66 (18.97)	21 (26.83)	6 (6.32)			15.00 (2.61 to 27.39)	Data extracted from graphs. SD derived from SE
263	Wang, 2000[63] (surgery + alternative)	C	RCT	3 days	Leg	VAS (0–10)	32	32	75.9 (23.2)	71.5 (25.5)	72.4 (23.8)	29.8 (17.5)			42.60 (32.36 to 52.84)	SD calculated from SE [e]Subgroup analysis of 64/145 (44%) patients who were given preoperative acupuncture ITT not used 13/145 (9%) dropped out, group allocation not stated (intervention = 32/67, control = 32/65)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs usual care																
606	Peul, 2007[87]	A	RCT	2 weeks	Leg	VAS (0–100)	140	141	67.2 (27.7)	64.4 (21.2)	28.5 (22.56)	44.2 (22.64)			–15.70 (–20.98 to –10.42) *Repeated measures analysis, difference between groups: 15.7 (95% CI 11.7 to 19.7)*	SD estimated from SE ITT based on LOCF used, but two patients lost to follow-up early on excluded (intervention = 1, control = 1)

A, acute; C, chronic; A + C, acute and chronic; LOCF, last observation carried forward; NR, not reported; NRS, numerical rating scale; SD, standard deviation.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Brown and Tompkins[76] included three treatment groups: chemonucleolysis using chymopapain (i), chemonucleolysis using collagenase (ii) and disc surgery (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 3*).

e Wang and Tronnier[63] compared the use of acupuncture plus disc surgery with placebo acupuncture plus disc surgery. Each intervention group was divided into two: half had preoperative acupuncture and half had postoperative acupuncture. Only patients who received preoperative acupuncture were included in our analyses.

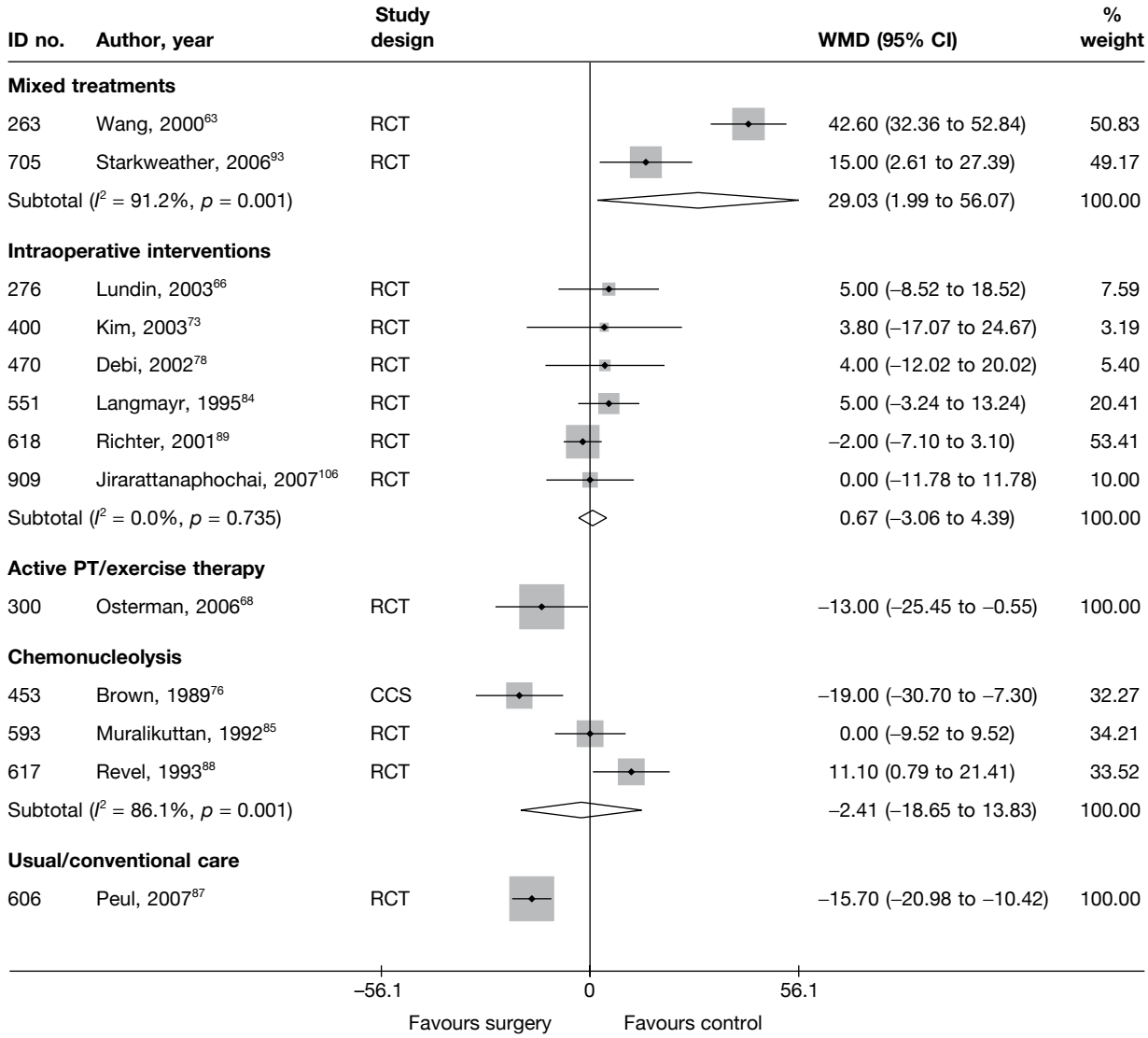

FIGURE 3 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for trials and observational studies comparing disc surgery with alternative interventions. PT, physical therapy. Note: weights are from random effects analysis.

whereas the other[88] included patients who had had previous surgery and also included a high proportion of men.

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 8* and the accompanying forest plot (*Figure 4*). Disc surgery was compared with usual care, exercise therapy, intraoperative interventions and chemonucleolysis. Most studies included patients with chronic sciatica.

One well-conducted RCT[87] compared early surgical intervention with conservative care in patients with severe sciatica for 6–12 weeks. Conservative care included exercise, pain medication and conservative treatment by their GP (or neurologist where necessary). Functional improvement was marginally, but statistically significantly, higher in patients in the conservative or usual care group than in those who received early surgery at 2 weeks. The findings reported by the authors based on repeated-measures analyses showed that patients in the control group had a greater improvement in functional status at 2 weeks (difference between groups for mean

TABLE 8 Summary of the findings of CSOMs at short-term follow-up for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs chemonucleolysis															
593	Muralikuttan, 1992[85]	A + C	RCT	6 weeks	Part of Waddell Disability Index	46	46	6.7	6.2	2.8 (1.21)	3.5 (1.21)	3.9	–2.7	–0.58 (–1.00 to –0.16)	SD for final means calculated from *p*-values (Mann–Whitney *U*-test); most outcomes showed skewed distribution
617	Revel, 1993[88]	NR	RCT	1 month	Waddell Disability Index and Main Scale	62	69	6 (2.55)	4.9 (2.49)	1.5 (3.15)	1.5 (1.21)	–1.05	–3.4	0.00 (–0.34 to 0.34)	SD derived from SE Dropouts: 24/165 (15%), group allocation not stated plus further 7/141 (5%); intervention = 7/69, control = 3/72
Disc surgery vs exercise therapy															
300	Osterman, 2006[68]	A + C	RCT	6 weeks	ODI	28	28	39 (15)	39 (14)	16 (16)	22 (16)	–23	–17	–0.38 (–0.90 to 0.15)	ITT (LOCF), but one patient who did not meet inclusion criteria was excluded from analysis
Disc surgery vs intraoperative interventions															
400	Kim, 2003[73]	NR	RCT	30 days	Composite scale	12	23	52.3 (22.7)	46.9 (21.3)	32.8 (22.2)	19.7 (20.5)	–19.4 (25.2)	–27.2 (26)	0.62 (–0.09 to 1.34)	

continued

TABLE 8 Summary of the findings of CSOMs at short-term follow-up for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
366	Lavyne, 1992[70]	A + C	Q-RCT	6 weeks	Scale based on analgesic use, functional status, hospital stay and return to work interval (max score 8)	36	42			7.44 (0.13)	7.3 (0.12)			1.12 (0.64 to 1.60)	ITT not used Dropouts 6 (7%): intervention = 0/42, control = 6/42
618	Richter, 2001[89]	NR	RCT	1 month	FFbH-R	177	180	50	49	27.3 (22.48)	28.7 (22.48)			–0.06 (–0.27 to 0.15)	SD calculated from weighted average SD for FFbH-R from long-term follow-up disc surgery studies ITT not used Dropouts 109 (27%): intervention = 52/199, control = 57/199
Disc surgery vs usual/conventional care															
606	Peul, 2007[87]	A	RCT	2 weeks	RMDQ	140	141	16.5 (4.4)	16.3 (3.9)	14.4 (5.92)	13 (5.96)	–2.1	–3.3	0.24 (0.00 to 0.47) *–1.6 (95% CI –2.8 to –0.3), repeated-measures analysis of variance based on final means*	SD derived from SE

A, acute; C, chronic; A + C, acute and chronic; FFbH-R, Hanover functional ability questionnaire (Funktionsgragebogen Hannover); LOCF, last observation carried forward; NR, not reported; SD, standard deviation.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

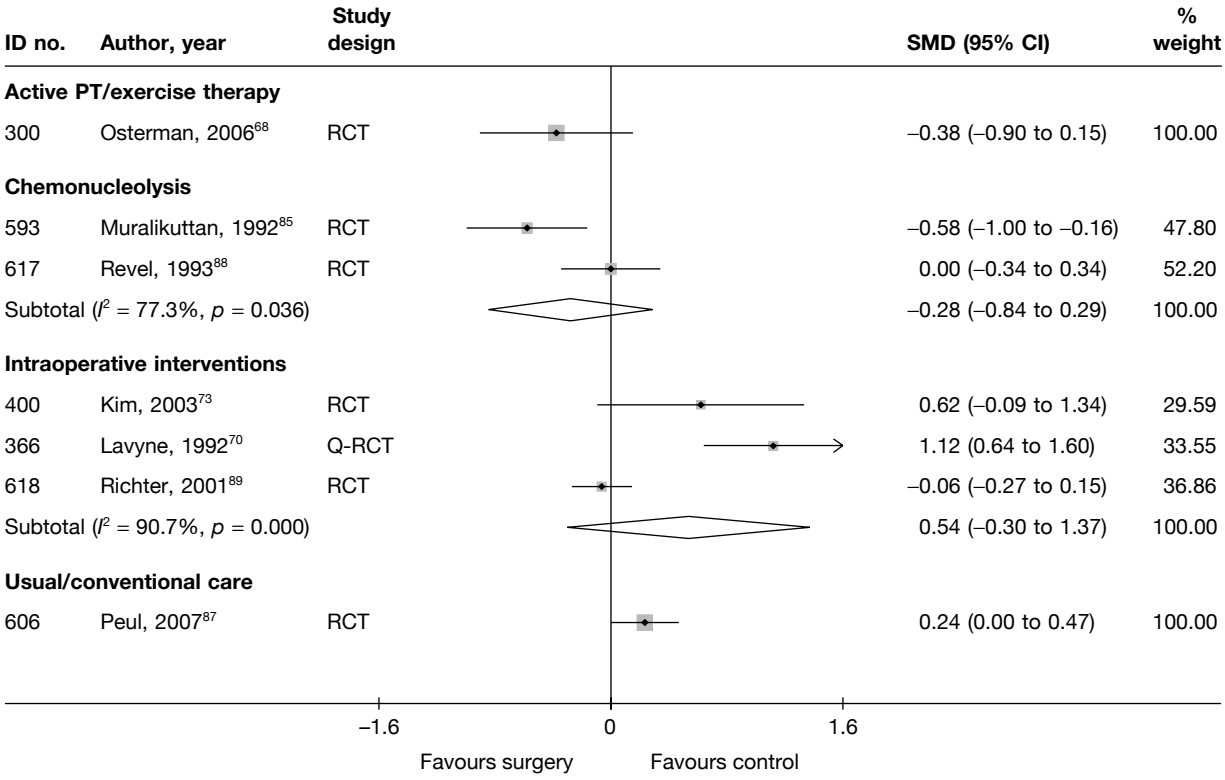

FIGURE 4 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for trials comparing disc surgery with alternative interventions (grouped by comparator then ordered by author). PT, physical therapy. Note: weights are from random effects analysis.

RMDQ: –1.6; 95% CI –2.8 to –0.3), which then reversed to show a greater improvement among patients treated with surgery at 8 weeks (difference between groups for mean RMDQ 3.1; 95% CI 1.7 to 4.3). Mean scores plotted over time showed that the curves crossed at 4 weeks.

One well-conducted RCT[68] found disc surgery plus exercise therapy to be superior to exercise therapy alone for acute sciatica due to an intervertebral disc extrusion or sequester, but the findings were not statistically significant.

Three studies[70,73,89] compared disc surgery with intraoperative interventions, for which the overall findings showed a greater improvement in functional status associated with disc surgery at 4–6 weeks, but the difference between the treatment groups was not statistically significant. The findings were heterogeneous. One study[70] included patients with either chronic or acute sciatica, but the chronicity of sciatica was not reported in the remaining two studies.[73,89] Two studies[73,89] were RCTs of moderate quality with adequate randomisation and allocation concealment, and the remaining study was a Q-RCT.[70]

Two moderate quality RCTs[85,88] compared disc surgery with chemonucleolysis. Pooled analysis showed a non-statistically significant difference between the intervention groups in favour of disc surgery.

Disc surgery results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 9* and the accompanying forest plot (*Figure 5*). Disc surgery was compared with usual care, non-opioids

TABLE 9 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
Disc surgery vs chemonucleolysis														
453	Brown, 1989[76] (i)[b] (chymopapain)	C	CCS	3 months	Overall improvement: excellent or good (vs fair, poor or failed)		19	16	0	51	26	0	5.13 (1.33 to 19.78)	Data reported as percentages
453	Brown, 1989[76] (ii)[b] (collagenase)	C	CCS	3 months	Overall improvement: excellent or good (vs fair, poor or failed)		19	16	0	15	9	0	3.56 (0.71 to 17.76)	Data reported as percentages
44	Javid, 1995[48]	C	CCS	6 months	Successful outcome: good or excellent (vs slight or no improvement)	Patient	100	85	0	100	88	0	0.77 (0.34 to 1.75)	
117	Lagarrigue, 1991[54] (French language)	C	CCS	2 months	MacNab criteria: excellent or good (vs mediocre, failure)	Patient and physician	751	675	0	334	238	0	3.58 (2.56 to 5.01)	Data reported as percentages
889	Lee, 1996[104] (German language) (i)[c] (APLD)	NR	CCS	2 months	Disappearance of back pain		100	35	?	100	29	?	1.32 (1.73 to 2.39)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 14%
889	Lee, 1996[104] (German language) (ii)[c] (PELD)	NR	CCS	2 months	Disappearance of back pain		100	8	?	100	29	?	0.21 (0.09 to 0.49)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 29%

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
45	Postacchini, 1987[49]	A + C	Non-RCT	3 months	Successful outcome: excellent or good (vs fair or poor)		84	65	0.03	72	51	0.03	1.41 (0.69 to 2.90)	Data inferred from graphs. Five lost to follow-up were excluded. Patients who had surgery in chemonucleolysis group regarded as failure
617	Revel, 1993[88]	NR	RCT	6 months	Treatment success: good or very good (vs none or moderate)	Patient	69	30	?	72	44	?	0.49 (0.25 to 0.96)	ITT not used. 24/165 patients dropped out at beginning, group allocation not stated
893	Watters,1988[105]	A + C	Non-RCT	Mean 46 days	Success of surgical results: excellent or good (vs fair or poor)	Physician	50	44	0.0	50	32	0.0	4.13 (1.47 to 11.56)	Data reported as percentages
672	Weinstein, 1986[92]	C	CCS	3–6 months	Recovered within 6–12 weeks, 2–6 weeks or immediate (vs no recovery or >12 weeks)		63	53	0.11	85	71	0.03	1.05 (0.43 to 2.53)	Data reported as percentages
Disc surgery vs exercise therapy														
300	Osterman, 2006[68]	A	RCT	6 months	Reported full recovery	Patient	28	5	0.03	28	4	0	1.30 (0.31 to 5.47)	
Disc surgery vs non-opioids														
475	Dubourg, 2002[80]	A	CCS	6 months	Recovery improvement (vs failure) according to change in VAS and muscle strength		32	25	0.18	25	24	0.11	0.15 (0.02 to 1.30)	

continued

TABLE 9 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
144	Rossi, 1993[57] (Italian language)	C	Non-RCT	6 months		Patient	?	68%	?	?	55%	?		Data reported as percentages; 40 patients included, but not stated how many were in each group. The study included three intervention groups, but all surgery patients (two groups) were compared with conservative treatment
Disc surgery vs usual care														
294	Koranda, 1995[67] (Czech language)	C	Q-RCT	3 months	Effective results: excellent, very good, good (vs satisfactory, poor or worse)	Patient	54	42	0.0	46	27	0.0	2.46 (1.03 to 5.88)	Duration of follow-up not clear; both groups had 3 months' conservative treatment then one group received surgery. Patients in control group who required surgery were classified as treatment failure. 28 patients in surgery group did not receive surgery as they got better during the conservative therapy period

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
606	Peul, 2007[87]	A	RCT	26 weeks	Satisfaction with recovery: 'complete' or 'nearly recovery complete' on a seven-point Likert scale (other 5 scores = unsatisfactory recovery)	Patient	140	108	0.01	141	100	0.01	1.38 (0.81 to 2.37) *Repeated measurements analysis adjusting for baseline values: 6.6% (95% CI –3.7% to 17.0%)*	Data presented as percentages. ITT using LOCF reported for mean Likert score
750	Weinstein, 2006[98] (a)	A + C	CCS	3 months	Satisfaction with current symptoms: very/somewhat satisfied	Patient	198	Change: 54% (SE 3.5)	0.19	211	Change: 43% (SE 3.4)	0.18	*Treatment effect 11.3% (95% CI 1.6% to 20.9%)*	Only mean percentage change and difference between groups reported. 19/222 patients who chose to be in non-operative group received surgery and 44/521 who chose to be in surgery group did not have surgery. Analysis based on treatment received not initial group allocation

continued

TABLE 9 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
751	Weinstein, 2006[99] (b)	A + C	RCT	3 months	Satisfaction with current symptoms: very/somewhat satisfied	Patient	466	Change: 68% (SE 2.3)	0.11	190	Change: 29% (SE 3.7)	0.14	*Treatment effect 38.7% (95% CI 30.0% to 47.7%)*	Only mean percentage change and difference between groups reported 472/501 included in ITT analysis using LOCF and longitudinal regression models Crossovers: intervention 117/232 (50%), control 71/240 (30%)

?, unclear; A, acute; A + C, acute and chronic; APLD, automated percutaneous lumbar discectomy; C, chronic; LOCF, last observation carried forward; NR, not reported; OR, odds ratio; PELD, percutaneous manual and laser discectomy.

a Results reported by study in italics.

b Brown and Tompkins[76] included three treatment groups: chemonucleolysis using chymopapain (i), chemonucleolysis using collagenase (ii) and disc surgery (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 5*).

c Lee *et al.*[104] included three treatment groups: APLD (i), PELD (ii) and chemonucleolysis (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 5*).

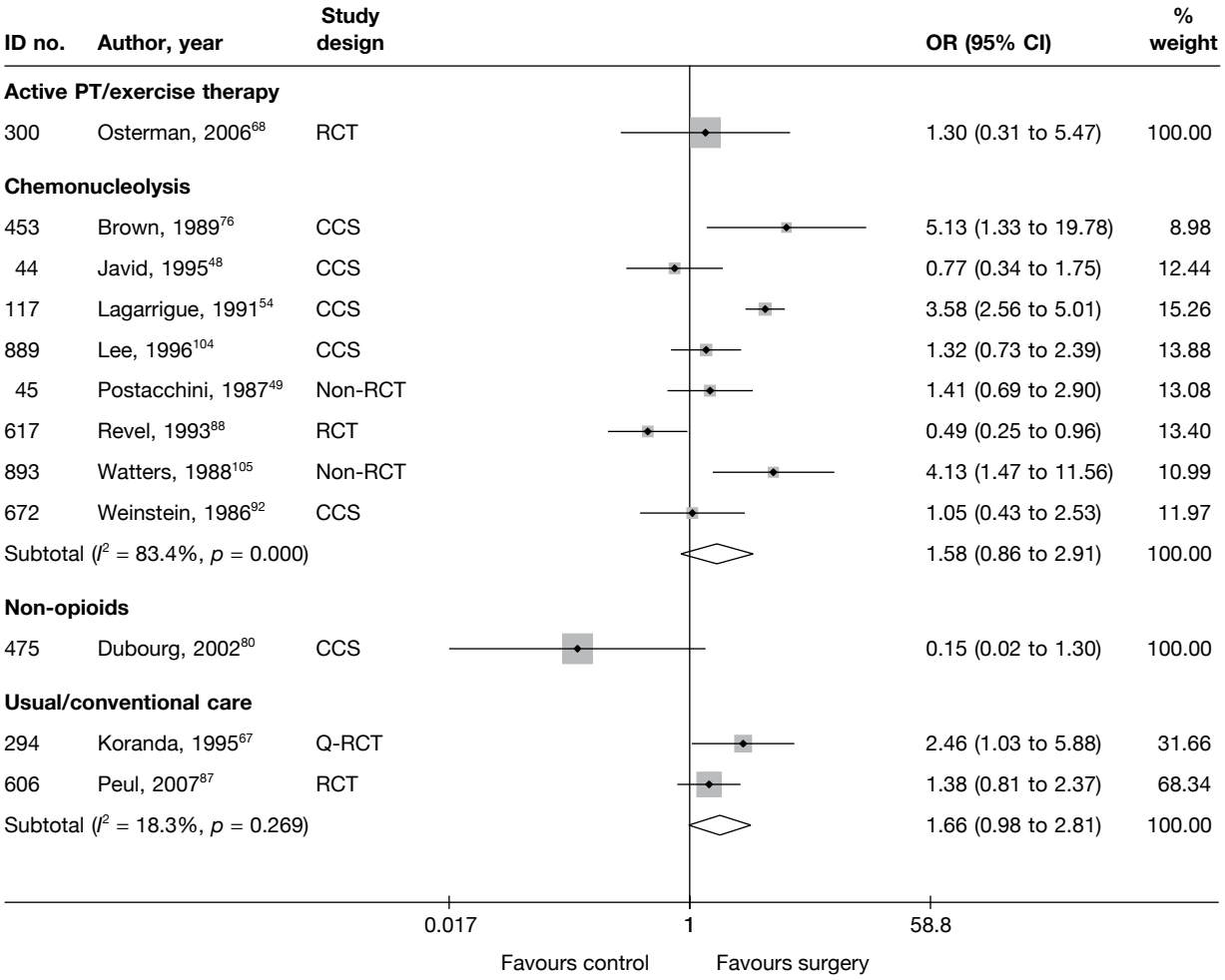

FIGURE 5 Summary of the findings of global effect at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions. PT, physical therapy. Note: weights are from random effects analysis.

and chemonucleolysis. One further study[68] compared disc surgery plus exercise therapy with exercise therapy alone for patients with acute sciatica due to an intervertebral disc extrusion or sequestered disc. Duration of follow-up ranged from 2 to 3 months.

Four studies[67,87,98,99] showed that disc surgery was superior to conservative treatment or usual care, but the meta-analysis of two studies[67,87] was not statistically significant. One was a well-conducted RCT[87] that included patients with acute sciatica and the other was a poorly reported and conducted Q-RCT[67] that included patients with chronic sciatica. The remaining two studies[98,99] could not be included in the meta-analysis because they only reported the percentage change and difference between groups. One was an RCT [the Spine Patient Outcomes Research Trial (SPORT)][99] and the other a parallel observational cohort study. Both included patients with acute or chronic sciatica. The RCT was well conducted and rated strong for external validity, but recruitment rates were poor and may have been affected by the fact that all patients had already tried non-operative treatment for 6 weeks. Adherence to treatment protocols was also low, with 71/240 (30%) patients in the usual care group having had surgery at 3 months (44 patients at 6 weeks) and only 115/232 (50%) patients in the surgery group having undergone surgery during the same interval (74 patients at 6 weeks). The analyses in both studies were adjusted for a number of covariates including missing data. Both studies reported statistically significant findings in favour of disc surgery.

According to a well-conducted RCT,[68] there was no real difference between disc surgery plus exercise therapy and exercise therapy alone in terms of reported full recovery at 6 months in patients with acute sciatica.

One poorly reported CCS[80] found non-opioids to be more effective than disc surgery for recovery or improvement in patients with acute sciatica, but the findings were not statically significant. A second poorly conducted study[57] found that more patients in the surgery group were satisfied with cure than those in the non-opioids group, but results were only reported as percentages without stating how many patients were in each group.

Eight studies[48,49,54,76,88,92,104,105] compared disc surgery with chemonucleolysis, for which there was no overall difference between the groups. Only one of these studies was an RCT,[88] of moderate quality, which found chemonucleolysis more effective than disc surgery. However, the withdrawal rate in the surgery group (at least 41%) was much greater than that of the chemonucleolysis group (at least 19%), with dropouts being given a poor outcome in the analysis. The duration, or chronicity of sciatica was not stated. The results and methods of the remaining studies were generally poorly reported. The funnel plot (*Figure 6*), for publication and other biases, does not appear to show asymmetry, but does not include many studies and demonstrates a lack of large studies.

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 10* and the accompanying forest plot (*Figure 7*). Disc surgery was compared with usual care, non-opioids, exercise therapy, epidurals, chemonucleolysis and intraoperative interventions.

One well-conducted RCT[87] showed that early surgical intervention, compared with usual care, resulted in a statistically significantly greater reduction in pain intensity in patients with severe sciatica for 6–12 weeks. However, the size of the effect, or reduction in pain, at 6 months was less than that at 2 weeks (WMD –6.10; 95% CI –11.38 to –0.82).

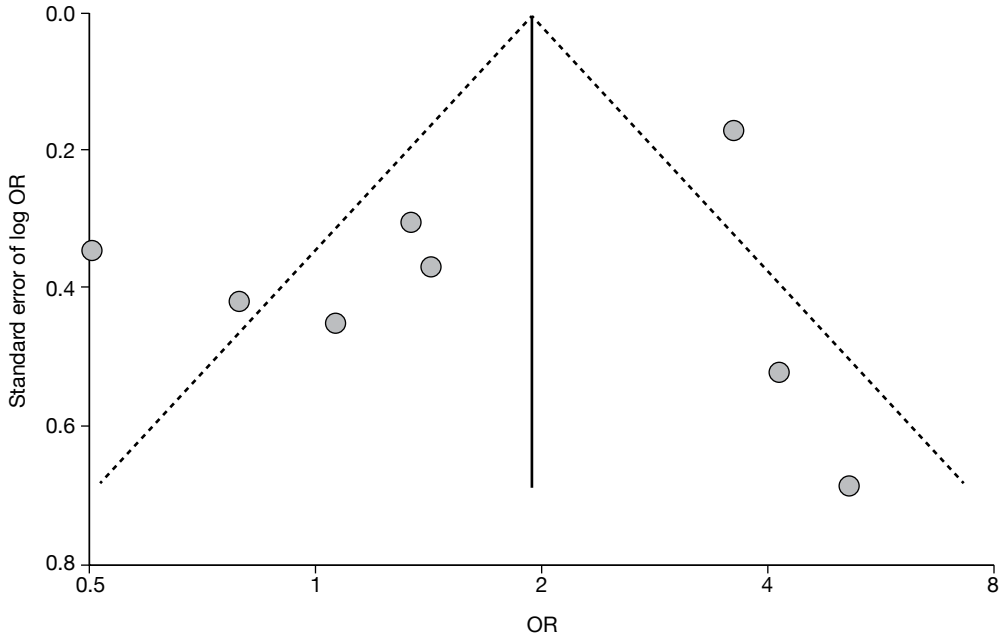

FIGURE 6 Funnel plot with pseudo 95% CIs for studies comparing disc surgery with chemonucleolysis at medium-term follow-up (>6 weeks to ≤6months).

TABLE 10 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs chemonucleolysis																
453	Brown, 1989[76] (i)[d] (chymopapain)	C	CCS	12 weeks	Leg	VAS (0–100)	19	51	70	60	4 (24.43)	14 (23.76)			–10.0 (–22.77 to 2.77)	SD imputed from weighted average
453	Brown, 1989[76] (ii)[d] (collagenase)	C	CCS	12 weeks	Leg	VAS (0–100)	19	15	70	58	4 (24.43)	22 (23.76)			–18.0 (–34.29 to –1.71)	SD imputed from weighted average
593	Muralikuttan, 1992[85]	A+C	RCT	3 months	Leg	VAS (0–100)	46	46	72	64	14 (24.43)	20 (23.76)			–6.00 (–15.85 to 3.85)	SD imputed from weighted average Most outcomes showed skewed distribution
617	Revel, 1993[88]	NR	RCT	6 months	Leg	VAS (0–100)	69	72	68.1 (21.6)	63.4 (24.61)	35.6 (34.89)	17.6 (23.76)			18.00 (8.11 to 27.89)	SD estimated from SE 24 patients excluded from analysis, group allocation not stated

continued

TABLE 10 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs epidural/intradiscal injection																
725	Buttermann, 2004[95]	C	RCT	4–6 months	Leg	VAS (0–10)									*Significant less pain experienced by surgery group at 1–3 months' and 4–6 months' follow-up:* $p < 0.0001$ *and* $p = 0.03$ *respectively, Student's t-test*	No data reported
Disc surgery vs exercise therapy																
300	Osterman, 2006[68]	A	RCT	6 months	Leg	VAS (0–100)	28	28	61 (20)	57 (21)	9 (20)	18 (29)			–9.00 (–22.05 to 4.05)	
Disc surgery vs intraoperative interventions																
268	Aminmansour, 2006[64] (i)[e] (40 mg dexamethasone)	NR	Q-RCT	2 months	Leg	VAS (0–10)	22	19	55.5 (14.3)	54.2 (15)	28.2 (26.7)	11.6 (12.4)			16.60 (4.13 to 29.07)	
268	Aminmansour, 2006[64] (ii)[e] (80 mg dexamethasone)	NR	Q-RCT	2 months	Leg	VAS (0–10)	22	20	55.5 (14.3)	53 (13.4)	28.2 (26.7)	11.5 (14.4)			16.70 (3.88 to 29.52)	
Disc surgery vs non-opioids																
475	Dubourg, 2002[80]	A	CCS	6 months	Overall	VAS (0–100)	36	28	52.2 (28.5)	47.7 (34)	13.2 (18.8)	14.8 (20.6)			–1.60 (–11.39 to 8.19)	Dropouts 7/67 (10%): intervention 4/39, control 3/28

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
909	Jirarattanaphochai, 2007[106]	NR	RCT	3 months	Leg	NRS (0–10)	52	51	80	80	0 (24.43)	0 (19.98)		4.80	0.0 (–8.61 to 8.61)	Median used as mean SD imputed from weighted average ITT using LOCF Dropouts 2/52 (4%): intraoperative 1/51, surgery 2/52
400	Kim, 2003[73]	NR	RCT	6 months	Leg	Composite scale (0–100)	11	22	65.8 (16.7)	57.8 (18.4)	20.6 (29.4)	15.8 (16)	–44.2 (32.5)	–40.9 (27.8)	4.80 (–13.82 to 23.42)	Pain scale 1–6 (also taking into account when patients had pain); six scores per patient combined into a single score (0–100) Change scores used for the meta-analysis. Dropouts 2/35 (6%): intervention 1/23, control 1/12

continued

TABLE 10 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
551	Langmayr, 1995[84]	A+C	RCT	6 months	Overall	VAS (0–100)	12	12	55 (11.54)	54 (21.27)	5 (24.43)	4 (19.98)			1.00 (–16.86 to 18.86) *Repeated-measures analysis: between subjects – use of steroids* p = *0.014; within subjects – time preoperative to 8 days postoperative* p < *0.001; interaction between time and steroids* p = *0.04*	SD imputed from weighted average Small sample size Dropouts 8%: intervention 1/13, control 1/13
276	Lundin, 2003[66]	C	RCT	26 weeks	Overall	VAS (0–100)	42	38	48	54	10 (24.43)	8 (19.98)			2.00 (–7.74 to 11.74)	SD imputed from weighted average Mean inferred from graphs
854	Rasmussen, 2008[101]	NR	RCT	2 months	Leg	Composite NRS (0–30)	100	100	68.3	70	43.3 (24.43)	23.3 (19.98)			20.0 (13.81 to 26.19)	Median used to represent mean SD imputed from weighted average Three separate pain measures using NRS (0–10) combined: pain now, worst, and average pain in the last 2 weeks, for back and leg pain separately

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
618	Richter, 2001[89]	NR	RCT	6 months	Leg	VAS (0–10)	176	180	75 (14.8)	78 (14.8)	20 (25.9)	23 (29.6)			–3.00 (–8.77 to 2.77)	SD estimated from IQR ITT not used Dropouts 42 (11%): intervention 23/199, control 19/199
Disc surgery vs usual care																
606	Peul, 2007[87]	A	RCT	26 weeks	Leg	VAS (0–100)	140	141	67.2 (27.7)	64.4 (21.2)	8.4 (22.56)	14.5 (22.64)			–6.10 (–11.38 to –0.82) *Repeated measures analysis, difference between groups: 6.1 (95% CI 2.2 to 10.0)*	SD estimated from SE ITT based on LOCF used, but two patients lost to follow-up early on excluded (intervention = 1, control = 1)

A, acute; A + C, acute and chronic; C, chronic; LOCF, last observation carried forward; NR, not reported; NRS, numerical rating scale; SD, standard deviation.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Brown and Tompkins[76] included three treatment groups: chemonucleolysis using chymopapain (i), chemonucleolysis using collagenase (ii) and disc surgery (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 7*).

e Aminmansour *et al.*[64] included three treatment groups: open fenestration with i.v. 40 mg dexamethasone (i), open fenestration with i.v. 80 mg dexamethasone (ii) and open fenestration with i.v. distilled water (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 7*).

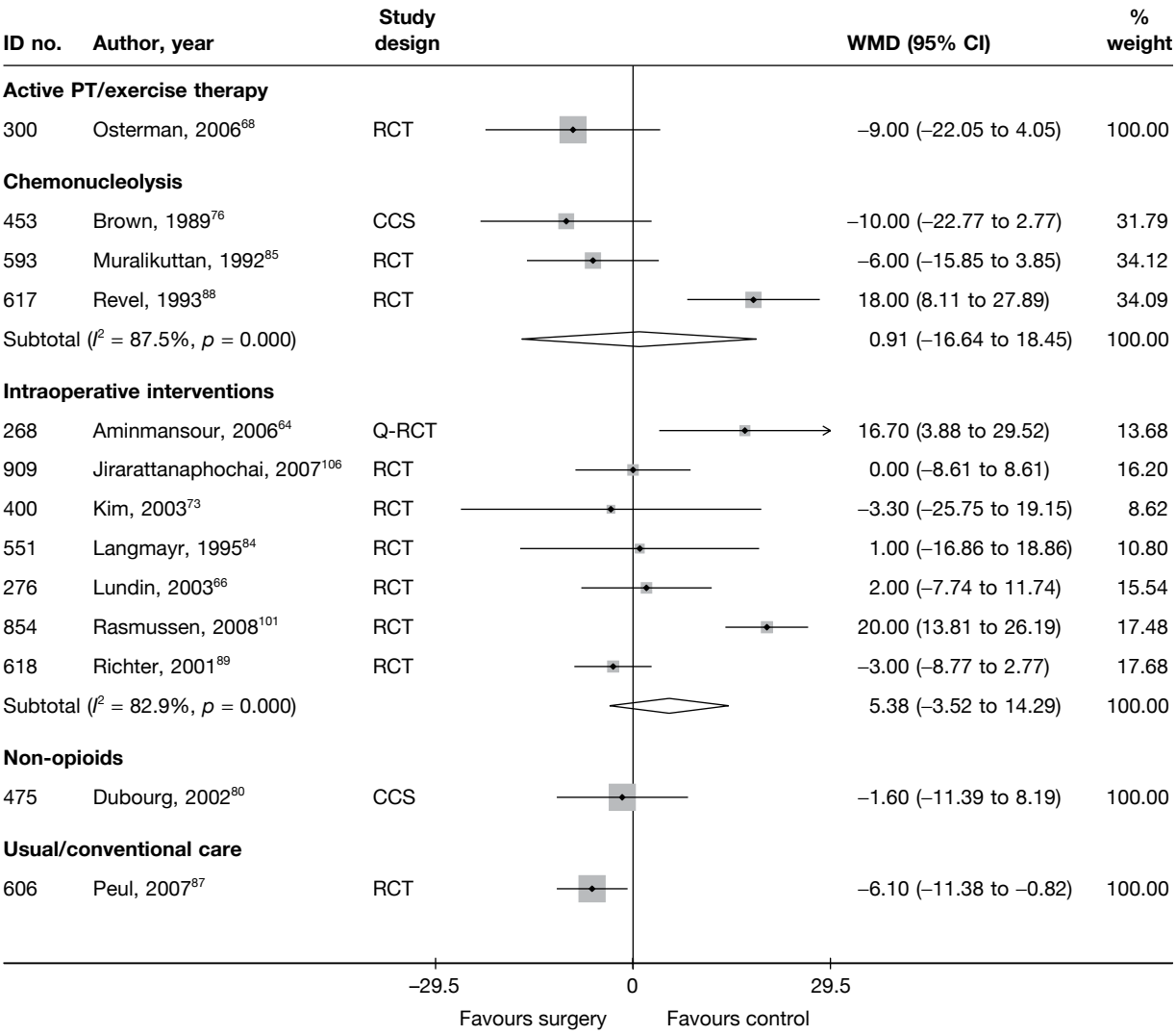

FIGURE 7 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions. PT, physical therapy. Note: weights are from random effects analysis.

One poorly reported CCS[80] found no important difference between disc surgery and non-opioids in reduction in pain intensity at 6 months.

As with the global effect, one well-conducted RCT[68] found non-statistically significant findings in favour of disc surgery plus exercise therapy, compared with exercise therapy alone, in patients with acute sciatica at 6 months' follow-up.

One poorly reported RCT[95] compared the use of epidurals with disc surgery in patients with chronic sciatica [mean 3.55 months, standard deviation (SD) 2.75 months], and found that patients in the disc surgery group experienced significant less leg pain at 1–3 months' and 4–6 months' follow-up than those in the control group ($p < 0.0001$ and $p = 0.03$ respectively; Student's t-test). The methods of randomisation and allocation concealment were not reported.

Six RCTs[66,73,84,89,101,106] and one Q-RCT[64] compared surgery with intraoperative interventions and found no overall statistically significant difference between treatment groups. The results were heterogeneous, with two studies[64,101] reporting statistically significant findings in favour of intraoperative interventions. One study[84] included patients with acute and chronic sciatica

(median symptom duration 35 days, range 14–150 days) and one[66] included patients with chronic sciatica (mean 4.5 months); duration of symptoms was not stated in the remaining studies. Duration of follow-up ranged from 2 months to 6 months. Four studies[73,89,101,106] were of moderate to good quality, with adequate randomisation in all four and allocation concealment in two.[73,89]

As with pain at short-term follow-up, these studies compared disc surgery with chemonucleolysis; two were RCTs[85,88] and one was a CCS.[76] Overall, there was no statistically significant difference between the intervention groups, but again the results were heterogeneous, with one study[88] showing statistically significant findings in favour of chemonucleolysis. This study included patients who had had previous surgery and also included a high proportion of men.

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 11* and the accompanying forest plot (*Figure 8*). Disc surgery was compared with usual care, exercise therapy, epidural, intraoperative interventions and chemonucleolysis.

Four studies[72,87,98,99] compared disc surgery with usual care, for which the pooled findings showed no statistically significant difference between the intervention groups at 3–6 months. However, the findings were very heterogeneous, with one CCS reporting statistically significant findings in favour of surgery and another CCS reporting statistically significant findings in favour of usual care. Pooled analysis of the two well-conducted RCTs showed marginally statistically significant findings in favour of surgery (SMD –0.15; 95% CI –0.30 to –0.00; the findings were homogeneous $I^2 = 0\%$, $p = 0.84$).

One well-conducted RCT[68] found non-statistically significant findings in favour of disc surgery plus exercise therapy compared with exercise therapy alone in patients with acute sciatica at 6 months' follow-up.

One poorly reported RCT[95] compared the use of epidurals with disc surgery in patients with chronic sciatica. The methods of randomisation and allocation concealment were not stated and insufficient data were reported to estimate the mean difference between the intervention groups. The authors reported that there was a significantly greater decrease in disability in the discectomy group than in the epidural group at the 1–3 month follow-up interval ($p < 0.015$, Student's t-test).

Four moderate RCTs[73,89,106,107] compared disc surgery with intraoperative interventions. Pooled analysis for three RCTs[73,89,107] showed no overall statistically significant difference between treatment groups at 6 months. The fourth RCT[106] did not report arm-level data, but also found no statistically significant difference between the intervention groups (at 3 months), based on repeated measures of analysis of variance using generalised estimating equation models (difference between groups –0.52, 95% CI –3.91 to 2.87, favouring intraoperative group; $p = 0.763$).

Three RCTs[85,88,96] compared disc surgery with chemonucleolysis, for which pooled analyses showed no important difference between the intervention groups at 3–6 months. However, the findings were heterogeneous.

Results at long-term follow-up (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 12* and the accompanying forest plot (*Figure 9*). Disc surgery was compared with usual care, active physical therapy (PT), intraoperative interventions, mixed treatments, chemonucleolysis and spinal cord

TABLE 11 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs chemonucleolysis															
727	Ejeskar, 1983[96]	A+C	RCT	6 months	Composite score	14	15			9.71 (4.79)	9.27 (6.62)			0.08 (–0.65 to 0.80)	
593	Muralikuttan, 1992[85]	A+C	RCT	3 months	Part of Waddell Disability index	46	46	6.7	6.2	2.3 (1.28)	3 (1.28)	–4.4	–3.2	–0.55 (–0.96 to –0.13)	SD for final means calculated from *p*-values (Mann–Whitney *U*-test); most outcomes showed skewed distribution
617	Revel, 1993[88]	NR	RCT	6 months	Waddell Disability Index and Main Scale	69	72	6 (3.9)	4.9 (2.55)	3.4 (3.32)	2.3 (4.65)	–2.6	–2.6	0.27 (–0.06 to 0.60)	SD calculated from SE Dropouts 24/165 (15%): group allocation not stated
Disc surgery vs epidural															
725	Buttermann, 2004[95]	A+C	RCT	1–3 months	ODI	50	50							*Significantly greater decrease in disability in discectomy group compared with epidural; p < 0.015, Student's t-test*	
Disc surgery vs exercise therapy															
300	Osterman, 2006[68]	A	RCT	6 months	ODI	28	28	39 (15)	39 (14)	8 (12)	12 (15)	–31	–27	–0.29 (–0.82 to 0.23)	ITT used LOCF, but one patient that did not meet inclusion criteria excluded from analysis

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs intraoperative interventions															
909	Jirarattanaphochai, 2007[106]	NR	RCT	3 months	ODI	52	51	49 (16)	54 (15)					*Repeated measures of analysis of variance using generalised estimating equation models: –0.52 (95% CI –3.91 to 2.87), p = 0.763*	ITT used LOCF Dropouts 3/103 (3%): intervention 2/52, control 1/51
400	Kim, 2003[73]	NR	RCT	6 months	Composite scale	11	22	52.3 (22.7)	46.9 (21.3)	19.4 (23.3)	17.6 (19.8)	–30.4 (25.8)	–28.1 (21.7)	0.09 (–0.64 to 0.81)	
618	Richter, 2001[89]	NR	RCT	6 months	FFbH-R	177	180	50	49	20 (22.48)	21.5 (22.48)			–0.07 (–0.27 to 0.14)	SD calculated from weighted average SD for FFbH-R from long-term follow-up disc surgery studies ITT not used Dropouts 42 (11%): intervention 19/199, control 23/199
915	de Tribolet, 1998[107]	NR	RCT	6 months		128	128			1.58 (0.99)	1.24 (1.02)			0.34 (0.09 to 0.59)	

continued

TABLE 11 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs usual/conventional care															
386	Atlas, 1996[72]	C	CCS	6 months	Modified RMDQ	236	181	17.8 (4)	13.6 (5.9)	7 (4)	9.7 (5.9)	–10.8	–3.9		Data inferred from graphs. No SDs reported. Baseline SD taken from 10-year follow-up data (see *Condition-specific outcome measures at long-term follow-up*), but this does not relate to same number of patients. Same SDs used for final means
606	Peul, 2007[87]	A	RCT	26 weeks	RMDQ	140	141	16.5 (4.4)	16.3 (3.9)	4 (5.94)	4.8 (5.96)	–12.5	–11.5	–0.13 (–0.37 to 0.10)	ITT using LOCF, but two patients lost to follow-up early on were not included in analysis; Number randomised: intervention 141, control 142, baseline data based on all patients (sensitivity analysis showed no difference between ITT and non-ITT)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
751	Weinstein, 2006[99]	A + C	RCT	3 months	MODEMS version of ODI	198	211	47.5 (21.4)	46.3 (20.6)	21.5 (21.4)	25 (20.6)	–26 (23.92)	–21.3 (23.24)	*Adjusted difference between groups based on change scores: –4.7 (95% CI –9.3 to –0.2)*	Baseline SD used for final mean ITT using LOCF and longitudinal mixed model controlling for covariates associated with missing values, but only included 472/501 patients with baseline data Dropouts: intervention 47/245 (19%), control 45/256 (18%) Crossovers: intervention 117/232 (50%), control 71/240 (30%)
750	Weinstein, 2006[98]	A + C	CCS	3 months	MODEMS version of ODI	466	190	56.7 (18.9)	35.9 (20.1)	20.6 (18.9)	15 (20.1)	–36.1 (18.78)	–20.9 (20.68)	*Adjusted difference between groups based on change scores: –15.2 (95% CI –18.5 to –11.8)*	Baseline SD used for final mean Dropouts 87/743 (12%): intervention 55/521, control 32/222. 19/222 patients who chose to be in the non-operative group received surgery and 44/521 who chose to be in the surgery group did not have surgery Analysis based on treatment received, not initial group allocation

A, acute; A + C, acute and chronic; B-U&LPI, Bergquist-Ullman and Larson, pain index; C, chronic; FFbH-R, Hanover functional ability questionnaire (Funktionsfragebogen Hannover); LBPRS, lower back pain rating scale; LOCF, last observation carried forward; MODEMS, Modified Oswestry Disability Index (American Academy of Orthopaedic Surgeons); NR, not reported.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

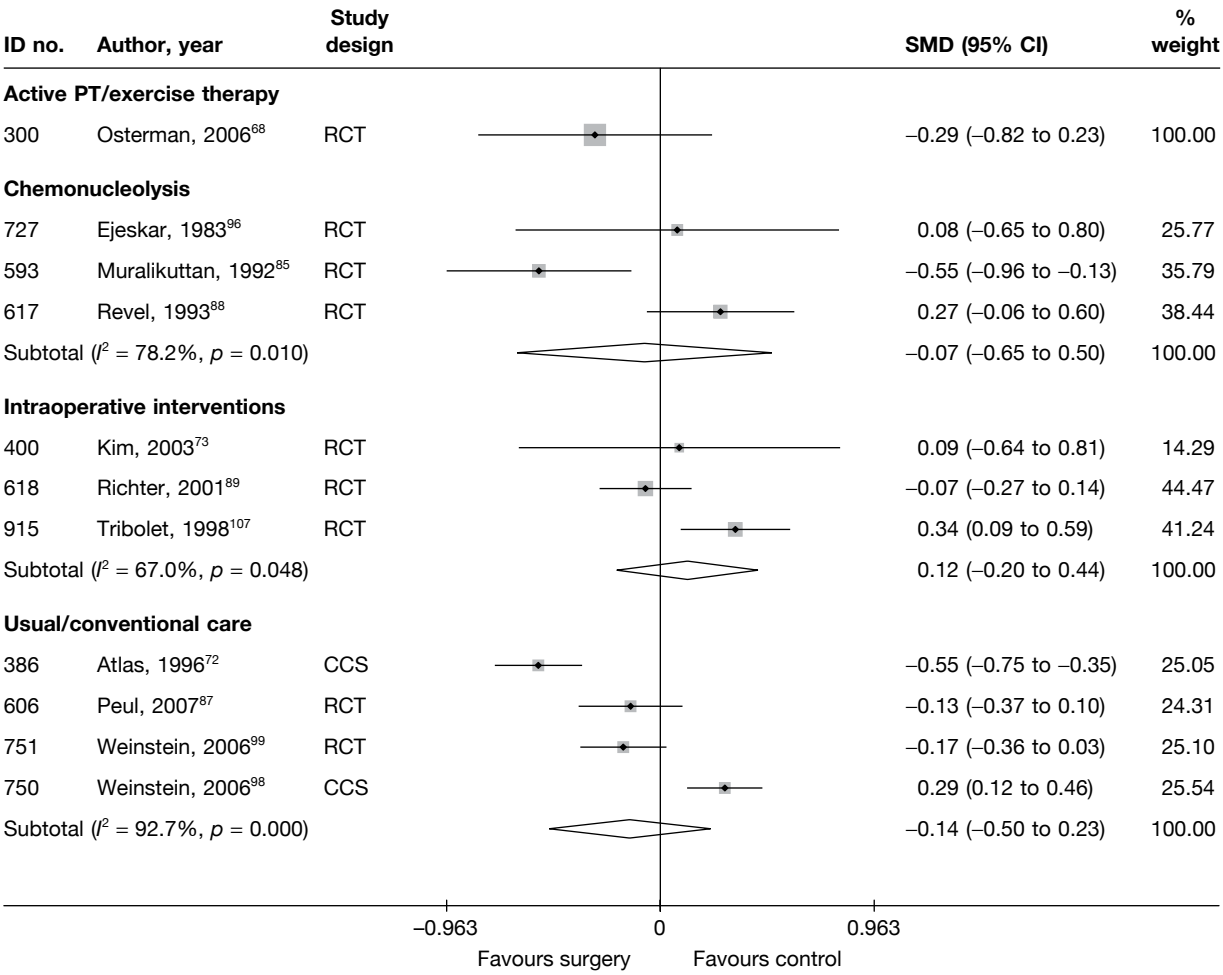

FIGURE 8 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6months) for studies comparing disc surgery with alternative interventions. PT, physical therapy. Note: weights are from random effects analysis.

stimulation (others). Duration of follow-up ranged from 1 year to 10 years. Most studies included patients with chronic sciatica or a mixture of chronic and acute symptoms.

Six studies[62,72,87,91,98,99] compared disc surgery with usual care; the overall findings for four[62,72,87,91] included in the meta-analysis showed a statistically significant difference in favour of surgery. Two were RCTs, for which the duration of follow-up ranged from 1 year to 10 years.[87,91] Only one RCT,[91] which included patients with chronic sciatica, reported statistically significant findings. The overall quality rating for this study was poor, with the method of randomisation not stated and allocation concealment considered partial. The study was published in 1983 and surgical techniques are likely to have changed since then. The remaining RCT[87] was published in 2007. It was a well-conducted study that included patients with acute sciatica. Two further studies[98,99] could not be included in the meta-analysis because they reported only the percentage change and difference between groups. One was a well-conducted RCT (SPORT)[99] and the other a parallel observational cohort study.[98] Both included patients with acute or chronic sciatica. The analyses in both studies were adjusted for a number of covariates including missing data. The treatment effect was much smaller in the RCT[99] than in the CCS[98] and the findings were not statistically significant. However, adherence to treatment protocols was low in the RCT, with 107/240 (45%) patients in the usual care group having surgery after 2 years and only 140/232 (60%) patients in the surgery group receiving surgery during the same 2-year period.

TABLE 12 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
Disc surgery vs chemonucleolysis														
884	Alexander, 1989[103]	C	CCS	Mean 14 (range 6–35) months	Satisfactory clinical outcome (vs unsatisfactory results)	Physician	49	39	0	51	40	0	1.07 (0.41 to 2.81)	Follow-up differed in each group: surgery mean 12 months (range 6–24 months), chemonucleolysis mean 16 months (range 6–35 months)
43	van Alphen, 1989[47]	C	RCT	12 months	Satisfied with final result of treatment: yes or largely (vs barely or no)	Patient	77	61	0.01	73	53	0	1.44 (0.68 to 3.06)	
441	Bonafe, 1993[75] (French language)	A + C	CCS	1 year	Overall treatment success using modified MacNab criteria: excellent or good (vs satisfactory or worse)		20	11	0	20	16	0	0.31 (0.07 to 1.25)	
166	Crawshaw, 1984[60]	NR	RCT	1 year	Overall outcome: excellent or good (vs poor)		26	23	0	24	11	0	9.06 (2.13 to 38.49)	
48	Dabezies, 1978[51]	NR	CCS	2 years	Treatment outcome: excellent or good (vs unimproved)	Patient	100	63	0	100	71	0	0.70 (0.38 to 1.26)	

continued

TABLE 12 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
132	Hoogmartens, 1976[56]	C	HCS	Mean 49 months	Satisfactory result for radicular pain: excellent or good (vs fair or poor)		53	37	0	44	24	0	1.93 (0.84 to 4.44)	Data inferred from percentages Follow-up differed for the two groups: surgery mean 58 months, chemonucleolysis mean 38 months
44	Javid, 1995[48]	C	CCS	1 year	Successful outcome: good or excellent (vs slight or no improvement)	Patient	100	82	0	100	87	0	0.68 (0.31 to 1.48)	
129	Lavignolle, 1987[55] (French language)	NR	RCT	Mean: surgery 24 months, chemonucleolysis 2 months	Overall success: MacNab type scores: good or medium (vs mediocre or bad)		182	150	0	176	141	0	1.16 (0.68 to 1.98)	
889	Lee, 1996[104] (German language) (i)[b] (APLD)	NR	CCS	1 year	Results of treatment: very good or good; (vs moderate or bad)	Patient	100	48	?	100	55	?	1.74 (0.98 to 3.09)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 29%
889	Lee, 1996[104] (German language) (ii)[b] (PELD)	NR	CCS	1 year	Results of treatment: very good or good; (vs moderate or bad)	Patient	100	68	?	100	55	?	0.76 (0.43 to 1.32)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 14%

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
593	Muralikuttan, 1992[85]	A + C	RCT	1 year	Completely pain free (vs residual back pain only or residual back and referred pain)		46	14	0	46	8	0	2.08 (0.77 to 5.58)	Reported as percentages One patient crossed over to surgery
47	Norton, 1986[50]	A + C	CCS	≥ 1 year	Treatment success: satisfactory (vs unsatisfactory) based on patient and physician report	Patient + physician	44	26	0	61	17	0	3.74 (1.64 to 8.50)	
45	Postacchini, 1987[49]	A + C	Non-RCT	> 20 months	Treatment success: excellent or good (vs fair or poor)	Patient + physician	84	70	0.03	72	54	0.03	1.67 (0.76 to 3.65)	Data inferred from graphs Five lost to follow-up were excluded
617	Revel, 1993[88]	NR	RCT	1 year	Overall success rate	Patient	69	25	> 0.41	72	48	> 0.19	0.28 (0.14 to 0.57)	High dropout rate 24/165 excluded patients dropped out at beginning, group allocation not stated A further 30% dropped out (surgery 28/69; chemonucleolysis 14/72), but included in analysis (given poor outcome)
641	Steffen, 1999[90] (German language)	C	RCT	1 year	MacNab criteria: good or very good (vs satisfactory or poor)		36	11	0	33	17	0	0.41 (0.15 to 1.11)	Reported as percentages only
61	Tregonning, 1991[53]	C	CCS	10 years	MacNab criteria: excellent or good (vs fair or poor)		91	51	0.13	145	47	0.12	2.66 (1.55 to 4.56)	

continued

TABLE 12 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
160	Watts, 1975[59]	C	CCS	2 years	Overall outcome: successful (vs failure)		174	134	0	100	59	0	2.33 (1.37 to 3.96)	
672	Weinstein, 1986[92]	C	CCS	> 1 year	Recovered within > 12 weeks, 6–12 weeks, 2–6 weeks or immediate (vs no recovery)		63	56	0.11	88	77	0.03	0.83 (0.28 to 2.43)	
150	Zeiger, 1987[58]	A + C	CCS	Mean 18 months (range 6–46 months)	Current level of discomfort: pain free or improvement (vs no better or worse)	Patient	81	72	0	45	27	0	5.33 (2.14 to 13.31)	Results included seven surgery patients who had had reoperation; five with good results
Disc surgery vs exercise therapy														
300	Osterman, 2006[68]	A	RCT	2 years	Full recovery	Patient	28	7	0.03	28	5	0	1.53 (0.42 to 5.58)	
Disc surgery vs intraoperative interventions														
436	Bernsmann, 2001[74]	NR	RCT	Median 24.2 months	Permanently free of complaints or permanent improvement (vs initially free of complaints then just improvement, same complaints, initially improvement then same complaints, initially improvement then worse or no effect)	Patient	94	70	0.06	92	77	0.08	0.57 (0.28 to 1.17)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
492	Gerszten, 2003[81]	C	RCT	1 year	Pain free or improvement (vs no improvement). Improvement = increases of ≥ 7 points on SF-36		5	3	0	5	5	0	0.13 (0.00 to 3.52)	
520	Jensen, 1996[83]	NR	RCT	1 year	Overall assessment: very satisfied or satisfied little discomfort (vs acceptable some discomfort, unchanged or aggravated)	Patient	49	36	?	50	37	?	0.97 (0.40 to 2.38)	19/118 (16%) dropped out; group allocation not stated
270	MacKay, 1995[65] (j)[c] (gelfoam)	C	RCT	1 year	Overall outcome: excellent or good (vs fair or poor)		50	40	?	54	46	?	0.70 (0.25 to 1.93)	36/190 excluded from analysis, group allocation not stated (three intervention groups)
270	MacKay, 1995[65] (ii)[c] (free fat graft)	C	RCT	1 year	Overall outcome: excellent or good (vs fair or poor)		50	40	?	50	42	?	1.14 (0.25 to 1.93)	36/190 excluded from analysis, group allocation not stated (three intervention groups)

continued

TABLE 12 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
856	Ronnberg, 2008[102]	NR	RCT	24 months	MacNab criteria: excellent or good (vs fair or poor)	Physician	48	30	?	60	41	?	0.77 (0.44 to 2.94)	Interim analysis based on first 40/61 patients (65%) to complete 12 months' follow-up (group allocation of remainder not stated) Dropouts at 6 months 10/61 (16%): intervention 5/20, control 5/20 All included in ITT analysis
Disc surgery vs other														
600	North, 2005[86] (spinal cord stimulation)	C	RCT	2 years	Success: ≥ 50% pain relief and patient satisfaction with treatment rated as success (vs failure)	Patient + physician	26	9	0.13	24	9	0.2	0.88 (0.28 to 2.80)	
Disc surgery vs usual care														
386	Atlas, 1996[72]	C	CCS	10 years	Improvement in predominant symptom: completely gone, much better or better (vs not improved or worse)	Patient	207	143	0.25	175	107	0.25	1.42 (0.93 to 2.17)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
606	Peul, 2007[87]	A	RCT	52 weeks	Satisfaction with recovery: 'complete' or 'nearly recovery complete' on seven-point Likert scale (other 5 scores = unsatisfactory recovery)	Patient	130	106	0.08	130	103	0.08	1.16 (0.63 to 2.14) *Repeated measurements analysis adjusting for baseline values: 2.4% (95% CI: –7.2% to 12.0%)*	Data presented as percentages ITT using LOCF reported for mean Likert score
211	Shvartzman, 1992[62]	A	HCS	2 years	Results categorised as good (vs satisfactory; poor) using composite scale based on functional (work-related) and perceptual (subjective-opinion) criteria	Patient	25	16	0	30	14	0	2.03 (0.69 to 6.02)	
664	Weber, 1983[91]	NR	RCT	10 years	Overall outcome: good or fair (vs poor or bad)	Physician	55	34	0.08	66	27	0	2.34 (1.12 to 4.87)	17 from control group received surgery, but analysed according to randomised group Seven patients registered as permanently incapacitated were categorised as 'fair' in final analysis

continued

TABLE 12 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
750	Weinstein, 2006[98] (a)	A + C	CCS	2 years	Satisfaction with current symptoms: very/ somewhat satisfied	Patient	456	Change: 72% (SE 2.2)	0.12	165	Change: 49% (SE 4.3)	0.26	*Adjusted treatment effect 22.4% (95% CI 12.8% to 32.0%)*	Only mean percentage change and difference between groups reported 48/222 patients who chose to be in non-operative group received surgery and 40/521 who chose to be in surgery group did not have surgery Analysis based on treatment received not initial group allocation Sensitivity analyses used to determine the impact of missing data

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
751	Weinstein, 2006[99] (b)	A + C	RCT	2 years	Satisfaction with current symptoms: very/ somewhat satisfied		186	Change: 68% (SE 3.4)	0.24	187	Change: 64% (SE 3.5)	0.37	*Adjusted treatment effect 4.0% (95% CI –5.6% to 13.5%)*	Only mean percentage change and difference between groups reported ITT included 472/501 using LOCF and longitudinal mixed model controlling for covariates associated with missed visits Crossovers: intervention 92/232 (40%), control 107/240 (45%)
Disc surgery vs mixed treatments														
734	Hoogland, 2006[97] (discectomy + chemonucleolysis)	C	Q-RCT	2 years	Satisfaction with results classified as excellent or good (vs fair or not satisfied)	Patient	119	101	0.16	116	108	0.16	0.42 (0.17 to 1.00)	Reported as percentages only
379	Prestar, 1995[71] (German language) (discectomy + non-opioids)	NR	RCT	1 year	Treatment success: very good or good (vs inadequate or poor).		34	9	0.32	34	13	0.32	0.58 (0.21 to 1.63)	

?, unclear; A, acute; A + C, acute and chronic; APLD, automated percutaneous lumbar discectomy; BVCF, baseline value carried forward; C, chronic; HCS, historical cohort study; LOCF, last observation carried forward; NR, not reported; PELD, percutaneous manual and laser discectomy; SF-36, Short Form questionnaire-36 items.

a Results reported by study in italics.

b Lee *et al.*[104] included three treatment groups: APLD (i), PELD (ii) and chemonucleolysis (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 9*).

c MacKay *et al.*[65] included three treatment groups: surgery + dura covered with gelfoam (i), surgery + dura covered with free fat graft (ii) and surgery + dura left uncovered (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 9*).

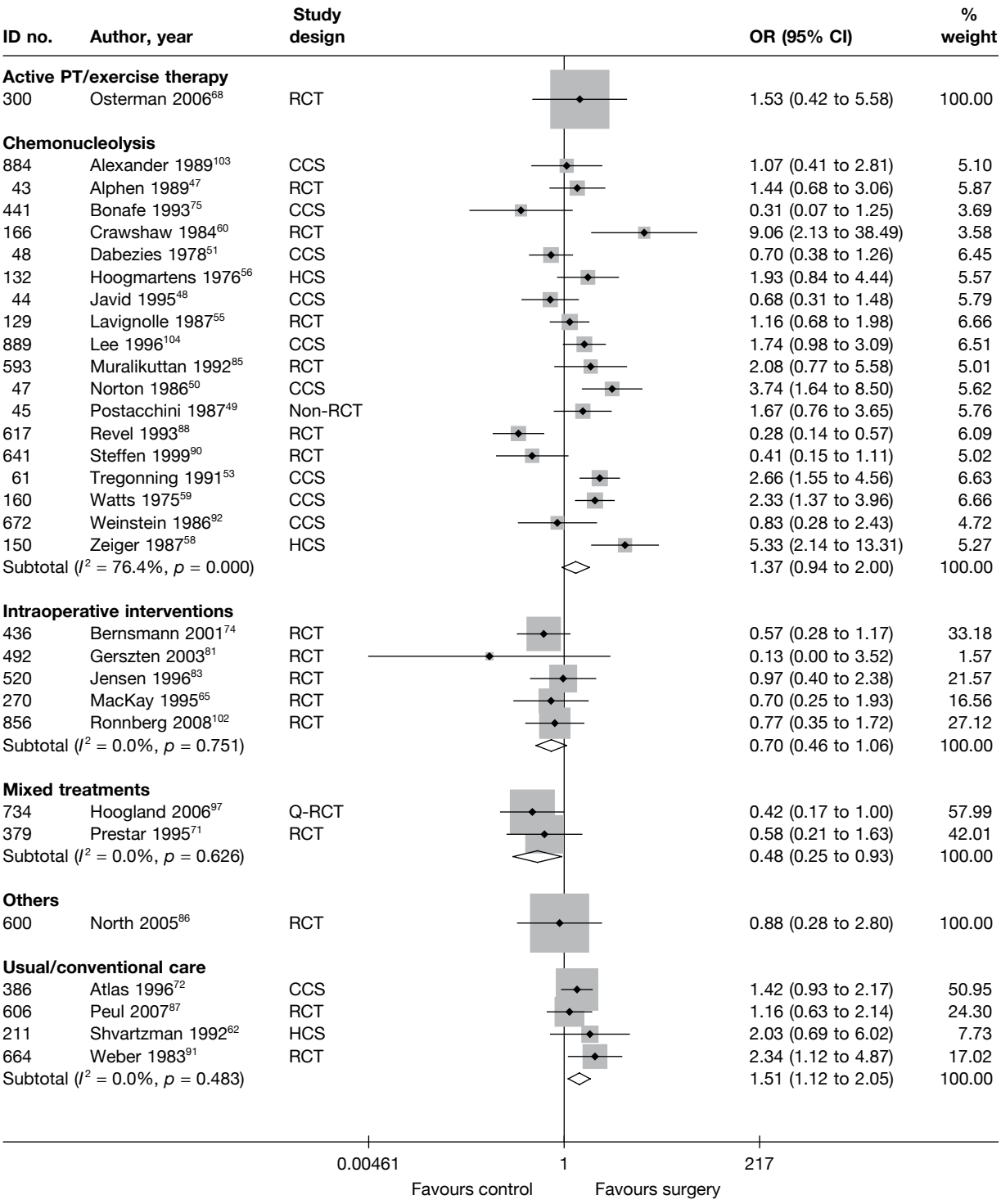

FIGURE 9 Summary of the findings of the global effect at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions. HCS, historical cohort study; PT, physical therapy. Note: weights are from random effects analysis.

According to a well-conducted RCT,[68] there was no real difference between disc surgery plus exercise therapy and exercise therapy alone in terms of reported full recovery at 2 years in patients with acute sciatica.

Intraoperative interventions were found to be superior to disc surgery alone in five RCTs,[65,74,81,83,102] but the overall findings were not statistically significant. One study[81] reported a large effect size, but had a very wide CI owing to a small sample size ($n = 10$).

Two studies[71,97] compared disc surgery with mixed treatments: chemonucleolysis plus surgery[97] and disc surgery plus non-opioids.[71] Both found non-statistically significant findings in favour of the combined interventions. One was a Q-RCT[97] and the other a poor-quality and poorly reported RCT,[71] for which the method of randomisation and allocation concealment were unclear. The withdrawal rate in this study was also high (32% in both intervention groups).

Eighteen studies[47,48–51,53,55,56,58–60,75,85,88,90,92,103,104] compared disc surgery and chemonucleolysis, for which the findings were very heterogeneous, giving a pooled result that was borderline statistically significant in favour of surgery. There was a mixture of study designs. The duration of follow-up ranged from 1 year to 10 years and duration of sciatica varied between studies. If only the six RCTs[47,55,60,85,88,90] were considered, the findings were still heterogeneous, although most reported findings in favour of disc surgery [pooled analysis: odds ratio (OR) 1.12; 95% CI 0.51 to 2.49]. One moderate-quality RCT[88] found chemonucleolysis to be more effective than disc surgery, but the study had a high withdrawal rate in the surgery group (at least 41%) compared with chemonucleolysis (at least 19%), with dropouts being given a poor outcome in the analysis. The funnel plot (*Figure 10*), for publication and other biases, does not appear to show asymmetry, but does indicate a lack of large studies.

According to one RCT,[86] there was no important difference between repeat disc surgery and spinal cord stimulation (others) in terms of treatment success for chronic sciatica following previous disc surgery.

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 13* and the accompanying forest plot (*Figure 11*). Disc surgery was compared with usual care, exercise therapy, epidural, intraoperative interventions, chemonucleolysis and mixed treatments.

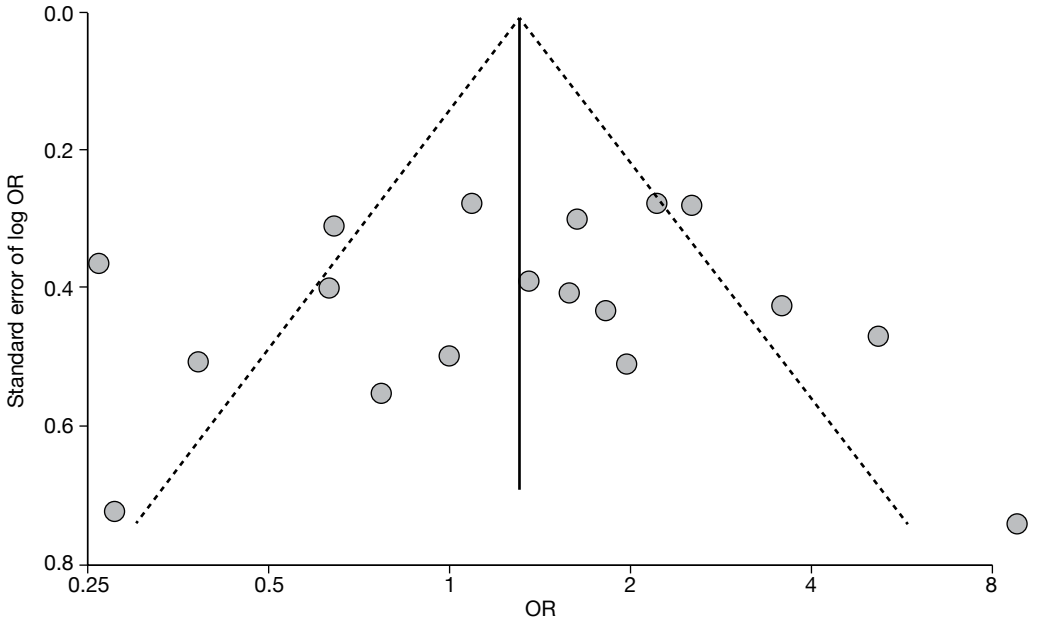

FIGURE 10 Funnel plot with pseudo 95% CIs for studies comparing disc surgery with chemonucleolysis at long-term follow-up (>6 months).

TABLE 13 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs chemonucleolysis																
454	Buric, 2005[77]	A + C	Non-RCT	18 months	Overall	VAS (0–10)	15	30	61 (31)	53 (22)	20 (13)	22 (13)	–41	–40	7.0 (–1.72 to 15.72)	Two patients crossed over to surgery, classed as treatment failures
593	Muralikuttan, 1992[85]	A + C	RCT	3 months	Leg	VAS (0–100)	46	46	72	64	14 (24.43)	20 (23.76)			–2.00 (–10.49 to 6.49)	SD imputed from weighted average Most outcomes showed skewed distribution
Disc surgery vs epidural																
725	Buttermann, 2004[95]	A + C	RCT	2–3 years	Back	VAS (0–10)									*No significant differences between groups, Student's t-test (p-value not given)*	No summary estimates reported
Disc surgery vs exercise therapy																
300	Osterman, 2006[68]	A	RCT	2 years	Leg	VAS (0–100)	28	28	61 (20)	57 (21)	6 (11)	15 (24)			–9.00 (–18.78 to 0.78)	ITT using LOCF Dropouts: surgery 2/29, exercise 4/28
Disc surgery vs intraoperative interventions																
470	Debi, 2002[78]	A + C	RCT	1 year	Leg	VAS (0–10)	35	26	71	58	13 (20.31)	13 (8.68)			0.0 (–7.51 to 7.51)	SD imputed from weighted average Mean inferred from graphs Dropouts 9/70 (13%): intervention 9/35, control 0/35

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
276	Lundin, 2003[66]	C	RCT	104 weeks	Overall	VAS (0–100)	42	38	48	54	14 (20.31)	8 (8.68)			6.00 (–0.73 to 12.73)	SD imputed from weighted average Mean inferred from graphs
854	Rasmussen, 2008[101]	NR	RCT	2 years	Leg	Composite NRS (0–30)	100	100	68.3	70	33.33 (20.31)	16.7 (8.68)			5.54 (1.21 to 9.87)	Median used to represent mean SD imputed from weighted average Three separate pain measures using NRS (0–10) combined: pain now, worst, and average pain in the last 2 weeks, for back and leg pain separately ITT using LOCF. Dropouts 2/200 (1%): group allocation not stated
316	Cengiz, 2007[69] (i)[c] (anti–adhesion barrier ADCON-L)	C	RCT	12 months	Overall	VAS (0–10)	18	21	100 (0.0)	92.8 (10.5)	46.6 (12.3)	44.7 (9.8)			1.90 (–5.16 to 8.96)	
316	Cengiz, 2007[69] (ii)[d] (anti-adhesion barrier Healon GV)	C	RCT	12 months	Overall	VAS (0–10)	18	21	100 (0.0)	97.1 (9.5)	46.6 (12.3)	48 (7.4)			–1.40 (–7.90 to 5.10)	
Disc surgery vs usual care																
716	Alaranta, 1990[94]	A + C	CCS	12 months		B-U&LPI (0–30)	235	122							*Surgery group had greatest decrease in pain indices* *Pain index: surgery vs control* $p < 0.001$; *surgery vs control not significant, Student's t-test*	Patients in control group had no disc herniation on rhizography or did not meet criteria for surgery Data presented in unusable graphical form

continued

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TABLE 13 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
772	Hansson, 2007[100]	A + C	CCS	2 years	Overall	Von Korff – pain scale (0–10)	92	92	71	70	45	59	–26 (34)	–11 (73.3)	–15 (–31.51 to 1.51)	SD for change score derived from *p*-value of *t*-test (individual group) converted to 0–100
606	Peul, 2007[87]	A	RCT	104 weeks	Leg	VAS (0–100)	130	130	67.2 (27.7)	64.4 (21.2)	11 (21.66)	9 (21.66)			2.0 (–3.27 to 7.27) *Repeated measures analysis, difference between groups: –2.0 (95% CI –6.0 to 2.0)*	Final SD based on SE Dropouts 23 (8%): intervention 11/141, control 12/142 ITT not done because no difference between ITT and non-ITT at 1-year follow-up
Disc surgery vs mixed treatments																
734	Hoogland, 2006[97] (surgery + chemonucleolysis)	C	Q-RCT	2 years	Leg	VAS (0–10)	119	116	80.5	82.2	20.2 (20.31)	18.5 (21.22)			1.70 (–3.61 to 7.01)	SD imputed from weighted average ITT not used Dropouts 45 (16%): intervention 23/142, control 22/138

A, acute; A + C, acute and chronic; B-U&LPI, Bergquist-Ullman and Larson, pain index; C, chronic; LOCF, last observation carried forward; NR, not reported; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Cengiz and Baysefer[69] included three treatment groups: surgery + anti-adhesion barrier ADCON-L (i), surgery + anti-adhesion barrier Healon GV (ii) and surgery + no adhesion barrier (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 11*).

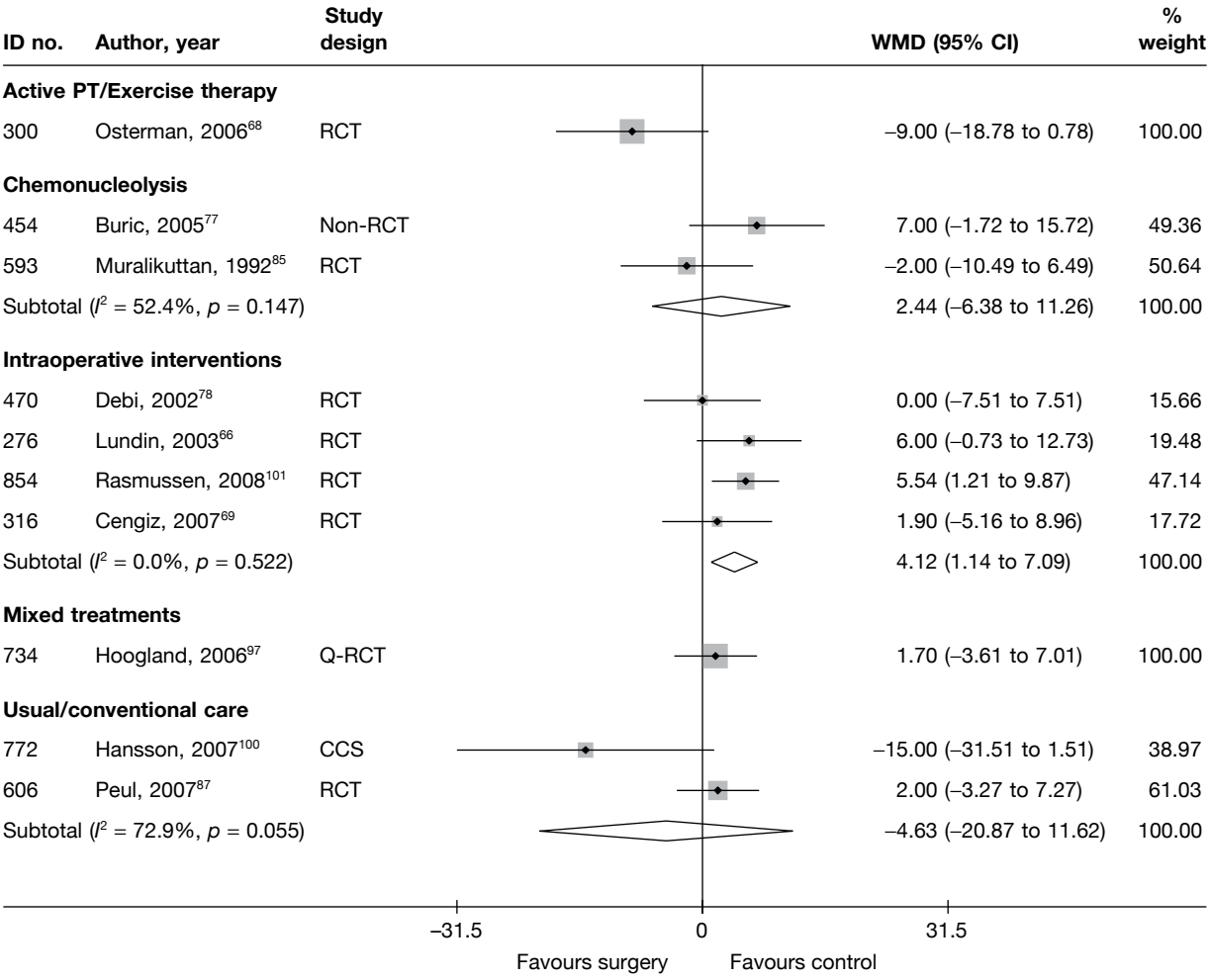

FIGURE 11 Summary of the findings of pain intensity at long-term follow-up studies (>6 months) comparing disc surgery with alternative interventions. Note: weights are from random effects analysis.

Three studies[87,94,100] compared disc surgery with usual care. One well-conducted RCT[87] included patients with severe sciatica for 6–12 weeks. The study did not find any important differences between the interventions groups for pain intensity at 104 weeks. The other two studies were CCSs that included patients with acute and chronic sciatica. Neither study used VAS as their pain scale. Only one study[94] found statistically significant findings in favour of surgery, but the data were reported in an unusable graphical format and could not be included in the meta-analysis. The study was poorly reported in general and had obvious selection bias, with patients in the comparator group including those with no disc herniation on rhizography or who were not eligible for disc surgery.

As with the global effect, one well-conducted RCT[68] found non-statistically significant findings in favour of disc surgery plus exercise therapy compared with exercise therapy alone in patients with acute sciatica at 2 years' follow-up.

One poorly reported study[95] compared the use of epidurals with disc surgery in patients with chronic sciatica [mean 3.55 months (SD 2.75 months)], and found no statistically significant difference between the intervention groups for back pain intensity at follow-up intervals of 7–12 months, 1–2 years or 2–3 years (Student's *t*-test). Results of leg pain were not reported beyond 6 months.

The pooled analysis of four RCTs[66,69,78,101] found a statistically significant improvement following intraoperative interventions compared with disc surgery alone. One study[78] included patients with acute and chronic sciatica (mean symptom duration 56 days, range 12–135 days), two studies[66,69] included patients with chronic sciatica, and duration of symptoms was not stated in the remaining study.[101] Duration of follow-up ranged from 1 year to 2 years. Overall study quality was moderate[66,69,101] or poor.[78]

Two studies[77,85] compared disc surgery with chemonucleolysis: one was an RCT[85] and the other a non-RCT.[77] Overall, there was no statistically significant difference between the intervention groups.

A Q-RCT[97] evaluated the use of chemonucleolysis plus surgery versus surgery alone in patients with chromic sciatica. There was no statistically significant difference between the intervention groups.

Condition-specific outcome measures at long-term follow-up

The results for CSOMs at long-term follow-up are presented in *Table 14* and the accompanying forest plot (*Figure 12*). Disc surgery was compared with usual care, exercise therapy, intraoperative interventions and chemonucleolysis.

Six studies[45,72,87,98–100] compared disc surgery with usual care, for which the pooled findings showed no statistically significant difference between the intervention groups at 1 year to 10 years[45,72] (median 2 years). Two studies[87,99] were well-conducted RCTs and the remaining four[45,72,98,100] were CCSs. Pooled analysis of the RCTs also showed no important differences between the intervention groups (SMD –0.01; 95% CI –0.16 to 0.15).

One well-conducted RCT[68] found non-statistically significant findings in favour of disc surgery plus exercise therapy compared with exercise therapy alone in patients with acute sciatica at 2 years' follow-up.

The pooled analysis of four RCTs[69,74,81,83] showed no important difference between disc surgery and intraoperative interventions for CSOMs at 1 year's[69,81,83] follow-up or a median of 2 years' follow-up.[74]

Four studies[77,85,92,96] compared disc surgery and chemonucleolysis: two were RCTs,[85,96] one was a non-RCT[77] and one was a CCS.[92] The CCS[92] reported insufficient data to be included in the meta-analysis. The results of six pain and disability outcome measures were analysed in a one-way multivariate analysis of variance (MANOVA), the results of which showed no significant relationship between pain outcome measures and treatment type (Wilks' criterion $F(6,54) = 1.18$; $p < 0.34$). Pooled analysis of the remaining three studies[77,85,96] showed no statistically significant difference between the intervention groups.

TABLE 14 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs chemonucleolysis															
454	Buric, 2005[77]	A+C	Non-RCT	18 months	RMDQ	15	30	12.4 (4.3)	9.1 (3.5)	2.1 (1.9)	2.2 (3.2)	–10.3	–6.9	–0.04 (–0.66 to 0.58)	ITT used but method not stated Dropouts: two, considered as treatment failure
727	Ejeskar, 1983[96]	A+C	RCT	12 months	Composite score	14	15			8.79 (6.02)	9.4 (6.88)			–0.08 (–0.3 to 0.21)	
593	Muralikuttan, 1992[85]	A+C	RCT	1 year	Part of the Waddell Disability Index	46	46	6.7	6.2	2.8 (1.21)	2.6 (1.21)	–3.9	–3.6	0.17 (–0.24 to 0.57)	SD for final means calculated from *p*-values (Mann–Whitney *U*-test); most outcomes showed skewed distribution ITT not used, but all patients included in analysis except one for psychological outcomes
672	Weinstein, 1986[92]	C	CCS	Mean 10.3 years	Composite score	71	85							*Results of MANOVA showed no significant relationship between pain outcome measures and treatment type [Wilks' criterion: F(6,54) = 1.18, p < 0.34]*	Pain + disability measured in six different scales Actual data not presented Dropouts: 3/159 (2%) (chemonucleolysis group)
Disc surgery vs exercise therapy															
300	Osterman, 2006[68]	A	RCT	2 years	ODI	28	28	39 (15)	39 (14)	6 (9)	11 (16)	–33	–28	–0.39 (–0.91 to 0.14)	ITT using LOCF, but one patient who did not meet inclusion criteria excluded from analysis

continued

TABLE 14 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Disc surgery vs intraoperative interventions															
436	Bernsmann, 2001[74]	NR	RCT	Median 24.2 months	FFbH-R	94	92			4.64 (22.48)	5.15 (22.48)			0.02 (–0.31 to 0.26)	Final SD imputed from weighted mean SDs of FFbH from other studies of disc surgery long-term follow-up ITT not used Dropouts 14 (7%): intervention 8/100, control 6/100
492	Gerszten, 2003[81]	C	RCT	1 year	ODI	5	5	31.4 (5.5)	32.6 (7.8)	21.2 (8.8)	20.4 (10.6)			0.08 (–1.16 to 1.32)	
520	Jensen, 1996[83]	NR	RCT	1 year	LBPRS	49	50	57.0	54.5	23.0 (10.85)	23.5 (10.85)			–0.05 (–0.44 to 0.35)	Median used for mean, final SD imputed from weighted mean of SDs of LBRS for post-operative interventions ITT not used Dropouts 19/118 (16%): group allocation not stated
316	Cengiz, 2007[69]	C	RCT	12 months	ODI	18	21			16.66 (12.5)	19.66 (9.59)			–0.27 (–0.90 to 0.36)	
Disc surgery vs usual/conventional care															
386	Atlas, 1996[72]	C	CCS	10 years	Modified RMDQ	188	152	17.7 (4)	13.5 (5.9)	6 (7)	7.6 (7)	–11.7 (7.2)	–5.8 (7.6)	–0.23 (–0.44 to –0.–1) *Difference between groups for change score* p < *0.001 using multiple linear regression models that control for baseline score*	Number of patients included in analysis was unclear

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
772	Hansson, 2007[100]	A+C	CCS	2 years	FFbH-R	92	92	47	58	35 (13.09)	36 (13.09)	18	6	–0.08 (–0.37 to 0.21)	Final SD imputed from weighted means of FFbH-R for usual care
606	Peul, 2007[87]	A	RCT	2 years	RMDQ	130	130	16.5 (4.4)	16.3 (3.9)	3.1 (5.7)	2.6 (5.7)	–13.4	–13.7	0.09 (–0.16 to 0.33) *Adjusted mean difference 0.5 (95% CI –0.8 to 1.8), repeated-measures analysis of variance; difference between groups based on AUC also reported*	SDs calculated from SE ITT not used because sensitivity analysis showed no difference between ITT and non-ITT at 1-year follow-up; 23 (8%) patients lost to follow-up; no randomised intervention 141, control 142
2	Thomas, 2007[45]	C	CCS	Intervention: 6 months; control: 12 months	NASS Lumbar Spine Q subscale – pain and disability	333	164	21.4 (10)	29 (10)	58.3 (10)	57.7 (10)	20.2	13.3	0.06 (–0.13 to 0.25) *Adjusted mean difference 3.46 (95% CI 0.17 to 6.75)* p = *0.04*	ITT used (method of dealing with missing values not reported) Dropouts 126 (20%): intervention 84/417, control 42/206
750	Weinstein, 2006[98]	A+C	CCS	2 years	MODEMS version of ODI	456	165	56.7 (18.9)	35.9 (20.1)	19.1 (18.9)	11.7 (20.1)	–37.6 (18.15)	–24.2 (21.84)	0.38 (0.21 to 0.56) *Adjusted mean difference –13.4 (95% CI –17.0 to –9.7);* n = *620/743*	Final score calculated from change score No final SD so baseline SD used, adjusted difference between groups based on change scores Missed visits adjusted for in analysis. 48/222 patients who chose to be in non-operative group received surgery and 40/521 who chose to be in surgery group did not have surgery Analysis based on treatment received not initial group allocation

continued

TABLE 14 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
751	Weinstein, 2006[99]	A+C	RCT	2 years	MODEMS version of ODI	186	187	47.5 (21.4)	46.3 (20.6)	16.1 (21.4)	17.6 (20.6)	–31.4	*–28.7*	–0.07 (–0.27 to 0.13) *Adjusted mean difference –2.7 (95% CI –7.4 to 1.9);* n = *472/501*	Final score calculated from change score No final SD so baseline SD used, adjusted difference between groups based on change scores ITT analysis included 472/501 patients using LOCF (longitudinal mixed model controlling for covariates associated with missing values) Dropouts: intraoperative 59/245 (24%), chemonucleolysis 69/256 (27%) Crossovers: intervention 92/232 (40%), control 107/240 (45%)

A, acute; AUC, area under the curve; A+C, acute and chronic; C, chronic; FFbH-R, Hanover functional ability questionnaire (Funktionsgragebogen Hannover); LBPRS, lower back pain rating scale; LOCF, last observation carried forward; MODEMS, Modified Oswestry Disability Index (American Academy of Orthopaedic Surgeons); NASS, North American Spine Society; NR, not reported.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

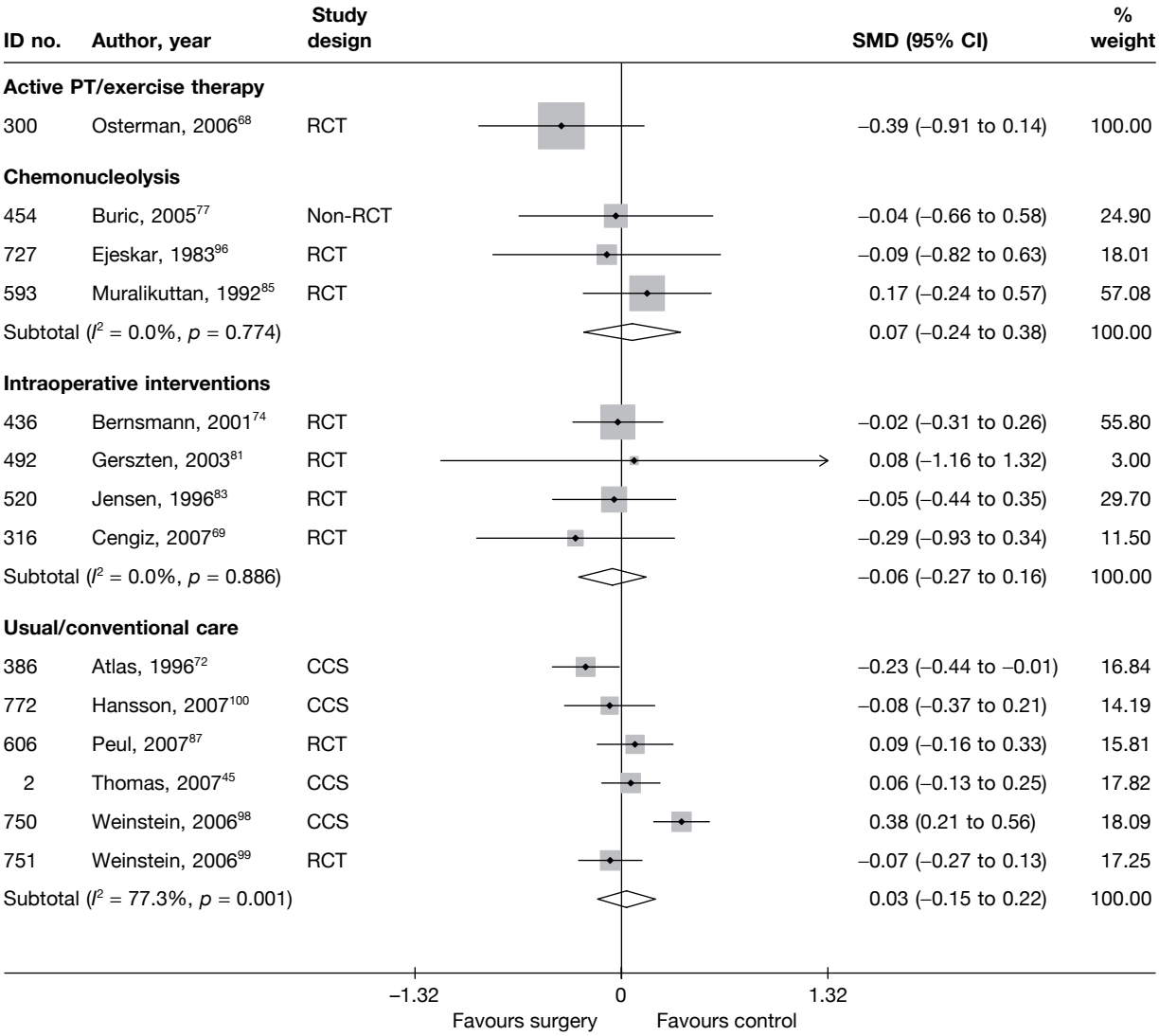

FIGURE 12 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing disc surgery with alternative interventions. Note: weights are from random effects analysis.

Analysis of adverse effects for disc surgery

Adverse events were very poorly reported in most studies. *Table 15* and *Figure 13* present the overall number of any adverse event that occurred.

There was a statistically significant greater number of adverse effects with disc surgery compared with usual care. Overall there was no statistically significant difference in the number of adverse effects following disc surgery compared with: epidural and exercise therapy, chemonucleolysis, epidural, intraoperative interventions, mixed treatments, non-opioids or others.

SUMMARY OF OVERALL FINDINGS FOR DISC SURGERY COMPARED WITH ALTERNATIVE INTERVENTIONS

Most disc surgery studies included patients with chronic sciatica or both acute and chronic sciatica. Four studies[62,68,80,87] included acute sciatica, for which the comparator included exercise

TABLE 15 Summary of the findings of any adverse effect for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Disc surgery vs chemonucleolysis							
884	Alexander, 1989[103]	CCS	8	49	8	51	1.05 (0.36 to 3.06)
43	van Alphen, 1989[47]	RCT	3	78	3	73	0.93 (0.18 to 4.78)
441	Bonafe, 1993[75]	CCS	1	20	10	20	0.05 (0.01 to 0.47)
183	Bouillet, 1983[61]	CCS	91	613	152	2136	2.28 (1.72 to 3.00)
453	Brown, 1989[76] (chemopapain)	CCS	NR	NR	NR	NR	
453	Brown, 1989[76] (collagenase)	CCS	NR	NR	NR	NR	
454	Buric, 2005[77]	Non-RCT	NR	NR	NR	NR	
166	Crawshaw, 1984[60]	RCT	0	27	1	25	0.30 (0.01 to 7.63)
48	Dabezies, 1978[51]	CCS	0	100	2	100	0.20 (0.01 to 4.14)
471	Dei-Anang, 1990[79] (German language)	CCS	NR	NR	NR	NR	
727	Ejeskar, 1983[96]	RCT	1	14	1	15	1.08 (0.06 to 19.05)
132	Hoogmartens, 1976[56]	HCS	19	53	3	44	7.64 (2.08 to 28.02)
44	Javid, 1995[48]	CCS	4	100	6	100	0.65 (0.18 to 2.39)
35	Krugluger, 2000[46]	RCT	1	10	5	12	0.16 (0.01 to 1.65)
117	Lagarrigue, 1991[54] (French language)	CCS	30	751	5	334	2.74 (1.05 to 7.12)
129	Lavignolle, 1987[55] (French language)	RCT	7	182	7	176	0.97 (0.33 to 2.81)
889	Lee, 1996[104] (APLD)	CCS	3	100	73	100	0.01 (0.00 to 0.04)
889	Lee, 1996[104] (PELD)	CCS	4	100	73	100	0.02 (0.01 to 0.05)
593	Muralikuttan, 1992[85]	RCT	0	46	1	46	0.33 (0.01 to 8.22)
47	Norton, 1986[50]	CCS	2	44	12	61	0.19 (0.04 to 0.92)
45	Postacchini, 1987[49]	Non-RCT	20	84	2	72	10.94 (2.46 to 48.65)
617	Revel, 1993[88]	RCT	15	69	35	72	0.29 (0.14 to 0.61)
641	Steffen, 1999[90]	RCT	NR	NR	NR	NR	
49	Stula, 1990[52] (German language)	RCT	NR	NR	NR	NR	
61	Tregonning, 1991[53]	CCS	4	145	5	91	0.49 (0.13 to 1.87)
893	Watters,1988[105]	Non-RCT	1	50	2	50	0.49 (0.04 to 5.58)
160	Watts, 1975[59]	CCS	2	174	3	100	0.38 (0.06 to 2.29)
672	Weinstein, 1986[92]	CCS	NR	NR	NR	NR	
150	Zeiger, 1987[58]	CCS	5	81	16	45	0.12 (0.04 to 0.36)
Disc surgery vs epidural/intradiscal injection							
725	Buttermann, 2004[95]	RCT	7	77	5	50	0.90 (0.27 to 3.01)
Disc surgery vs active PT/exercise therapy							
300	Osterman, 2006[68]	RCT	1	28	0	28	3.11 (0.12 to 79.64)
Disc surgery vs intraoperative interventions							
268	Aminmansour, 2006[64] (control = 40 mg)	Q-RCT	1	22	0	19	3.46 (0.13 to 89.95)

TABLE 15 Summary of the findings of any adverse effect for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
268	Aminmansour, 2006[64] (control = 80 mg)	Q-RCT	1	22	0	20	2.72 (0.10 to 70.79)
436	Bernsmann, 2001[74]	RCT	0	94	0	92	
470	Debi, 2002[78]	RCT	0	26	0	35	
492	Gerszten, 2003[81]	RCT	1	5	1	5	1.00 (0.05 to 22.18)
497	Glasser, 1993[82] (control = LA)	RCT	NR	NR	NR	NR	
497	Glasser, 1993[82] (control = steroid + LA)	RCT	NR	NR	NR	NR	
520	Jensen, 1996[83]	RCT	NR	NR	NR	NR	
909	Jirarattanaphochai, 2007[106]	RCT	2	51	1	52	2.08 (0.18 to 23.70)
400	Kim, 2003[73]	RCT	NR	NR	NR	NR	
551	Langmayr, 1995[84]	RCT	NR	NR	NR	NR	
366	Lavyne, 1992[70]	Q-RCT	0	42	0	42	
276	Lundin, 2003[66]	RCT	1	42	0	38	2.78 (0.11 to 70.39)
270	MacKay, 1995[65] (control = free fat graft)	RCT	NR	NR	NR	NR	
270	MacKay, 1995[65] (control = gelfoam membrane)	RCT	NR	NR	NR	NR	
379	Prestar, 1995[71] (German language)	RCT	6	34	0	34	15.74 (0.85, 291.46)
854	Rasmussen, 2008[101]	RCT	NR	NR	NR	NR	
618	Richter, 2001[89]	RCT	3	177	3	180	1.02 (0.20 to 5.11)
856	Ronnberg, 2008[102]	RCT	NR	NR	NR	NR	
316	Cengiz, 2007[69] (control = Adcon-L)	RCT	1	18	0	21	3.69 (0.14 to 96.22)
316	Cengiz, 2007[69] (control = Healon GV)	RCT	1	18	0	21	3.69 (0.14 to 96.22)
705	Starkweather, 2006[93]	RCT	NR	NR	NR	NR	
915	de Tribolet, 1998[107]	RCT	81	141	65	128	1.31 (0.81 to 2.12)
Disc surgery vs mixed treatments							
734	Hoogland, 2006[97]	Q-RCT	3	119	2	116	1.47 (0.24 to 8.99)
600	North, 2005[86]	RCT	0	26	1	19	0.23 (0.01 to 6.03)
263	Wang, 2000[63]	RCT	NR	NR	NR	NR	
Disc surgery vs non-opioids							
475	Dubourg, 2002[80]	CCS	1	39	0	28	2.22 (0.09 to 56.54)
144	Rossi, 1993[57] (surgery = microdiscectomy)	Non-RCT	0	NR	1	NR	
144	Rossi, 1993[57] (surgery = percutaneous discectomy)	Non-RCT	0	NR	1	NR	
Disc surgery vs usual/conventional care							
716	Alaranta, 1990[94]	CCS	NR	NR	NR	NR	
386	Atlas, 1996[72]	CCS	16	275	0	232	29.57 (1.76 to 495.56)

continued

TABLE 15 Summary of the findings of any adverse effect for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
772	Hansson, 2007[100]	CCS	NR	NR	NR	NR	
294	Koranda, 1995[67]	Q-RCT	NR	NR	NR	NR	
606	Peul, 2007[87]	RCT	NR	NR	NR	NR	
211	Shvartzman, 1992[62]	HCS	NR	NR	NR	NR	
2	Thomas, 2007[45]	CCS	NR	NR	NR	NR	
664	Weber, 1983[91]	RCT	NR	NR	NR	NR	
750	Weinstein, 2006[98]	CCS	2	538	0	216	2.02 (0.10 to 42.20)
751	Weinstein, 2006[99]	RCT	24	232	0	240	56.52 (3.42 to 935.13)

APLD, automated percutaneous lumbar discectomy; HCS, historical cohort study; LA, local anaesthetic; NR, not reported; PELD, percutaneous manual and laser discectomy.

therapy,[68] non-opioids[80] and usual care.[62,87] Just over half of the disc surgery studies were RCTs. There were only a small number of good-quality studies, two of which compared disc surgery with usual care (*Table 16*).

One well-conducted RCT[87] found that early disc surgery resulted in a statistically significant improvement in pain at short- and medium-term follow-up compared with usual care, with a greater reduction at short-term follow-up. The same RCT found that functional status after disc surgery was significantly worse than usual care for the first 4 weeks, but significantly better after 4 weeks. However, there was no statistically significant difference between the treatment groups at medium-term follow-up. Pooled data from two RCTs[67,87] showed a small improvement, which was not statistically significant, in favour of surgery for the global effect at medium-term follow-up. One further RCT[99] (that could not be included in the meta-analysis) showed a small but statistically significant effect in favour of surgery for satisfaction with symptoms. Pooled data showed disc surgery to be better than usual care for the global effect at long-term follow-up [two RCTs,[87,91] one CCS,[72] one historical cohort study (HCS)[62]]. There were no statistically significant differences between intervention groups for pain intensity[87,100] or CSOMs at long-term follow-up.[45,72,87,98–100] The number of adverse effects was statistically significantly higher following disc surgery than after usual care (one RCT,[99] two CCSs[72,98]).

Disc surgery was significantly better than epidural at reducing pain intensity at medium-term follow-up but not at long-term follow-up (one poor-quality RCT[95]). There was no statistically significant difference between the intervention groups for adverse effects.

There was no statistically significant difference between disc surgery and non-opioids for global effect (one non-RCT,[57] one CCS[80]) and pain intensity (one CCS[80]) at medium-term follow-up, or for adverse effects, according to two poor-quality studies.[57,80] Disc surgery in combination with non-opioids led to a greater reduction in pain intensity than disc surgery alone at short-term follow-up (one poor-quality RCT[93]), but there was no statistically significant difference between similar comparisons at long-term follow-up for global effect (one poor-quality RCT[71]).

There was no statistically significant difference between disc surgery plus exercise therapy and exercise therapy alone in terms of reported full recovery, pain intensity or functional status

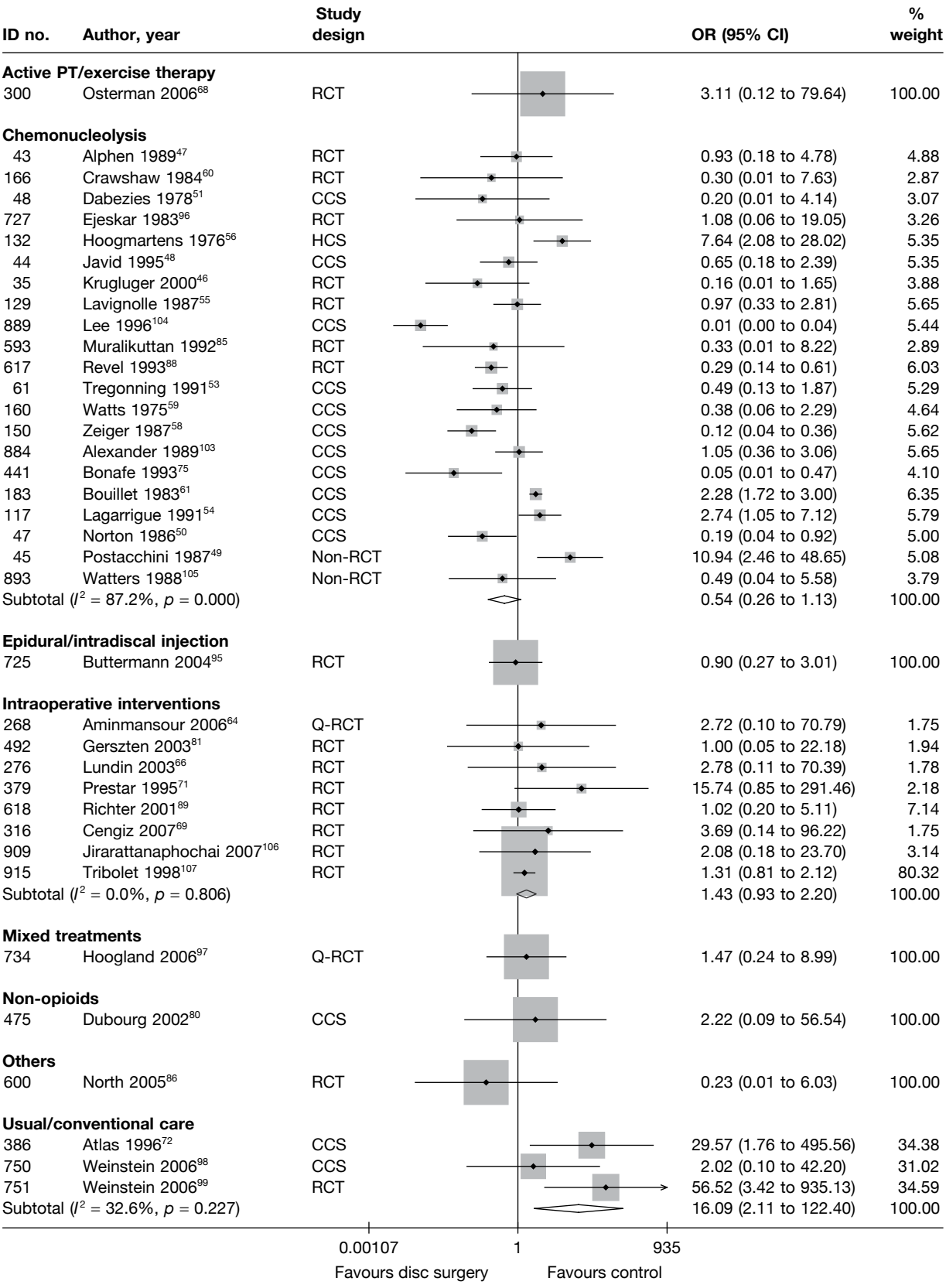

FIGURE 13 Summary of the findings of any adverse effect for studies comparing disc surgery with alternative interventions. Note: weights are from random effects analysis.

TABLE 16 Summary of the disc surgery studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Disc surgery vs chemonucleolysis	27 (29)	29–1085 (126)	8/27 (30)	0/27 (0)	0/27 (0)	27/27 (100)	22/27 (81)	1/27 (4)	1/27 (4)	3/27 (11)	22/27 (81)	3/27 (11)
Disc surgery vs epidural/ Intradiscal injection	1 (1)	100 (100)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
Disc surgery vs exercise therapy	1 (1)	57 (57)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)
Disc surgery vs intraoprative interventions	17 (17)	10–398 (84)	15/17 (88)	0/17 (0)	0/17 (0)	17/17 (100)	15/17 (88)	1/17 (6)	4/17 (24)	2/17 (12)	9/17 (53)	1/17 (6)
Disc surgery vs mixed treatments	4 (5)	70–280 (123)	3/4 (75)	0/4 (0)	0/4 (0)	4/4 (100)	4/4 (100)	0/4 (0)	1/4 (24)	0/4 (0)	3/4 (75)	2/4 (50)
Disc surgery vs non-opioids	2 (3)	40–67 (54)	0/2 (0)	0/2 (0)	1/2 (50)	2/2 (100)	2/2 (100)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)
Disc surgery vs others	1 (1)	60 (60)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
Disc surgery vs usual/ conventional care	10 (10)	55–743 (320)	3/10 (30)	2/10 (20)	2/10 (20)	10/10 (100)	8/10 (80)	1/10 (10)	2/10 (20)	0/10 (0)	5/10 (50)	1/10 (10)
Total (for disc surgery studies)	**62 (65)**	**10–1085 (105)**	**32/62 (52)**	**2/62 (3)**	**4/62 (6)**	**62/62 (100)**	**53/62 (85)**	**3/62 (5)**	**10/62 (16)**	**6/62 (10)**	**41/62 (62)**	**10/62 (16)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

at short-, medium- or long-term follow-up in patients with acute sciatica (one small, well-conducted RCT[68]). There was also no significant difference between the intervention groups in terms of adverse effects.

One poorly reported RCT[63] (moderate quality) found that disc surgery in combination with acupuncture led to a greater reduction in pain intensity than disc surgery alone at short-term follow-up.

Intraoperative interventions led to a greater reduction in pain intensity at long-term follow-up than did disc surgery alone (four moderate- to poor-quality RCTs[66,69,78,101]). However, there was no statistically significant difference between the intervention groups for global effect (at short-[71,82] and long-term[65,74,81,83,102] follow-up), pain intensity (at short-[66,73,78,84,89,106] and medium-term[64,66,73,84,89,101,106] follow-up), CSOMs (at short-[70,73,89] and medium-term[73,89,107] follow-up) and adverse effects (according to a number of studies, ranging from good to poor quality[64,66,69,71,81,89,106,107]).

Pooled analysis of 18 studies[47–51,53,55,56,58–60,75,85,88,90,92,103,104] showed marginally statistically significant findings in favour of disc surgery, compared with chemonucleolysis, for the global effect at long-term follow-up (see *Figure 9*). However, there was no statistically significant difference between the intervention groups for the global effect at short-[48,49,52,79,92,104] and medium-term[48,49,54,76,88,92,104,105] follow-up; pain intensity at short-,[76,85,88] medium-[76,85,88] and long-term[77,85] follow-up; CSOMs at short-,[85,88] medium-[85,88,96] and long-term[77,85,96] follow-up; or adverse effects[46–51,53–56,58–61,75,85,88,96,103–105] (according to a number of studies, ranging from good to poor quality). There was no statistically significant difference between disc surgery in combination with chemonucleolysis and disc surgery alone, at long-term follow-up, for global effect, pain, or for adverse effects (one poor-quality Q-RCT[97]).

There was no statistically significant difference between repeat disc surgery and spinal cord stimulation for the global effect at long-term follow-up or adverse effects of patients with chronic sciatica following previous disc surgery (one RCT[86]).

Epidural/intradiscal injection

This category includes the use of epidural (injection into the epidural space) or intradiscal (injection into disc) injection of steroid and/or local anaesthetic in various combinations, as well as spinal nerve block using local anaesthetic. Studies that evaluate the use of an alternative class of medication via epidural or intradiscal injection have been classified according to the medication used. The use of a peripheral nerve block is not included in this section.

Description of epidural/intradiscal injection studies

Summary of interventions

Sixty-three studies evaluated the use of epidural/intradiscal injection for sciatica[95,143–204] (eight studies had more than two treatment arms[146,149,161,163,167,169,183,197]), of which 35[95,143–176] compared epidural/intradiscal injection with alternative interventions; the type of interventions being compared are listed in *Table 17a.* Five of these did not report usable data for pain, global or CSOMs,[146,161,164,169,172] but three[146,161,169] provided data on adverse effects. (Two studies[161,169] were pilot studies that reported only baseline data for main outcome measures and follow-up data for adverse effects and cost.)

Thirty studies[149,167,177–204] compared different types (in terms of content) of epidural/intradiscal injections, 10 studies[181,183–185,187,193,194,197,200,202] (two studies had more than two treatment arms[183,197]) compared different modes of administering epidural/intradiscal injections and 20 studies[149,167,177–180,182,186,188–192,195,196,198,199,203,204,207] compared the use of different epidural/intradiscal injections. Details of the interventions are summarised in *Table 17b*, but the findings of these studies are not considered any further here.

Two further studies[142,166] evaluated mixed treatments which included epidural. One study[166] compared the use of epidural plus traction and exercise therapy with traction and exercise therapy without epidural.

One further study[142] compared disc surgery plus epidural (mixed treatments) with conventional care given while waiting for surgery. However, the study reported only health-care utilisation and employment-related outcomes.

Summary of study participants for epidural/intradiscal injections

Summary data for included participants are presented in *Table 18*. The number of participants included in the 28 studies that reported outcome data for global, pain or CSOMs ranged from 23 to 278 (median 74). Most epidural studies included patients with either acute or chronic sciatica. Only two studies[145,176] included patients with acute sciatica (one epidural vs activity restriction and one epidural vs inactive control), with a mean of 34 days[145] or a median 4 weeks[176] for symptom duration of the current episode. One study[94] only included patients with the first episode of sciatica (epidural vs disc surgery) and one study[154] only included patients with recurrent symptoms (epidural vs usual care). The remaining studies included first and recurrent episodes or more usually did not report this information. Fifteen studies included patients who had received previous treatment for their current episode of sciatica; this information was not stated for the remaining studies. Two studies included patients who had previously received an epidural for their current episode, but this information was not reported for most studies. Three studies[94,156,169] included patients who had had previous disc surgery, one of which[169] did not report data on global effect, pain or CSOMs. (One study[95] compared the use of epidural with disc surgery.) Two studies[156,166] (comparator included non-opioids) included some patients with spinal stenosis and one study[94] (epidural vs disc surgery) included patients with sequestered discs.

TABLE 17a Summary of the interventions used when comparing epidural/intradiscal injection with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Treatment description	Control description
Epidural vs activity restriction				
140	Coomes, 1961[145]	Non-RCT	Sacral epidural injection local anaesthetic 50–60 ml procaine	Bed rest at home on fracture-boards
Epidural vs alternative/non-traditional				
667	Wehling, 1997[167] (German language)	CCS	Nerve root blockade with local anaesthetic 5 ml mepivacaine twice a week for 5 weeks	Acupuncture and herbal medication
667	Wehling, 1997[167] (German language)	CCS	Nerve root blockade with steroid triamcinolone 20 mg + local anaesthetic 5 ml mepivacaine twice a week for 5 weeks	Acupuncture and herbal medication
Epidural vs biological agents				
321	Becker, 2007[149]	RCT	Epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (group 2)	Epidural injection of autologous conditioned serum (group 1)
321	Becker, 2007[149]	RCT	Epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (group 3)	Epidural injection of autologous conditioned serum (group 1)
Epidural vs chemonucleolysis				
720	Bontoux, 1990[168] (French language)	RCT	Intradiscal injection of triamcinolone 70 mg	Chemonucleolysis with chymopapain 4000 U
447	Bourgeois, 1988[160] (French language)	RCT	Intradiscal injection of triamcinolone 80 mg	Chemonucleolysis with chymopapain 4000 U
729	Gallucci, 2007[170]	RCT	Intraforaminal and intradiscal injections of steroid triamcinolone 80 mg + local anaesthetic 2–4 ml ropivacaine (group A)	Intraforaminal and intradiscal injections of steroid triamcinolone 80 mg + local anaesthetic 2–4 ml ropivacaine plus ozone–oxygen (group B)
50	Graham, 1976[144]	Non-RCT	Intradiscal hydrocortisone injection (dose not stated)	Chemonucleolysis with chymopapain (dose not stated)
Epidural vs disc surgery				
725	Buttermann, 2004[95]	RCT	Epidural injection of steroid betamethasone 10–15 mg up to three injections	Discectomy
Epidural vs education/advice				
722	Bronfort, 2004[169]	RCT	Three ESIs over 12 weeks	Self-care education
Epidural vs inactive control				
203	Bush, 1991[147]	RCT	Caudal epidural injection of steroid (80 mg of triamcinolone acetonide) + local anaesthetic (0.5% procaine hydrochloride)	Caudal injection of 25 ml normal saline
350	Carette, 1997[152]	RCT	Epidural injection of steroid methylprednisolone 80 mg, 1–3 injections	Normal saline epidural injections
383	Dilke, 1973[157]	RCT	Lumbar epidural injection of steroid methylprednisolone 80 mg	Injection of saline into interspinous ligament
512	Helliwell, 1985[162]	RCT	Epidural injection of steroid methylprednisolone 80 mg (EDI)	Interspinous saline injections (control)

continued

TABLE 17a Summary of the interventions used when comparing epidural/intradiscal injection with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	Treatment description	Control description
739	Karppinen, 2001[171]	RCT	Periradicular injection of steroid methylprednisolone 40 mg + local anaesthetic bupivacaine	Periradicular saline injection
539	Klenerman, 1984[163]	RCT	Epidural injection of steroid methylprednisolone 80 mg	Epidural injection of saline
539	Klenerman, 1984[163]	RCT	Epidural injection of local anaesthetic 20 ml bupivacaine	Epidural injection of saline
905	Mathews, 1987[176]	RCT	Caudal epidural injection Injections of 20 ml of 0.125% bupivacaine and 2 ml (80 mg) methylprednisolone acetate given at fortnightly intervals, up to three times as needed	Control injection Injection of 2 ml lidocaine over the sacral hiatus or into a tender spot
778	Price, 2005[173]	RCT	Epidural injection of steroid triamcinolone 80 mg and local anaesthetic 10 ml bupivacaine	Saline injection into interspinous ligament (placebo)
620	Ridley, 1988[165]	RCT	Epidural injection of steroid methylprednisolone 80 mg	Saline injection into interspinous ligament (placebo)
240	Snoek, 1977[148]	RCT	Epidural injection of steroid methylprednisolone 80 mg	Epidural injection of saline
406	Vad, 2002[158]	RCT	Transforaminal epidural steroid injections with betamethasone 9 mg and 1.5 ml xylocaine, 1–3 injections	Trigger-point saline injections epidural steroid injections, 1–2 injections
351	Valat, 2003[153]	RCT	Three interlaminar epidural injections of steroid methylprednisolone 50 mg at two day intervals	Three interlaminar epidural injections of saline at 2-day intervals
175	Yates, 1978[146]	RCT (crossover)	Caudal epidural injections of steroid	Caudal epidural injections of saline
175	Yates, 1978[146]	RCT (crossover)	Caudal epidural injections of local anaesthetic	Caudal epidural injections of saline
175	Yates, 1978[146]	RCT (crossover)	Caudal epidural injections of steroid + local anaesthetic	Caudal epidural injections of saline
Epidural vs manipulation				
451	Bronfort, 2000[161]	RCT	Epidural injection of steroid injections, 1–3 injections	Chiropractic spinal manipulation
722	Bronfort, 2004[169]	RCT	Three epidural steroid injections over 12 weeks	Chiropractic spinal manipulation
Epidural vs mixed treatment				
439	Blonna, 2004[159] (Italian language)	RCT	Epidural steroid + local anaesthetic injections (4 mg betamethasone + 3 ml ropovicaine 0.2%)	(Epidural + non-opioids) Epidural steroid + local anaesthetic injections (4 mg betamethasone + 3 ml ropovicaine 0.2%) and oral gabapentin (Neurontin®, Pfizer) (up to 900 mg daily)
348	Pirbudak, 2003[150]	RCT	Epidural injection of steroid betamethasone 14 mg and local anaesthetic bupivacaine + oral placebo for 9 months	(Epidural + non-opioids) Epidural injection of steroid betamethasone 14 mg and local anaesthetic bupivacaine + oral amitriptyline 10 mg daily for 9 months
Epidural vs non-opioids				
451	Bronfort, 2000[161]	RCT	Epidural injection of steroid injections, 1–3 injections	Paracetamol, NSAIDs, activity modification
20	Dincer, 2007[143]	RCT	Caudal epidural injection 40 mg methylprednisolone acetate, 8 mg dexamethasone phosphate, 7 ml of 2% prilocaine	Oral diclofenac 75 mg for 14 days (NSAID)
771	Lafuma, 1997[172]	RCT	Epidural steroid (125 mg prednisolone) injections at admission	Usual care (rest + NSAIDs) without epidural injections during hospital admission

TABLE 17a Summary of the interventions used when comparing epidural/intradiscal injection with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	Treatment description	Control description
362	Wilson-MacDonald, 2005[156]	RCT	Epidural injection of steroid methylprednisolone 80 mg and local anaesthetic 8 ml bupivacaine	Intramuscular injections of steroid methylprednisolone 80 mg and local anaesthetic 8 ml bupivacaine
846	Murata, 2009[175]	RCT	L2 nerve block using steroid (3.3 mg dexamethasone sodium phosphate) and local anaesthetic (2 ml of 1% lidocaine)	Injection of steroid (3.3 mg dexamethasone sodium phosphate) and local anaesthetic (7 ml of 1% lidocaine) in the back muscles of L2 area (control block)
Epidural vs passive PT				
9	Veihelmann, 2006[155]	RCT	Epidural injection via epidural catheter (neuroplasty) of steroid triamcinolone 40 mg and ropivacaine	Conservative physiotherapy
Epidural vs usual/conventional care				
349	Buchner, 2000[151]	RCT	Three epidural injections of steroid methylprednisolone 100 mg and 10 ml bupivacaine plus conservative therapy and graded rehabilitation	Conservative therapy and graded rehabilitation without epidural injections
828	Laiq, 2009[174]	Q-RCT	Epidural steroid (80 mg methylprednisolone) + local anaesthetic (3 ml of 2% plain xylocaine) + 3 ml normal saline (steroid group)	Bed rest, NSAIDs, muscle relaxants and opioids (Conservative group)
581	Matyjek, 1986[164] (Polish language)	CCS	Caudal epidural injection. Seven doses of hydrocortisone acetate 0.025 g and a final injection of methylprednisolone 0.04 g	Control group treated by various other methods which were not stated
358	Popiolek, 1991[154] (Polish language)	Non-RCT	Epidural injection of steroid and local anaesthetic. Injected with separate syringes of 5 ml of 0.5% bupivacaine then 40 mg methylprednisolone (n = 15) or 40 mg triamcinolone (n = 15). Repeated after 14 days if necessary	No epidural injection
Mixed treatment incorporating epidural vs mixed treatment without epidural				
644	Styczynski, 1997[166] (Polish language)	Non-RCT	Epidural, traction and therapeutic exercises	Traction and therapeutic exercises

U, units.

TABLE 17b Summary of the interventions used when comparing alternative forms of epidural (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Treatment category	Treatment description	Control category	Control description
Comparison of different modes of administration						
326	Acherman, 2007[183]	RCT	Epidural/ intradiscal injection	Intralaminar epidural injections of steroid triamcinolone 40 mg	Epidural/ intradiscal injection	Caudal epidural injections of steroid triamcinolone 40 mg
326	Acherman, 2007[183]	RCT	Epidural/ intradiscal injection	Transforaminal epidural injection of steroid triamcinolone 40 mg	Epidural/ intradiscal injection	Caudal epidural injections of steroid triamcinolone 40 mg
389	Candido, 2008[187]	RCT	Epidural/ intradiscal injection	Epidural steroid injection (80 mg prednisolone with lidocaine) using parasagittal interlaminar approach	Epidural/ intradiscal injection	ESIs (80 mg prednisolone with lidocaine) using transforaminal approach

continued

TABLE 17b Summary of the interventions used when comparing alternative forms of epidural (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	Treatment category	Treatment description	Control category	Control description
302	Jeong, 2007[181]	RCT	Epidural/ intradiscal injection	Transforaminal epidural steroid injection (ganglionic group)	Epidural/ intradiscal injection	Transforaminal epidural steroid injection (preganglionic group)
328	Kolsi, 2000[184]	RCT	Epidural/ intradiscal injection	Nerve root injections of steroid cortivazol 3.75 mg + local anaesthetic 2 ml lidocaine	Epidural/ intradiscal injection	Interspinous epidural injection of steroid cortivazol 3.75 mg + local anaesthetic 2 ml lidocaine
556	Lee, 2006[193]	HCS	Epidural/ intradiscal injection	Preganglionic epidural injection of steroid triamcinolone 40 mg and 0.5 ml bupivacaine (preganglionic)	Epidural/ intradiscal injection	Interlaminar or caudal epidural injection of steroid triamcinolone 40 mg and 0.5 ml bupivacaine (conventional)
830	Lee, 2009[197]	CCS	Epidural/ intradiscal injection	Translaminar epidural steroid (40 mg triamcinolone) and local anaesthetic (8 ml of 0.5% lidocaine) injection	Epidural/ intradiscal injection	Caudal epidural steroid (40 mg triamcinolone) and local anaesthetic (15 ml of 0.5% lidocaine) injection
830	Lee, 2009[197]	CCS	Epidural/ intradiscal injection	Translaminar epidural steroid (40 mg triamcinolone) and local anaesthetic (8 ml of 0.5% lidocaine) injection	Epidural/ intradiscal injection	Transforaminal epidural steroid (40 mg triamcinolone) and local anaesthetic (2 ml of 0.5% lidocaine) injection; small volume group
830	Lee, 2009[197]	CCS	Epidural/ Intradiscal injection	Translaminar epidural steroid (40 mg triamcinolone) and local anaesthetic (8 ml of 0.5% lidocaine) injection	Epidural/ intradiscal injection	Transforaminal epidural steroid (40 mg triamcinolone) and local anaesthetic (2 ml of 0.5% lidocaine) injection; large volume group
842	Mendoza-Lattes[200]	CCS	Epidural/ intradiscal injection	Caudal epidural steroid (either 2 ml of 80 mg methylprednisolone or 3 ml of 18 mg betamethasone) injection	Epidural/ intradiscal injection	Transforaminal epidural injection of steroid [methylprednisolone (40 mg/ml) or betamethasone (6 mg/ml)] and local anaesthetic (1.5–2.0 cc 1 : 1 solution of bupivacaine 0.25%) injections
630	Schaufele, 2006[194]	CCS	Epidural/ intradiscal injection	Interlaminar epidural injection of steroid methylprednisolone 80 mg + 3 ml lidocaine	Epidural/ intradiscal injection	Transforaminal epidural injection of steroid methylprednisolone 80 mg + 2 ml lidocaine
330	Thomas, 2003[185]	RCT	Epidural/ intradiscal injection	Interspinous epidural injection of steroid dexamethasone 5 mg	Epidural/ intradiscal injection	Transforaminal epidural injection of steroid dexamethasone 5 mg
895	Winnie, 1972[202]	RCT	Epidural/ intradiscal injection	Epidural corticosteroid (80 mg of methylprednisolone). Average of 2.1 injections	Epidural/ intradiscal injection	Intrathecal corticosteroid (80 mg of methylprednisolone). Average of 2.1 injections
Comparison of different type of epidurals (content)						
896	Anwar, 2005[203]	RCT	Epidural/ intradiscal injection	Caudal epidural steroid injection with triamcinolone (40 mg) and local anaesthetic (5 ml of 1% lignocaine)	Epidural/ intradiscal injection	Caudal epidural steroid injection with methylprednisolone (40 mg) and local anaesthetic (5 ml of 1% lignocaine)
321	Becker, 2007[149]	RCT	Epidural/ intradiscal injection	Epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (group 2)	Epidural/ intradiscal injection	Epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (group 3)
141	Beliveau, 1971[177]	Q-RCT	Epidural/ intradiscal injection	Epidural injection of steroid 80 mg methylprednisolone + local anaesthetic 40 ml procaine	Epidural/ intradiscal injection	Epidural injection of 42 ml procaine
437	Blankenbaker, 2005[189]	HCS	Epidural/ intradiscal injection	Selective lumbar nerve root block with triamcinolone 40 mg	Epidural/ intradiscal injection	Selective lumbar nerve root block with betamethasone 6 mg
450	Breivik, 1976[190]	RCT	Epidural/ intradiscal injection	Epidural steroid + local anaesthetic injections (80 mg depot methylprednisolone + 20 ml bupivacaine 0.25%)	Epidural/ intradiscal injection	Epidural bupivacaine injections 20 ml
803	Cocelli, 2009[195]	RCT	Epidural/ intradiscal injection	Epidural injection of betamethasone (10 mg) and bupivacaine (0.125% in 20 ml), 1–3 injections (group 1)	Epidural/ intradiscal injection	Epidural injection of triamcinolone (80 mg) and bupivacaine (0.125% in 20 ml), 1–3 injections (group 2)

TABLE 17b Summary of the interventions used when comparing alternative forms of epidural (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	Treatment category	Treatment description	Control category	Control description
413	Cuckler, 1985[188]	RCT	Epidural/ intradiscal injection	Epidural injection of steroid methylprednisolone 80 mg and local anaesthetic 5 ml procaine	Epidural/ intradiscal injection	Epidural injection of saline and local anaesthetic 5 ml procaine
149	Dashfield, 2005[178]	RCT	Epidural/ intradiscal injection	Targeted injection during spinal endoscopy of steroid 40 mg triamcinolone + 10 ml lidocaine	Epidural/ intradiscal injection	Caudal epidural injection of steroid 40 mg triamcinolone + local anaesthetic 10 ml lidocaine
483	Faraj, 2006[191]	RCT	Epidural/ intradiscal injection	Nerve root infiltration using steroid + local anaesthetic (40 mg + 0.5 ml of 0.5% bupivacaine) with the aid of nerve stimulator	Epidural/ intradiscal injection	Nerve root infiltration using steroid + local anaesthetic (40 mg + 0.5 ml bupivacaine 0.5%) without the aid of nerve stimulator
500	Gronemeyer, 1995[192] (German language)	RCT	Epidural/ intradiscal injection	Epidural injection of steroid triamcinolone 40 mg. 2–11 treatments over 3–8 weeks	Epidural/ intradiscal injection	Epidural injection of steroid triamcinolone 10 mg. 2–11 treatments over 3–8 weeks
814	Hagihara, 2009[196]	Q-RCT	Epidural/ intradiscal injection	Selective nerve root block with steroid (4 mg in 1 ml betamethasone) and local anaesthetic (2 ml of lidocaine hydrochloride)	Epidural/ intradiscal injection	Selective nerve root block of local anaesthetic only (3 ml of lidocaine hydrochloride)
838	Manchikanti, 2008[198]	RCT	Epidural/ intradiscal injection	Caudal epidural steroid (either 6 mg of betamethasone or 40 mg of methylprednisolone) and local anaesthetic (9 ml of 0.5% lidocaine) injections (steroid group)	Epidural/ intradiscal injection	Caudal epidural local anaesthetic (10 ml of lidocaine 0.5%) injections (local anaesthetic group)
908	Manchikanti, 2009[204]	RCT	Epidural/ intradiscal injection	Caudal epidural steroid (either 6 mg of betamethasone or 40 mg of methylprednisolone) and local anaesthetic (9 ml of 0.5% lidocaine) injections (steroid group)	Epidural/ intradiscal injection	Caudal epidural injections of local anaesthetic (0.5% lidocaine 9 ml) (local anaesthetic group)
839	Manchikanti, 2009[199]	RCT	Epidural/ intradiscal injection	Caudal epidural steroid (either 6 mg of betamethasone or 40 mg of methylprednisolone) and local anaesthetic (9 ml of 0.5% lidocaine) injections (steroid group)	Epidural/ intradiscal injection	Caudal epidural local anaesthetic (10 ml of lidocaine 0.5%) injections (local anaesthetic group)
318	Ng, 2005[182]	RCT	Epidural/ intradiscal injection	Periradicular injection of steroid methylprednisolone 40 mg + local anaesthetic 2 ml bupivacaine	Epidural/ intradiscal injection	Periradicular injection of local anaesthetic 2 ml bupivacaine
176	Owlia, 2007[179]	RCT	Epidural/ intradiscal injection	Epidural injection of 80 mg methylprednisolone acetate (80 mg steroid group)	Epidural/ intradiscal injection	Epidural injection of 40 mg methylprednisolone acetate (40 mg steroid group)
273	Riew, 2000[180]	RCT	Epidural/ intradiscal injection	Nerve root injection of steroid betamethasone 6 mg + local anaesthetic 1 ml bupivacaine up to four injections	Epidural/ intradiscal injection	Nerve root injection of local anaesthetic 1 ml bupivacaine up to four injections
365	Rogers, 1992[186]	RCT	Epidural/ intradiscal injection	Epidural injection of steroid methylprednisolone 80 mg and local anaesthetic 14 ml lidocaine	Epidural/ intradiscal injection	Epidural injection of local anaesthetic 14 ml lidocaine
866	Tafazal, 2009[201]	RCT	Epidural/ intradiscal injection	Periradicular infiltration of steroid (40 mg methylprednisolone) and bupivacaine (2 ml of 0.25%) injection	Epidural/ intradiscal injection	Periradicular infiltration bupivacaine (2 ml of 0.25%)
667	Wehling, 1997[167] (German language)	CCS	Epidural/ intradiscal injection	Nerve root blockade with steroid triamcinolone 20 mg + local anaesthetic 5 ml mepivacaine, twice a week for 5 weeks	Epidural/ intradiscal injection	Nerve root blockade with local anaesthetic 5 ml mepivacaine, twice a week for 5 weeks

TABLE 18 Summary of sciatica type and study population details for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?	Any previous epidural?
Epidural vs activity restriction														
140	Coomes, 1961[145]	Non-RCT	40	Mean 43 (range 16–70)	26 (65)	Mean 34 days	Nerve root pain	No	NR	No	No	Yes	NR	NR
Epidural vs alternative/non-traditional														
667	Wehling, 1997[167] (German language)	CCS	278	NR	NR	At least 3 months	Nerve root pain and referred pain	No	NR	No	No	NR	NR	Yes
Epidural vs biological agents														
321	Becker, 2007[149]	RCT	90	Mean 53.9 (range 29–81)	52 (62)	At least 6 weeks	Nerve root pain	Yes	NR	No	No	NR	NR	No epidural in last 3 months
Epidural vs chemonucleolysis														
720	Bontoux, 1990[168] (French language)	RCT	80	Mean 40	50 (63)	At least 2 months; >6 months 34%	Nerve root pain	Yes	NR	No	No	Yes	NR	Yes
447	Bourgeois, 1988[160] (French language)	RCT	60	Mean 37 (range 26–62)	40 (67)	Mean 178 (range 50–700) days	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	NR	Yes
729	Gallucci, 2007[170]	RCT	159	Mean 41.5 (range 18–71)	86 (54)	Mean 15 weeks	Nerve root pain	Yes	NR	No	No	Yes		

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?	Any previous epidural?
50	Graham, 1976[144]	Non-RCT	40 (23 with sciatica)	Mean 42 Sciatica patients: mean 41 (range 24–66)	25 (63). Sciatica patients: 13 (57)	Mean back pain or sciatica for whole group 5.35 years. Sciatica patients median 1 year (range 12 weeks–25 years)	Nerve root pain and referred pain	Yes	NR	No	No	Yes	NR	NR
Epidural vs disc surgery														
725	Buttermann, 2004[95]	RCT	100	Mean 40.5 (SD 12)		Mean 3.55 months (SD 2.75 months)	Nerve root pain	Yes	First episode	No	Yes	Yes	Yes	NR
Epidural vs education/advice														
722	Bronfort, 2004[169]	RCT	32	Mean 49.0 (SD 9.1)	18 (56)	1–3 months 19%, 4–6 months 6%, 7–12 months 9%, >12 months 66%	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	Yes	NR
Epidural vs inactive control														
203	Bush, 1991[147]	RCT	23	Mean 37.8 (range 23–71)	15 (65)	Mean 4.7 months (range 1–13 months)	Nerve root pain	No	NR	No	No	NR	NR	NR
350	Carette, 1997[152]	RCT	158	Mean 39.8 (SD 10.2)	103 (65)	Median 13 weeks	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	No	No epidural in last year
383	Dilke, 1973[157]	RCT	100	Mean 40.4 (range 18–75)	55 (56)	1–4 weeks 10%, 4 weeks–3 months 27%, 3–6 months 33%, 6–12 months 17%, 1–2 years 10%, >2 years 2%	Nerve root pain	No	Recurrent and first episode	No	No	NR	No	NR

continued

TABLE 18 Summary of sciatica type and study population details for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?	Any previous epidural?
512	Helliwell, 1985[162]	RCT	39	Mean 46 (range 20–69)	9 (23)	Mean 10.7 months (range 2.5–48 months)	Nerve root pain	No	NR	No	No	NR	No	NR
739	Karppinen, 2001[171]	RCT	160	Mean 43.8 (SD 13)	115 (72)	2.5 months (SD 1.5 months)	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	No	No
539	Klenerman, 1984[163]	RCT	74	NR	NR	< 6 months	Nerve root pain	No	NR	No	No	NR	No	NR
905	Mathews, 1987[176]	RCT	57	Median 40 (range 18–59)	43 (75)	Median 4 weeks (range 3 days–3 months)	Nerve root pain	No	NR	NR	NR	NR	NR	NR
778	Price, 2005[173]	RCT	228	Mean 43.5 (SD 12)	121 (53)	< 4 months 37%, 4–18 months 63%	Nerve root pain	No	Recurrent and first episode	No	No	Yes	No	No
620	Ridley, 1988[165]	RCT	39	Mean 39 (SD 10)	15 (43)	Mean 8.2 months (SD 6.8 months)	Nerve root pain	No	Recurrent and first episode	No	No	NR	No	None for current episode
240	Snoek, 1977[148]	RCT	51	Mean 45 (range 26–67)	26 (51)	Mean 11.2 weeks (range 12 days–36 weeks)	Nerve root pain	Yes	NR	No	No	NR	No	NR
406	Vad, 2002[158]	RCT	50	Mean 41.5	NR	> 6 weeks	Nerve root pain	Yes	NR	No	No	Yes	No	No
351	Valat, 2003[153]	RCT	85	Mean 41 (SD 10.4)	46 (54)	> 15 days and < 180 days	Nerve root pain and refereed pain	No	Recurrent and first episode	No	No	NR	No	No spinal injection in last month
175	Yates, 1978[146]	RCT	20	NR	NR	NR	Nerve root pain and referred pain	No	NR	No	No	NR	NR	NR

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?	Any previous epidural?
Epidural vs mixed treatment														
439	Blonna, 2004[159] (Italian language)	RCT	50	Mean 61 (SD 15)	NR	Mean 84 days (SD 48 days)	Nerve root pain	Yes	NR	Yes	NR	Yes	No	No
348	Pirbudak, 2003[150]	RCT	92	Mean 49 (SD 12.1)	30 (33)	Median 16.5 months (range 6–48 months)	Nerve root pain	Yes	NR	No	No	Yes	No	No epidural in last year
Epidural vs non-opioids														
451	Bronfort, 2000[161]	RCT	20	Mean 44.5 (SD 10.6)	12 (60)	≤3 weeks $n=6$, 4–12 weeks $n=14$	Nerve root pain and refereed pain	No	NR	No	No	Yes	No	NR
20	Dincer, 2007[143]	RCT	64	Mean 28 (SD 5)	46 (72)	1–12 months	Nerve root pain and refereed pain	Yes	NR	No	No	NR	No	NR
771	Lafuma, 1997[172]	RCT	108	Mean 42.1 (SD 10.6)	66 (61)	Mean 56 days (range 1–854 days)	Nerve root pain	NR	Recurrent and first episode	No	NR	Yes	NR	NR
362	Wilson-MacDonald, 2005[156]	RCT	93	Mean 49 (range 23–79)	37 (40)	>6 weeks, exact duration NR	Nerve root pain	Yes	NR	Yes	No	Yes	Yes	Partial (seven patients had previous epidural)
846	Murata, 2009[175]	RCT	246 (136 radicular pain)	Mean 68 (SD 12, range 27–90)	90 (37)	Median 31 months (SD 52 months)	Nerve root pain	No	NR	NR	NR	Yes	No	No

continued

TABLE 18 Summary of sciatica type and study population details for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?	Any previous epidural?
Epidural vs passive PT														
359	Veihelmann, 2006[155]	RCT	99	Mean 44.5 (SD 24)	45 (45)	NR	Nerve root pain	Yes	NR	No	No	Yes	NR	NR
Epidural vs usual/conventional care														
349	Buchner, 2000[151]	RCT	36	Mean 34.3 (range 20–50)	23 (64)	Median 8 weeks (range 1–150 weeks)	Nerve root pain	Yes	NR	No	No	NR	No	NR
828	Laiq, 2009[174]	Q-RCT	52	Mean 40.5 (SD 2.3)	32 (62)	> 2 weeks	Nerve root pain	Yes	NR	No	NR	NR	NR	No
581	Matyjek, 1986[164] (Polish language)	CCS	629	NR	NR	NR	Nerve root pain	No	NR	NR	NR	NR	NR	NR
358	Popiolek, 1991[154] (Polish language)	Non-RCT	60	Mean 41.3 (range 27–63)	39 (65)	Mean 1.95 months	Nerve root pain	Yes	Recurrent	NR	NR	NR	NR	NR
Mixed treatment incorporating epidural vs mixed treatment without epidural														
644	Styczynski, 1997[166] (Polish language)	Non-RCT	103	Range 27–85	57 (55)	Mean 4 weeks one group; 5 months	Nerve root pain	Yes	NR	Yes	NR	NR	No	NR

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included otherwise reported as no.

Summary of study design and quality for epidural/intradiscal injection studies

Summary information on study details is presented in *Table 19*, excluding studies[146,161,164,169,172] that did not report outcome data for global effect, pain intensity or CSOMs. Most included epidural studies were RCTs (24/29, 83%); however, the proportion that were deemed good quality was very low (4/29, 14%), all of which compared epidural with inactive control. Although 10 studies[149,152,153,156,160,163,165,168,171,173] used and adequate method for generating a random number sequence, eight of these used sealed envelopes to conceal allocation, which is a partially adequate method. Only one study had good external validity.[171]

Epidural/intradiscal injection results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 20* and the accompanying forest plot (*Figure 14*). Epidural/intradiscal injections were compared with inactive control, usual care and chemonucleolysis (not widely used in the UK NHS). One study[176] included only patients with acute sciatica, and the remaining studies included patients with either acute or chronic sciatica. The duration of follow-up ranged from 24 hours[148] to 6 weeks.[173]

Six RCTs[148,152,153,165,173,176] compared epidural injections with inactive control; the overall findings were found to be in favour of epidural, but were not statistically significant. Three RCTs[152,153,173] were good quality. The study that had the largest effect size in favour of epidural injections,[165] and the only study to have statistically significant results, was of poor quality.

One poorly reported non-RCT[154] found that epidural injections were much better than usual care, in terms of the global effect at 21 days, in patients who had had sciatica for a mean of 2 months.

One moderate-quality RCT[170] found no statistically significant difference between intraforaminal and intradiscal injections of steroid plus local anaesthetic (categorised as epidural) compared with intraforaminal and intradiscal injections of steroid, local anaesthetic and ozone–oxygen (categorised as chemonucleolysis). The study included patients with both acute and chronic sciatica, with a mean duration of symptoms of 15 weeks.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 21* and the accompanying forest plot (*Figure 15*). Epidural injections/nerve block were compared with inactive control, usual care, non-opioids, alternative therapy and mixed treatments. Three studies[150,167,175] included patients with chronic sciatica, one study[174] did not report the duration of symptoms, and the remaining studies included patients with either acute or chronic sciatica. The duration of follow-up ranged from post treatment to 6 weeks.[158,173]

The overall findings from seven RCTs[147,152,153,158,162,171,173] found a statistically significant reduction in pain intensity for epidural injections compared with inactive control. Four of these RCTs[152,153,171,173] were good quality; three were moderate quality. One study[171] was also considered as having good external validity, whereas four[147,153,158,162] of the seven were rated as poor. One further RCT[165] found epidural injection to be superior to inactive control, but reported data only for median percentage improvement.

One moderate-quality RCT[151] and one Q-RCT[174] compared epidural injections with usual care. The Q-RCT[174] reported a statistically significant improvement in favour of epidural injection; the RCT[151] reported a smaller improvement which was not statistically significant. When the results were combined in a meta-analysis, there was no statistically significant difference.

TABLE 19 Summary of the study details for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Epidural vs activity restriction										
140	Coomes, 1961[145]	40	9 weeks	Non-RCT	No	No	80–100	No	Weak	Weak
Epidural vs alternative/non-traditional										
667	Wehling, 1997[167] (German language)	278	5 weeks	CCS	No	No	80–100	No	Weak	Weak
Epidural vs biological agents										
321	Becker, 2007[149]	90	22 weeks	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
Epidural vs chemonucleolysis										
720	Bontoux, 1990[168] (French language)	80	3 months	RCT	Yes	Unclear	80–100	Yes	Moderate	Weak
447	Bourgeois, 1988[160] (French language)	60	6 months	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
729	Gallucci, 2007[170]	159	6 months	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
50	Graham, 1976[144]	40 (23 with sciatica)	2 years	Non-RCT	No	No	80–100	Yes	Weak	Weak
Epidural vs disc surgery										
725	Buttermann, 2004[95]	100	2–3 years	RCT	Unclear	Unclear	80–100	No	Moderate	Moderate
Epidural vs education/advice										
722	Bronfort, 2004[169]	32	52 weeks	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Epidural vs inactive control										
203	Bush, 1991[147]	23	1 year	RCT	Unclear	Unclear	60–79	Yes	Moderate	Weak
350	Carette, 1997[152]	158	3 months	RCT	Yes	Partial	60–79	Yes	Strong	Moderate
383	Dilke, 1973[157]	100	3 months	RCT	Unclear	Unclear	60–79	Yes	Moderate	Weak
512	Helliwell, 1985[162]	39	3 months	RCT	Unclear	Unclear	80–100	Unclear	Moderate	Weak
739	Karppinen, 2001[171]	160	1 year	RCT	Yes	Partial	80–100	Yes	Strong	Strong
539	Klenerman, 1984[163]	74	2 months	RCT	Yes	Partial	80–100	Yes	Weak	Weak
905	Mathews,1987[176]	57	12 months	RCT	Partial	Unclear	60–79	Yes	Moderate	Moderate
778	Price, 2005[173]	228	12 months	RCT	Yes	Partial	80–100	Yes	Strong	Moderate
620	Ridley, 1988[165]	39	6 months	RCT	Yes	Unclear	80–100	Yes	Moderate	Weak
240	Snoek, 1977[148]	51	Ranged from 8 to 20 months	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak

TABLE 19 Summary of the study details for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
406	Vad, 2002[158]	50	Mean 16 months (range 12–21 months)	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
351	Valat, 2003[153]	85	35 days	RCT	Yes	Partial	80–100	Yes	Strong	Weak
175	Yates, 1978[146]	20	1 month	RCT	Unclear	Unclear	Cannot tell	Unclear	Weak	Weak
Epidural vs mixed treatment										
439	Blonna, 2004[159] (Italian language)	50	60 days	RCT	Unclear	Partial	80–100	Unclear	Weak	Moderate
348	Pirbudak, 2003[150]	92	9 months	RCT	Partial	No	80–100	Yes	Moderate	Weak
Epidural vs non-opioids										
451	Bronfort, 2000[161]	20	12 weeks	RCT	Unclear	Partial	80–100	NA	Moderate	Weak
20	Dincer, 2007[143]	64	3 months, assessment at day 15, first month and third month	RCT	Unclear	Unclear	80–100	Yes	Moderate	Moderate
771	Lafuma, 1997[172]	108	3 months	RCT	Unclear	Unclear	80–100	No	Weak	Weak
362	Wilson-MacDonald, 2005[156]	93	35 days	RCT	Yes	Partial	80–100	Unclear	Moderate	Moderate
846	Murata, 2009[175]	246 (136 radicular pain)	7 days	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Epidural vs passive PT										
359	Veihelmann, 2006[155]	99	12 months	RCT	Partial	Yes	< 60	Yes	Moderate	Weak
Epidural vs usual/conventional care										
349	Buchner, 2000[151]	36	6 months	RCT	Partial	Partial	80–100	Unclear	Moderate	Weak
828	Laiq, 2009[174]	52	6 months	Q-RCT	No	No	80–100	No	Weak	Weak
581	Matyjek, 1986[164] (Polish language)	629	Not stated	CCS	No	No	80–100	No	Weak	Weak
358	Popiolek, 1991[154] (Polish language)	60	21 days	Non-RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Mixed treatment incorporating epidural vs mixed treatment without epidural										
644	Styczynski, 1997[166] (Polish language)	103	10 days	Non-RCT	No	No	80–100	No	Weak	Weak

NA, not applicable.

TABLE 20 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Epidural vs chemonucleolysis														
729	Gallucci, 2007[170]	A + C	RCT	2 weeks	Treatment success: ODI ≤ 20%		82	72	0	77	69	0	0.83 (0.31 to 2.24)	
Epidural vs inactive control														
350	Carette, 1997[152]	A + C	RCT	3 weeks	Marked or very marked improvement		75	42	0.04	78	44	0.03	1.15 (0.58 to 2.27)	Data reported as percentages. ITT reported for study using LOCF, but data missing for three patients for global outcome; not stated how missing data handled for binary outcomes
905	Mathews, 1987[176]	A	RCT	1 month	Recovered: pain score of 5 or 6 (vs not recovered: scores of 1–4)		21	14	0.09	32	18	0.06	1.56 (0.50 to 4.89)	Number of dropouts reported were different to the number missing from the analysis
778	Price, 2005[173]	A + C	RCT	6 weeks	Global improvement: 75% improvement in ODI		120	20	0	108	16	0	1.15 (0.56 to 2.35)	
620	Ridley, 1988[165]	A + C	RCT	2 weeks	Reported some improvement	Patient	19	17	0.10	16	3	2	36.83 (5.35 to 253.62)	
240	Snoek, 1977[148]	A + C	RCT	24 hours	Improvement in radiating pain		27	7	0	24	3	0	2.45 (0.56 to 10.81)	
351	Valat, 2003[153]	A + C	RCT	35 days	Overall success	Patient	43	21	0	42	20	0	1.05 (0.45 to 2.46)	
Epidural vs usual/conventional care														
358	Popiolek, 1991[154] (Polish language)	A + C	Non-RCT	21 days	Overall improvement: large improvement or moderate improvement (vs no improvement)		30	28	0	30	8	0	38.50 (7.42 to 199.87)	

A, acute; A + C, acute and chronic; LOCF, last observation carried forward.

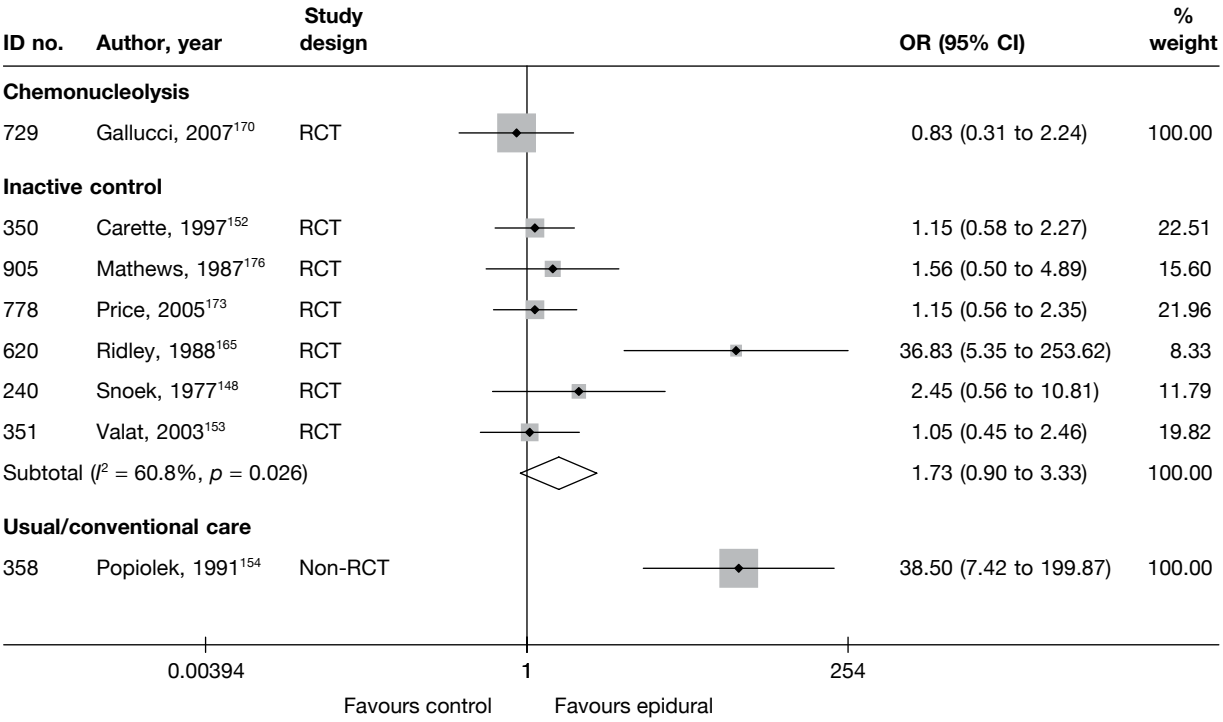

FIGURE 14 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing epidural/interdiscal injection with alternative interventions. Note: weights are from random effects analysis.

Epidural injections were found to be significantly better than non-opioids at reducing pain at 1 week to 1 month, according to two poorly reported RCTs of weak to moderate quality.[143,175] One further poorly reported RCT,[156] of moderate quality, found epidural to be significantly better than non-opioids for pain relief at 35 days ($p < 0.004$, statistical test not stated), but did not report any summary statistics.

Two RCTs[150,159] compared the use of epidural injection with epidural injection plus non-opioids (mixed treatments) at 2–6 weeks, and found no overall benefit. One RCT[150] was of moderate quality, and included blinding of participants, clinicians and outcome assessors. Patients were randomly assigned to the two groups by one of the authors by drawing sealed envelopes from a box. The second RCT[159] was poorly reported and of poor quality. The SDs for this study were not reported and have been imputed using the weighted mean.

One CCS[167] found no important difference between nerve root block and acupuncture plus herbal medicine for pain relief at 5 weeks in patients with chronic sciatica.

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 22* and the accompanying forest plot (*Figure 16*). Epidural injections were compared with inactive control, usual care, biological agents and mixed treatments. One study[150] included patients with chronic sciatica, and the remaining studies included patients with either acute or chronic symptoms. The duration of follow-up ranged from post treatment to 6 weeks.[149–151,158,173]

The overall findings from five RCTs[152,153,158,171,173] showed epidural injections to be significantly better than inactive control for improving function. The findings were heterogeneous, with one poor-quality RCT[158] reporting a large effect size in favour of epidural injection. The quality of the

TABLE 21 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs alternative																
667	Wehling, 1997[167] (i)[c] (German language) (steroid + local anaesthetic)	C	CCS	5 weeks	Overall	Percentage improvement (0–100)	26	230					–66 (24)	–62 (28)	–4.0 (–18.18 to 10.18)	Results reported as percentage improvement (100% improvement = no pain; 0% pain reduction = pain the same as before treatment)
667	Wehling, 1997[167] (ii)[c] (German language)	C	CCS	5 weeks	Overall	Percentage improvement (0–100)	26	230					–48 (24)	–62 (28)	14.0 (–2.84 to 30.84)	Results reported as percentage improvement (100% improvement = no pain; 0% pain reduction = pain the same as before treatment)
Epidural vs inactive control																
203	Bush, 1991[147]	A + C	RCT	4 weeks	Overall	VAS (0–100)	12	11	38.5	49.2	16.0 (22.48)	45.0 (23.67)			–29.00 (–50.71 to –7.29)	SD imputed from weighted average Dropouts 22%: intervention 1/12, control 4/11 ITT analysis based on LOCF
350	Carette, 1997[152]	A + C	RCT	3 weeks	Overall	VAS (0–100)	77	79	65.6 (21.6)	61.5 (21.4)	44.9	49.1	–21 (29.2)	–12.4 (27.3)	–8.60 (–17.48 to 0.28)	
512	Helliwell, 1985[162]	C	RCT	1 month	Overall	VAS (0–10)	20	19					–27.0 (21.0)	–7 (14)	–20.00 (–31.15 to –8.85)	Summary statistics derived from graphs

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
739	Karppinen, 2001[171]	A + C	RCT	4 weeks	Leg	VAS (0–100)	80	80	71.0 (18)	75.2 (19)	36.9 (35.66)	43.9 (35.66)			–2.80 (–13.76 to 8.16) *Multivariate analysis (adjusted change from baseline): 2.3 (95% CI –8.7 to 13.4)*	SDs (and SEs) for change estimated from 95% CI of difference between treatment groups Two patients lost to follow-up from steroid group
778	Price, 2005[173]	A + C	RCT	6 weeks	Leg	VAS (0–100)	120	108	52 (23)				–15 (32)	–15 (32)	0.00 (8.32 to 8.32)	
620	Ridley, 1988[165]	A + C	RCT	2 weeks	Overall	VAS (0–100)	19	16					–46	0	–46	Only median percentage improvement and range reported
406	Vad, 2002[158]	A + C	Non-RCT	Post-treatment	Overall	VAS (0–10)	25	25	88 (14)	94 (14)	16 (8)	36 (11)			–2.70 (–12.52 to 7.12)	
351	Valat, 2003[153]	A + C	RCT	35 days	Overall	VAS (0–100)	43	42	57.5 (16.3)	58 (16.6)	22.1 (20.1)	24.8 (25.7)			–10.73 (–18.47 to –2.99)	
Epidural vs mixed treatments																
439	Blonna, 2004[159] (Italian language)	A + C	RCT	14 days	Overall	VAS (0–10)	24	26	80.4 (10.0)	83.5 (12.6)	34.3 (22.48)	35.6 (22.86)			–1.30 (–22.07 to 19.47)	SD imputed from weighted average ITT using LOCF, dropouts 3 (6%): intervention 3/26, control 0/24
348	Pirbudak, 2003[150]	C	RCT	6 weeks	Overall	VAS (0–10)	46	46	84.0 (17.0)	78.1 (40.0)	40	11.0	–44.0 (22.0)	–49.0 (10.0)	5.00 (–1.98 to 11.98)	

continued

TABLE 21 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs non-opioids																
20	Dincer, 2007[143]	A + C	RCT	1 month	Overall	VAS (0–10)	34	30	69 (10)	68 (10)	32 (11)	44 (13)			–12.00 (–17.94 to –6.06)	
846	Murata, 2009[175]	C	RCT	7 days	Leg	VAS (0–100)	69	65			43 (22.48)	67 (22.86)			–24.00 (–31.63 to –16.37)	SD imputed from weighted average Subgroup analysis based on 136/246 (55%) with radicular pain; intervention 71/122, control 65/124. Dropouts: 8/246 (3%); no further details
362	Wilson-MacDonald, 2005[156]	NR	RCT	35 days	Overall	Oxford pain chart									*Significant difference in pain relief between groups, in favour of epidural (p < 0.004, test not stated)*	Summary statistics not reported Dropouts 14/93 (15%): group allocation not stated

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs usual/conventional care																
349	Buchner, 2000[151]	A + C	RCT	2 weeks	Overall	VAS (0–100)	17	19	84.4	81	30.8 (12.47)	37.1 (12.47)			–6.30 (–14.46 to 1.86)	2-week data used instead of 6-weeks because *p*-value for one-sided *t*-test available to calculate SD Dropouts 9/31 (29%): intervention 4/16, control 5/15
828	Laiq, 2009[174]	NR	Q-RCT	1 month	Overall	VAS (0–10)	25	25			20 (15)	45 (14.8)			–15.64 (–33.96 to 2.69)	Dropouts 2/52 (4%): intervention 1/26, control 1/26
Mixed treatment incorporating epidural vs mixed treatment without epidural																
644	Styczynski, 1997[166] (Polish language)	A + C	Non-RCT	10 days	Overall	VAS (1–100)	58	45	100	100	39.8	53.8			14	Pain scale used was not stated SD not reported and no statistical analysis undertaken

A + C, acute and chronic; C, chronic; LOCF, last observation carried forward; NR, not reported.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Wehling and Reinecke[167] included three treatment groups: epidural injection of local anaesthetic (i), epidural injection of steroid + local anaesthetic (ii), and acupuncture + herbal medicine (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 15*).

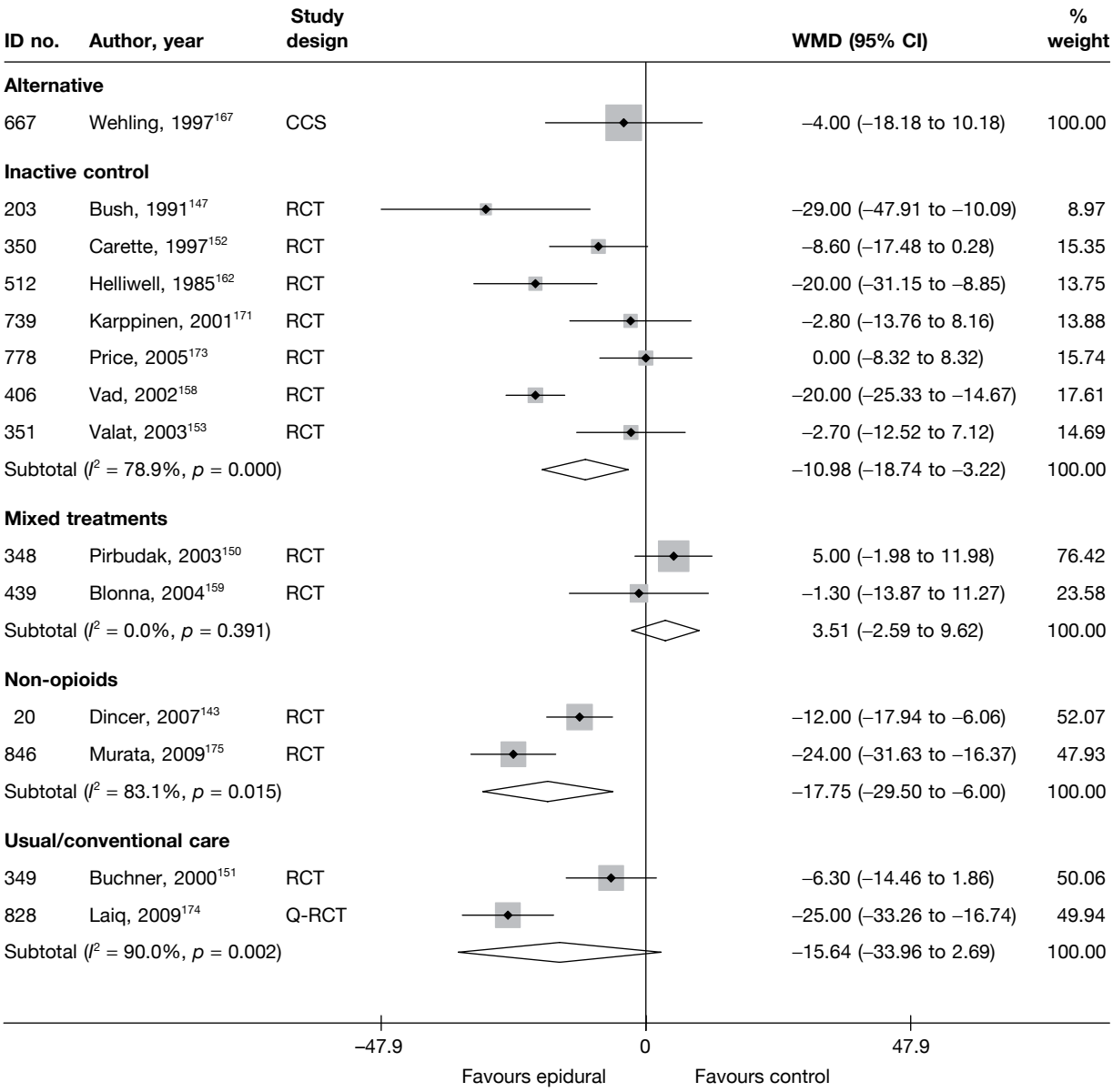

FIGURE 15 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

remaining RCTs[152,153,171,173] was good, and pooled analysis showed a significant difference in favour of epidural (SMD −0.19; 95% CI −0.34 to −0.03).

One moderate-quality RCT[151] found epidural to be significantly better than usual care for improving functional status at 6 weeks' follow-up.

One moderate-quality RCT[143] found epidural to be significantly better than non-opioids for improving functional status at 4 weeks' follow-up. The methods of randomisation and allocation concealment were not stated.

One moderate-quality RCT[150] found no statistically significant difference between epidural injection in combination with non-opioids (mixed treatments) and epidural injection alone for improving functional status for patients with chronic sciatica at 6 weeks' follow-up.

TABLE 22 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

						Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)			
ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Mean difference (95% CI)[a]	Comment/conversion[b]
Epidural vs biological agents															
321	Becker, 2007[149] (i)[c] (5 mg)	A+C	RCT	6 weeks	ODI	27	32	20.6 (8.1)	22.0 (8.3)	12.1 (9.0)	13.8 (9.8)			–0.18 (–0.69 to 0.33)	
321	Becker, 2007[149] (ii)[c] (10 mg)	A+C	RCT	6 weeks	ODI	25	32	19.4 (9.9)	22.0 (8.3)	11.0 (9.5)	13.8 (9.8)			–0.29 (–0.82 to 0.24)	
Epidural vs inactive control															
350	Carette, 1997[152]	A+C	RCT	3 weeks	Modified ODI	77	80	49.6 (15.7)	50 (15.5)	41.6 (15.7)	44.5 (15.5)	–8 (15.3)	–5.5 (14.3)	–0.19 (–0.50 to 0.13)	Final SD missing, so baseline SD used ITT using LOCF: one dropout excluded Analysis of variance results not reported
739	Karppinen, 2001[171]	A+C	RCT	4 weeks	ODI	80	80	42.9 (16)	43.5 (15)	26.8 (16)	29.1 (15)	–16.1 (18.88)	–14.4 (18.88)	–0.15 (–0.46 to 0.16) *Adjusted change from baseline –0.4 (95% CI –7.0 to 6.2)*	Final SD missing, so baseline SD used
778	Price, 2005[173]	A+C	RCT	6 weeks	ODI	120	108	44 (15)	45 (18)	31 (15)	35 (18)	–13 (17)	–10 (18)	–0.24 (–0.50 to 0.02)	Final mean calculated from change scores Baseline SD used ITT using LOCF
406	Vad, 2002[158]	A+C	RCT	Post-treatment	RMDQ	25	25	8.8 (1.2)	9.6 (1.3)	0.9 (1.6)	4.7 (2.1)	13.3	8.7	–2.04 (–2.72 to –1.35)	

continued

TABLE 22 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
351	Valat, 2003[153]	A + C	RCT	35 days	RMDQ	43	42	15.1 (4.7)	14.2 (4.2)	8.5 (5.4)	9.1 (5.4)	–6.6	–5.1	–0.11 (–0.54 to 0.31)	ITT using LOCF Dropouts 22/85 (26%): intervention 9/43, control 13/42
Epidural vs non-opioids															
20	Dincer, 2007[143]	A + C	RCT	1 month	ODI	34	30	35.8 (6.7)	34.4 (6.7)	17 (7.3)	22.2 (8.6)	–18.8	–12.2	–0.66 (–1.16 to –0.15)	
Epidural vs mixed treatments															
348	Pirbudak, 2003[150]	C	RCT	6 weeks	ODI	46	46	49.6 (15.5)	50.2 (15.2)	32 (15.5)	28 (15.2)	–17.6 (20.5)	–21.8 (24.5)	0.26 (–0.15 to 0.67)	Final SD missing, so baseline SD used
Epidural vs usual/conventional care															
349	Buchner, 2000[151]	A + C	RCT	6 weeks	Hannover Functional Ability	17	19	38.5	39.9	36.3 (6.01)	42.5 (6.01)			–1.03 (–1.73 to –0.33)	2-week data used instead of 6-week data because *p*-value for one-sided *t*-test available to calculate SD

A + C, acute and chronic; C, chronic; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Becker *et al.*[149] included three treatment groups: epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of autologous conditioned serum (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 16*).

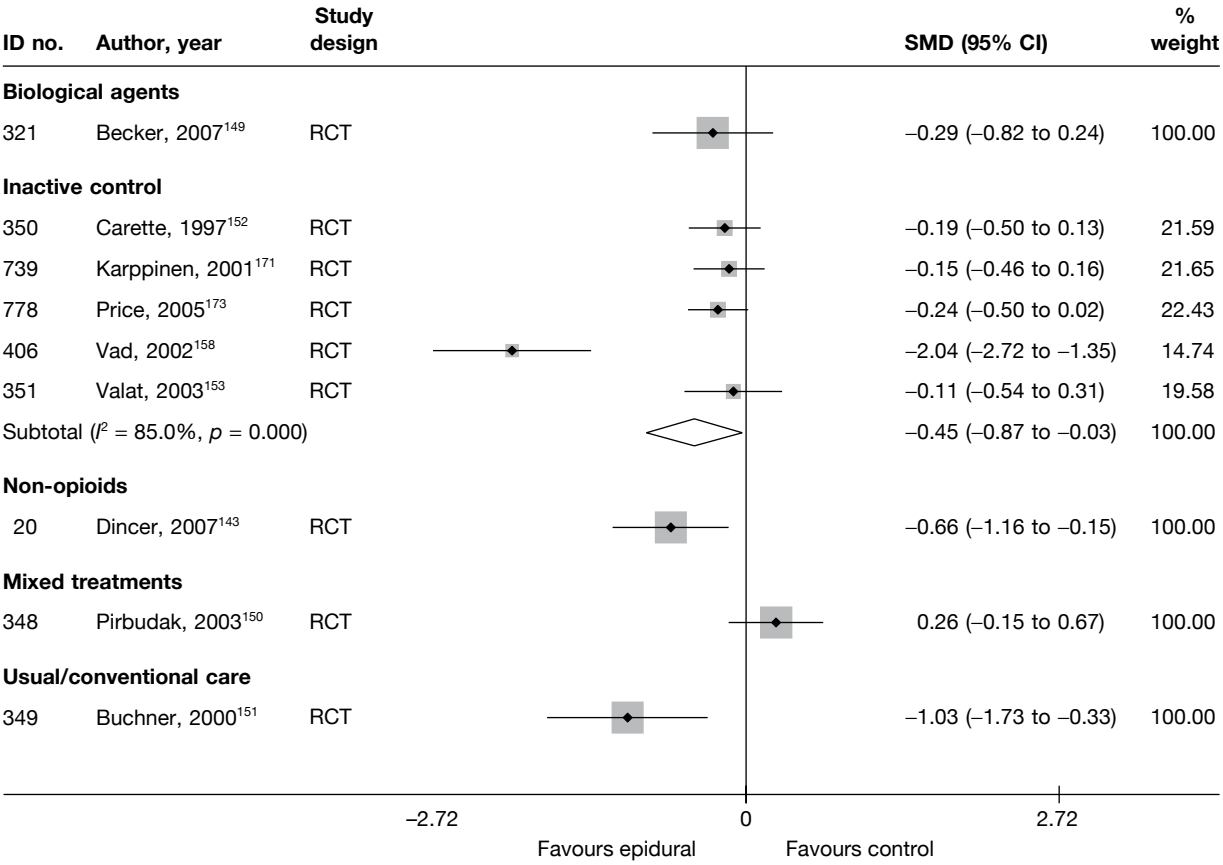

FIGURE 16 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

One moderate-quality RCT[149] compared epidural using two different dosages of steroid with an epidural injection of autologous conditioned serum (biological agent). There was no statistically significant difference between either dose of epidural steroid and the biological agent at 6 weeks.

One poorly conducted non-RCT,[166] reported a greater decrease in pain intensity for patients treated with epidural, traction and exercise therapy than those treated with traction and exercise therapy without epidural.

Epidural/intradiscal injections results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 23* and the accompanying forest plot (*Figure 17*). Epidural/intradiscal/nerve block injections were compared with inactive intervention, usual care, activity restriction, non-opioids, passive PT and chemonucleolysis. One study[145] included only patients with acute sciatica, whereas five studies[155,160,162,168,175] included only patients with chronic symptoms. The remaining studies included patients with either acute or chronic sciatica, or did not state the duration of symptoms.[174] The duration of follow-up ranged from 2 months[163,175] to 6 months.[151,155,160,170,174]

Five RCTs[152,157,162,163,173] compared epidural injections with inactive control; the overall findings were in favour of epidural at 2–3 months, but the difference was not statistically significant. Two of these RCTs[152,173] were good quality and two[157,162] were of moderate quality.

TABLE 23 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)[a]	Comments
Epidural vs activity restriction														
140	Coomes, 1961[145]	A	Non-RCT	9 weeks	Neurological state: completely relieved or improved (vs not changed or worse)	Physician	20	12	0	20	5	0	4.50 (1.17 to 17.37)	
Epidural vs chemonucleolysis														
720	Bontoux, 1990[168] (French language)	C	RCT	3 months	Overall improvement: very good or good (vs mediocre or bad; other cases)		40	27	0	40	26	0	1.12 (0.44 to 2.83)	
447	Bourgeois, 1988[160] (French language)	C	RCT	6 months	Overall pain relief: very good or good (vs failure)		30	16	0	30	20	0	0.57 (0.20 to 1.62)	
729	Gallucci, 2007[170]	A+C	RCT	6 months	Treatment success: ODI ≤ 20%		77	36	0	82	61	0	3.31 (1.70 to 6.45)	
Epidural vs inactive control														
350	Carette, 1997[152]	A+C	RCT	3 weeks	Marked or very marked improvement		77	25	0.01	78	23	0.03	0.98 (0.52 to 1.86) *Treatment effect –0.4% (95% CI –16.5% to 15.7%); not clear if adjusted for baseline values*	Data reported as percentages ITT reported for study using LOCF, but data missing for five patients for global outcome; not stated how missing data handled for binary outcomes
383	Dilke, 1973[157]	A+C	RCT	3 months	Pain: not severe or none (vs severe and unknown)	Patient	44	40	0.14	38	28	0.21	3.57 (1.02 to 12.54)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
512	Helliwell, 1985[162]	C	RCT	3 months	Definitive improvement	Patient	20	14	0	19	5	0	6.53 (1.61 to 26.47)	
539	Klenerman, 1984[163] (i)[b] (steroid)	A+C	RCT	2 months	Treatment success based on overall pain (VAS) and physical examination: not failed, i.e. improved or cured (vs failed)	Physician	19	15	?	16	11	?	1.70 (0.37 to 7.85)	Number randomised unclear
539	Klenerman, 1984[163] (ii)[b] (anaestheticd)	A+C	RCT	2 months	Treatment success based on overall pain (VAS) and physical examination: not failed, i.e. improved or cured (vs failed)	Physician	16	11	?	16	11	?	1.00 (0.22 to 4.46)	Number randomised unclear
778	Price, 2005[173]	A+C	RCT	12 weeks	Global improvement: ≥ 75% improvement in ODI		120	22	0	108	26	0	0.71 (0.37 to 1.34)	Data inferred from graphs reporting percentages ITT using LOCF
Epidural vs non-opioids														
846	Murata, 2009[175]	C	RCT	24 weeks	Adequate recovery from leg pain		71	11	?	65	5	?	2.20 (0.72 to 6.72)	Subgroup analysis of 136/246 (55%) patients with radicular pain: intervention 71/122, control 65/124 8/246 patients dropped out, group allocation or radicular pain not stated

continued

TABLE 23 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Epidural vs passive PT														
359	Veihelmann, 2006[155]	C	RCT	6 months	Gerbershagen score (chronification index), GHS I (vs GHS II, III)		46	31	0.02	27	8	0.48	4.91 (1.75 to 13.76)	
Epidural vs usual/conventional care														
349	Buchner, 2000[151]	A+C	RCT	6 months	Overall assessment: very good or good based on VAS, SLR and functional status		17	15	0	19	14	0	2.68 (0.45 to 16.11)	ITT used
828	Laiq, 2009[174]	NR	Q-RCT	6 months	Successfully treated: ≥50% reduction in pain using VAS		25	21	0.04	25	19	0.04	1.66 (0.41 to 6.78)	Findings reported in terms of treatment failure

?, unclear; A, acute; A+C, acute and chronic; C, chronic; LOCF, last observation carried forward; NR, not reported.

a Results reported by study in italics.

b Klenerman *et al.*[163] included three treatment groups: epidural steroid injection (i), epidural anaesthetic injection (ii) and epidural saline injection (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see forest plot).

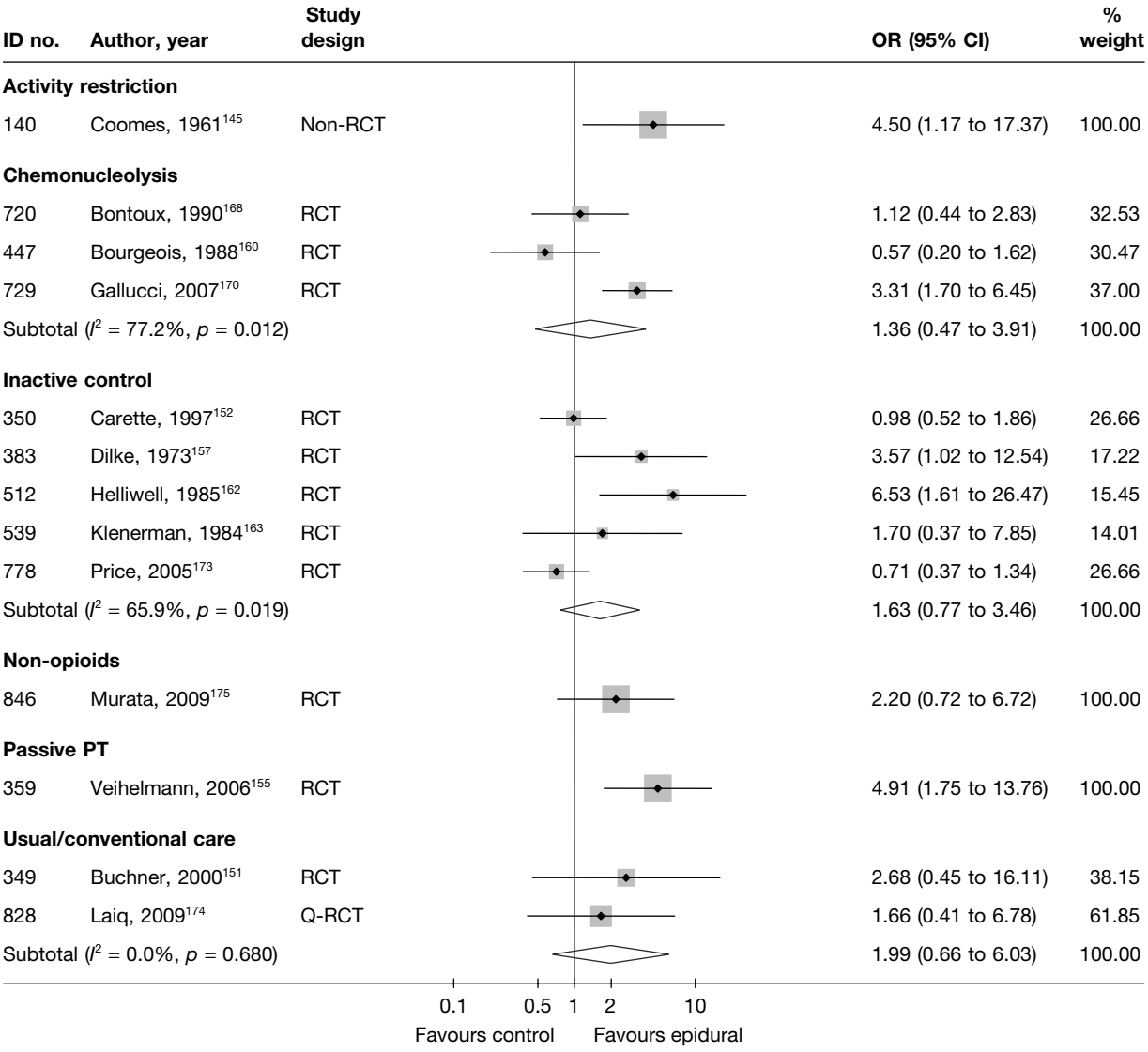

FIGURE 17 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

Two moderate- or poor-quality RCTs[151,174] compared epidural injection with usual care; the overall finding was in favour of epidural at 6 months, but the difference was not statistically significantt.

Epidural injection was found to be significantly better than activity restriction for overall improvement in neurological state for patients with acute sciatica (mean duration of symptoms 34 days) at 9 weeks. But these findings are based on a poor-quality non-RCT,[145] which also had poor external validity.

One poor-quality RCT[175] reported non-statistically significant findings in favour of epidural, compared with non-opioids, for adequate recovery from leg pain at 24 weeks. The findings were based on a subgroup analysis of 136/246 (55%) patients with radicular pain.

One moderate-quality RCT[155] found epidural injections to be significantly better than passive PT in terms of the number for patients with Gerbershagen pain chronicity score I (vs II or III; pain staging system) at 6 months. However, the withdrawal rate was very high in the control group

(48%) compared with the intervention group (2%). Patients in the control group had the choice to cross over to the epidural group after 3 months of unsatisfactory treatment with PT. These patients were then excluded from analysis ($n = 12/52$).

Two moderate-quality RCTs[160,168] compared intradiscal injection with chemonucleolysis using chymopapain for chronic sciatica, and one poorly reported but moderate-quality RCT[170] compared intraforaminal/intradiscal injections of steroid plus local anaesthetic (epidural) with intraforaminal/intradiscal injections of steroid, local anaesthetic and ozone–oxygen (chemonucleolysis). The first RCTs[160,168] found no statistically significant difference between the intervention groups, while the third RCT[170] found statistically significant findings in favour of the epidural group for patients who had had symptoms for a mean of 15 weeks.

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 24* and the accompanying forest plot (*Figure 18*). Epidural injections were compared with inactive control, usual care, passive PT, mixed treatments, disc surgery and biological agents. Three studies[150,155,162] included only patients with chronic sciatica, one study[174] did not report the duration of symptoms, and the remaining studies included patients with either acute or chronic sciatica. The duration of follow-up ranged from 60 days[159] to 6 months.[150,151,155,171,174]

Four RCTs[152,162,171,173] compared epidural injections with inactive control, for which pooled analyses showed no important difference between the groups at 3[152,162,173] and 6[171] months. However, the findings were heterogeneous. The overall quality for three trials[152,171,173] was good. The fourth study[162] was small ($n = 39$), poorly reported and of moderate quality, and, unlike the remaining studies, found statistically significant findings in favour of epidural. One RCT[171] also reported findings based on ANCOVA, adjusted for baseline values, which favoured inactive control for leg pain at 3 months (–12.2; 95% CI –23.5 to –1.0, $p = 0.003$; negative values indicate a negative effect). The same analyses showed no statistically significant difference between the groups at 12 months.

Two studies[151,174] compared epidural injections with usual care; the overall findings at 6 months were in favour of epidural, but were not statistically significant. One was a moderate-quality RCT and the other a Q-RCT.

One moderate-quality RCT[155] reported a non-statistically significant reduction in pain intensity at 6 months in favour of epidural, compared with passive PT. The withdrawal rate was much higher in the control group (48%) than in the intervention group (2%). Patients in the control group had the choice to cross over to the epidural group after 3 months of unsatisfactory treatment with PT. These patients were then excluded from the analysis ($n = 12/52$).

Two RCTs[150,159] compared the use of epidural injection with epidural injection plus non-opioids (mixed treatments) at 2 months[159] or 6 months.[150] Overall, there was a non-statistically significant finding in favour of the mixed treatments. A much greater (and statistically significant) reduction in pain was achieved by the better-quality RCT[150] than by the poor-quality and poorly reported study.[159]

One poorly reported RCT[95] of moderate quality compared epidural with disc surgery. The method of randomisation and allocation concealment were not reported. The level of leg pain experienced by the epidural group was significantly more than that of the disc surgery group at 4–6 months' follow-up ($p = 0.03$, Student's t-test). No summary statistics were reported and, therefore, the study is not presented in *Figure 18*.

TABLE 24 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs biological agents																
321	Becker, 2007[149] (i)[d] (5 mg)	A + C	RCT	22 weeks	Overall	VAS (0–100)	27	32	82	78					*–13.5 (95% CI –27.4 to 0.4); repeated measures analysis of variance*	Summary statistics not reported
321	Becker, 2007[149] (ii)[c] (10 mg)	A + C	RCT	22 weeks	Overall	VAS (0–100)	24	32	85	78					*–9.3 (95% CI –23.5 to 4.9); repeated measures analysis of variance*	Summary statistics not reported One patient in epidural group dropped out
Epidural vs disc surgery																
725	Buttermann, 2004[95]	A + C	RCT	4–6 months	Leg	VAS (0–10)	50	50							*Statistically significant greater pain experienced by epidural group (p < 0.03, Student's t-test)*	Summary statistics not reported
Epidural vs inactive control																
350	Carette, 1997[152]	A + C	RCT	3 months	Overall	VAS (0–100)	77	79	65.6 (21.6)	61.5 (21.4)	38.9	39.5	–26.5 (36)	–22.5 (34.4)	–4.00 (–15.05 to 7.05)	ITT analysis used
512	Helliwell, 1985[162]	C	RCT	3 months	Overall	VAS (0–100)	20	19					–27 (21)	–4 (21)	–23.00 (–36.19 to –9.81)	

continued

TABLE 24 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
739	Karppinen, 2001[171]	A + C	RCT	6 months	Leg	VAS (0–100)	78	80	71 (18)	75.2 (19)	30.7 (33.99)	21.6 (33.99)			13.30 (2.78 to 23.82) *Multivariate analysis (adjusted change from baseline): –16.2 (95% CI –26.8 to –5.6)*	SDs (and SEs) for change estimated from 95% CI of difference between treatment groups ITT not used Two patients lost to follow-up from steroid group
778	Price, 2005[173]	A + C	RCT	12 weeks	Leg	VAS (0–100)	120	108	52 (23)	56 (22)			–13 (33)	–18 (33)	5.00 (–3.58 to 13.58)	
Epidural vs passive PT																
359	Veihelmann, 2006[155]	C	RCT	6 months	Leg	VAS (0–10)	46	27	72 (135.6)	67 (103.9)	23 (142.4)	58 (114.3)			–35.00 (–94.60 to 24.60)	SD derived from SE 26 (26%) dropped out: intervention 1/47, control 25/52
Epidural vs mixed treatments																
439	Blonna, 2004[159] (Italian language)	A + C	RCT	60 days	Overall	VAS (0–10)	24	26	80.4 (10.0)	83.5 (12.6)	16.9 (12.8)	10.2 (18.0)			6.70 (–1.91 to 15.31)	SD imputed from weighted average from non-opioids for intervention ITT using LOCF Dropouts: intervention 3/26, control 0/24
348	Pirbudak, 2003[150]	C	RCT	6 months	Overall	VAS (0–10)	46	46	84 (17)	78.1 (40.0)	42	8.0	–42.0 (17.0)	–70.0 (5.0)	28.00 (22.88 to 33.12)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs usual/conventional care																
349	Buchner, 2000[151]	A + C	RCT	6 months	Overall	VAS (0–100)	17	19	84.4	81	32.9 (20.35)	39.2 (20.35)			–6.30 (–19.62 to 7.02)	One-sided *t*-test (comparing final means) used to calculate SD
828	Laiq, 2009[174]	NR	Q-RCT	6 months	Overall	VAS (0–10)	25	25			60 (14.5)	65 (13)			–5.00 (–12.63 to 2.63)	ITT not used Dropouts 2/52 (4%): intervention 1/26, control 1/26

A, acute; A + C, acute and chronic; C, chronic; LOCF, last observation carried; NR, not reported.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Becker *et al.*[149] included three treatment groups: epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of autologous conditioned serum (iii).

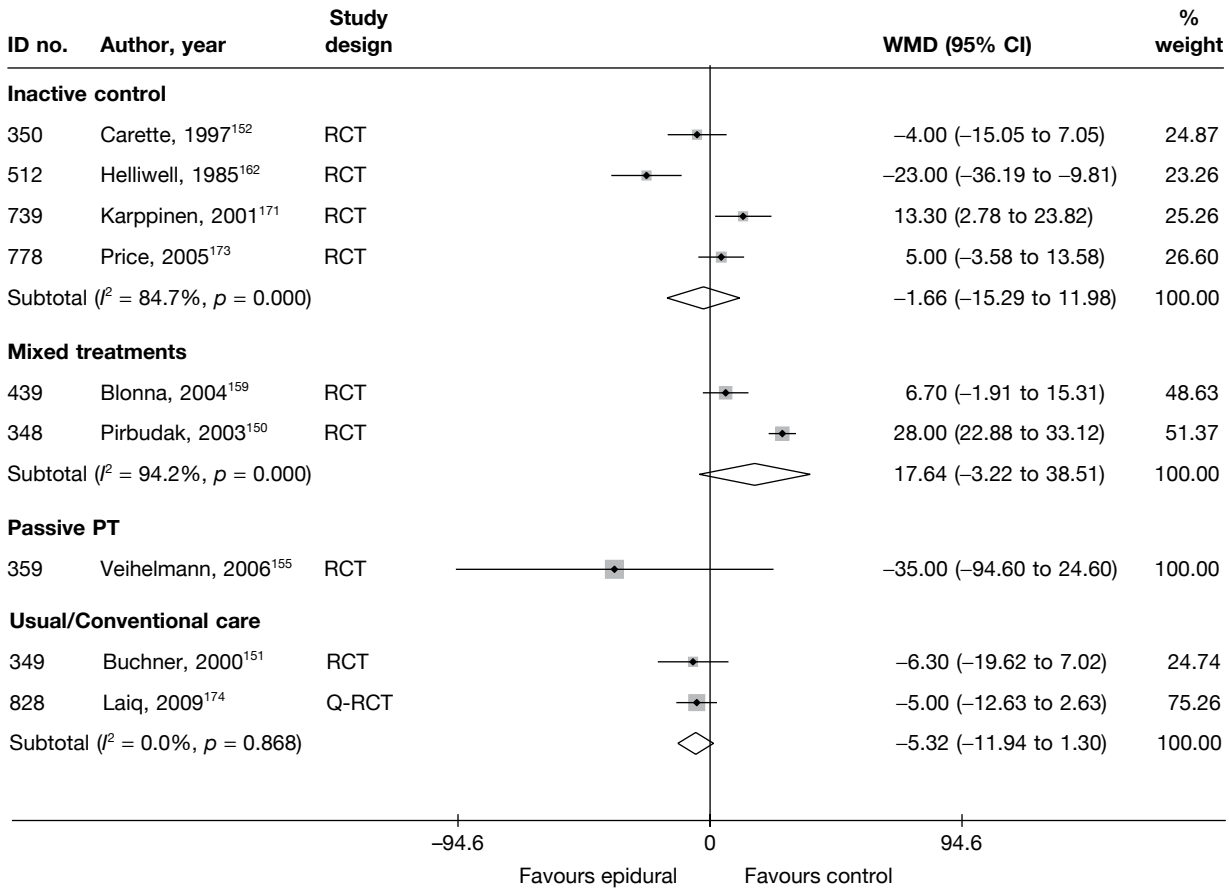

FIGURE 18 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

One moderate-quality RCT[149] compared two types of epidural (containing local anaesthetic plus triamcinolone at a dose of either 5 mg or 10 mg) with biological agents (epidural injection of autologous conditioned serum). Insufficient data were reported to include the study in *Figure 18*. Pair-wise analysis showed a non-statistically significant difference in favour of the biological agent for pain reduction at 22 weeks.

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 25* and the accompanying forest plot (*Figure 19*). Epidural injections were compared with inactive control, usual care, non-opioids, passive PT, biological agents and mixed treatments. Two studies[150,155] only included patients with chronic sciatica, and the remaining studies[143,149,151,152,171,173] included patients with either acute or chronic sciatica. The duration of follow-up ranged from 3[95] to 6 months.[150,151,155,171]

There was no overall statistically significant difference between epidural and inactive control for improving functional status, according to three good-quality RCTs.[152,171,173] The duration of follow-up ranged from 3 months[152,173] to 6 months.[171] All three studies included patients with either acute or chronic sciatica.

One moderate-quality RCT[151] reported non-statistically significant findings in favour of epidural compared with usual care for improving functional status at 6 months' follow-up.

TABLE 25 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs biological agents															
321	Becker, 2007[149] (i)[c] (5 mg)	A + C	RCT	22 weeks	ODI	27	32	20.6 (8.1)	22.0 (8.3)	11.1 (7.1)	11.7 (9.2)			–0.07 (–0.58 to 0.044)	Dropouts 7 (8%): Number originally randomised to each group not stated
321	Becker, 2007[149] (ii)[c] (10 mg)	A + C	RCT	22 weeks	ODI	25	32	19.4 (9.9)	22.0 (8.3)	11.0 (9.5)	11.7 (9.2)			–0.08 (–0.60 to 0.45)	Dropouts 7 (8%): Number originally randomised to each group not stated
Epidural vs disc surgery															
725	Buttermann, 2004[95]	A + C	RCT	1–3 months	ODI									*There was a significantly greater decreasing in disability in the discectomy group compared with the epidural group at the 1–3 month follow-up interval;* p *< 0.015, Student's* t*-test*	
Epidural vs inactive control															
350	Carette, 1997[152]	A + C	RCT	3 months	Modified ODI	77	79	49.6 (15.7)	50 (15.5)	32.2 (15.7)	34.6 (15.5)	–17.3 (20.6)	–15.4 (25.5)	–0.15 (–0.47 to 0.16)	Final SD missing so baseline SD used ITT used LOCF Two patient dropouts excluded Analysis of variance, but results not reported
739	Karppinen, 2001[171]	A + C	RCT	6 months	ODI	78	80	42.9 (16)	43.5 (15)	18.9 (16)	15.8 (15)	–24 (21.0)	–27.7 (21.0)	0.20 (–0.11 to 0.51) *Adjusted change from baseline* –5.9 (95% CI –12.4 to 7.0)	Final SD missing, so baseline SD used ITT not used; two patients lost to follow-up from steroid group

continued

TABLE 25 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
778	Price, 2005[173]	A + C	RCT	12 weeks	ODI	120	108	44 (15)	45 (18)	32 (15)	27 (18)	–12 (19)	–12 (21)	0.30 (0.04 to 0.56)	Final score calculated from change score Final SD missing so baseline SD used ITT used LOCF
Epidural vs non-opioids															
20	Dincer, 2007[143]	A + C	RCT	3 months	ODI	34	30	35.8 (6.7)	28.4 (5.4)	16.2 (9.4)	20.3 (10.1)	–19.6	–8.1	–0.42 (–0.92 to 0.08)	
Epidural vs mixed treatments															
348	Pirbudak, 2003[150]	C	RCT	6 months	ODI	46	46	49.6 (15.5)	50.2 (15.2)	45 (15.5)	25 (15.2)	–7.6 (15.3)	–13.2 (15.5)	1.30 (0.85 to 1.75)	
Epidural vs passive PT															
359	Veihelmann, 2006[155]	C	RCT	6 months	ODI	46	27	23.1	21.4	10.8 (50.19)	22.5 (55.58)			–0.22 (–0.70 to 0.25)	SD based on weighted average Dropouts 26 (26%): intervention 1/47, control 25/52
Epidural vs usual/conventional care															
349	Buchner, 2000[151]	A + C	RCT	6 months	Hannover Functional Ability (0–100)	17	17	38.5	39.9	38.2 (13.09)	42.8 (13.09)			–0.35 (–1.03 to 0.33)	SD calculated from SE Dropouts 26 (26%): intervention 1/47, control 25/52

A + C, acute and chronic; C, chronic; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Becker *et al.*[149] included three treatment groups: epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of autologous conditioned serum (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 19*).

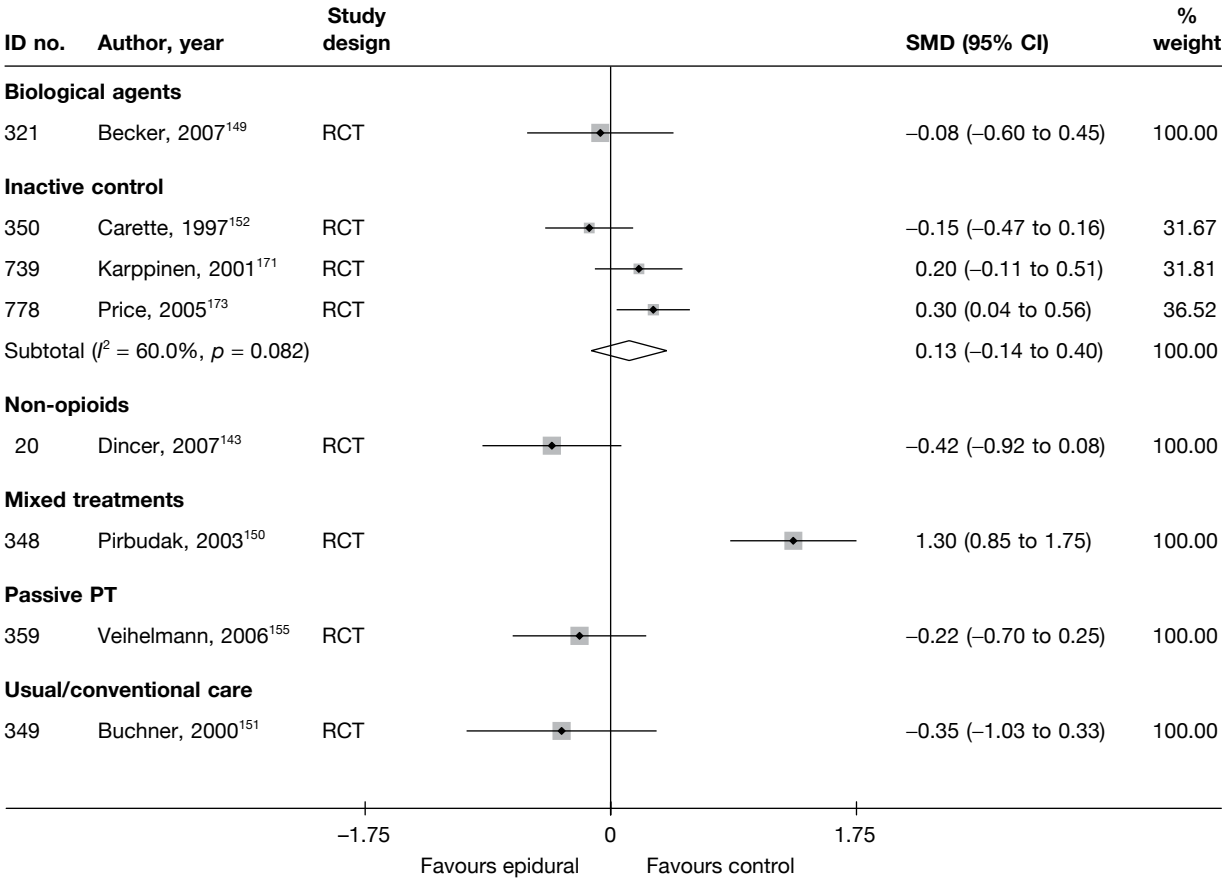

FIGURE 19 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

One moderate-quality RCT[143] reported non-statistically significant findings in favour of epidural compared with non-opioids for improving functional status at 3 months' follow-up. The methods of randomisation and allocation concealment were not stated.

One moderate-quality RCT[150] found epidural used in combination with non-opioids (mixed treatments) to be significantly better than epidural used alone for improving functional status at 6 months' follow-up. The study included patients with duration of symptoms ranging from 1 month to 12 months.

There was no statistically significant difference between epidural and passive PT in terms of improvement in functional status for chronic sciatica at 6 months. This was according to one moderate-quality study[155] with a differential dropout rate in favour of epidural.

There was no important difference between epidural using either a low- or high-dose steroid and biological agents, in terms of functional status at 22 weeks. This was according to one moderate-quality RCT[149] that included patients with chronic or acute sciatica.

One poorly reported RCT[95] of moderate quality compared epidural with disc surgery. The method of randomisation and allocation concealment were not reported. There was a significantly greater decreasing in disability in the discectomy group compared with the epidural group at the 1–3 month follow-up interval ($p < 0.015$, Student's t-test). No summary statistics were reported and, therefore, the study is not presented in *Figure 19*.

Results at long-term follow-up for epidural/intradiscal injections (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 26* and the accompanying forest plot (*Figure 20*). Epidural/intradiscal injections were compared with inactive control, passive PT and chemonucleolysis. One study[158] only included patients with acute sciatica, two studies[144,155] only included patients with chronic sciatica and the remaining two studies[158,173] included patients with either acute or chronic sciatica. The duration of follow-up ranged from 1 year[155,173] to 2 years.[144]

Two studies[158,173] compared epidural injections with inactive control in patients with either acute or chronic sciatica, for which there was a non-statistically significant overall findings in favour of epidural. One study was a good-quality RCT,[173] whereas the other was a poorly reported non-RCT.[158]

As with medium-term follow-up, one RCT,[155] of moderate quality, found epidural injections to be significantly better than passive PT at 12 months. However, the withdrawal rate was very high in the control group (48%) compared with the intervention group (2%). Patients in the PT group were able to cross over to an epidural injection after 3 months of unsatisfactory treatment, but were then excluded from the analysis ($n = 12/52$).

One poorly reported non-RCT[144] found chemonucleolysis to be significantly more effective than epidural injection in terms of overall recovery according to the physician, for patients with chronic sciatica at 2 years. All patients had been treated by the author. The findings were based on a subgroup of included patients with sciatica, for whom symptom duration ranged from 12 weeks to 25 years (median 1 year). All patients had already tried various treatments for at least 3 months.

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 27* and the accompanying forest plot (*Figure 21*). Epidural injections were compared with inactive control, passive PT, mixed treatments and disc surgery. Two studies[150,155] included patients with chronic

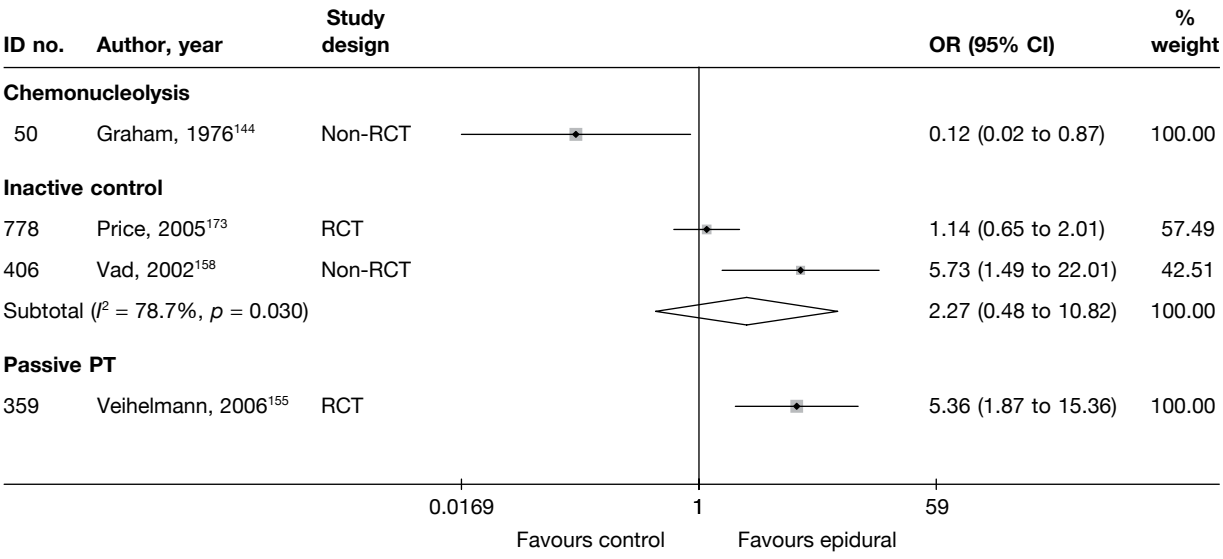

FIGURE 20 Summary of the findings of global effect at long-term follow-up (>6 months) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

TABLE 26 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
Epidural vs chemonucleolysis														
50	Graham, 1976[144]	C	Non-RCT	2 years	Perceived effect: good (vs fair or unimproved)	Physician	13	2	0	10	6	0	0.12 (0.02 to 0.87)	Only sciatica patients included here (23/40)
Epidural vs inactive control														
778	Price, 2005[173]	A + C	RCT	52 weeks	Global improvement: ≥ 75% improvement in ODI		120	39	0	108	32	0	1.14 (0.65 to 2.01)	Data inferred from graphs reporting percentages ITT using LOCF
406	Vad, 2002[158]	A + C	Non-RCT	Mean 1.4 years (range 12–21 months)	Successful outcome: patient satisfaction (score of 2 or 3), improvement on the RMDQ (≥ 5), and pain reduction (≥ 50%)	Patient + physician	25	21	0	23	11	0.09	5.73 (1.49 to 22.01)	
Epidural vs passive PT														
359	Veihelmann, 2006[155]	C	RCT	12 months	Gerbershagen score (chronification index), GHS I (vs GHS II, III)		46	30	0.02	27	7	0.48	2.52 (1.87 to 15.36)	Almost half of patients in control group missing ITT not used

A + C, acute and chronic; C, chronic; LOCF, last observation carried forward.

TABLE 27 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs disc surgery																
725	Buttermann, 2004[95]	A + C	RCT	2–3 years	Back	VAS (0–10)	50	50							*There were no significant differences between intervention groups (Student's t-test)*	Summary statistics not reported Dropouts 4/100 (4%): intervention 3/50, control 1/50
Epidural vs inactive control																
203	Bush, 1991[147]	C	RCT	52 weeks	Overall	VAS (0–100)	12	11	38.5	49.2	14.2 (15.94)	29.6 (23.67)			–15.40 (–32.04 to 1.24)	SD imputed from weighted average Dropouts 22%: intervention 1/12, control 4/11 ITT analysis based on LOCF
739	Karppinen, 2001[171]	A + C	RCT	12 months	Leg	VAS (0–100)	78	80	71 (18)	75.2 (19)	23.9 (17.15)	24.2 (17.15)			3.90 (–6.37 to 14.17) *Multivariate analysis (adjusted change from baseline) –5.3 (95% CI –15.7 to 5.0)*	SDs (and SEs) for change estimated from 95% CI of difference between treatment groups Two patients lost to follow-up from steroid group ITT not used
778	Price, 2005[173]	A + C	RCT	52 weeks	Leg	VAS (0–100)	120	108	52 (23)	56 (22)			–17 (36)	–20 (34)	3.00 (–6.09 to 12.09)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs passive PT																
359	Veihelmann, 2006[155]	C	RCT	12 months	Leg	VAS (0–10)	46	27	72 (135.6)	67 (103.92)	28 (189.91)	59 (119.51)			–31.00 (–102.02 to 40.02)	SD estimated from SE Dropouts 26%: intervention 1/47, control 25/52 Almost half of control group dropped out
Epidural vs mixed treatments																
348	Pirbudak, 2003[150]	C	RCT	9 months	Overall	VAS (0–10)	46	46	84 (17)	78.1 (40.0)	75	16	–9 (18)	–62.0 (8.0)	53.00 (47.31 to 58.69)	

A + C, acute and chronic; C, chronic; LOCF, last observation carried forward.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

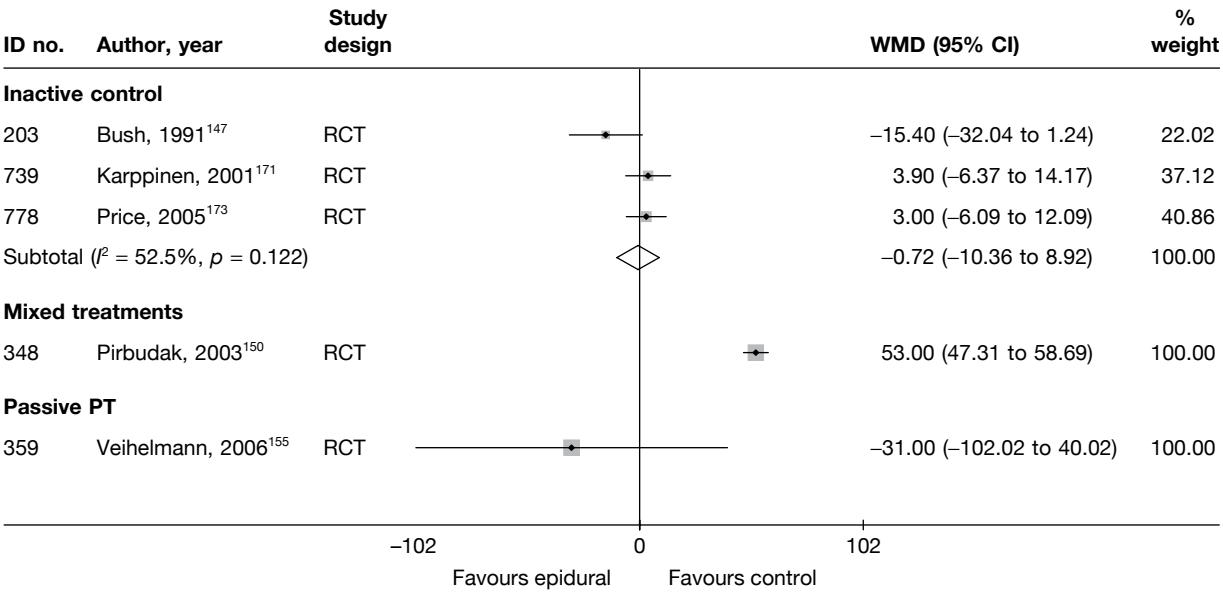

FIGURE 21 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

sciatica and the remaining studies included patients with either acute or chronic sciatica. The duration of follow-up ranged from 9 months[150] to 2–3 years.[95]

Three RCTs[147,171,173] compared epidural injections with inactive control, for which pooled analyses showed no important difference between the groups at 12 months. The overall quality of two trials[171,173] was good. The third study[147] was small ($n = 23$), poorly reported and of moderate quality. The method of randomisation and allocation concealment were not stated, but the study included blind outcome assessment. SDs for final mean were not reported, so were imputed using the weighted mean. Unlike the remaining studies, the WMD for this study was statistically significant in favour of epidural. One of the RCTs[171] also reported findings based on ANCOVA, adjusted for baseline values, which favoured inactive control for leg pain at 6 months (−16.2; 95% CI −26.8 to −5.6, $p = 0.003$; negative values indicate a negative effect). The same analysis showed no statistically significant difference between the groups at 12 months.

One moderate-quality RCT[155] found epidural injection to be significantly better than passive PT in terms of pain reduction in chronic sciatica at 12 months. The withdrawal rate was much higher in the control group (48%) than the intervention group (2%).

One moderate-quality RCT[150] found epidural injection in combination with non-opioids (mixed treatments) to be significantly better than epidural injection alone in terms of pain reduction in chronic sciatica at 9 months' follow-up.

One poorly reported RCT[94] of moderate quality, compared epidural injection with disc surgery. The method of randomisation and allocation concealment were not reported. There were no significant differences between the epidural injection and disc surgery groups at 2–3 years follow-up for low back pain (Student's *t*-test). No summary statistics were reported and, therefore, the study is not presented in *Figure 21*.

Condition-specific outcome measures at long-term follow-up

The results for CSOMs at long-term follow-up are presented in *Table 28* and the accompanying forest plot (*Figure 22*). Epidural injections were compared with inactive control, passive PT and

TABLE 28 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Epidural vs inactive control															
739	Karppinen, 2001[171]	A + C	RCT	12 months	ODI	78	80	42.9 (16)	43.5 (15)	15.9 (16)	16.3 (15)	–27 (21.16)	–27.2 (21.16)	–0.3 (–0.34 to 0.29) *Adjusted change from baseline –0.4 (95% CI –7.0 to 6.2)*	No final SD so baseline SD used Two patients lost to follow-up from steroid group
778	Price, 2005[173]	A + C	RCT	52 weeks	ODI	120	108	44 (15)	45 (18)	28 (15)	27 (18)	–16 (23)	–14 (24)	0.06 (–0.20 to 0.32)	Final score calculated from change score No final SD, so baseline SD used ITT used LOCF
Epidural vs mixed treatment															
348	Pirbudak, 2003[150]	C	RCT	9 months	ODI	46	46	49.6 (15.5)	50.2 (15.2)	46 (15.5)	26 (15.2)	–7.6 (15.3)	–13.2 (15.5)	1.30 (0.85 to 1.75)	No final SD, so baseline SD used
Epidural vs passive PT															
359	Veihelmann, 2006[155]	C	RCT	12 months	ODI	46	27	23.1	21.4	11.6 (13.04)	21.6 (13.04)			–0.77 (–1.26 to –0.28)	Final SD imputed from weighted mean of SDs of ODI for epidural Dropouts 26 (26%): intervention 1/47, control 25/52

A + C, acute and chronic; C, chronic; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

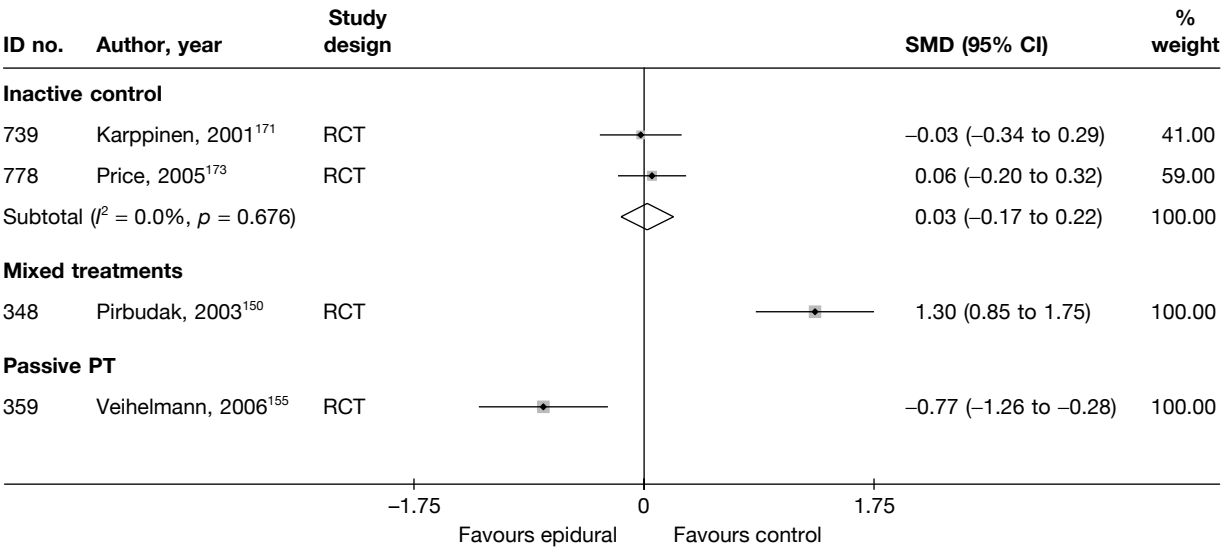

FIGURE 22 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing epidural/intradiscal injections with alternative interventions. Note: weights are from random effects analysis.

mixed treatments. Two studies[150,155] included patients with chronic sciatica and the remaining studies included patients with either acute or chronic sciatica. The duration of follow-up ranged from 9 months[150] to 12 months.[155,171,173]

Two good-quality RCTs[171,173] compared epidural injections with inactive control; the pooled analyses showed no statistically significant difference between the groups at 12 months.

One moderate-quality RCT[155] found epidural injections to be significantly better than passive PT for improving functional status for patients with chronic sciatica at 12 months. However, the withdrawal rate was much higher in the control group (48%) than in the intervention group (2%).

One moderate-quality RCT[150] found epidural injection in combination with non-opioids (mixed treatments) to be significantly better than epidural injection alone for improving functional status in patients with chronic sciatica at 9 months' follow-up.

Analysis of adverse effects for epidural/intradiscal injections

The results for the occurrence of any reported adverse effects are presented in *Table 29* and the accompanying forest plot (*Figure 23*). The incidence of adverse effects were significantly greater for epidural injections compared with either education/advice, passive PT or usual care. Overall there was no statistically significant difference in the number of adverse effects when comparing epidural injections with either activity restriction, biological agents, chemonucleolysis, disc surgery, manipulation, mixed treatments, non-opioids or inactive control.

SUMMARY OF OVERALL FINDINGS FOR EPIDURAL/INTRADISCAL INJECTIONS COMPARED WITH ALTERNATIVE INTERVENTIONS

Most epidural injection studies included patients with chronic sciatica or both acute and chronic sciatica. One study included acute sciatica.[145] Less than half of the studies were RCTs. Apart from studies comparing epidural with inactive control, the quality of studies was poor (*Table 30*).

TABLE 29 Summary of the findings of any adverse effect for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Epidural vs activity restriction							
140	Coomes, 1961[145]	Non-RCT	1	20	0	20	3.15 (0.12 to 82.16)
Epidural vs alternative							
667	Wehling, 1997[167] (epidural = steroid + LA)	CCS	NR	NR	NR	NR	
667	Wehling, 1997[167] (epidural = LA)	CCS	NR	NR	NR	NR	
Epidural vs biological agents							
321	Becker, 2007[149] (epidural = 10 mg steroid)	RCT	1	27	1	32	1.19 (0.07 to 20.01)
321	Becker, 2007[149] (epidural = 5 mg steroid)	RCT	1	25	1	32	1.29 (0.08 to 21.73)
Epidural vs chemonucleolysis							
720	Bontoux, 1990[168]	RCT	NR	NR	NR	NR	
447	Bourgeois, 1988[160]	RCT	0	30	3	30	0.13 (0.01 to 2.61)
729	Gallucci, 2007[170]	RCT	0	82	0	77	
50	Graham, 1976[144]	Non-RCT	NR	NR	NR	NR	
Epidural vs disc surgery							
725	Buttermann, 2004[95]	RCT	5	50	7	77	1.11 (0.33 to 3.72)
Epidural vs education/advice							
722	Bronfort, 2004[169]	RCT	10	10	0	10	441.00 (7.98 to 24,372.70)
Epidural vs inactive control							
203	Bush, 1991[147]	RCT	1	12	0	11	3.00 (0.11 to 81.61)
350	Carette, 1997[152]	RCT	22	77	17	79	1.46 (0.70 to 3.03)
383	Dilke, 1973[157]	RCT	6	51	0	48	13.86 (0.76 to 253.00)
512	Helliwell, 1985[162]	RCT	0	20	0	19	
739	Karppinen, 2001[171]	RCT	1	80	0	80	3.04 (0.12 to 75.69)
539	Klenerman, 1984[163] (epidural = LA)	RCT	0	16	0	16	
539	Klenerman, 1984[163] (epidural = steroid)	RCT	1	19	0	16	2.68 (0.10 to 70.31)
905	Matthews, 1987[176]	RCT	NR	NR	NR	NR	
778	Price, 2005[173]	RCT	12	120	11	108	0.98 (0.41 to 2.32)
620	Ridley, 1988[165]	RCT	2	21	0	18	4.74 (0.21 to 106.00)
240	Snoek, 1977[148]	RCT	0	27	0	24	
406	Vad, 2002[158]	Non-RCT	0	25	0	25	
351	Valat, 2003[153]	RCT	2	42	3	42	0.65 (0.10 to 4.10)

continued

TABLE 29 Summary of the findings of any adverse effect for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
175	Yates, 1978[146] (epidural = LA)	RCT (crossover)	0	20	0	20	
175	Yates, 1978[146] (epidural = steroid)	RCT (crossover)	0	20	0	20	
175	Yates, 1978[146] (epidural = steroid + LA)	RCT (crossover)	0	20	0	20	
Epidural vs manipulation							
451	Bronfort, 2000[161]	RCT	6	6	3	7	16.71 (0.68 to 409.09)
722	Bronfort, 2004[169]	RCT	10	10	6	11	17.77 (0.84 to 377.00)
Epidural vs mixed treatment							
439	Blonna, 2004[159]	RCT	0	24	3	26	0.14 (0.01 to 2.80)
348	Pirbudak, 2003[150]	RCT	0	46	0	46	
Epidural vs non-opioids							
451	Bronfort, 2000[161]	RCT	6	6	4	6	7.22 (0.28 to 189.19)
20	Dincer, 2007[143]	RCT	2	34	0	30	4.69 (0.22 to 102.00)
771	Lafuma, 1997[172]	RCT	NR	NR	NR	NR	
362	Wilson-MacDonald, 2005[156]	RCT	NR	NR	NR	NR	
846	Murata, 2009[175]	RCT	NR	NR	NR	NR	
Epidural vs passive PT							
359	Veihelmann, 2006[155]	RCT	16	46	0	39	42.74 (2.47 to 741.00)
Epidural vs usual care							
349	Buchner, 2000[151]	RCT	NR	NR	NR	NR	
828	Laiq, 2009[174]	Q-RCT	8	52	0	52	24.77 (1.34 to 458.00)
581	Matyjek, 1986[164]	CCS	NR	NR	NR	NR	
358	Popiolek, 1991[154]	Non-RCT	NR	NR	NR	NR	
Mixed treatments including epidural vs mixed treatments without epidural							
913	Saberski, 2000[142]	RCT	NR	NR	NR	NR	
644	Styczynski, 1997[166]	Non-RCT	NR	NR	NR	NR	

LA, local anaesthetic; NR, not reported.

Meta-analysis of the mainly good-quality RCTs (up to seven studies) showed epidural injections to be significantly better than the inactive control at short-term follow-up for reducing pain[147,152,153,158,162,171,173] and improving functional status.[152,153,158,171,173] However, there was no statistically significant difference between intervention groups for the global effect.[148,152,153,165,173,176] Furthermore, there was no statistically significant difference between epidural injection and inactive control for global effect,[152,157,162,163,173] pain intensity[152,162,171,173] or CSOMs[152,171,173] at medium-term follow-up or global effect,[158,173] pain intensity[147,171,173] or CSOMs[171,173] at long-term follow-up, or in terms of the number of adverse effects.[146–148,152,153,157,158,162,163,165,171,173] A similar pattern was found for epidural injection compared with usual care. There was a statistically significant difference in favour of epidural for overall recovery (one non-RCT[154]) and functional

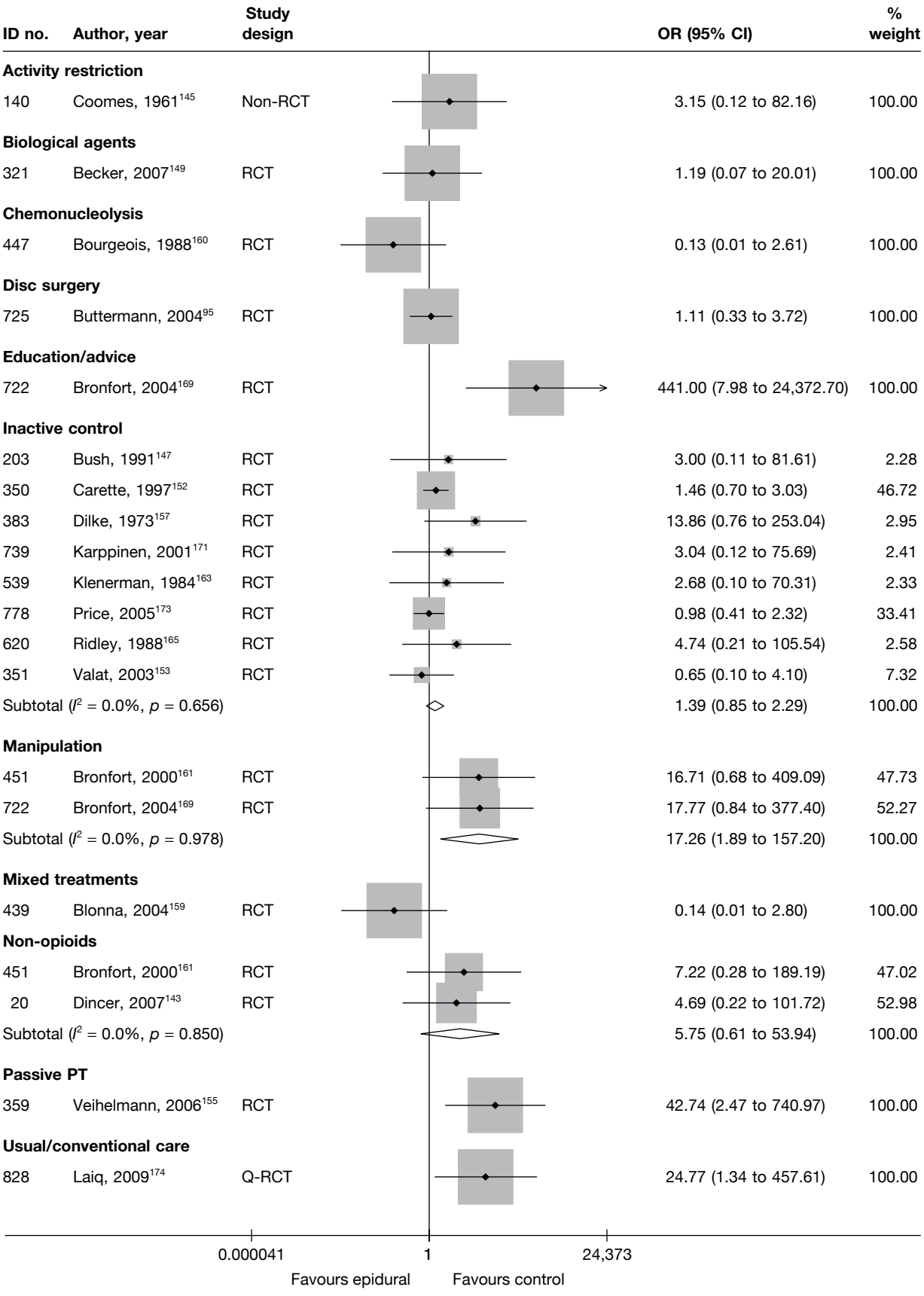

FIGURE 23 Summary of the findings of any adverse effect for studies comparing epidural/intradiscal injections with alternative interventions (grouped by comparator then ordered by author). Note: weights are from random effects analysis.

TABLE 30 Summary of epidural studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Epidural vs activity restriction	1 (1)	40 (40)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Epidural vs alternative/non-traditional	1 (2)	278 (278)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Epidural vs biological agents	1 (1)	90 (90)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Epidural vs chemonucleolysis	4 (4)	40–159 (70)	3/4 (75)	0/4 (0)	0/4 (0)	4/4 (100)	4/4 (100)	0/4 (0)	0/4 (0)	0/4 (0)	4/4 (100)	0/4 (0)
Epidural vs disc surgery	1 (1)	100 (100)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
Epidural vs inactive control	12 (13)	23–288 (67)	12/12 (100)	4/12 (33)	1/12 (8)	12/12 (100)	4/12 (33)	0/12 (0)	0/12 (0)	0/12 (0)	2/12 (17)	0/12 (0)
Epidural vs mixed treatment	2 (2)	50–92 (71)	2/2 (100)	0/2 (0)	0/2 (0)	2/2 (100)	2/2 (100)	1/2 (50)	0/2 (0)	0/2 (0)	2/2 (100)	0/2 (0)
Epidural vs non-opioids	3 (3)	64–246 (93)	3/3 (100)	0/3 (0)	0/3 (0)	3/3 (100)	2/3 (67)	1/3 (33)	0/3 (0)	0/3 (0)	2/3 (67)	1/3 (33)
Epidural vs passive PT	1 (1)	99 (99)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Epidural vs usual/ conventional care	3 (3)	36–60 (52)	1/3 (33)	0/3 (0)	0/3 (0)	3/3 (100)	3/3 (100)	0/3 (0)	0/3 (0)	0/3 (0)	0/3 (0)	0/3 (0)
Total (results for epidural studies)	**29 (31)**	**23–278 (74)**	**24/29 (83)**	**4/29 (14)**	**2/29 (7)**	**29/29 (100)**	**18/29 (62)**	**2/29 (7)**	**1/29 (3)**	**1/29 (3)**	**13/29 (45)**	**2/29 (7)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

status (one RCT[151]) at short-term follow-up, but not for pain intensity (one RCT,[151] one Q-RCT[174]). There were no statistically significant difference between epidural injection and usual care at medium-term follow-up for global effect,[151,174] pain intensity[151,174] or CSOMs.[151] However, usual care was associated with significantly fewer adverse effects than epidural injection (one Q-RCT[174]).

Epidural injections were found to be better than non-opioids for reducing pain and improving functional status at short-term follow-up according to three poorly reported RCTs.[143,156,175] There was no statistically significant difference between epidural and non-opioids for global effect (one RCT[175]) or CSOMs (one RCT[143]) at medium-term follow-up or adverse effects (two RCTs[143,161]). One poorly reported RCT found that epidural injection in combination with non-opioids was better than epidural injection alone for reducing pain and improving functional status at long-term follow-up.[150] However, there was no statistically significant difference between the intervention groups at short- and medium-term follow-up for pain (two poorly reported RCTs[150,159]) and CSOMs (RCT[150]) or in terms of the number of adverse effects.[150,159]

Chemonucleolysis using chymopapain was found to be better than epidural injection for the global effect at long-term follow-up (one poor-quality non-RCT[144]). There was no statistically significant difference between epidural injection and chemonucleolysis for the global effect at short-term (one poorly reported RCT[170] using ozone–oxygen) or medium-term follow-up (three RCTs;[160,168,170] one RCT[170] used ozone–oxygen). There was no statistically significant difference in the number of adverse effects experienced with epidural than with chemonucleolysis (one RCT[160]).

Statistically significant findings in favour of epidural injection were found when compared with passive PT for global effect (at medium-[155] and long-term[155] follow-up) and activity restriction for global effect (medium-term follow-up[145]), but these findings were reported by a single RCT[155] or non-RCT.[145] Disc surgery was found to be significantly better than epidural injection at reducing pain intensity at medium-term follow-up, but not at long-term follow-up (one poor-quality RCT[95]). There was also no statistically significant difference in pain intensity between epidural injection and acupuncture (CCS[167] at short-term follow-up) and biological agents (poorly reported RCT[149] at medium-term follow-up).

Chemonucleolysis

Description of chemonucleolysis studies

Summary of interventions

Forty studies evaluated chemonucleolysis for sciatica,[46–56,58–61,75–77,79,85,88,90,92,96,103–105,144,160,168,170,205–213] 37[46–56,58–61,75–77,79,85,88,90,92,96,103–105,144,160,168,170,205–210] of which compared chemonucleolysis with alternative interventions. The type of interventions evaluated by these latter studies are listed in *Table 31a*. One of these studies,[46] which compared disc surgery with chemonucleolysis, did not include comparative data and reported only descriptive results for change from baseline for each group.[46] One further study[61] did not report any global effect, pain intensity or CSOM data.[61]

Three studies compared different types of chemonucleolysis[211–213] and one study[213] included three intervention arms.The types of chemonucleolysis being compared are listed in *Table 31b*, but the findings of these studies are not considered any further than this.

Summary of study participants for chemonucleolysis

The summary data for included participants are presented in *Table 32*. The number of participants included in the 36 studies that reported outcome data for global effect, pain or CSOMs ranged from 22 to 1085 participants (median 100 participants). A similar number of studies included patients with chronic sciatica or included patients with either chronic or acute sciatica. One study (comparing chemonucleolysis with disc surgery),[103] included some patients with spinal stenosis and none included patients with sequestered or extruded discs. The diagnosis of sciatica, or the presence of herniated disc, was confirmed by imaging in 31 (84%) studies. Two studies[49,105] compared the use of chemonucleolysis with disc surgery in only patients who had sciatica for the first time, and one study[50] compared the same intervention in patients who had recurrent sciatica. The remaining studies included a mixture of patients with either first episode or recurrent sciatica or, more usually, did not report this information. The majority of studies included patients who had received previous treatment for their current episode of sciatica, with this information not being stated in the remaining studies. Three studies[56,59,88] that compared chemonucleolysis with disc surgery, included patients who had received previous disc surgery.

Summary of study design and quality for chemonucleolysis studies

Summary information on study details are presented in *Table 33*. Fewer than half (17/36, 47%) of chemonucleolysis studies were RCTs, and only one of these[206] was good quality (comparator was inactive control). Eleven studies[47,85,88,160,168,170,205,207–210] were of moderate quality. One study[206] used both adequate randomisation and allocation concealment (comparator included inactive control). A further five studies[85,88,160,205,210] used adequate randomisation, but not allocation concealment (although two studies[160,210] used sealed envelopes), and one study[69] used adequate allocation concealment but not randomisation. One multicentre study[209] reported that separate randomisation sequences were provided for each participating institute, but gave no details on how these sequences were generated. One study[47] had strong external validity (comparator included inactive control).

Chemonucleolysis results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 34* and the accompanying forest plot (*Figure 24*). Chemonucleolysis was compared with inactive control, disc surgery and epidural. Five studies[46,48,52,92,205] included only patients with chronic sciatica, four studies[49,170,206,207] included patients with either acute or chronic sciatica and the remaining studies did not report the duration of symptoms. The duration of follow-up ranged from 72 hours[206] to 6 weeks.[46,48,79,104,205,209]

TABLE 31a Summary of the interventions used when comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Chemonucleolysis description	Control description
Chemonucleolysis vs disc surgery				
884	Alexander, 1989[103]	CCS	Chymopapain chemonucleolysis (2000 U)	Disc surgery (removal of protruding disc fragment only + free fat graft)
43	van Alphen, 1989[47]	RCT	Chemonucleolysis with 4000 U chymopapain	Discectomy with emptying of disc space
441	Bonafe, 1993[75] (French language)	CCS	Nucleolysis using chymopapain (4000 U)	Percutaneous automated nucleotomy
183	Bouillet, 1983[61]	CCS	Chemonucleolysis by chymopapain injections	Conventional lumbar disc surgery
453	Brown, 1989[76]	CCS	Chemonucleolysis with chymopapain	Disc surgery
453	Brown, 1989[76]	CCS	Collagenase chemonucleolysis	Disc surgery
454	Buric, 2005[77]	Non-RCT	Chemonucleolysis with ozone–oxygen mixture	Standard microdiscectomy
166	Crawshaw, 1984[60]	RCT	Chemonucleolysis with 4000 U chymopapain	Disc surgery
48	Dabezies, 1978[51]	CCS	Chemonucleolysis using 2 ml chymopapain	Laminectomy with or without fusion
471	Dei-Anang, 1990[79] (German language)	CCS	Chemonucleolysis with 4000 U chymopapain or 600 units collagenase	Percutaneous nucleotomy
727	Ejeskar, 1983[96]	RCT	Chemonucleolysis with chymopapain 400 IU	Discectomy with unilateral laminotomy and removal of disc hernia only
132	Hoogmartens, 1976[56]	HCS	Chymopapain chemonucleolysis	Discectomy
44	Javid, 1995[48]	CCS	Chemonucleolysis with 3000 IU chymopapain	Partial hemilaminectomy using magnification and fat graft
35	Krugluger, 2000[46]	RCT	Chemonucleolysis using 4000 U chymodiactin	Automated percutaneous discectomy
117	Lagarrigue, 1991[54] (French language)	CCS	Chemonucleolysis with 2000–5000 U chymopapain	Discectomy with minimal bony resection
129	Lavignolle, 1987[55] (French language)	RCT	Chemonucleolysis with 4000 U chymopapain	Microscopic discectomy. Unilateral limited interlaminar
889	Lee, 1996[104] (German language)	CCS	Chemonucleolysis with chymopapain	Percutaneous manual and laser discectomy
889	Lee, 1996[104] (German language)	CCS	Chemonucleolysis with chymopapain	Automated percutaneous lumbar discectomy
593	Muralikuttan, 1992[85]	RCT	Chemonucleolysis with chymopapain 2000 U	Standard discectomy with fenestration, disc space cleared
47	Norton, 1986[50]	CCS	Chymopapain chemonucleolysis	Conventional surgical discectomy
45	Postacchini, 1987[49]	Non-RCT	2 ml chymopapain chemonucleolysis	Disc excision using unilateral laminotomy
617	Revel, 1993[88]	RCT	Chemonucleolysis	Automated percutaneous lumbar discectomy
641	Steffen, 1999[90] (German language)	RCT	Chemonucleolysis with 2 ml chymodiactin	Laser disc decompression
49	Stula, 1990[52] (German language)	RCT	Chemonucleolysis with 500 U chymopapain	Conventional disc surgery
61	Tregonning, 1991[53]	CCS	Chemonucleolysis with chymopapain	Fenestration or partial laminectomy removing extruded disc material
893	Watters,1988[105]	Non-RCT	Chemonucleolysis using chymopapain (4000 U)	Microdiscectomy with free fat graft over exposed dura
160	Watts, 1975[59]	CCS	Chemonucleolysis with chymopapain 4 mg	Discectomy with laminotomy and foraminotomy
672	Weinstein, 1986[92]	CCS	Chemonucleolysis with chymopapain	Discectomy
150	Zeiger, 1987[58]	CCS	Chemonucleolysis with 2.5 ml chymodiactin	Microdiscectomy with intraoperative injection into intervertebral space with steroid 125 mg methylprednisolone + morphine 4 mg used to reduce postoperative pain and morbidity

continued

TABLE 31a Summary of the interventions used when comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	Chemonucleolysis description	Control description
Chemonucleolysis vs epidural				
720	Bontoux, 1990[168] (French language)	RCT	Chemonucleolysis with chymopapain 4000 U	Intradiscal injection of triamcinolone 70 mg
447	Bourgeois, 1988[160] (French language)	RCT	Chemonucleolysis with chymopapain 4000 U	Intradiscal injection of triamcinolone 80 mg
729	Gallucci, 2007[170]	RCT	Intraforaminal and intradiscal injections of steroid triamcinolone 80 mg + local anaesthetic 2–4 ml ropivacaine plus ozone–oxygen (group B)	Intraforaminal and intradiscal injections of steroid triamcinolone 80 mg + local anaesthetic 2–4 ml ropivacaine (group A)
50	Graham, 1976[144]	Non-RCT	Chemonucleolysis with chymopapain (dose not stated)	Intradiscal hydrocortisone injection (dose not stated)
Chemonucleolysis vs inactive control				
726	Dabezies, 1988[209]	RCT	Chemonucleolysis using 8 mg chymopapain	Placebo injections
244	Feldman, 1986[207] (French language)	RCT	Chemonucleolysis with 4000 U chymopapain	Intradiscal injection of distilled water
55	Gogan, 1992[205]	RCT	Chemonucleolysis with 8 mg chymopapain	Intradiscal injection of normal saline 2 ml
738	Javid, 1983[210]	RCT	Chymopapain injections of 3.0 ml (3000 U/ 1.5 ml)	Placebo group (3 ml of sterile pyrogen-free saline solution)
236	Schwetschenau, 1976[206]	RCT	Chemonucleolysis by 4 mg chymopapain	Intradiscal injection of inactive control (placebo group)
Chemonucleolysis vs manipulation				
723	Burton, 2000[208]	RCT	Chemonucleolysis with 400 U chymopapain	Osteopathic spinal manipulation for up to 12 weeks

IU, international units; U, units

TABLE 31b Summary of the interventions used when comparing alternative forms of chemonucleolysis (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Chemonucleolysis description	Control description
Chemonucleolysis vs chemonucleolysis				
435	Benoist, 1993[212]	RCT	Chemonucleolysis using low-dose chymopapain 2000 U	Chemonucleolysis using standard-dose chymopapain 4000 U
453	Brown, 1989[76]	CCS	Chemonucleolysis with chymopapain	Collagenase chemonucleolysis
511	Hedtmann, 1987[213]	Q-RCT	Chemonucleolysis with collagenase 600 ABC U (high dose)	Chemonucleolysis with chymopapain 400 ABC U
511	Hedtmann, 1987[213]	Q-RCT	Chemonucleolysis with collagenase 400 ABC U (low dose)	Chemonucleolysis with chymopapain 400 ABC U
407	Wittenberg, 2001[211]	RCT	Chemonucleolysis with 4000 IU chymopapain	Chemonucleolysis with 400 ABC U collagenase

IU, international units; U, units.

Chemonucleolysis was compared with an inactive control in four RCTs,[205–207,209] for which the pooled analysis showed a non-statistically significant difference in favour of the chemonucleolysis group. One RCT[206] was good quality and the remaining three were of moderate quality, with most using adequate randomisation. Unlike the remaining RCTs, this study[206] reported non-statistically significant findings in favour of the inactive control.

TABLE 32 Summary of sciatica type and study population details for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Chemonucleolysis vs disc surgery													
884	Alexander, 1989[103]	CCS	100	Mean 33.5 (range 18–65)	90 (90)	Mean 5.5 months	Nerve root pain	Yes	NR	No	Yes	Yes	No
43	van Alphen, 1989[47]	RCT	151	Mean 34 (range 18–45)	99 (66)	< 6 months 55%; > 6 months 45%	Nerve root pain	Yes	NR	No	No	Yes	No
441	Bonafe, 1993[75] (French language)	CCS	40	Mean 46 (range 27–68)	28 (70)	Mean 3 months (range several days to 15 months)	Nerve root pain	Yes	NR	No	NR	Yes	NR
183	Bouillet, 1983[61]	CCS	2749	NR	NR	Range (weeks to months)	Nerve root pain	Yes	NR	No	NR	Yes	NR
453	Brown, 1989[76]	CCS	85	Mean 37.6	59 (69)	At least 3 months	Nerve root pain	Yes	NR	No	No	Yes	No
454	Buric, 2005[77]	Non-RCT	45	Mean 45 (SD 14.2, range 19–77)	23 (51)	Mean 203.9 days (SD 129.6, range 21 to > 365 days)	Nerve root pain	Yes	NR	No	No	Yes	No
166	Crawshaw, 1984[60]	RCT	52	Mean 37	NR	NR	Nerve root pain	Yes	NR	No	No	Yes	No
48	Dabezies, 1978[51]	CCS	200	Mean 39	132 (66)	NR	Nerve root pain and referred pain	Clinical	Recurrent and first episode	No	No	Yes	NR
471	Dei-Anang, 1990[79] (German language)	CCS	201	NR	NR	NR	Nerve root pain	NR	NR	No	No	NR	NR
727	Ejeskar, 1983[96]	RCT	29	Mean 39.3	21 (72)	Mean 4.5 months (SD 3 months)	Nerve root pain	Yes	NR	No	No	NR	No

continued

TABLE 32 Summary of sciatica type and study population details for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
132	Hoogmartens, 1976[56]	HCS	97	Mean 35.5	48 (49)	25–35 months	Nerve root pain	NR	Recurrent and first episode	No	No	Yes	Yes
44	Javid, 1995[48]	CCS	200	Mean 39 (range 17–81)	134 (67)	Mean 7.2 months	Nerve root pain	Yes	NR	No	No	Yes	No
35	Krugluger, 2000[46]	RCT	22	Mean 40 (range 24–60)	16 (73)	Mean 7 months	Nerve root pain	Yes	NR	No	No	Yes	NR
117	Lagarrigue, 1991 (French language)[54]	CCS	1085	Mean 42 (range 14–83)	682 (63)	Mean 13.4 months	Nerve root pain	Clinical	NR	Yes	No extrusion	Yes	NR
129	Lavignolle, 1987[55] (French language)	RCT	358	Mean 41 (SD 12.03)	225 (63)	NR	Nerve root pain	NR	NR	No	No	NR	NR
889	Lee, 1996[104] (German language)	CCS	300	<30 50%; >40 25%	213 (71)	NR	Nerve root pain	Yes	NR	No	No	Yes	NR
593	Muralikuttan, 1992[85]	RCT	92	Mean 35 (range 19–60)	55 (60)	Mean 24 weeks	Nerve root pain	Yes	NR	No	No	Yes	NR
47	Norton, 1986[50]	CCS	105	Mean 40 (range 20–67)	86 (82)	Mean 18.5 months (range 5 days–128 months)	Nerve root pain	Yes	Recurrent	NR	NR	Yes	No
45	Postacchini, 1987[49]	Non-RCT	161	NR	NR	Mean 8.75 months (range 1.2–36.0 months)	Nerve root pain and referred pain	Yes	First episode	No	No	Yes	No
617	Revel, 1993[88]	RCT	165	Mean 39 (SD 9, range 21–65)	96 (68)	NR	Nerve root pain	Yes	NR	No	No	Yes	Yes

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
641	Steffen, 1999[90] (German language)	RCT	69	NR	NR	10.6 months	Nerve root pain	Yes	NR	No	No	Yes	No
49	Stula, 1990[52] (German language)	RCT	69	Range 22–54	57 (83)	< 1 year	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	No
61	Tregonning, 1991[53]	CCS	268	Mean 40.4 (range 20–65)	135 (68)	NR	Nerve root pain	Yes	NR	No	No	Yes	No
893	Watters,1988[105]	Non-RCT	100	Mean 36.5	59 (59)	Mean 13 weeks	Nerve root pain	Yes	First episode	No	NR	NR	NR
160	Watts, 1975[59]	CCS	274	Range 24–62	55 (55)	NR	Nerve root pain and referred pain	Yes	Recurrent and first episode	No	Unclear	Yes	Yes
672	Weinstein, 1986[92]	CCS	159	Mean 41 (range 28–57)	64 (41)	Minimum period of 3 months	Nerve root pain	Yes	First episode	No	No	Yes	No
150	Zeiger, 1987[58]	CCS	126	NR	NR	≥ 4 weeks	Nerve root pain	Yes	NR	No	No	Yes	No
Chemonucleolysis vs epidural													
720	Bontoux, 1990 (French language)[168]	RCT	80	Mean 40	50 (63)	At least 2 months, > 6 months 34%	Nerve root pain	Yes	NR	No	No	Yes	NR
447	Bourgeois, 1988[160] (French Language)	RCT	60	Mean 37 (range 26–62)	40 (67)	Mean 178 (range 50–700) days	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	NR
729	Gallucci, 2007[170]	RCT	159	Mean 41.5 (range 18–71)	86 (54)	Mean 15 weeks	Nerve root pain	Yes	NR	No	No	Yes	No

continued

TABLE 32 Summary of sciatica type and study population details for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
50	Graham, 1976[144]	Non-RCT	40 (23 with sciatica)	Mean 42 Sciatica patients: mean 41 (range 24–66)	25 (63) Sciatica patients: 13 (57%)	Mean whole group 5.35 years Sciatica patients median 1 year (range 12 weeks–25 years)	Nerve root pain and referred pain	Yes	NR	No	No	Yes	NR
Chemonucleolysis vs inactive control													
726	Dabezies, 1988[209]	RCT	173	NR	NR	NR	Nerve root pain	Yes	Recurrent and first episode	No	NR	Yes	No
244	Feldman, 1986[207] (French language)	RCT	39	Mean 42.5 (range 21–77)	19 (49)	Mean 6.6 months (range 1–18 months)	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	NR
55	Gogan, 1992[205]	RCT	60	Mean 37 (range 19–69)	39 (65)	< 6 weeks 10%, 6 weeks to 6 month 75%, > 6 months 15%	Nerve root pain	Yes	NR	No	No	Yes	NR
738	Javid, 1983[210]	RCT	108	NR	NR	Mean 26 weeks	Nerve root pain	Yes	NR	No	NR	Yes	No
236	Schwetschenau, 1976[206]	RCT	66	Mean 36.2 (SE 1.9)	44 (67)	Mean 11.6 weeks (SE 1.9 weeks)	Nerve root pain	Yes	NR	No	NR	Yes	No
Chemonucleolysis vs manipulation													
723	Burton, 2000[208]	RCT	40	Mean 41.9 (SD 10.6)	19 (48)	Mean 31 weeks (SD 35 weeks)	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	No

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 33 Summary of the study details for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Chemonucleolysis vs disc surgery										
884	Alexander, 1989[103]	100	Mean 14 (range 6–35) months	CCS	No	No	80–100	Unclear	Weak	Weak
43	van Alphen, 1989[47]	151	12 months	RCT	Partial	Unclear	80–100	No	Moderate	Strong
441	Bonafe, 1993[75] (French language)	40	Mean 15 (range 3–36) months	CCS	No	No	80–100	Unclear	Weak	Weak
183	Bouillet, 1983[61]	2749	NR	CCS	No	No	NA	No	Weak	Moderate
453	Brown, 1989[76]	85	3 months	CCS	No	No	80–100	Yes	Weak	Weak
454	Buric, 2005[77]	45	18 months	Non-RCT	No	No	80–100	NA	Weak	Weak
166	Crawshaw, 1984[60]	52	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Moderate
48	Dabezies, 1978[51]	200	2 years	CCS	No	No	Cannot tell	No	Weak	Moderate
471	Dei-Anang, 1990[79] (German language)	201	1 year	CCS	No	No	NA	Unclear	Weak	Weak
727	Ejeskar, 1983[96]	29	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Moderate
132	Hoogmartens, 1976[56]	97	58 months for discectomy and 38 months for chemonucleolysis	HCS	No	No	NA	NA	Weak	Moderate
44	Javid, 1995[48]	200	1 year	CCS	No	No	80–100	No	Weak	Moderate
35	Krugluger, 2000[46]	22	2 years	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
117	Lagarrigue, 1991[54] (French language)	1085	Mean 17.2 (range 12–84) months	CCS	No	No	80–100	Unclear	Weak	Moderate
129	Lavignolle, 1987[55] (French language)	358	Mean 25 months for surgery and 22 months for chemonucleolysis	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
889	Lee, 1996[104] (German language)	300	1 year	CCS	No	No	Cannot tell	Unclear	Weak	Weak
593	Muralikuttan, 1992[85]	92	1 year	RCT	Yes	Unclear	80–100	Unclear	Moderate	Moderate
47	Norton, 1986[50]	105	At least 1 year	CCS	No	No	NA	Unclear	Weak	Weak
45	Postacchini, 1987[49]	161	Mean 2.9 years (range 20–38 months) in chemonucleolysis group Mean 2.8 years (range 21–42 months in surgery) group	Non-RCT	No	No	80–100	No	Weak	Moderate

continued

TABLE 33 Summary of the study details for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
617	Revel, 1993[88]	165	1 year	RCT	Yes	Unclear	80–100	Unclear	Moderate	Weak
641	Steffen, 1999[90] (German language)	69	1 year	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
49	Stula, 1990[52] (German language)	69	Postoperative	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
61	Tregonning, 1991[53]	268	10 years	CCS	No	No	80–100	No	Weak	Moderate
893	Watters,1988[105]	100	3 years	Non-RCT	No	No	80–100	No	Weak	Weak
160	Watts, 1975[59]	274	2 years	CCS	No	No	80–100	Unclear	Weak	Weak
672	Weinstein, 1986[92]	159	Mean 10.3 (range 10.0–13.5) years	CCS	No	No	80–100	NA	Weak	Weak
150	Zeiger, 1987[58]	126	Range 6–46 months, with an average time from treatment procedure to follow-up evaluation of 18 months	CCS	No	No	NA	Yes	Weak	Weak
Chemonucleolysis vs epidural										
720	Bontoux, 1990[168] (French language)	80	3 months	RCT	Yes	Unclear	80–100	Yes	Moderate	Weak
447	Bourgeois, 1988[160] (French language)	60	6 months	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
729	Gallucci, 2007[170]	159	6 months	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
50	Graham, 1976[144]	40 (23 with sciatica)	2 years	Non-RCT	No	No	80–100	Yes	Weak	Weak

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Chemonucleolysis vs inactive control										
726	Dabezies, 1988[209]	173	6 months	RCT	Partial	Yes	60–79	Yes	Moderate	Weak
244	Feldman, 1986[207] (French language)	39	3 months	RCT	Unclear	Unclear	80–100	Unclear	Moderate	Moderate
55	Gogan, 1992[205]	60	10 Years	RCT	Yes	Unclear	80–100	Yes	Moderate	Moderate
738	Javid, 1983[210]	108	6 months	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
236	Schwetschenau, 1976[206]	66	1 year	RCT	Yes	Yes	80–100	Yes	Strong	Moderate
Chemonucleolysis vs manipulation										
723	Burton, 2000[208]	40	12 months	RCT	No	No	60–79	Yes	Moderate	Weak
Chemonucleolysis vs mixed treatments										
534	Khoromi, 2007[214]	55	36 weeks	RCT (crossover)	Yes	Yes	<60	Yes	Moderate	Strong

NA, not applicable; NR, not reported.

TABLE 34 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
Chemonucleolysis vs disc surgery														
471	Dei-Anang, 1990[79] (German language)	NR	CCS	42 days	Reported absence of pain	Patient	101	79	0	100	72	0	1.40 (0.73 to 2.66)	Data inferred from percentages reported in graphs
44	Javid, 1995[48]	C	CCS	6 weeks	Successful outcome: good or excellent (vs slight or no improvement)	Patient	100	82	0	100	92	0	0.40 (0.16 to 0.96)	
889	Lee, 1996[104] (German language) (i)[a] (APLD)	NR	CCS	6 weeks	Disappearance of back pain		100	16	?	100	16	?	1.00 (0.47 to 2.13)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 14%
889	Lee, 1996[104] (German language) (ii)[a] (PELD)	NR	CCS	6 weeks	Disappearance of back pain		100	16	?	100	29	?	0.47 (0.23 to 0.93)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 29%
45	Postacchini, 1987[49]	A + C	Non-RCT	1 month	Treatment success: excellent or good (vs fair or poor)		72	39	0.03	84	52	0.03	0.40 (0.16 to 0.96)	Data inferred from graphs Five lost to follow-up were excluded Patients in chemonucleolysis group who had surgery regarded as failure
49	Stula, 1990[52] (German language)	C	RCT	Postoperative	Therapeutic success: good (vs unsatisfactory)	Physician	25	22	0.43	44	40	0.76	0.73 (0.38 to 1.38)	Per protocol analysis with 19 crossed over to surgery

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ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
672	Weinstein, 1986[92]	C	CCS	< 6 weeks	Recovered within 2–6 weeks or immediate (vs no recovery, 6–12 weeks recovery or > 12 weeks recovery)	Patient	88	61	0.04	71	39	0.13	1.56 (0.78 to 3.13)	
Chemonucleolysis vs epidural/intradiscal injection														
729	Gallucci, 2007[170]	A + C	RCT	2 weeks	Treatment success: ODI ≤ 20%		82	72	0	77	69	0	1.20 (0.45 to 3.21	
Chemonucleolysis vs inactive control														
726	Dabezies, 1988[209]	NR	RCT	6 weeks	Treatment success: pain free or moderate improvement (vs unimproved or worse)		77	56	0.11	81	42	0.06	2.48 (1.27 to 4.81)	
244	Feldman, 1986[207] (French language)	A + C	RCT	1 month	Favourable results – based on VAS pain assessment: very good or good (vs mediocre, bad or failures)	Patient	20	11	0	19	5	0	3.42 (0.89 to 13.18)	
55	Gogan, 1992[205]	C	RCT	6 weeks	Treatment success (yes or no)	Patient	30	22	0	30	11	0	4.45 (1.58 to 14.25)	Data inferred from graphs
236	Schwetschenau, 1976[206]	A + C	RCT	72 hours	Symptom improvement: excellent or good (vs fair)		31	8	0.	35	13	0	0.59 (0.20 to 1.69)	

?, unclear; A + C, acute and chronic; APLD, automated percutaneous lumbar discectomy; C, chronic; NA, not applicable; NR, not reported; PELD, percutaneous manual and laser discectomy.

a Lee *et al.*[104] included three treatment groups: APLD (i), PELD (ii) and chemonucleolysis (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 24*).

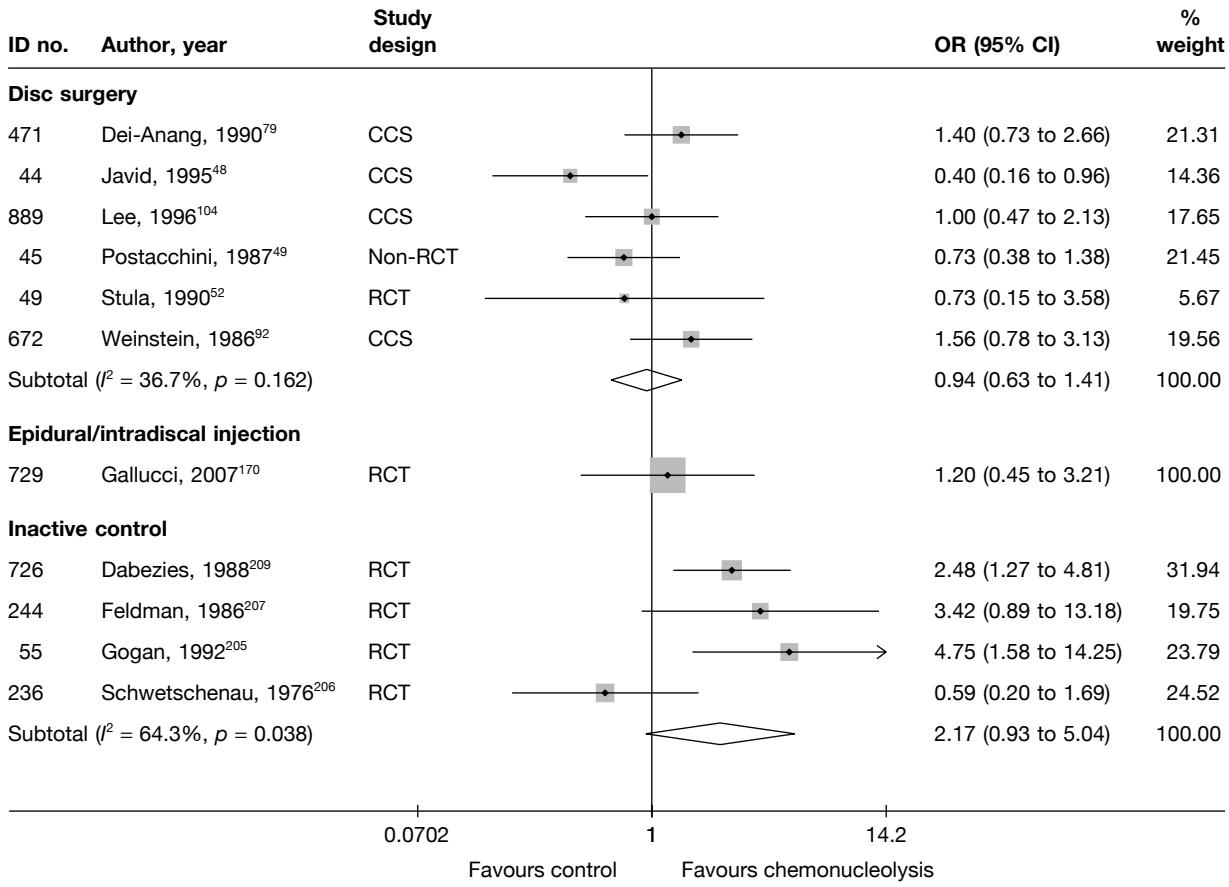

FIGURE 24 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

Six studies[48,49,52,79,92,104] compared chemonucleolysis with disc surgery, for which there was no overall statistically significant difference between the groups. Only one of these studies was a RCT,[52] which was poorly reported with method of randomisation and allocation concealment not stated. Nineteen patients in the chemonucleolysis group crossed over to receive surgery and were analysed accordingly. The results and methods of the remaining studies were also poorly reported.

One poorly reported RCT,[170] of moderate quality, compared intraforaminal and intradiscal injections of steroid, local anaesthetic and ozone–oxygen (categorised as chemonucleolysis) with intraforaminal and intradiscal injections of steroid plus local anaesthetic (epidural), for which there was no overall difference between the groups. The study included patients with mainly acute sciatica (mean duration of symptoms of 15 weeks).

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 35* and the accompanying forest plot (*Figure 25*). Chemonucleolysis was compared with inactive control, disc surgery and manipulation. One study[76] included patients with chronic sciatica, three studies[85,207,208] included patients with either acute or chronic sciatica, and the remaining study[88] did not report the duration of symptoms. The duration of follow-up ranged from 4 weeks[88,207] to 6 weeks.[76,85,208]

TABLE 35 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Chemonucleolysis vs disc surgery																
453	Brown, 1989[76] (i)[d] (chymopapain)	C	CCS	6 weeks	Leg	VAS (0–100)	51	19	60	70	22 (25.48)	3 (20.87)			19.00 (7.30 to 30.70)	SD imputed from weighted average
453	Brown, 1989[76] (ii)[d] (collagenase)	C	CCS	6 weeks	Leg	VAS (0–100)	15	19	58	70	46 (25.48)	3 (20.87)			43.00 (27.05 to 58.95)	SD imputed from weighted average
593	Muralikuttan, 1992[85]	A + C	RCT	6 weeks	Leg	VAS (0–100)	46	46	6	72	19 (25.48)	19 (20.87)			0.00 (–9.52 to 9.52)	SD imputed from weighted average (one study)
617	Revel, 1993[88]	NR	RCT	1 month	Leg	VAS (0–100)	68	62	63.4 (24.6)	68.1 (21.6)	28.3 (27.21)	39.4 (32.28)			–11.10 (–21.41 to –0.79)	SD derived from SE Dropouts 24/165 (15%): intervention 4/72, control 7/69 A further 24 patients were also excluded from the analysis, group allocation not stated

continued

TABLE 35 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Chemonucleolysis vs inactive control																
244	Feldman, 1986[207] (French language)	A + C	RCT	28 days	Leg	VAS (0–100)	20	19	64.0	54.1	30.3 (25.48)	40.2 (23.67)			–9.90 (–25.33 to 5.53)	SD imputed from weighted average (one study)
Chemonucleolysis vs manipulation																
723	Burton, 2000[208]	A + C	RCT	6 weeks	Leg	Annotated thermometer (0–6)	18	19	60.8 (26.5)	66.7 (14.7)	45.3 (17.0)	44.7 (26.7)			0.63 (–13.72 to 14.98)	Missing data: intervention 2/20, control 1/20

A + C, acute and chronic; C, chronic; NR, not reported.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Brown and Tompkins[76] included three treatment groups: chemonucleolysis using chymopapain (i), chemonucleolysis using collagenase (ii) and disc surgery (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 25*).

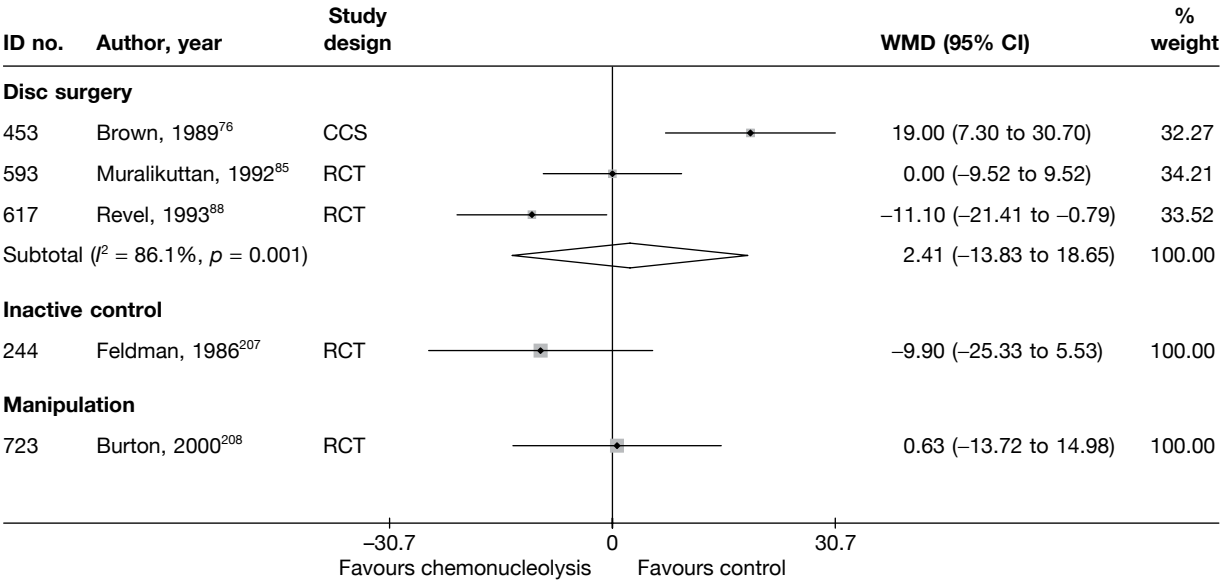

FIGURE 25 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

One poorly reported RCT,[207] of moderate quality, showed non-statistically significant findings in favour of chemonucleolysis compared with inactive control, for reduction in leg pain at 28 days.

Three studies[76,85,88] compared chemonucleolysis with disc surgery, for which there was no overall statistically significant difference between the intervention groups. However, the results were heterogeneous. One CCS[76] reported findings in favour of disc surgery and one RCT[88] reported findings in favour of chemonucleolysis, whereas the remaining RCT[85] reported no statistically significant difference between the interventions. One study[76] included patients who had not received previous disc surgery, whereas the other[88] included patients who had had previous surgery and also had a high proportion of men.

According to one RCT,[208] there was no important difference between chemonucleolysis and osteopathic manipulation at 6 weeks in terms of pain reduction. However, although the randomisation sequence was generated by computer and treatment allocated using envelopes, some patients were not randomised according to the predetermined order because of administrative problems.

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 36* and the accompanying forest plot (*Figure 26*). Chemonucleolysis was compared with disc surgery and manipulation. Two studies[46,92] included patients with chronic sciatica, two studies[85,208] included patients with either acute or chronic symptoms, and the remaining study[88] did not report this information. The duration of follow-up ranged from 1 month[88] to 6 weeks.[46,85,208]

Two studies compared chemonucleolysis with disc surgery; one was an RCT[85] and one was a non-RCT.[77] Overall, there was a non-statistically significant difference between the intervention groups in favour of disc surgery.

One moderate-quality RCT[208] showed a non-statistically significant improvement in function in favour of manipulation, compared with chemonucleolysis, at 6 weeks. The study experienced problems with the randomisation process.

TABLE 36 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Chemonucleolysis vs disc surgery															
593	Muralikuttan, 1992[85]	A + C	RCT	6 weeks	Part of Waddell Disability Index	46	46	6.2	6.7	3.5 (1.21)	2.8 (1.21)	–2.7	3.9	0.58 (0.16 to 1.00)	SD imputed from weighted average Most outcomes showed skewed distribution
617	Revel, 1993[88]	NR	RCT	1 month	Waddell Disability Index and Main Scale	69	62	4.9 (2.49)	6 (2.55)	1.5 (2.55)	1.5 (3.15)	–3.4	–1.05	–0.00 (–0.34 to 0.34)	Final SDs derived from SEs 24 patients were excluded from analysis, group allocation not stated, plus further 10/141 (7%): intervention 3/72, control 7/69
Chemonucleolysis vs manipulation															
723	Burton, 2000[208]	A + C	RCT	6 weeks	RMDQ	18	19	11.95 (5.83)	11.9 (5.48)	11 (5.69)	7.79 (6.65)	–0.95	–4.11		

A + C, acute and chronic; NR, not reported.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

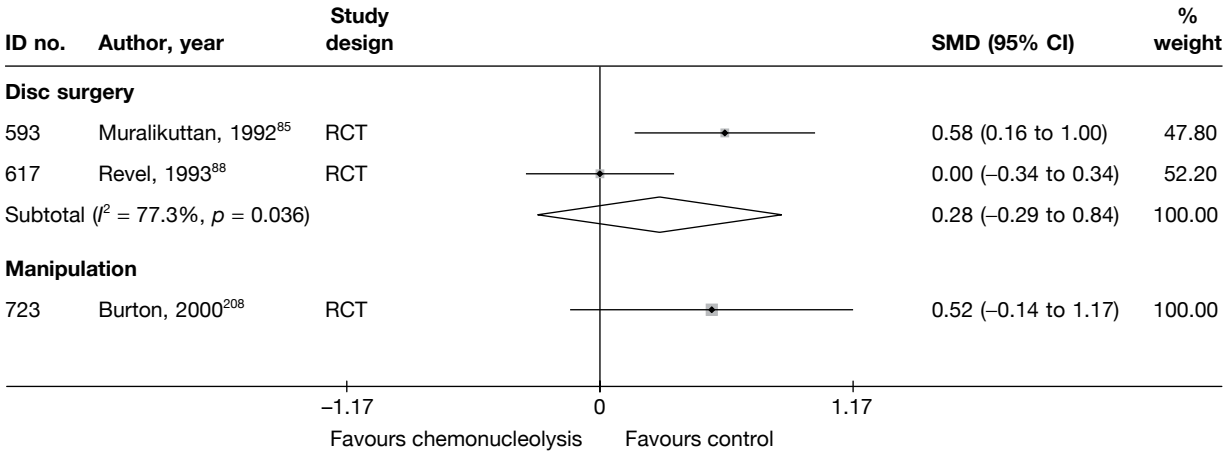

FIGURE 26 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

Chemonucleolysis results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 37* and the accompanying forest plot (*Figure 27*). Chemonucleolysis was compared with inactive intervention, disc surgery, and epidural. Eight studies[48,54,76,92,160,168,205,210] only included patients with chronic symptoms. The remaining studies included patients with either acute or chronic sciatica[49,105,170,206,207] or did not state the duration of symptoms.[88,104,209] The duration of follow-up ranged from 2 to 6 months, or mean 13[105] to 23 weeks.[206]

Pooled analysis of five RCTs[205–210] showed chemonucleolysis to be significantly better than inactive control for overall recovery at 3–6 months[205,207,209,210] or mean 23 weeks.[206]

Eight studies[48,49,54,76,88,92,104,105] compared chemonucleolysis and disc surgery, for which there was no overall difference between the groups. One moderate-quality RCT[88] found chemonucleolysis to be more effective than disc surgery. However, the withdrawal rate in the surgery group (at least 41%) was much greater than that in the chemonucleolysis group (at least 19%), with dropouts being given a poor outcome in the analysis. The remaining studies were observational or non-RCTs, the results and methods of which were generally poorly reported.

Three RCTs[160,168,170] compared chemonucleolysis with epidural, two of which used chymopapain[160,168] and one[170] used injections of steroid, local anaesthetic, and ozone–oxygen. The first two RCTs found no important difference between the intervention groups for chronic sciatica, whereas the third RCT[170] found statistically significant findings in favour of the epidural group for patients who had had symptoms for a mean of 15 weeks. However, the study was poorly reported (with method of randomisation not stated) and of moderate quality. The first two studies were also of moderate quality overall, but used an adequate method of randomisation.

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 38* and the accompanying forest plot (*Figure 28*). Chemonucleolysis was compared with inactive control and disc surgery. One study[76] only included patients with chronic sciatica, one study[88] did not report the duration of symptoms and the remaining studies[207,85] included patients with either acute or chronic sciatica. The duration of follow-up ranged from 60 days[159] to 6 months.[150,151,155,171,174]

TABLE 37 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Chemonucleolysis vs disc surgery														
453	Brown, 1989[76] (i)[a] (chymopapain)	C	CCS	3 months	Final outcome: excellent or good (vs fair, poor or failed)	NR	51	26	0	19	16	0	0.19 (0.05 to 0.75)	Data reported as percentages
453	Brown, 1989[76] (ii)[a] (collagenase)	C	CCS	3 months	Final outcome: excellent or good (vs fair, poor or failed)	NR	15	9	0	19	16	0	0.28 (0.06 to 1.41)	Data reported as percentages
44	Javid, 1995[48]	C	CCS	6 months	Successful outcome: good or excellent (vs slight or no improvement)	Patient	100	88	0	100	85	0	1.29 (0.57 to 2.93)	
117	Lagarrigue, 1991[54] (French language)	C	CCS	2 months	MacNab criteria: excellent or good (vs mediocre or failure)	Patient + physician	334	238	0	751	675	0	0.28 (0.20 to 0.39)	Data reported as percentages
889	Lee, 1996[104] (German language) (i)[b] (APLD)	NR	CCS	2 months	Disappearance of back pain		100	?	29	100	35	?	0.76 (0.42 to 1.38)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 14%
889	Lee, 1996[104] (German language) (ii)[b] (PELD)	NR	CCS	2 months	Disappearance of back pain		100	?	29	100	8	?	4.70 (2.02 to 10.90)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 29%

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
45	Postacchini, 1987[49]	A + C	Non-RCT	3 months	Treatment success: excellent or good (vs fair or poor)		72	51	0.03	84	65	0.03	0.71 (0.35 to 1.46)	Data inferred from graphs Five lost to follow-up were excluded Patients who had surgery in chemonucleolysis group regarded as failure
617	Revel, 1993[88]	NR	RCT	6 months	Treatment success categorised as: very good or good (vs none or moderate)	Patient	72	44	?	69	30	?	2.04 (1.04 to 4.00)	ITT not used. 24/165 (15%) patients excluded from analysis, group allocation not stated
893	Watters,1988[105]	A + C	Non-RCT	Mean 46 days	Success of surgical results: excellent or good (vs fair or poor)	Physician	50	32	0	50	44	0	0.24 (0.09 to 0.68)	Reported as percentages only
672	Weinstein, 1986[92]	C	CCS	3–6 months	Recovered within 2–6 weeks, 6–12 weeks or immediate (vs no recovery, > 12 weeks)	Patient	85	71	0.03	63	53	0.11	0.96 (0.39 to 2.32)	Data reported as percentages
Chemonucleolysis vs epidural/intradiscal injection														
720	Bontoux, 1990[168] (French language)	C	RCT	3 months	Overall improvement: very good or good (vs mediocre or bad)		40	26	0	40	27	0	0.89 (0.35 to 2.26)	
447	Bourgeois, 1988[160] (French language)	C	RCT	6 months	Overall pain relief: very good or good (vs failure)		30	20	0	30	16	0	1.75 (0.62 to 4.97)	
729	Gallucci, 2007[170]	A + C	RCT	6 months	Treatment success: ODI ≤ 20%		82	61	0	77	36	0	0.30 (0.15 to 0.59)	

continued

TABLE 37 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Chemonucleolysis vs inactive control														
726	Dabezies, 1988[209]	NR	RCT	6 months	Treatment success: pain free or moderate improvement (vs unimproved or worse)		62	44	0.29	74	33	0.14	3.04 (1.49 to 6.21)	
244	Feldman, 1986[207] (French language)	A + C	RCT	3 months	Favourable results – based on VAS pain assessment: very good or good (vs mediocre, bad or failures)		20	13	0	19	8	0	2.55 (0.70 to 9.31)	
55	Gogan, 1992[205]	C	RCT	6 months	Treatment success (yes or no)	Patient	30	24	0	30	17	0	3.06 (0.97 to 9.66)	Data inferred from graphs
738	Javid, 1983[210]	C	RCT	6 months	Success (vs failure)		55	40	0	53	22	0	3.76 (1.68 to 8.42)	
236	Schwetschenau, 1976[206]	A + C	RCT	Mean 23 weeks	Symptom improvement: excellent or good (vs fair)		31	9	0	35	11	0	0.89 (0.31 to 2.56)	

?, unclear; APLD, automated percutaneous lumbar discectomy; A + C, acute and chronic; C, chronic; NR, not reported; PELD, percutaneous manual and laser discectomy.

a Brown and Tompkins[76] included three treatment groups: chemonucleolysis using chymopapain (i), chemonucleolysis using collagenase (ii) and disc surgery (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 27*).

b Lee *et al.*[104] included three treatment groups: APLD (i), PELD (ii) and chemonucleolysis (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 27*).

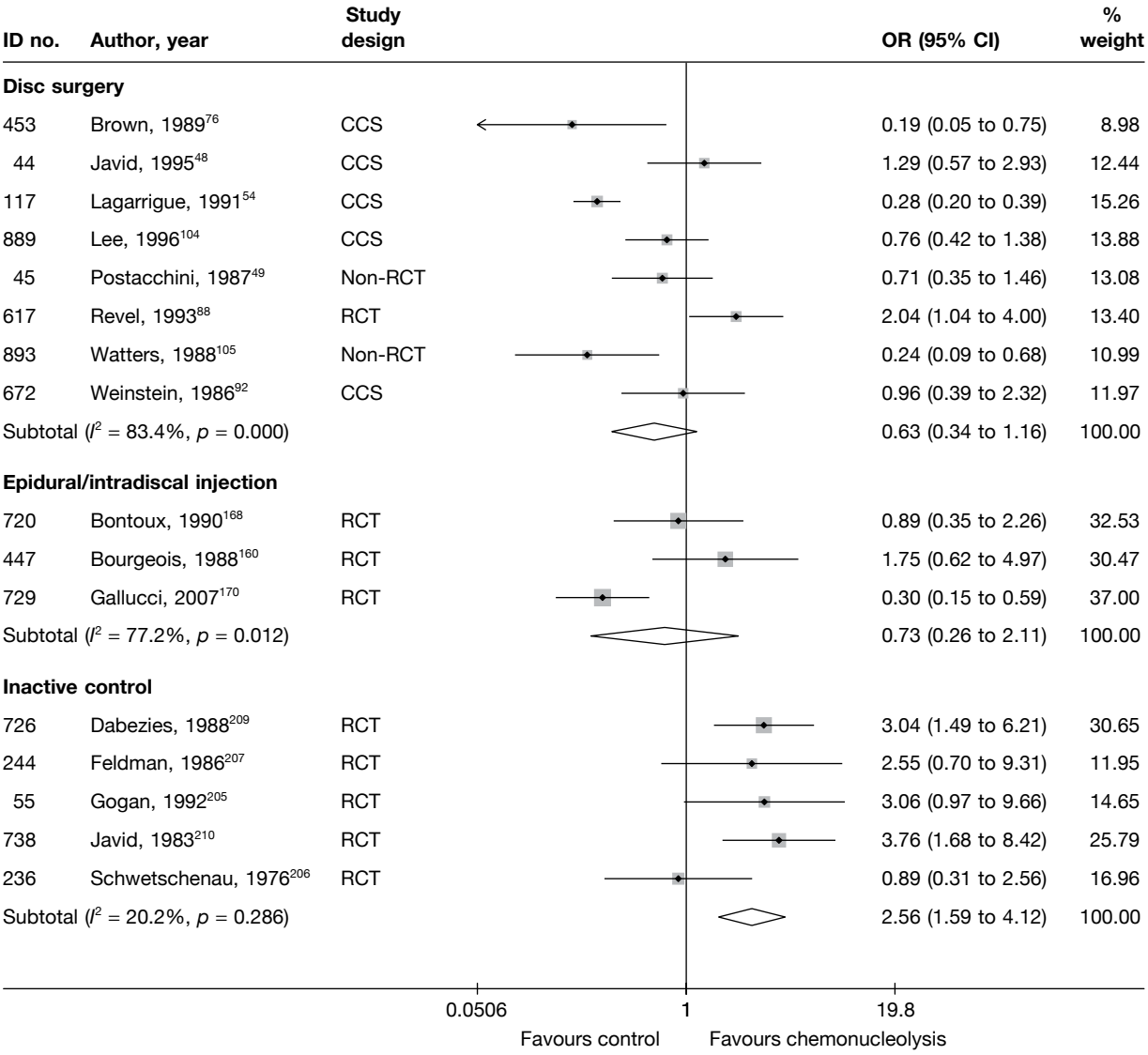

FIGURE 27 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

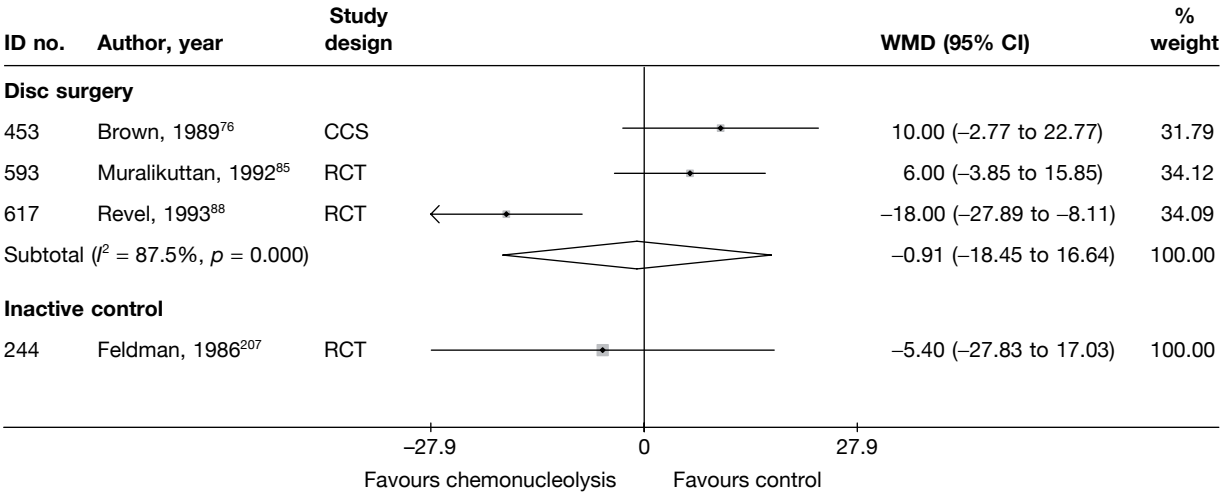

FIGURE 28 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

TABLE 38 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Chemonucleolysis vs disc surgery																
453	Brown, 1989[76] (i)[d] (chymopapain)	C	CCS	12 weeks	Leg	VAS (0–100)	51	19	60	70	14 (23.76)	4 (24.43)			10.00 (–2.77 to 22.77)	SD imputed from weighted average
453	Brown, 1989[76] (ii)[d] (collagenase)	C	CCS	12 weeks	Leg	VAS (0–100)	15	19	58	70	22 (23.76)	4 (24.43)			18.00 (1.71 to 34.29)	SD imputed from weighted average
593	Muralikuttan, 1992[85]	A+C	RCT	3 months	Leg	VAS (0–100)	46	46	64	72	20 (23.76)	14 (24.43)			6.00 (–3.85 to 15.85) *Statistically significant difference between groups,* $p < 0.05$, *Mann–Whitney U-test*	SD imputed from weighted average Most outcomes showed skewed distribution
617	Revel, 1993[88]	NR	RCT	6 months	Leg	VAS (0–100)	72	69	63.4 (24.61)	68.1 (21.6)	17.6 (23.76)	35.6 (34.89)			–18.00 (–27.89 to –8.11)	SDs derived from SEs 24 patients were excluded from the analysis, group allocation not stated
Chemonucleolysis vs inactive control																
244	Feldman, 1986[207] (French language)	A+C	RCT	90 days	Leg	VAS (0–100)	14	10	64.0	54.1	8.7 (23.76)	14.1 (30.1)			–5.40 (–27.83 to 17.03)	SD imputed from weighted average Missing data: intervention 6/20, control 9/19

A+C, acute and chronic; C, chronic; NR, not reported.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Brown and Tompkins[76] included three treatment groups: chemonucleolysis using chymopapain (i), chemonucleolysis using collagenase (ii) and disc surgery (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 28*).

One small, poorly reported RCT of moderate quality, showed a non-statistically significant findings in favour of chemonucleolysis, compared with inactive control, at 90 days. The number of dropouts for the study was quite high, and more patients were lost to follow-up in the control group (47%) than in the intervention group (30%).

Three studies[76,85,88] compared chemonucleolysis with disc surgery; two were RCTs[85,88] and one was a CCS.[76] Overall, there was no statistically significant difference between the intervention groups, but the results were heterogeneous, with one RCT[88] showing statistically significant findings in favour of chemonucleolysis. This study included patients who had had previous surgery and also included a high proportion of men.

Condition-specific outcome measures at medium-term follow-up

The results for the CSOMs at medium-term follow-up are presented in *Table 39* and the accompanying forest plot (*Figure 29*). Chemonucleolysis was compared with disc surgery.

Three RCTs[85,88,96] compared chemonucleolysis with disc surgery; the pooled analysis showed no statistically significant difference between the intervention groups at 3–6 months. However, the findings were heterogeneous.

Results at long-term follow-up (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 40* and the accompanying forest plot (*Figure 30*). Chemonucleolysis was compared with inactive control, disc surgery and epidural. Ten studies[47,48,53,56,59,90,92,103,144,205] included patients with chronic sciatica and six studies included patients with either acute or chronic sciatica,[49,50,58,75,85,206] although the remaining five studies did not report this information.[51,55,60,88,104] The duration of follow-up ranged from < 1 year[92] to 10 years.[53,205]

Two RCTs, which were good to moderate quality,[205,206] compared chemonucleolysis with inactive control. Pooled analysis showed no statistically significant difference between the intervention groups, but there was some degree of heterogeneity between the studies. The duration of follow-up ranged from 1 year[206] to 10 years.[205] The mean duration of symptoms was 11.6 weeks in one study,[206] whereas in the second study[205] 75% of participants had symptoms for between 6 weeks and 6 months and a further 15% had symptoms for > 6 months. The second study[205] reported statistically significant better outcomes in patients treated with chemonucleolysis than in those who received inactive control.

Eighteen studies[47–51,53,55,56,58–60,75,85,88,90,92,103,104] compared chemonucleolysis with disc surgery, the findings of which were very heterogeneous. The pooled result were borderline statistically significant in favour of surgery. There was a mixture of study designs. The duration of follow-up ranged from 1 year to 10 years and duration of sciatica varied between studies. Even when considering the six RCTs on their own,[47,55,60,85,88,90] the findings were still heterogeneous, although most reported findings in favour of disc surgery (pooled analysis: OR 1.12; 95% CI 0.51 to 2.49). One moderate-quality RCT[88] found chemonucleolysis to be more effective than disc surgery. But the study had a high withdrawal rate in the surgery group (at least 41%), compared with chemonucleolysis (at least 19%), with dropouts being given a poor outcome in the analysis.

One poorly reported non-RCT[144] found chemonucleolysis to be significantly better than epidural in terms of overall recovery, according to the physician, among patients with chronic sciatica at 2 years. All patients had been treated by the author. The study included patients with long-term back pain or sciatica, and these findings are based on a subgroup of patients with sciatica (23/40), among whom symptom duration ranged from 12 weeks to 25 years (median 1 year). All patients had already tried various treatments for at least 3 months.

TABLE 39 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing chemonucleolysis with alternative interventions (ordered by author)

						Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)			
ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Mean difference (95% CI)[a]	Comment/ conversion[b]
Chemonucleolysis vs disc surgery															
727	Ejeskar, 1983[96]	A+C	RCT	6 months	Composite score	15	14			9.27 (6.62)	9.71 (4.79)			–0.08 (–0.80 to 0.65)	
593	Muralikuttan, 1992[85]	A+C	RCT	3 months	Part of Waddell Disability Index	46	46	6.2	6.7	3 (1.28)	2.3 (1.28)	–3.2	–4.4	0.55 (0.13 to 0.96)	SD for final means calculated from *p*-values (Mann–Whitney *U*-test); most outcomes showed skewed distribution
617	Revel, 1993[88]	NR	RCT	6 months	Waddell Disability Index and Main Scale	72	69	4.9 (2.55)	6 (3.9)	2.3 (4.65)	3.4 (3.32)	–2.6	–2.6	–0.27 (–0.60 to 0.06)	SD calculated from SE Dropouts 24/165 (15%): group allocation not stated

A+C, acute and chronic; NR, not reported.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

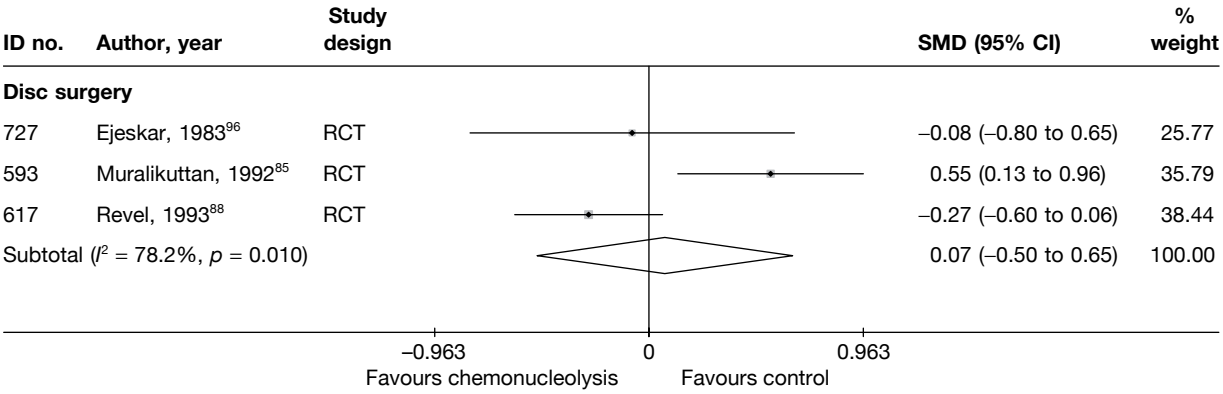

FIGURE 29 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

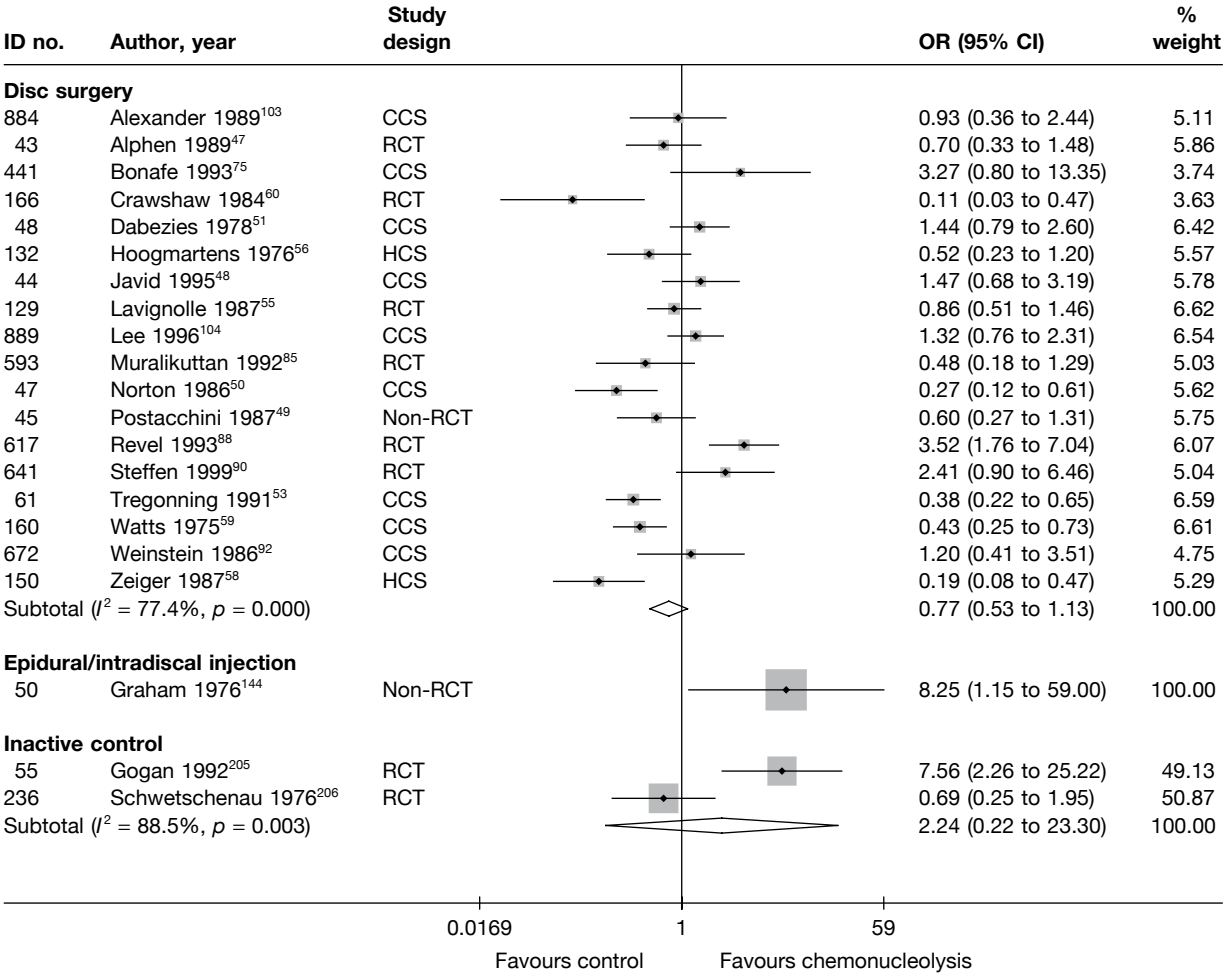

FIGURE 30 Summary of the findings of the global effect at long-term follow-up (>6 months) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

TABLE 40 Summary of the findings of the global effect at long-term follow-up (>6 months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Chemonucleolysis vs disc surgery														
884	Alexander, 1989[103]	C	CCS	Mean 14 (range 6–35) months	Satisfactory clinical outcome (vs unsatisfactory results)	Physician	51	40	0	49	39	0	0.93 (0.36 to 2.44)	Follow-up differed in each groups: chemonucleolysis mean 16 (range 6–35) months, surgery mean 12 (range 6–24) months
43	van Alphen, 1989[47]	C	RCT	12 months	Satisfaction with final result of treatment: yes or largely; (vs barely or no)	Patient	73	53	0	77	61	1	0.70 (0.33 to 1.48)	
441	Bonafe, 1993[75] (French language)	A + C	CCS	1 year	Overall treatment success using modified MacNab criteria: excellent or good (vs satisfactory or worse)		20	16	0	20	11	0	3.27 (0.80 to 13.35)	
166	Crawshaw, 1984[60]	NR	RCT	1 year	Overall outcome: excellent or good (vs poor)		24	11	0. 04	26	23	0.04	0.11 (0.03 to 0.47)	
48	Dabezies, 1978[51]	NR	CCS	2 years	Results categorised as excellent or good (vs unimproved)	Patient	100	71	0	100	63	0	1.44 (0.79 to 2.60)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
132	Hoogmartens, 1976[56]	C	HCS	Mean 49 months	Satisfactory result for amount of radicular pain: excellent or good (vs fair or poor)		44	24	0	53	37	0	0.52 (0.23 to 1.20)	Data inferred from percentages Follow-up differed for the two groups: surgery mean 58 months, chemonucleolysis mean 38 months
44	Javid, 1995[48]	C	CCS	1 year	Success categorised as: good or excellent (vs slight or no improvement)	Patient	100	87	0	100	82	0	1.47 (0.68 to 3.19)	
129	Lavignolle, 1987[55] (French language)	NR	RCT	Mean: surgery 25 months; chemonucleolysis 22 months	Overall success using MacNab type score: good or medium (vs mediocre or bad)	Patient	176	141	0	182	150	0	0.86 (0.51 to 1.46)	
889	Lee, 1996[104] (German language) (i)[a] (APLD)	NR	CCS	1 year	Results of treatment: very good or good; (vs moderate or bad)	Patient	100	55	?	100	48	?	1.32 (0.76 to 2.31)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 29%
889	Lee, 1996[104] (German language) (ii)[a] (PELD)	NR	CCS	1 year	Results of treatment: very good or good (vs moderate or bad)	Patient	100	55	?	100	68	?	0.58 (0.32 to 1.02)	Number randomised not stated, 300 included in analysis Excluded: chemonucleolysis 29%, surgery 14%
593	Muralikuttan, 1992[85]	A + C	RCT	1 year	Completely pain free (vs residual back pain only, residual back and referred pain)		46	8	0	46	14	0	0.48 (0.18 to 1.29)	Reported as percentages One patient crossed over to surgery

continued

TABLE 40 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
47	Norton, 1986[50]	A + C	CCS	≥ 1 year	Treatment success: satisfactory (vs unsatisfactory) based on patient and physician report	Patient + physician	61	17	0	44	26	0	0.27 (0.12 to 0.61)	
45	Postacchini, 1987[49]	A + C	Non-RCT	> 20 months	Treatment success: excellent or good (vs fair or poor)	Patient + physician	72	54	0.03	84	70	0.03	0.60 (0.27 to 1.31)	Data inferred from graphs Five lost to follow-up were excluded
617	Revel, 1993[88]	NR	RCT	1 year	Treatment success	Patient	58	48	?	41	25	?	3.52 (1.76 to 7.04)	24/165 (15%) patients dropped out at beginning, group allocation not stated A further 30% dropped out (surgery: 28/69; chemonucleolysis 14/72), but included in analysis (given poor outcome)
641	Steffen, 1999[90] (German language)	C	RCT	1 year	MacNab criteria: good or very good (vs satisfactory or poor)		33	17	0	36	11	0	2.41 (0.90 to 6.46)	Reported as percentages only
61	Tregonning, 1991[53]	C	CCS	10 years	MacNab criteria: excellent or good (vs fair or poor)		145	47	0.12	91	51	0.13	0.38 (0.22 to 0.65)	
160	Watts, 1975[59]	C	CCS	2 years	Overall outcome: success (vs failure)		100	59	0	174	134	0	0.43 (0.25 to 0.73)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
672	Weinstein, 1986[92]	C	CCS	>1 year	Recovered within 2–6 weeks, 6–12 weeks, >12 weeks or immediate (vs no recovery)	Patient	88	77	3	71	56	8	1.20 (0.41 to 3.51)	
150	Zeiger, 1987[58]	A+C	CCS	Mean 18 (range 6–46) months	Current level of discomfort: pain free or improvement (vs no better or worse)		45	27	0	81	72	0	0.19 (0.08 to 0.47)	Results included seven surgery patients who had had reoperation; five with good results
Chemonucleolysis vs epidural/intradiscal injection														
50	Graham, 1976[144]	C	Non-RCT	2 years	Results categorised as good (vs fair or unimproved)	Physician	10 sciatica patients	6	0	13	2	0	8.25 (1.15 to 59.00)	
Chemonucleolysis vs inactive control														
55	Gogan, 1992[205]	C	RCT	10 years	Treatment success (yes or no)	Patient	30	24	0	26	9	4	7.56 (2.26 to 25.22)	Data inferred from graphs
236	Schwetschenau, 1976[206]	A+C	RCT	1 year	Symptom improvement: excellent or good (vs fair)		31	9	0	35	13	0	2.24 (0.22 to 23.30)	

?, unclear; APLD, automated percutaneous lumbar discectomy; A+C, acute and chronic; C, chronic; NR, not reported; PELD, percutaneous manual and laser discectomy.

a Lee *et al.*[104] included three treatment groups: APLD (i), PELD (ii) and chemonucleolysis (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 30*).

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 41* and the accompanying forest plot (*Figure 31*). Chemonucleolysis was compared with disc surgery and manipulation. Three studies[77,85,208] included patients with either acute or chronic symptoms. The duration of follow-up ranged from 12[85,208] to 18 months.[77]

Two studies compared chemonucleolysis with disc surgery; one was a moderate-quality RCT[85] and one was a non-RCT.[77] Overall, there was a non-statistically significant difference between the intervention groups, in favour of chemonucleolysis.

One moderate-quality RCT[208] showed a non-statistically significant reduction in pain intensity in favour of manipulation, compared with chemonucleolysis, at 12 months. As previously stated the study experienced problems with the randomisation process.

Condition-specific outcome measures at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 42* and the accompanying forest plot (*Figure 32*). Chemonucleolysis was compared with disc surgery and

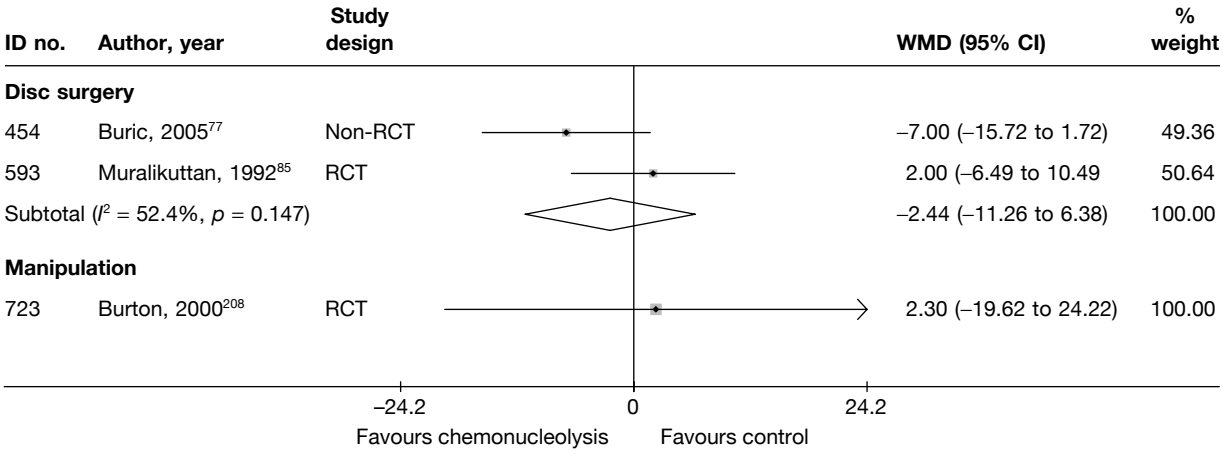

FIGURE 31 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

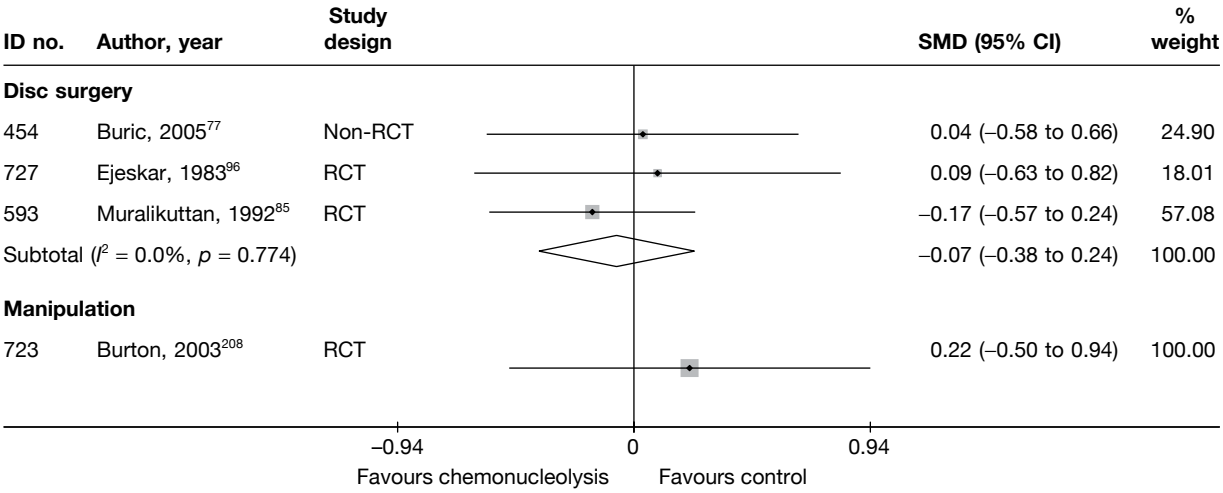

FIGURE 32 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

TABLE 41 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Chemonucleolysis vs disc surgery																
454	Buric, 2005[77]	A+C	Non-RCT	18 months	Overall	VAS (0–10)	30	15	53 (22)	61 (31)	13 (16)	20 (13)	–40.0	–41	–7.00 (–15.7 to 1.72)	Two patients crossed over to surgery, classed as treatment failures
593	Muralikuttan, 1992[85]	A+C	RCT	1 year	Leg	VAS (0–100)	46	46	64	72	18 (21.22)	16 (20.31)			2.00 (–6.49 to 10.49)	SD imputed from weighted average Most outcomes showed skewed distribution
Chemonucleolysis vs manipulation																
723	Burton, 2000[208]	A+C	RCT	12 months	Leg	Annotated thermometer (0–6)	15	15	60.8 (26.5)	66.7 (14.2)	37.8 (29.2)	35.5 (32)			2.30 (–19.62 to 24.22)	Missing data: intervention 5/20, control 5/20

A+C, acute and chronic.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 42 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Chemonucleolysis vs disc surgery															
454	Buric, 2005[77]	A + C	Non-RCT	18 months	RMDQ	30	15	9.1 (3.5)	12.4 (4.3)	2.2 (3.2)	2.1 (1.9)	–6.9	–10.3	0.04 (–0.58 to 0.66)	ITT used but method not stated Dropouts: two, considered as treatment failure
727	Ejeskar, 1983[96]	A + C	Non-RCT	12 months	Composite score	15	14			9.4 (6.88)	8.79 (6.02)			–0.07 (–0.38 to 0.24)	
593	Muralikuttan, 1992[85]	A + C	RCT	1 year	Part of Waddell Disability Index	46	46	6.2	6.7	2.6 (1.21)	2.8 (1.21)	–3.6	–3.9	–0.17 (–0.57 to 0.24)	SD for final means calculated from *p*-values (Mann–Whitney *U*-test); most outcomes showed skewed distribution ITT not used, but all patients included in analysis except one for psychological outcomes
672	Weinstein, 1986[92]	C	CCS	Mean 10.3 years	Composite score	81	71	–						*Results of MANOVA showed no significant relationship between pain outcome measures and treatment type, Wilks' criterion* F*(6, 54) = 1.18,* p *< 0.34*	Pain + disability measured on six different scales Actual data not presented Dropouts 3/159 (2%): (chemonucleolysis group)
Chemonucleolysis vs manipulation															
723	Burton, 2000[208]	A + C	CCS	12 months	RMDQ	15	15	11.95 (5.83)	11.9 (5.48)	7.27 (6.65)	5.87 (5.96)	–4.68	–6.03	0.22 (–0.50 to 0.94)	

A + C, acute and chronic; C, chronic.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

manipulation. Three studies[77,85,208] included patients with either acute or chronic symptoms. The duration of follow-up ranged from 12[85,208] to 18 months.[77]

Four studies[77,85,92,96] compared chemonucleolysis with disc surgery. Pooled analysis of three weak-to-moderate quality studies[77,85,96] showed a non-statistically significant difference between the intervention groups in favour of chemonucleolysis. One CCS[88] reported insufficient data to be included in the meta-analysis. The study followed patients for a mean of 10.3 years. The results of six pain and disability outcome measures were analysed in a one-way MANOVA, the results of which showed no significant relationship between pain outcome measures and treatment type (Wilks' criterion $F(6,54) = 1.18$; $p < 0.34$).

One moderate-quality RCT[208] showed a non-statistically significant reduction in functional status in favour of manipulation, compared with chemonucleolysis, at 12 months. As previously stated, the study experienced problems with the randomisation process.

Analysis of adverse effects for chemonucleolysis

The results for the occurrence of any reported adverse effects are presented in *Table 43* and the accompanying forest plot (*Figure 33*).

The number of adverse effects were significantly less with chemonucleolysis compared with epidural injection. Pooled analyses showed no statistically significant differences between the intervention groups in the number of adverse effects when comparing chemonucleolysis with disc surgery, manipulation or inactive control.

Serious adverse effects (as considered by the review team) reported by patients receiving chemonucleolysis included nerve root injury, dural defect with subsequent leakage of cerebrospinal fluid, phlebitis, disc space infection, discitis, pulmonary embolus and deep-vein thrombosis plus pulmonary embolism.[47,48,51,56,205] However, these were experienced by only one or two participants within each study (that compared chemonucleolysis with another types of treatment). One study[211] that compared two types of chemonucleolysis (with 5 years' follow-up data) reported slightly higher levels of serious adverse effects. When combining data from both treatment arms ($n = 50$), 12 participants experienced severe pain and 11 experienced neurological deficit.

SUMMARY OF OVERALL FINDINGS FOR CHEMONUCLEOLYSIS COMPARED WITH ALTERNATIVE INTERVENTIONS

Most of the chemonucleolysis studies included patients with chronic sciatica or both acute and chronic sciatica. Almost half (47%) of the studies were RCTs. One study was deemed to be of good quality (comparator was inactive control[206]) and 12 studies[47,85,88,160,168,170,205,207–210,214] (36%) were of moderate quality, most of which compared chemonucleolysis with an inactive control or epidural. One study had good external validity (comparator was disc surgery[47]) (*Table 44*).

Meta-analysis of five RCTs[205–207,209,210] deemed to be moderately or well conducted showed chemonucleolysis to be significantly better than the inactive control, in terms of improved global effect, at medium-term follow-up. However, there was no significant difference between the intervention groups in terms of global effect (four RCTs[205–207,209]) or pain intensity (one small RCT[207]) at short-term follow-up; in terms of pain intensity at medium term (one small RCT with fairly high dropout rate[207]); global effect (two good- to moderate-quality RCTs[205,206]) at long-term follow-up for; or for overall adverse effects.[205,207,209,210]

TABLE 43 Summary of the findings of any adverse effect for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Chemonucleolysis vs disc surgery							
884	Alexander, 1989[103]	CCS	8	51	8	49	1.64 (0.50 to 5.40)
43	van Alphen, 1989[47]	RCT	3	73	3	78	1.07 (0.21 to 4.57)
441	Bonafe, 1993[75]	CCS	0	20	1	20	0.32 (0.01 to 8.26)
183	Bouillet, 1983[61]	CCS	152	2136	91	613	0.44 (0.33 to 0.58)
453	Brown, 1989[76] (chymopapain)	CCS	NR	NR	NR	NR	
453	Brown, 1989[76] (collagenase)	CCS	NR	NR	NR	NR	
454	Buric, 2005[77]	Non-RCT	NR	NR	NR	NR	
166	Crawshaw, 1984[60]	RCT	1	25	0	27	3.37 (0.13 to 86.55)
48	Dabezies, 1978[51]	CCS	2	100	0	100	5.10 (0.24 to 107.62)
471	Dei-Anang, 1990[79]	CCS	NR	NR	NR	NR	
727	Ejeskar, 1983[96]	RCT	1	15	1	14	0.93 (0.05 to 16.42)
132	Hoogmartens, 1976[56]	HCS	3	44	19	53	0.13 (0.04 to 0.48)
44	Javid, 1995[48]	CCS	4	100	6	100	0.65 (0.18 to 2.39)
35	Krugluger, 2000[46]	RCT	5	12	1	10	6.43 (0.60 to 68.31)
117	Lagarrigue, 1991[54]	CCS	5	334	30	751	0.37 (0.14 to 0.95)
129	Lavignolle, 1987[55]	RCT	7	176	7	182	1.04 (0.36 to 3.02)
889	Lee, 1996[104] (control = APLD)	CCS	73	100	3	100	87.42 (25.53 to 299.34)
889	Lee, 1996[104] (control = PELD)	CCS	73	100	4	100	64.89 (21.75 to 193.63)
593	Muralikuttan, 1992[85]	RCT	1	46	0	46	3.07 (0.12 to 77.24)
47	Norton, 1986[50]	CCS	12	61	2	44	5.14 (1.09 to 24.29)
45	Postacchini, 1987[49]	Non-RCT	2	72	0	84	5.99 (0.28 to 126.89)
617	Revel, 1993[88]	RCT	35	72	15	69	3.41 (1.63 to 7.10)
641	Steffen, 1999[90]	RCT	NR	NR	NR	NR	
49	Stula, 1990[52]	RCT	NR	NR	NR	NR	
61	Tregonning, 1991[53]	CCS	4	145	5	91	0.49 (0.13 to 1.87)
893	Watters,1988[105]	Non-RCT	2	50	1	50	2.04 (0.18 to 23.27)
160	Watts, 1975[59]	CCS	3	100	32	174	0.14 (0.04 to 0.46)
672	Weinstein, 1986[92]	CCS	NR	NR	NR	NR	
150	Zeiger, 1987[58]	CCS	16	45	5	81	8.39 (2.82 to 24.98)
Chemonucleolysis vs epidural							
447	Bourgeois, 1988[160]	RCT	3	30	30	30	0.00 (0.00 to 0.04)
720	Bontoux, 1990[168]	RCT	NR	NR	NR	NR	
729	Gallucci, 2007[170]	RCT	0	82	0	77	
50	Graham, 1976[144]	Non-RCT	NR	NR	NR	NR	
Chemonucleolysis vs inactive control							
726	Dabezies, 1988[209]	RCT	14	87	1	86	16.3 (2.09 to 126.97)
244	Feldman, 1986[207]	RCT	0	14	2	10	0.12 (0.01 to 2.74)
55	Gogan, 1992[205]	RCT	2	30	2	26	2.07 (0.18 to 24.15)
738	Javid, 1983[210]	RCT	28	55	7	53	6.81 (2.62 to 17.71)
236	Schwetschenau, 1976[206]	RCT	0	31	0	35	

TABLE 43 Summary of the findings of any adverse effect for studies comparing chemonucleolysis with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Chemonucleolysis vs manipulation							
723	Burton, 2000[208]	RCT	4	15	5	15	0.73 (0.15 to 3.49)

APLD, automated percutaneous lumbar discectomy; NR, not reported; PELD, percutaneous manual and laser discectomy.

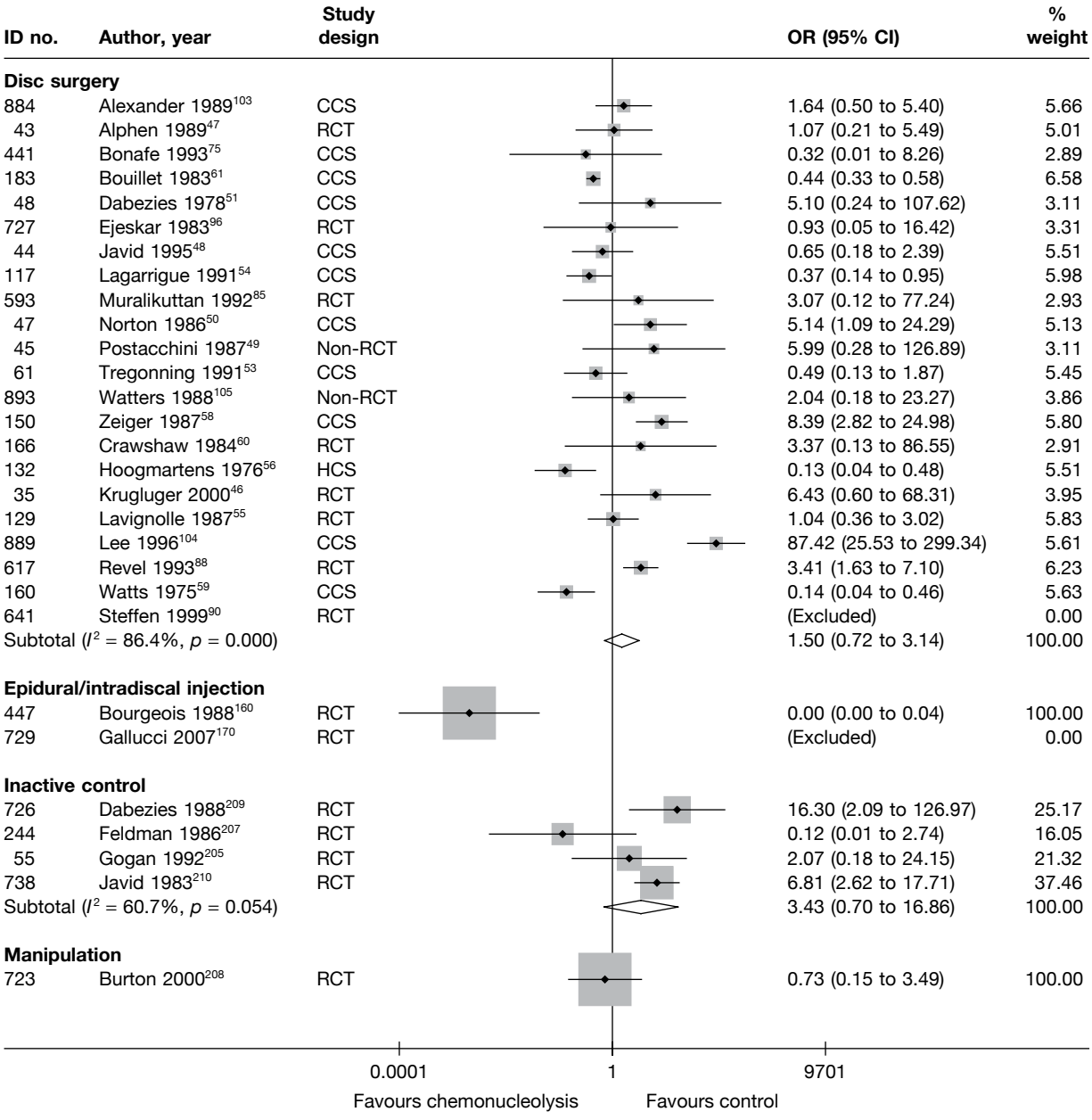

FIGURE 33 Summary of the findings of any adverse effect for studies comparing chemonucleolysis with alternative interventions. Note: weights are from random effects analysis.

TABLE 44 Summary of chemonucleolysis studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Chemonucleolysis vs disc surgery	26 (29)	29–1085 (116)	8/26 (31)	0/26 (0)	0/26 (0)	26/26 (100)	21/26 (81)	1/26 (4)	1/26 (4)	3/26 (12)	21/26 (81)	3/26 (12)
Chemonucleolysis vs epidural/intradiscal injection	4 (4)	40–159 (70)	3/4 (75)	0/4 (0)	0/4 (0)	4/4 (100)	4/4 (100)	0/4 (0)	0/4 (0)	0/4 (0)	4/4 (100)	0/4 (0)
Chemonucleolysis vs inactive control	5 (5)	39–173 (66)	5/5 (100)	1/5 (20)	0/5 (0)	5/5 (100)	5/5 (100)	0/5 (0)	0/5 (0)	0/5 (0)	5/5 (100)	0/5 (0)
Chemonucleolysis vs manipulation	1 (1)	40 (40)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total (for chemonucleolysis results)	**36 (39)**	**29–1085 (100)**	**17/36 (47)**	**1/36 (3)**	**0/36 (0)**	**36/36 (100)**	**31/36 (86)**	**1/36 (3)**	**1/36 (3)**	**3/36 (8)**	**30/36 (83)**	**3/36 (8)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Pooled analysis of 18 studies[47–51,53,55,56,58–60,75,85,88,90,92,103,104] showed marginally statistically significant findings in favour of disc surgery, compared with chemonucleolysis, for the global effect at long-term follow-up (see *Figure 30*). However, there was no statistically significant difference between the intervention groups for the global effect at short-[48,49,52,79,92,104] and medium-term[48,49,54,76,88,92,104,105] follow-up; pain intensity at short-,[76,85,88] medium-[76,85,88] and long-term[77,85] follow-up; CSOMs at short-,[85,88] medium-[85,88,96] and long-term[77,85,96] follow-up; or adverse effects[46–51,53–56,58–61,75,85,88,96,103–105] (according to a number of studies, ranging from good to poor quality). There was no statistically significant difference between disc surgery in combination with chemonucleolysis and disc surgery alone, at long-term follow-up, for global effect, pain, or for adverse effects (one poor-quality Q-RCT[97]).

Chemonucleolysis using steroid plus ozone–oxygen was found to be better than epidural for overall recovery at short-term follow-up (one poorly reported RCT[170]) and chemonucleolysis using chymopapain better than epidural at long-term follow-up (one poor-quality non-RCT[144]). There was no statistically significant difference between epidural and chemonucleolysis for overall recovery at medium-term follow-up (three RCTs,[160,168,170] one of which used ozone–oxygen[170]). There were more adverse effects experienced with epidural injections than with chemonucleolysis (one RCT[160]).

There was no statistically significant difference between chemonucleolysis and osteopathic manipulation, in terms of pain intensity and functional status, at short- or medium-term follow-up (one RCT[208]).

Non-opioids

Description of non-opioids studies

Summary of interventions

Thirty-six studies evaluated the use of non-opioids for sciatica,[6,57,80,143,156,161,172,175,214–241] 25 of which compared non-opioids with alternative interventions.[6,57,80,143,156,162,173,176,214–230] (Two studies were reported in a single publication;[223] studies 696 and 99999.) Seven studies included more than two arms.[57,166,214,215,223,227,229] The types of intervention being evaluated by the studies are presented in *Table 45a*. Three studies[161,172,226] did not report any pain, global or CSOM data.[161,172,226]

Fifteen studies compared different types of non-opioids[223,227,229,231–241] (seven of which were three-arm studies[57,215,223,227,229] and two studies of which were reported in a single publication[223]). The types of non-opioids being compared are presented in *Table 45b* but the findings are not considered further.

Summary of study participants for non-opioids

Summary data for included participants are presented in *Table 46*. The number of participants included in the 22 studies that reported outcome data for global effect, pain or CSOMs ranged from 10 to 532 participants (median 65 participants). Nine studies (41%) included patients with acute sciatica and six studies (27%) included patients with chronic sciatica, whereas the majority of the remaining studies included patients with either acute or chronic sciatica (one study did not report this information). Two studies (one in which the comparator was epidural[156] and one in which the comparator was opioids[229]) included some patients with spinal stenosis and none included patients with sequestered or extruded discs. The diagnosis of sciatica, or the presence of herniated disc, was confirmed by imaging in eight studies (38%). One study[57] compared the use of non-opioids with disc surgery in patients who had recurrent sciatica. The remaining studies included a mixture of patients with either first-episode or recurrent sciatica or, more likely, did not report this information. One study (comparator was inactive control)[6] included patients who had not received any previous treatment for their current episode of sciatica. Eleven studies (50%) included patients who had received previous treatment for their current episode of sciatica and this information was not stated in the remaining studies. Two studies that compared non-opioids with disc surgery[80] or epidural[156] included patients who had received previous disc surgery.

Summary of study quality for non-opioids studies

Summary information on study details is presented in *Table 47*. Most of the non-opioid studies were RCTs (17/21, 81%), but none was good quality. Ten studies[6,143,161,214,218,220,223,224,227,228] were of moderate quality, most of which compared non-opioids with inactive control. Two of these studies[214,227] used adequate methods for random sequence generation and allocation concealment (comparators included inactive control, opioids and mixed treatment). A further two studies[156,224] used adequate randomisation, but not allocation concealment, although both used sealed envelopes. Two studies[218,222] used adequate allocation concealment, but the method of randomisation was unclear. Only one study[214] had strong external validity, although it had a high attrition rate.

Non-opioids results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 48* and the accompanying forest plot (*Figure 34*). Non-opioids were compared with inactive control and opioids. One study[221] included only patients with chronic sciatica, five studies[218,220,223,224,227]

TABLE 45a Summary of the interventions used when comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Treatment description	Control description
Non-opioids vs alternative/non-traditional				
801	Chen, 2009[215]	RCT	Western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG)	Warming acupuncture by burning moxa daily for 10 days (WAG)
801	Chen, 2009[215]	RCT	Western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG)	Anisodamine (2 mg) point injections into acupoints daily for 10 days (PIG)
Non-opioids vs biological agents				
323	Genevay, 2004[216]	HCS	Three intravenous injections of methylprednisolone 250 mg	Three subcutaneous injections of etanercept (Enbrel®, Wyeth Pharmaceuticals) 25 mg (anti-TNF-α)
Non-opioids vs disc surgery				
475	Dubourg, 2002[80]	CCS	Non-operative intervention group. Some received steroids	Disc surgery (operative group) (various surgical techniques)
144	Rossi, 1993[57] (Italian language)	RCT	Oral dexamethasone 8 mg for 9 days, naproxen 500–1000 mg for 5 days (group Ib)	Percutaneous discectomy (groups Ia and IIa)
144	Rossi, 1993[57] (Italian language)	RCT	Oral dexamethasone 8 mg for 9 days, naproxen 500–1000 mg for 5 days (group Ib)	Microdiscectomy (group IIb)
Non-opioids vs epidural/intradiscal injection				
451	Bronfort, 2000[161]	RCT	Paracetamol, NSAIDs, activity modification	Epidural injection of steroid injections, 1–3 injections
20	Dincer, 2007[143]	RCT	Oral diclofenac 75 mg for 14 days (NSAID)	Caudal epidural injection 40 mg methylprednisolone acetate, 8 mg dexamethasone phosphate, 7 ml of 2% prilocaine
771	Lafuma, 1997[172]	RCT	Usual care (rest + NSAIDs) without epidural injections during hospital admission	Epidural steroid (125 mg prednisolone) injections at admission
362	Wilson-MacDonald, 2005[156]	RCT	Intramuscular injections of steroid methylprednisolone 80 mg and local anaesthetic 8 ml bupivacaine	Epidural injection of steroid methylprednisolone 80 mg and local anaesthetic 8 ml bupivacaine
846	Murata, 2009[175]	RCT	Injection of steroid (3.3 mg dexamethasone sodium phosphate) and local anaesthetic (7 ml 1% lidocaine) in the back muscles of L2 area (control block)	L2 nerve block using steroid (3.3 mg dexamethasone sodium phosphate) and local anaesthetic (2 ml of 1% lidocaine)
Non-opioids vs inactive control				
696	Dreiser, 2001[223]	RCT	Oral meloxicam (NSAID) 7.5 mg for 7 days (M I)	Oral placebo for 7 days
696	Dreiser, 2001[223]	RCT	Oral meloxicam (NSAID) 15 mg for 7 days (M II)	Oral placebo for 7 days
334	El-Zahaar, 1995[221]	RCT	Intravenous injections of colchicine 1 mg twice weekly for 3 weeks	Intravenous injections of saline twice weekly for 3 weeks
728	Finckh, 2006[224]	RCT	Intravenous steroid methylprednisolone 500 mg	Intravenous saline infusion (placebo)
62	Gibson, 1975[217]	Non-RCT	Chymoral tablets (proteolytic enzymes) for 7 days	Placebo tablets for 7 days

continued

TABLE 45a Summary of the interventions used when comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	Treatment description	Control description
97	Goldie, 1968[218]	RCT	Oral indomethacin 75 mg daily	Oral placebo
732	Grevsten, 1975[225]	RCT	Phenylbutazone (NSAID) 300–600 mg for 15 days	Intramuscular and oral placebo
312	Hedeboe, 1982[220]	RCT	Intramuscular injection dexamethasone (8–64 mg) for 7 days	Intramuscular injection of saline
816	Herrmann, 2009[227]	RCT	Lornoxicam 8 mg	Placebo
816	Herrmann, 2009[227]	RCT	Diclofenac 50 mg	Placebo
817	Holve, 2008[228]	Q-RCT	Steroid oral tablets (prednisolone decreasing dose from 60 mg to 20 mg every 3 days) + standard medical + PT	Placebo tablets + standard medical + PT
736	Jacobs, 1968[226]	Q-RCT	Oral indomethacin (NSAID) 75–100 mg for 7 days	Oral placebo for 7 days
534	Khoromi 2007[214]	RCT (crossover)	Oral nortriptyline (Allegron®, King Pharmaceuticals) plus inert placebo (up to 100 mg/day for 7.5 weeks)	Oral benztropine (active placebo) plus inert placebo (0.25–1 mg/day for 8.5 weeks)
611	Porsman, 1979[222]	RCT	Intramuscular dexamethasone 8–64 mg for 7 days	Intramuscular saline for 7 days (placebo)
665	Weber, 1993[6]	RCT	Oral pirixicam (NSAID) 20–40 mg for 14 days	Oral placebo for 14 days
297	Yildirim, 2003[219]	RCT	Oral gabapentin 900–3600 mg for 2 months	Oral placebo for 2 months
Non-opioids vs manipulation				
451	Bronfort, 2000[161]	RCT	Paracetamol, NSAIDs, activity modification	Chiropractic spinal manipulation
Non-opioids vs mixed treatment				
534	Khoromi 2007[214]	RCT (crossover)	Oral nortriptyline plus inert placebo (up to 100 mg/day for 7.5 weeks)	(Opioids + non-opioids). Morphine plus nortriptyline (oral morphine up to 90 mg/day for 8.5 weeks; oral nortriptyline up to 100 mg/day for 7.5 weeks)
Non-opioids vs opioids				
534	Khoromi 2007[214]	RCT (crossover)	Oral nortriptyline plus inert placebo (up to 100 mg/day for 7 weeks)	Sustained-release morphine (oral) plus inert placebo (up to 90 mg/day for 7 weeks)
368	Kwasucki, 2002[229] (Polish language)	RCT	Fluvoxamine (10 mg oral)	Tramadol (100 mg intramuscular injection)
368	Kwasucki, 2002[229] (Polish language)	RCT	Imipramine (25 mg oral)	Tramadol (100 mg intramuscular injection)
547	Kwasucki, 1993[230] (Polish language)	RCT	Dexamethasone. First and second days 24 mg (16 mg at 7 AM, 8 mg at 7 PM); third day 8 mg twice daily; fourth and fifth days 4 mg twice daily; sixth and seventh days 4 mg once daily	Tramadol. First 5 days 100 mg twice daily; sixth and seventh days 100 mg once daily

M, meloxican; PIG, point injection group; TNF-α, tumour necrosis factor-alpha; WAG, warming acupuncture group; WMG, western medicine group.

TABLE 45b Summary of the interventions used when comparing alternative forms of non-opioids (ordered by author)

ID no.	Author, year	Study design	Treatment description	Control description
238	Andersen, 1978[235]	RCT	Oral proquazone (NSAID)	Oral naproxen (NSAID)
122	Blazek, 1986[232]	RCT	Oral proquazone	Oral diclofenac
159	Borms, 1988[234]	RCT	Intramuscular tiaprofenic acid	Intramuscular ketoprofen
721	Braun, 1982[238] (German language)	RCT	Intramuscular injection of ketoprofen	Intramuscular injection of corticosteroid containing antirheumatic combination preparation (sodium phenylbutazone, dexamethasone, lidocaine, cyanocobalamin)
136	Desnuelle, 1986[56] (French language)	RCT	Intramuscular indomethacin injections	Intramuscular diclofenac injections
696	Dreiser, 2001[223]	RCT	Oral meloxicam (NSAID) 7.5 mg for 7 days (M I)	Oral meloxicam (NSAID) 15 mg for 7 days (M II)
9999	Dreiser, 2001[223]	RCT	NSAID (low-dose meloxicam, M I)	Traditional NSAID (diclofenac)
9999	Dreiser, 2001[223]	RCT	NSAID (high-dose meloxicam, M II)	Traditional NSAID (diclofenac)
810	Friedman, 2008[239]	RCT	Steroid intramuscular injection (160 mg of methylprednisolone acetate) + oral naproxen + oral oxycodone/acetaminophen	Placebo intramuscular injection + oral naproxen + oral oxycodone/acetaminophen
816	Herrmann, 2009[227]	RCT	Lornoxicam 8 mg	Diclofenac 50 mg
527	Kanayama, 2005[237]	RCT	5-HT_{2A} receptor inhibitor. Sarpogrelate hydroxychloride 300 mg orally for 2 weeks	NSAID. Sodium diclofenac 75 mg orally for 2 weeks
368	Kwasucki, 2002[229] (Polish language)	RCT	Fluvoxamine (10 mg oral)	Imipramine (25 mg oral)
841	Memeo, 2008[240]	Q-RCT	Acetyl-L-carnitine 1180 mg/day	Thiotic acid 600 mg/day
109	Schuermans, 1988[231]	RCT	Intramuscular tiaprofenic acid	Intramuscular alclofenac
241	Stevanovic, 1986[236]	RCT	Intramuscular injection of tenoxicam	Intramuscular injection of piroxicam
871	Toroudi, 2009[241]	RCT	500 mg of oral ibuprofen prescribed three times a day for 9 days	400 mg of oral mesalamine prescribed three times a day for 9 days

5-HT_{2A}, 5-hydroxytryptamine$_{2A}$; M, meloxican.

included only patients with acute sciatica and the remainder included patients with either acute or chronic sciatica. The duration of follow-up ranged from 1 day[224] to 19 days.[230]

Pooled analysis of nine studies[217,218,220–226] showed non-opioids to be significantly better than inactive control at 1 day[224] to 21 days.[221] Eight studies were RCTs and one was a non-RCT. There was much heterogeneity between studies ($I^2 = 82.6\%$), with one RCT, which evaluated the use of intravenous injections of colchicine for patients with chronic sciatica, having a larger effect size than the other studies. Excluding this study reduced the effect size to an OR of 1.63 (95% CI 1.03 to 2.59) and improved homogeneity ($I^2 = 44.3\%$); follow-up ranged from 1 day[224] to 14 days.[218,225]

Non-opioids were compared with opioids in two RCTs;[229,230] the pooled analysis showed a non-statistically significant difference in favour of non-opioids. Both studies were poorly reported and conducted. Follow-up ranged from 14[229] to 19 days.[230]

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 49* and the accompanying forest plot (*Figure 35*). Non-opioids were compared with inactive control, opioids, epidural, alternative therapy and biological agents. Five studies[216,223,224,227,228] included only patients with acute sciatica, three[175,215,219] included only patients with chronic sciatica, one[156] did not report the duration of symptoms and the remaining studies included patients with acute or chronic sciatica. The duration of follow-up ranged from 8 hours[227] to 36 days.[215]

TABLE 46 Summary of sciatica type and study population details for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Non-opioids vs alternative/non-traditional													
801	Chen, 2009[215]	RCT	90	Mean 34.5 (SD 7.7)	63 (70)	Mean 5.3 years (SD 4.14 years)	Nerve root pain	No	NR	No	No	NR	NR
Non-opioids vs biological agents													
323	Genevay, 2004[216]	HCS	10	Mean 47.3 (SD 13.3, range 1 to >18)	10 (50)	Mean 3.2 weeks (SD 3.7 weeks)	Nerve root pain	No	NR	No	No	NR	NR
Non-opioids vs disc surgery													
475	Dubourg, 2002[80]	CCS	67	Mean 48.8 (SD 13.9, range 28–81)	42 (63)	Mean 25.7 days (SD 28.7 days)	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	Yes
144	Rossi, 1993[57] (Italian language)	RCT	40	Mean 42.5 (SD 10.5, range 20–65)	NR	< 6 months	Nerve root pain	Yes	Recurrent	No	No	NR	NR
Non-opioids vs epidural/intradiscal injection													
451	Bronfort, 2000[161]	RCT	20	Mean 44.5 (SD 10.6)	12 (60)	≤ 3 weeks $n=6$; 4–12 weeks $n=14$	Nerve root pain and refereed pain	No	NR	No	No	Yes	No
20	Dincer, 2007[143]	RCT	64	Mean 28 (SD 5)	46 (72)	1–12 months	Nerve root pain and refereed pain	Yes	NR	No	No	NR	No
771	Lafuma, 1997[172]	RCT	108	Mean 42.1 (SD 10.6)	66 (61)	Mean 56 days (range 1–854 days)	Nerve root pain	NR	Recurrent and first episode	No	No	Yes	NR
362	Wilson-MacDonald, 2005[156]	RCT	93	Mean 49 (range 23–79)	37 (40)	> 6 weeks, exact duration NR	Nerve root pain	Yes	NR	Yes	No	Some had	Yes
846	Murata, 2009[175]	RCT	246 (136 radicular pain)	Mean 68 (SD 12, range 27–90)	90 (37)	Median 31 months (SD 52 months)	Nerve root pain	No	NR	No	No	Yes	No

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Non-opioids vs inactive control													
696	Dreiser, 2001[223]	RCT	532	Mean 47 years	234 (44)	93% within 3 days	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	No
334	El-Zahaar, 1995[221]	RCT	100	Mean 38.7 (range 26–58)	NR	NR	Nerve root pain and referred pain	Yes	Recurrent and first episode	No	No	Yes	NR
728	Finckh, 2006[224]	RCT	65	Mean 47.2 (SD 15.2)	29(48)	Median 15 days	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	No
62	Gibson, 1975[217]	Non-RCT	93	Mean 40 (range 19–67)	55 (59)	< 1–6 months	Nerve root pain and referred pain	No	NR	No	No	NR	No
97	Goldie, 1968[218]	RCT	50	Range 15–65	26 (52)	1 week 34%; 2 weeks 56%; 3 weeks 10%	Nerve root pain and referred pain	No	NR	No	No	NR	NR
732	Grevsten, 1975[225]	RCT	36	Range 23–62	17 (47)	Days to years	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	NR
312	Hedeboe, 1982[220]	RCT	39	Mean 41.8 (range 24–63)	25 (64)	< 2 weeks 36%, 2–8 weeks 28%, > 2 months 36%	Nerve root pain and referred pain	No	NR	No	No	Yes	NR
816	Herrmann, 2009[227]	RCT	171	Mean 50.2 (SD12.6)	76 (44)	< 72 hours	Nerve root pain	No	Recurrent and first episode	No	No	No	NR
817	Holve, 2008[228]	Q-RCT	29	Mean 43.7	17 (59)	< 1 week	Nerve root pain	No	First episode	No	No	NR	NR
736	Jacobs, 1968[226]	Q-RCT	110 (50 sciatica)	NR	NR	Inclusion criteria acute and chronic	Nerve root pain	No	NR	No	No	NR	NR
534	Khoromi, 2007[214]	RCT (cross–over)	55	Median 53 (range 19–65)	30 (55)	Median 5 years (range 0.3–37.0 years)	Nerve root pain	Yes	Recurrent and first episode	NR	NR	Yes	NR

continued

TABLE 46 Summary of sciatica type and study population details for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
611	Porsman, 1979[222]	RCT	52	Mean 44.8 (range 21–67)	33 (67)	Range few days–6 months	Nerve root pain	No	Recurrent and first episode	No	No	Yes	NR
665	Weber, 1993[6]	RCT	214	Mean 48	NR	Recruited at onset sciatica	Nerve root pain	No	NR	No	No	No	NR
297	Yildirim, 2003[219]	RCT	50	Mean 39.3 (SD 8.2, range 25–60)	18 (36)	Mean 68.5 months (SD 60.2, range 3–240 months)	Nerve root pain	Yes	NR	No	No	Yes	No
Non-opioids vs manipulation													
451	Bronfort, 2000[161]	RCT	20	Mean 44.5 (SD 10.6)	12 (60)	≤3 weeks $n=6$; 4–12 weeks $n=14$	Nerve root pain and refereed pain	No	Not reported	No	No	Yes	No
Non-opioids vs mixed treatment													
534	Khoromi, 2007[214]	RCT (cross–over)	55	Median 53 (range 19–65)	30 (55)	Median 5 years (range 0.3–37.0 years)	Nerve root pain	Yes	Recurrent and first episode	NR	NR	Yes	NR
Non-opioids vs opioids													
534	Khoromi, 2007[214]	RCT (cross–over)	55	Median 53 (range 19–65)	30 (55)	Median 5 years (range 0.3–37.0 years)	Nerve root pain	Yes	Recurrent and first episode	NR	NR	Yes	NR
368	Kwasucki, 2002[229] (Polish language)	RCT	70	Mean 42.8 (range 23–68)	51 (73)	Range 1 week–8 months	Nerve root pain	Yes	Recurrent and first episode	Yes	No	Yes	NR
547	Kwasucki, 1993[230] (Polish language)	RCT	43	Mean 43.2 (range 27–69)	37 (86)	Mean 6.3 weeks (range 1 week–8 months)	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	NR

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 47 Summary of the study details for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Non-opioids vs alternative/non-traditional										
801	Chen, 2009[215]	90	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Moderate
Non-opioids vs biological agents										
323	Genevay, 2004[216]	10	6 weeks	HCS	No	No	80–100	No	Weak	Moderate
Non-opioids vs disc surgery										
144	Rossi, 1993[57] (Italian language)	40	6 months	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
475	Dubourg, 2002[80]	67	6 months	CCS	No	No	80–100	No	Weak	Weak
Non-opioids vs epidural/intradiscal injection										
451	Bronfort, 2000[161]	20	12 weeks	RCT	Unclear	Partial	80–100	NA	Moderate	Weak
20	Dincer, 2007[143]	64	3 months Assessment at day 15, first month and third month	RCT	Unclear	Unclear	80–100	Yes	Moderate	Moderate
771	Lafuma, 1997[172]	108	3 months	RCT	Unclear	Unclear	80–100	No	Weak	Weak
362	Wilson-MacDonald, 2005[156]	93	35 days	RCT	Yes	Partial	80–100	Unclear	Moderate	Weak
846	Murata, 2009[175]	246 (136 RP)	7 days	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Non-opioids vs inactive control										
696	Dreiser, 2001[223]	532	7 days	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
334	El-Zahaar, 1995[221]	100	3 weeks	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
728	Finckh, 2006[224]	65	30 days	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
62	Gibson, 1975[217]	93	3 months	Non-RCT	No	No	80–100	Unclear	Weak	Weak
97	Goldie, 1968[218]	50	14 days	RCT	Unclear	Yes	80–100	Yes	Moderate	Weak
732	Grevsten, 1975[225]	36	2 weeks	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
312	Hedeboe, 1982[220]	39	3 months	RCT	Partial	Partial	80–100	Unclear	Moderate	Moderate

continued

TABLE 47 Summary of the study details for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
816	Herrmann, 2009[227]	171	5 days	RCT	Yes	Yes	80–100	Unclear	Moderate	Weak
817	Holve, 2008[228]	29	6 months	Q-RCT	No	Partial	80–100	Yes	Moderate	Weak
736	Jacobs, 1968[226]	110 (50 NRP, 60 BP)	1 week	Q-RCT	No	Unclear	80–100	Yes	Weak	Weak
534	Khoromi, 2007[214]	55	36 weeks	RCT (cross–over)	Yes	Yes	< 60	Yes	Moderate	Strong
611	Porsman, 1979[222]	52	9 days	RCT	Unclear	Yes	80–100	Yes	Weak	Moderate
665	Weber, 1993[6]	214	4 weeks	RCT	Unclear	Unclear	80–100	No	Moderate	Weak
297	Yildirim, 2003[219]	50	2 months	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Non-opioids vs manipulation										
451	Bronfort, 2000[161]	20	12 weeks	RCT	Unclear	Partial	80–100	NA	Moderate	Weak
Non-opioids vs mixed treatment										
534	Khoromi, 2007[214]	55	36 weeks	RCT (cross–over)	Yes	Yes	< 60	Yes	Moderate	Strong
Non-opioids vs opioids										
534	Khoromi, 2007[214]	55	36 weeks	RCT (cross–over)	Yes	Yes	< 60	Yes	Moderate	Strong
368	Kwasucki, 2002[229] (Polish language)	70	19 days	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
547	Kwasucki, 1993[230] (Polish language)	43	2 weeks	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak

BP, back pain; NRP, nerve root pain; RP, radicular pain.

TABLE 48 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Non-opioid vs inactive control														
696	Dreiser, 2001[223] (i)[a] (7.5 mg)	A	RCT	7 days	Global efficacy: good or satisfactory (vs not satisfactory or bad)	Patient	171	130	0	180	117	0	1.71 (1.07 to 2.72)	Data inferred from graphs reporting percentages ITT using worst-case analysis
696	Dreiser, 2001[223] (ii)[a] (15 mg)	A	RCT	7 days	Global efficacy: good or satisfactory (vs not satisfactory or bad)	Patient	181	138	0	180	117	0	1.73 (1.09 to 2.74)	Data inferred from graphs reporting percentages ITT using worst-case analysis
334	El-Zahaar, 1995[221]	C	RCT	3 weeks	Number of patients with pain improvement for sciatica, low back pain and sciatica, and low back pain		49	46	0.02	48	2	0.04	352.00 (56.27 to 2210.11)	
728	Finckh, 2006[224]	A	RCT	1 day	Responders: decrease in VAS > 20 mm		31	15	?	29	8	?	2.46 (0.84 to 7.22)	Dropouts 5/65 (8%): group allocation not stated ITT where missing values assumed to be missing at random and imputed using longitudinal regression model
62	Gibson, 1975[217]	A + C	Non-RCT	7 days	Fully recovered	Physician	45	7	0.02	44	10	0.06	0.63 (0.21 to 1.83)	
97	Goldie, 1968[218]	A	RCT	14 days	Relief from pain: complete (vs fair or none)	Patient	25	14	0	25	16	0	0.72 (0.23 to 2.23)	

continued

TABLE 48 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
732	Grevsten, 1975[225]	A + C	RCT	2 weeks	Overall improvement (vs uncertain or not improved)		18	15	0	18	8	0	6.25 (1.33 to 29.43)	
312	Hedeboe, 1982[220]	A	RCT	9 days	Overall pain improvement: better (vs unchanged or worst)	Patient	19	13	0	20	7	0	4.02 (1.06 to 15.28)	
816	Herrmann, 2009[227] (i)[b] (lornoxicam)	A	RCT	5 days	Overall assessment of efficacy and tolerability: very good or good (vs fair or poor)	Patient	57	38	0	57	32	0	1.56 (0.73 to 3.34)	ITT reported; seven patients dropped out: lornoxicam 4/57, diclofenac 2/57, placebo 1/57
816	Herrmann, 2009[227] (ii)[b] (diclofenac)	A	RCT	5 days	Overall assessment of efficacy and tolerability: very good or good (vs fair or poor)	Patient	57	42	0	57	32	0	2.19 (0.99 to 4.81)	ITT reported; seven patients dropped out: lornoxicam 4/57, diclofenac 2/57, placebo 1/57
611	Porsman, 1979[222]	A + C	RCT	9 days	Treatment effective (vs not effective)		25	13	0.07	24	14	0.04	0.77 (0.25 to 2.39)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Non-opioid vs opioids														
547	Kwasucki, 1993[230] (Polish language)	A + C	RCT	2 weeks	Improvement in pain: cessation of symptoms or clear improvement (vs no improvement or mild improvement)		21	16	0	22	8	0	5.60 (1.48 to 21.13)	Data extracted from histograms of raw pain scores
368	Kwasucki, 2002[229] (Polish language) (i)[c] (fluvoksamine)	A + C	RCT	19 days (end of treatment)	Overall improvement: complete relief or improvement (vs no improvement)	Patient	24	18	0	22	17	0	0.88 (0.23 to 3.44)	
368	Kwasucki, 2002[229] (Polish language) (ii)[c] (imipramine)	A + C	RCT	19 days (end of treatment)	Overall improvement: complete relief or improvement (vs no improvement)	Patient	24	06	0	22	17	0	0.59 (0.16 to 2.18)	

?, unclear; A, acute; A + C, acute and chronic; C, chronic.

a Dreiser *et al.*[223] included three treatment groups: oral meloxicam (NSAID) 7.5 mg (M I) (i), oral meloxicam (NSAID) 15 mg (M II) (ii) and oral placebo (P) (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 34*).

b Herrmann and Geertsen[227] included three treatment groups: lornoxicam (LNX) 8 mg (i), diclofenac 50 mg (ii) and placebo (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 34*).

c Kwasucki *et al.*[229] included three treatment groups: fluvoksamine (10 mg oral) (i), imipramine (25 mg oral) (ii) and tramadol (100 mg intramuscular injection) (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 34*).

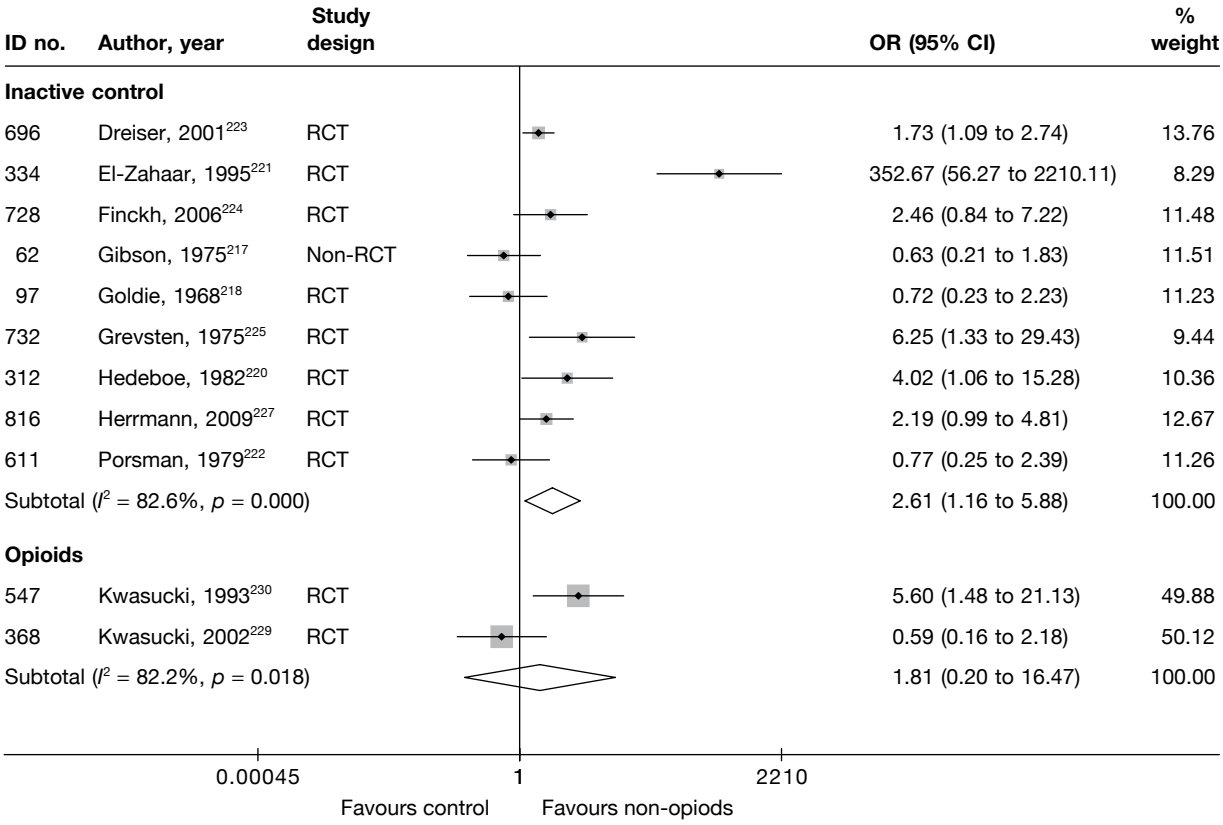

FIGURE 34 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

The overall findings from five studies[219,223,224,227,228] showed non-opioids to be significantly better than inactive control for reducing pain. Four studies included patients with acute sciatica, and one poorly reported and poorly conducted RCT[219] included patients with chronic sciatica (evaluating the use of oral gabapentin). As with the global effect, excluding the study with chronic sciatica improved homogeneity (I^2 = 0%), giving a pooled WMD for four studies of –6.45 (95% CI –10.60 to –2.30). Three of the four studies were moderate-quality RCTs;[223,224,227] the remaining study[228] was a Q-RCT.

Pooled analysis from two RCTs[229,230] showed non-opioids to be significantly better than opioids for reducing pain. Both studies were poorly reported and conducted. Follow-up ranged from 14[229] to 19 days.[230]

According to two RCTs,[143,175] non-opioids were significantly less effective than epidural at reducing pain at 1 week[175] to 1 month.[143] Both were poorly reported and of weak to moderate quality. One further poorly reported RCT[156] of moderate quality also found non-opioids to be statistically significantly less effective than epidural for pain relief at 35 days (p < 0.004; statistical test not stated), but did not report any summary statistics.

One poorly reported and poorly conducted RCT[215] found non-opioids to be significantly better than warming acupuncture (alternative therapy) for reducing pain in patients with chronic sciatica at the end of a 35-day treatment period.

A small HCS (323, n = 20) found biological agents to be significantly better than non-opioids for reducing pain intensity in patients with acute severe sciatica.

TABLE 49 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Non-opioids vs alternative																
801	Chen, 2009[215] (i)[d] (WAG)	C	RCT	36 days (end of treatment)	Leg	Not stated	30	30	1.42 (0.37)	1.56 (0.35)	2.42 (0.33)	5.74 (0.25)			–3.32 (–3.47 to –3.17)	Outcome = improvement in clinical symptoms (scale and range not stated) Reported separately for: sciatica, lumbago, aggravated pain on coughing, aggravated pain on sneezing, aggravated pain on defaecation
801	Chen, 2009[215] (ii)[d] (PIG)	C	RCT	36 days (end of treatment)	Leg	Not stated	30	30	1.42 (0.37)	1.75 (0.32)	2.42 (0.33)	2.75 (0.32)			–0.33 (–0.49 to –0.17)	Outcome = improvement in clinical symptoms (scale and range not stated) Reported separately for: sciatica, lumbago, aggravated pain on coughing, aggravated pain on sneezing, aggravated pain on defecation
Non-opioids vs biological agents																
323	Genevay, 2004[216]	A	HCS	6 weeks	Leg	VAS (0–100)	10	10	75.1 (14.2)	74.4 (12.9)	52.9 (25.1)	12.4 (13.2)			40.50 (22.92 to 58.08)	
Non-opioids vs epidural/intradiscal injection																
20	Dincer, 2007[143]	A + C	RCT	1 month	Overall	VAS (0–100)	30	34	68 (10)	69 (10)	44 (13)	32 (11)			12.00 (6.06 to 17.94)	

continued

TABLE 49 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
846	Murata, 2009[175]	C	RCT	7 days	Leg	VAS (0–100)	65	71	74	69	67 (22.86)	43 (22.48)			24.00 (16.37 to 31.63)	SD imputed from weighted average Subgroup analysis based on 136/246 (55%) with radicular pain: intervention 71/122, control 65/124 Dropouts 8/246 (3%): no further details
362	Wilson-MacDonald, 2005[156]	NR	RCT	35 days	Overall	Oxford pain chart	36	36							*There was a significant difference in pain relief between the two groups with the epidural group being better* ($p < 0.004$)	No data other than *p*-values presented Dropouts 23%: non-opioids 12/44, epidural 8/44
Non-opioids vs inactive control																
696	Dreiser, 2001[223]	A	RCT	7 days	Overall	VAS (0–100)	171	180	75.6 (11.4)	76 (10.7)			–46 (26.15)	–40 (26.83)	–6.00 (–11.54 to –0.46)	SD estimated from SE ITT using LOCF Dropouts 32/532 (6%): low dose 6/171, placebo 12/180
696	Dreiser, 2001[223]	A	RCT	7 days	Overall	VAS (0–100)	181	180	75.4 (10.6)	76 (10.7)			–45 (26.91)	–40 (26.83)	–5.00 (–10.54 to 0.54)	SD estimated from SE ITT using LOCF Dropouts 32/532 (6%): high dose 14/181, placebo 12/180

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
728	Finckh, 2006[224]	A	RCT	30 days	Leg	VAS (0–100)	31	29	67.1 (22.1)	63.3 (20.7)	36.1 (22.1)	45.3 (20.7)	–31	–18	–9.20 (–20.03 to 1.63) *Significantly greater pain reduction in steroid group during the first 3 days (p = 0.04), but both groups similar after 3 days (p = 0.22); linear spline regression model*	Final mean calculated using change score and baseline SD used Dropouts 5/65 (8%): group allocation not stated ITT where missing values assumed to be missing at random and imputed using longitudinal regression model
816	Herrmann, 2009[227]	A	RCT	8 hours	Overall	VAS (0–100)	57	57	84.9 (7.5)	83.2 (7.0)	62.9 (22.86)	69.5 (23.67)	–22.0	–13.7	–6.60 (–15.14 to 1.94)	Final mean derived from change scores and SD imputed from weighted average Treatment administered over 4 days (with an optional 5 days), but PID was measured at day 1 and therefore only evaluates the effectiveness of the loading dose Mean PID using VAS (0–100) compared with baseline

continued

TABLE 49 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
816	Herrmann, 2009[227]	A	RCT	8 hours	Overall	VAS (0–100)	57	57	83.9 (6.7)	83.2 (7.0)	59.8 (22.86)	69.5 (23.67)	–24.1	–13.7	–9.70 (–18.24 to –1.16)	Mean PID using VAS (0–100) compared with baseline Final mean derived from change scores and SD imputed from weighted average Treatment administered over 4 days (with an optional 5 days), but PID was measured at day 1 and therefore only evaluates the effectiveness of the loading dose
817	Holve, 2008[228]	A	Q-RCT	4 weeks	Overall	RMDQ subscale (0–5)	13	14	76	62	32 (22.86)	32 (23.67)	–24.1	–13.7	0.00 (–17.55 to 17.55)	SD imputed from weighted average RMDQ (scored on a pain thermometer range 0–5) ITT not used Dropouts 2/29 (7%): intervention 2/15, control 0/14
297	Yildirim, 2003[219]	C	RCT	1 month	Overall	Pain severity (0–3)	23	20	53.3 (31.3)	56.0 (22.3)	24.3 (25.0)	49.0 (23.0)			–24.70 (–39.05 to –10.35)	ITT not used Dropouts 7 (14%): intervention 2/25, control 5/25
Non-opioids vs opioids																
547	Kwasucki, 1993[230] (Polish language)	A + C	RCT	2 weeks	Overall	NRS (0–4)	21	22	77.5 (12.5)	77.5 (15)	27.5 (17.5)	50.0 (22.5)			–22.50 (–34.52 to –10.48)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
368	Kwasucki, 2002[229] (Polish language) (i)[e] (fluvoxamine)	A + C	RCT	19 days	Overall	NRS (0–4)	24	22	67.5 (15)	70.0 (17.5)	30 (20)	50.0 (25)			–20.00 (–33.16 to –6.84)	Data derived from histograms of pain scores
368	Kwasucki, 2002[229] (Polish language) (ii)[e] (imipramine)	A + C	RCT	19 days	Overall	NRS (0–4)	24	22	75 (25)	70.0 (17.5)	37.5 (25)	50.0 (25)			–12.50 (–26.96 to 1.96)	Data derived from histograms of pain scores

A, acute; A + C, acute and chronic; C, chronic; LOCF, last observation carried forward; NRS, numerical rating scale; PID, pain intensity difference; PIG, point injections group; WAG, warming acupuncture group; WMG, western medicine group.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Chen *et al.*[215] included three treatment groups: point injections of anisodamine (2 mg) into acupoints (PIG) (ii), warming acupuncture group with needles warmed by burning moxa (WAG) (i) and western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG) (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 35*).

e Kwasucki *et al.*[229] included three treatment groups: fluvoxamine (10 mg oral) (i), imipramine (25 mg oral) (ii); and tramadol (100 mg intramuscular injection) (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 35*).

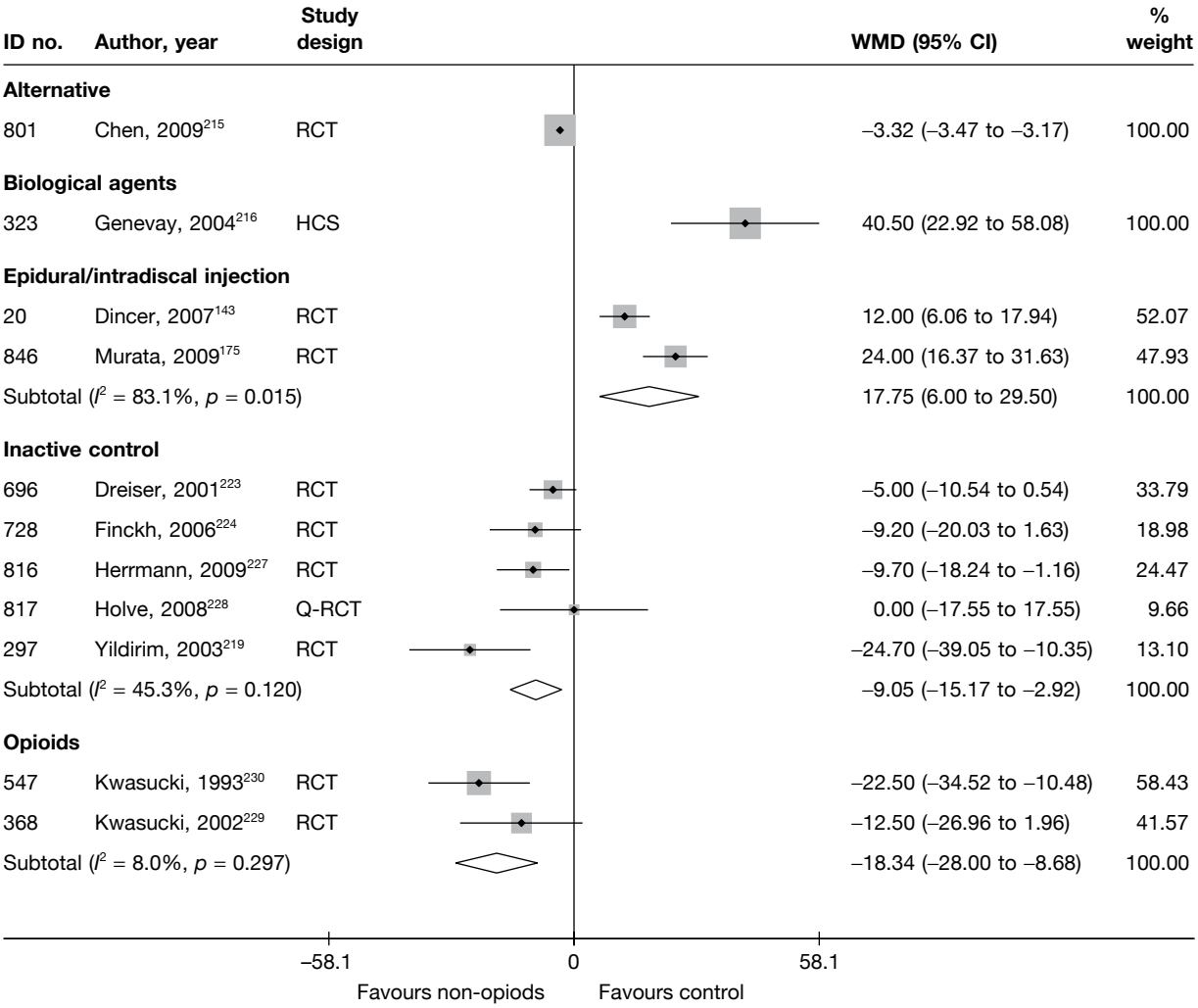

FIGURE 35 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 50* and the accompanying forest plot (*Figure 36*). Epidural injections were compared with inactive control, epidural injections and biological agents. Three studies[6,216,228] included only patients with acute sciatica and the remaining study[143] included patients with either acute or chronic symptoms. The duration of follow-up ranged from 4[6,143,228] to 6 weeks.[216]

Two studies[6,228] compared non-opioids with inactive control; there was an overall non-statistically significant finding in favour of inactive control at 4 weeks. One was a moderate-quality RCT[6] that did not report the methods of randomisation and allocation concealment and the other was a Q-RCT.[228]

One moderate-quality RCT[143] found epidural to be significantly better than non-opioids for improving functional status in patients with acute or chronic sciatica. The methods of randomisation and allocation concealment were not stated.

A small (n = 20) historical cohort study[216] found biological agents to be significantly better than non-opioids for improving functional status in patients with acute severe sciatica at 6 weeks.

TABLE 50 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/ conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Non-opioids vs biological agents															
323	Genevay, 2004[216]	A	HCS	6 weeks	RMDQ	10	10	15.5 (2.9)	17.8 (3.3)	11.1 (4.6)	5.8 (5.5)			1.05 (0.10 to 1.99)	
Non-opioids vs epidural/intradiscal injection															
20	Dincer, 2007[143]	A + C	RCT	1 month	ODI	30	34	34.4 (6.7)	35.8 (6.7)	22.2 (8.6)	17 (7.3)	–12.2	–18.8	0.66 (0.15 to 1.16)	
Non-opioids vs inactive control															
817	Holve, 2008[228]	A	Q-RCT	4 weeks	RMDQ	13	14	16	16	8 (4.6)	9.2 (4.47)			–0.26 (–1.02 to 0.49)	Final SD imputed from weighted mean of SDs from other studies ITT not used Dropouts 2/29 (7%): intervention 2/15, control 0/14
665	Weber, 1993[6]	A	RCT	4 weeks	Disability, Roland's Functional Test (0–17)	120	94	55 (14)	54 (12)	22 (14)	16 (14)	–33	–38	0.43 (0.16 to 0.70)	

A, acute; A + C, acute and chronic.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

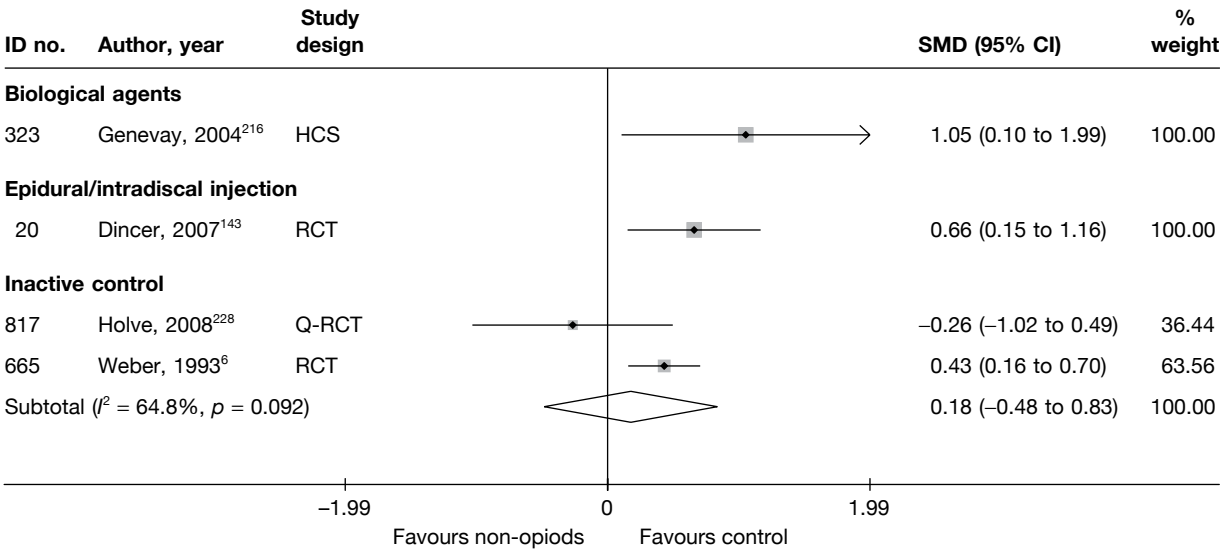

FIGURE 36 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

Non-opioid results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 51* and the accompanying forest plot (*Figure 37*). Non-opioids were compared with inactive intervention, epidural injections, disc surgery, opioids and mixed treatment. Two studies[220,80] included only patients with acute sciatica and the remaining three studies[175,214,220] included only patients with chronic sciatica. The duration of follow-up ranged from 9 weeks[214] to 6 months.[57,175]

Two moderate-quality RCTs[214,220] compared non-opioids with inactive control; there was a non-statistically significant finding in favour of non-opioids, for both acute and chronic sciatica. One study[214] was a four-arm crossover RCT with a high dropout rate; only 44% of patients who completed the study were included in the analysis.

One poor-quality RCT[175] reported non-statistically significant findings in favour of epidural, compared with non-opioids, for adequate recovery from leg pain at 24 weeks. The findings were based on a subgroup analysis of 136/246 (55%) patients with chronic radicular pain.

Two studies compared disc surgery with non-opioids. One poorly reported CCS[80] found non-opioids to be more effective than disc surgery for recovery or improvement in patients with acute sciatica, but the findings were not statistically significant. A second poorly conducted study[57] found that more patients in the surgery group (68%) than in the non-opioids group (55%) were satisfied with cure, but the findings were reported only as percentages, and the number of patients in each treatment group was not stated. The study was essentially two studies that were very poorly reported, and which included the comparison of two surgical procedures (percutaneous discectomy and microdiscectomy) with medical treatment. Patients (n = 40) were initially divided into two groups according to the type of disc herniation they had, with patients in one group randomised to one of two surgical procedures; the other group does not appear to have been randomised.

A moderate-quality crossover RCT[214] compared non-opioids with opioids or a combination of both opioids and non-opioids (mixed treatments). There was no statistically significant difference between non-opioids and opioids, but combination therapy (mixed treatments) resulted in

TABLE 51 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
Non-opioids vs disc surgery														
144	Rossi, 1993[57] (Italian language)	C	Non-RCT	6 months	Reduction of pain	Patient	?	68		?	55			Study included three comparative groups, but the two surgical groups were combined for the analysis of global effect Total number of participants was 40, but number in each group not stated and results reported only as percentages, therefore could not include in the meta-analysis
475	Dubourg, 2002[80]	A	CCS	6 months	Recovery improvement (vs failure) according to change in VAS and muscle strength		25	24	0.11	32	25	0.18	6.72 (0.77 to 58.79)	
Non-opioids vs epidural/intradiscal injection														
846	Murata, 2009[175]	C	RCT	24 weeks	Satisfactory clinical outcome (vs unsatisfactory results)	Physician	65	5	?	71	11	?	0.45 (0.15 to 1.39)	Subgroup analysis of 136/246 (55%) patients with radicular pain: intervention 71/122, control 65/124 Eight patients dropped out, group allocation or radicular pain not stated

continued

TABLE 51 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Non-opioids vs inactive control														
312	Hedeboe, 1982[220]	A	RCT	3 months	Overall pain improvement: better (vs unchanged or worst)	Patient	19	6	0	20	5	0	1.38 (0.34 to 5.62)	
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Global pain relief (GPR): worse pain or no pain relief		33	11	0.40	32	13	0.42	1.26 (0.45 to 3.51)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Non-opioids vs mixed treatment														
534	Khoromi, 2007[214] (opioids + non-opioids)	C	RCT (crossover)	9 weeks (end of treatment)	Global pain relief (GPR): worse pain or no pain relief		28	18	0.49	32	13	0.42	0.35 (0.12 to 1.01)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Non-opioids vs opioids														
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Global pain relief (GPR): worse pain or no pain relief		31	12	0.44	32	13	0.42	0.92 (0.34 to 2.53)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

?, unclear; A, acute; C, chronic

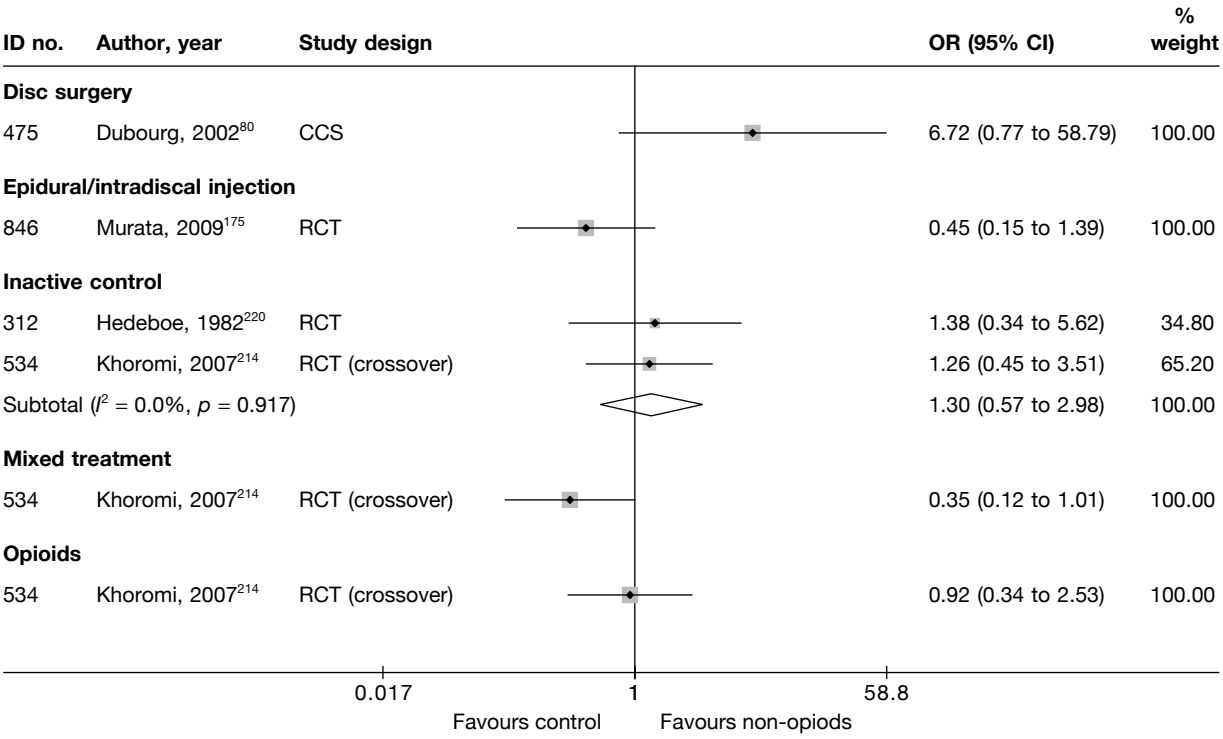

FIGURE 37 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

marginally statistically significant better outcomes than non-opioids used alone. Only 28 patients (44%) who completed the study were included in the analysis.

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 52* and the accompanying forest plot (*Figure 38*). Non-opioids were compared with inactive control and disc surgery, opioids and mixed treatments. Two studies[80,228] included patients with acute sciatica and two studies[214,219] included patients with chronic sciatica. The duration of follow-up ranged from 2[219] to 6 months.[80,228]

Pooled analysis from three studies[214,219,228] showed non-opioids to be significantly better than the inactive control for reducing the overall pain of acute[228] or chronic[214,219] sciatica. One was a four-arm crossover RCT, one was a Q-RCT[228] and the other a poor-quality RCT.[219] Follow-up ranged from 2[219] to 6 months.[228] Two studies were of moderate quality.[214,228]

One poorly reported CCS[80] found no important difference between non-opioids and disc surgery for reducing pain intensity of acute sciatica at 6 months.

One moderate-quality crossover RCT[214] compared non-opioids with opioids or a combination of both opioids and non-opioids (mixed treatments) for reducing pain intensity at 9 weeks. There was a non-statistically significant difference between the intervention groups in favour of non-opioids for both comparators. Only 28 patients (44%) who completed the study were included in the analysis.

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 53* and the accompanying forest plot (*Figure 39*). Non-opioids were compared with the inactive control,

TABLE 52 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Non-opioids vs disc surgery																
475	Dubourg, 2002[80]	A	CCS	6 months	Overall	VAS (0–100)	28	36	47.7 (34)	52.2 (28.5)	14.8 (20.6)	13.2 (18.8)			1.60 (–8.19 to 11.39)	Dropouts 7/67 (10%): intervention 4/39, control 3/28
Non-opioids vs inactive control																
817	Holve, 2008[228]	A	Q-RCT	6 months	Overall	RMDQ subscale (0–5)	13	14	76	62	8 (22.76)	32 (30.1)			–24.00 (–44.04 to –3.96)	SD imputed from weighted average ITT not used Dropouts 2/29 (7%): intervention 2/15, control 0/14
297	Yildirim, 2003[219]	C	RCT	2 months	Overall	NRS (0–3)	23	20	53.33 (31.33)	56 (22.33)	18.67 (19.33)	45.33 (19.67)			–26.66 (–38.35 to –14.97)	Dropouts: intervention 2/25, control 5/25
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Leg	NRS (0–10)	28	28	49 (24.3)	49 (24.3)	30.0 (27)	37.0 (27)			–7.00 (–21.14 to 5.38)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Non-opioids vs mixed treatment																
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Leg	NRS (0–10)	28	28	49 (24.3)	49 (24.3)	30.0 (27)	38.0 (24)			–8.00 (–21.38 to 5.38)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Non-opioids vs opioids																
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Leg	NRS (0–10)	28	28	49 (24.3)	49 (24.3)	30.0 (27)	34 (28)			–4.00 (–18.41 to 10.41)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

A, acute; C, chronic; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

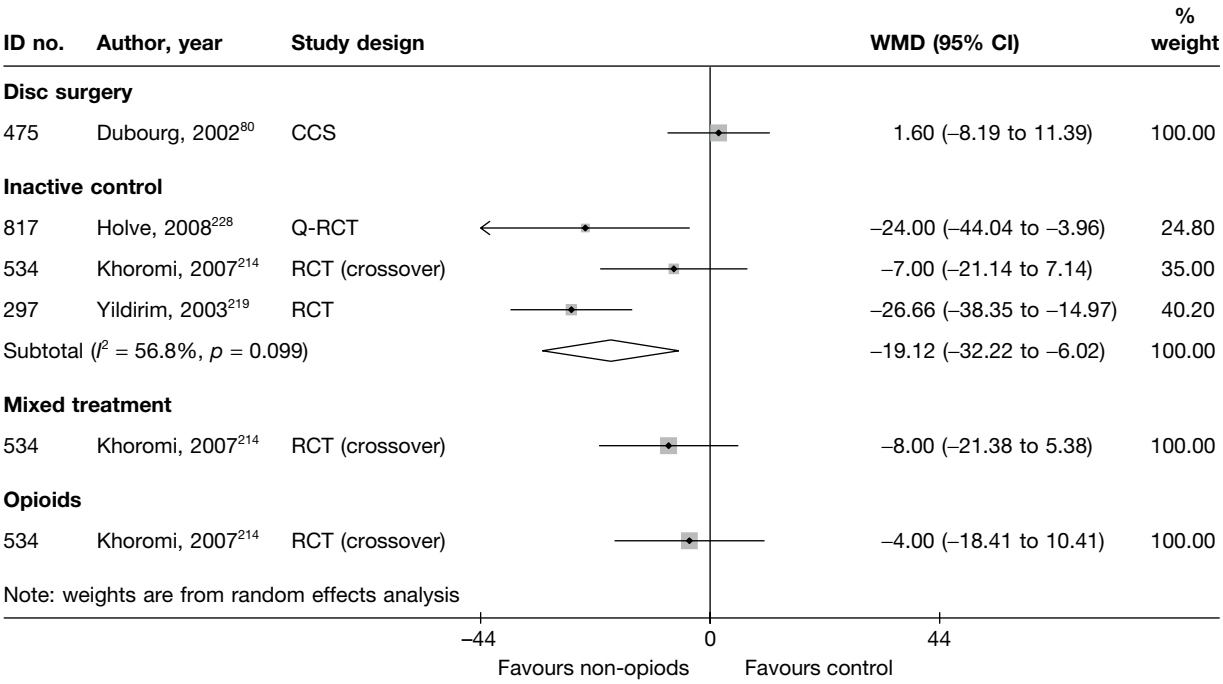

FIGURE 38 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

and epidural injections, opioids and mixed treatments. One study[228] included patients with acute sciatica and two studies[143,214] included patients with either acute or chronic sciatica. The duration of follow-up ranged from 9 weeks[214] to 6 months.[228]

Pooled analysis of two studies showed a non-statistically significant finding in favour of non-opioids at 2[214]–6[228] months, when compared with inactive control. One study was a moderate-quality, four-arm crossover RCT[214] with adequate randomisation and allocation concealment but only 44% of patients were included in the analysis. The second study was a Q-RCT.[228] Patients were sequentially entered into the study by the pharmacy department, with odd-numbered patients given prednisone and even-numbered patients given the placebo. The principal investigator and research nurse were blind to the specific group allocation and to the methods used to make that assignment.

One moderate-quality RCT[143] reported non-statistically significant findings in favour of epidural compared with non-opioids for improving functional status at 3 months' follow-up. The methods of randomisation and allocation concealment were not stated.

A moderate-quality, crossover RCT[214] compared non-opioids with opioids or a combination of opioids and non-opioids (mixed treatments). There was no statistically significant difference between the intervention groups for either comparison.

Results at long-term follow-up (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 54* and the accompanying forest plot (*Figure 40*).

One study[215] compared the overall success of the use of non-opioids or warming acupuncture in patients with chronic sciatic at 1 year's follow-up. The study was a poorly conducted RCT

TABLE 53 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID No.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Non-opioids vs epidural/intradiscal injection															
20	Dincer, 2007[143]	A+C	RCT	3 months	ODI	30	34	28.4 (5.4)	35.8 (6.7)	20.3 (10.1)	16.2 (9.4)	–8.1	–19.6	0.42 (–0.08 to 0.92)	Final SD imputed from weighted mean of SDs for RMDQ at short-term follow-up Dropouts 2/29 (7%): intervention 2/15, control 0/14
Non-opioids vs inactive control															
817	Holve, 2008[228]	A	Q-RCT	6 months	RMDQ	13	14	16	16	1.1 (4.6)	2.1 (4.47)			–0.22 (–0.98 to 0.54)	
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	ODI	28	28	30 (15)	30 (15)	27.5 (16.7)	30.5 (15.9)			0.18 (–0.71 to 0.34)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Non-opioids vs mixed treatment															
534	Khoromi, 2007[214]	C	RCT (crossover)	9-weeks (end of treatment)	ODI	28	28	30 (15)	30 (15)	27.5 (16.7)	27.4 (15.4)			0.01 (–0.52 to 0.53)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Non-opioids vs opioids															
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	ODI	28	28	30 (15)	30 (15)	27.5 (16.7)	25.7 (16.5)			0.11 (–0.42 to 0.63)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

A, acute; A+C, acute and chronic; C, chronic.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

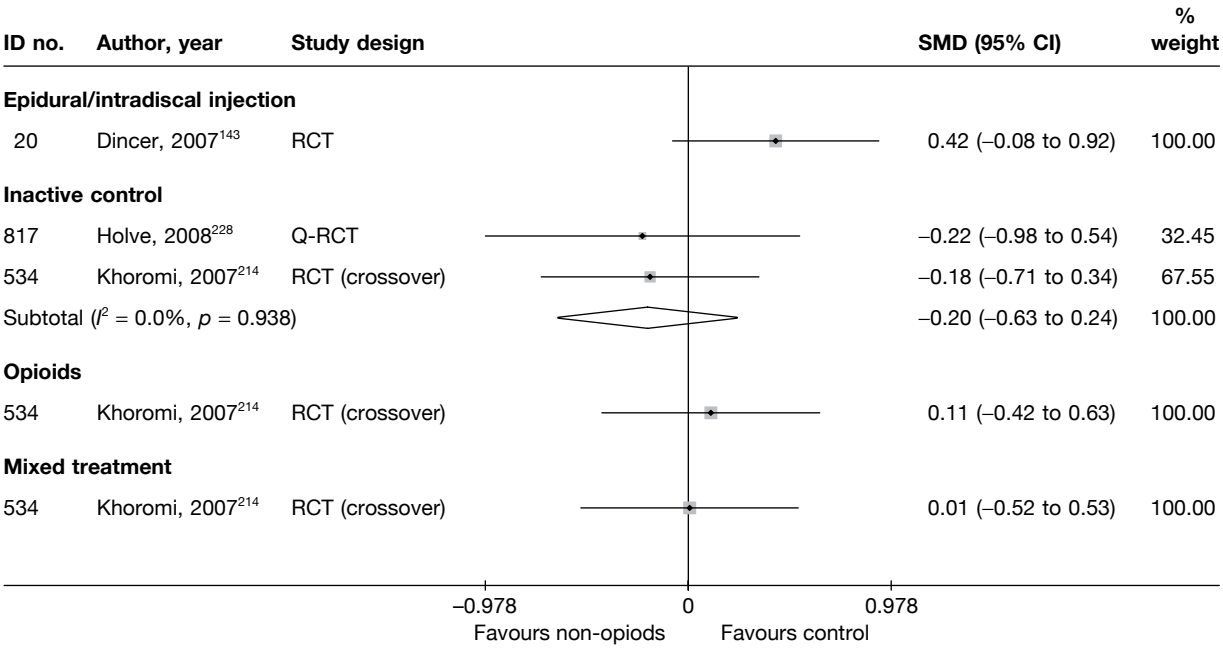

FIGURE 39 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

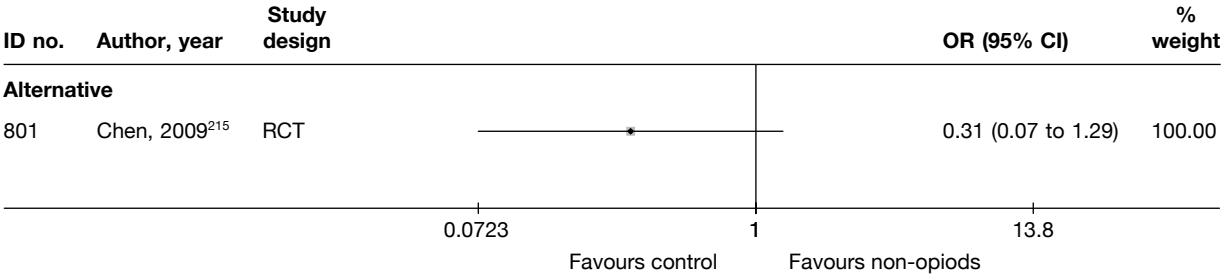

FIGURE 40 Summary of the findings of the global effect at long-term follow-up (>6 months) for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

and found a non-statistically significant difference between the intervention groups, in favour of acupuncture.

Pain intensity at long-term follow-up

No study reported long-term outcome in terms of pain intensity.

Condition-specific outcome measures at long-term follow-up

No study reported long-term outcome in terms of CSOMs.

Analysis of adverse effects for non-opioids

The results for the occurrence of any reported adverse effects are presented in *Table 55* and the accompanying forest plot (*Figure 41*).

The incidence of adverse effects associated with non-opioids was statistically significantly greater than the incidence of adverse events associated with inactive control and significantly lower than the incidence of adverse events associated with mixed treatments (opioids plus non-opioids). Pooled analyses showed no statistically significant differences between the intervention groups for the number of adverse effects when comparing non-opioids with disc surgery, epidural, mixed treatments (morphine plus nortriptyline) or opioids.

TABLE 54 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing non-opioids to alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Non-opioid vs alternative														
801	Chen, 2009[215] (i)[a] (WAG)	C	RCT	1 year	Success: cured or improved (vs no improvement)	Patient	30	22	0	30	27	0	0.31 (0.07 to 1.29)	Data inferred from graphs reporting percentages ITT using worst-case analysis (with non-opioids as the control group)
801	Chen, 2009[215] (ii)[a] (PIG)	C	RCT	1 year	Success: cured or improved (vs no improvement)	Patient	30	22	0	30	19	0	1.59 (0.53 to 4.77)	Data inferred from graphs reporting percentages ITT using worst-case analysis (with non-opioids as the control group)

C, chronic.

a Chen *et al.*[215] included three treatment groups: point injections of anisodamine (2 mg) into acupoints (point injection group) (ii), warming acupuncture group with needles warmed by burning moxa (warming acupuncture group) (i) and western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (western medicine group) (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 40*).

TABLE 55 Summary of the findings of any adverse effect for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Non-opioids vs alternative treatment							
801	Chen, 2009[215] (warming acupuncture)	RCT	NR	NR	NR	NR	
801	Chen, 2009[215] [anisodamine (2 mg) point injections]	RCT	NR	NR	NR	NR	
Non-opioids vs biological agent							
323	Genevay, 2004[216]	HCS	NR	NR	NR	NR	
Non-opioids vs disc surgery							
475	Dubourg, 2002[80]	CCS	0	28	1	39	0.45 (0.02 to 11.46)
144	Rossi, 1993[57] (microdiscectomy)	RCT	1	NR	0	NR	
144	Rossi, 1993[57] (percutaneous discectomy)	RCT	1	NR	0	NR	
Non-opioids vs epidural							
451	Bronfort, 2000[161]	RCT	4	6	6	6	0.14 (0.01 to 3.63)
20	Dincer, 2007[143]	RCT	0	30	2	34	0.21 (0.01 to 4.62)
771	Lafuma, 1997[172]	RCT	NR	NR	NR	NR	
362	Wilson-MacDonald, 2005[156]	RCT	NR	NR	NR	NR	
846	Murata, 2009[175]	RCT	NR	NR	NR	NR	
Non-opioids vs inactive control							
696	Dreiser, 2001[223] (low dose)	RCT	10	171	9	180	1.18 (0.47 to 2.98)
696	Dreiser, 2001[223] (high dose)	RCT	13	181	9	180	1.47 (0.61 to 3.53)
334	El-Zahaar, 1995[221]	RCT	3	50	0	50	7.44 (0.37 to 148.00)
728	Finckh, 2006[224]	RCT	3	31	0	29	7.25 (0.36 to 147.00)
62	Gibson, 1975[217]	Non-RCT	NR	NR	NR	NR	
97	Goldie, 1968[218]	RCT	8	25	5	25	1.88 (0.52 to 6.84)
732	Grevsten, 1975[225]	RCT	3	18	4	18	0.70 (0.13 to 3.70)
312	Hedeboe, 1982[220]	RCT	6	19	1	20	8.77 (0.94 to 81.70)
816	Herrmann, 2009[227]	RCT	11	57	7	57	1.71 (0.61 to 4.78)
816	Herrmann, 2009[227] (diclofenac)	RCT	6	57	7	57	0.84 (0.26 to 2.68)
817	Holve, 2008[228]	Q-RCT	0	15	0	14	
736	Jacobs, 1968[226]	Q-RCT	28	55	20	55	1.81 (0.85 to 3.89)
534	Khoromi, 2007[214]	RCT (crossover)	37	55	28	55	1.98 (0.92 to 4.29)
611	Porsman, 1979[222]	RCT	1	25	1	24	0.96 (0.06 to 16.24)
665	Weber, 1993[6]	RCT	22	120	13	94	1.4 (0.66 to 2.95)
297	Yildirim, 2003[219]	RCT	2	23	0	20	4.77 (0.22 to 105.00)

TABLE 55 Summary of the findings of any adverse effect for studies comparing non-opioids with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Non-opioids vs manipulation							
451	Bronfort, 2000[161]	RCT	4	6	3	7	2.67 (0.28 to 25.64)
Non-opioids vs opioids							
534	Khoromi, 2007[214]	RCT (crossover)	37	55	51	55	0.16 (0.05 to 0.52)
368	Kwasucki, 2002[229] (fluvoxamine)	RCT	2	24	1	22	1.91 (0.16 to 22.66)
368	Kwasucki, 2002[229] (imipramine)	RCT	12	24	1	22	21.00 (2.42 to 182.00)
547	Kwasucki, 1993[230]	RCT	NR	NR	NR	NR	NR
Non-opioids vs mixed treatment							
534	Khoromi, 2007[214]	RCT (crossover)	37	55	49	55	0.25 (0.09 to 0.70)

NR, not reported.

SUMMARY OF OVERALL FINDINGS FOR NON-OPIOIDS COMPARED WITH ALTERNATIVE INTERVENTIONS

Almost half (9/22,[6,80,216,218,220,223,224,227,228] 41%) of the non-opioid studies included patients with acute sciatica; 27% (6/22[57,175,214,215,219,221]) included patients with chronic sciatica. Most of the non-opioid studies (77%) were RCTs. None of the studies was deemed good quality overall; although two[214,227] included adequate randomisation and allocation concealment, one[214] of these studies had a high dropout rate. Both compared non-opioids with inactive control (one also included comparisons with opioids and mixed treatments[214]) (*Table 56*).

Non-opioids resulted in a statistically significant greater proportion of patients who recovered at short term follow-up than inactive control (eight RCTs[218,220–225,227] and one non-RCT[217]). Non-opioids were also significantly better than inactive control for reducing pain intensity of acute (three RCTs[223,224,227] and one Q-RCT,[228] all moderate quality) and chronic sciatica (one poor-quality RCT[219]) at short-term follow-up. However, there were no statistically significant difference between the intervention groups in terms of functional status (one RCT[6] and one Q-RCT[228]) during the same follow-up period. Non-opioids were significantly better than inactive control for reducing pain intensity of acute (one moderate-quality Q-RCT[228]) and chronic sciatica (one poor-quality RCT[219] and one moderate-quality crossover RCT[214]) at medium-term follow-up. There was no statistically significant difference between the intervention groups in terms of the proportion of patients who recovered (two moderate-quality RCTs[214,220]) or functional status (one moderate-quality Q-RCT[228] and one moderate-quality crossover RCT[214]) at medium-term follow-up. Non-opioids resulted in significantly more adverse effects than inactive control.[6,214,217–227]

There was no statistically significant difference between non-opioids and disc surgery for global effect (one non-RCT[57] and one CCS[80]) and pain intensity (one CCS[80]) at medium-term follow-up or for adverse effects, according to two poor-quality studies.[57,80]

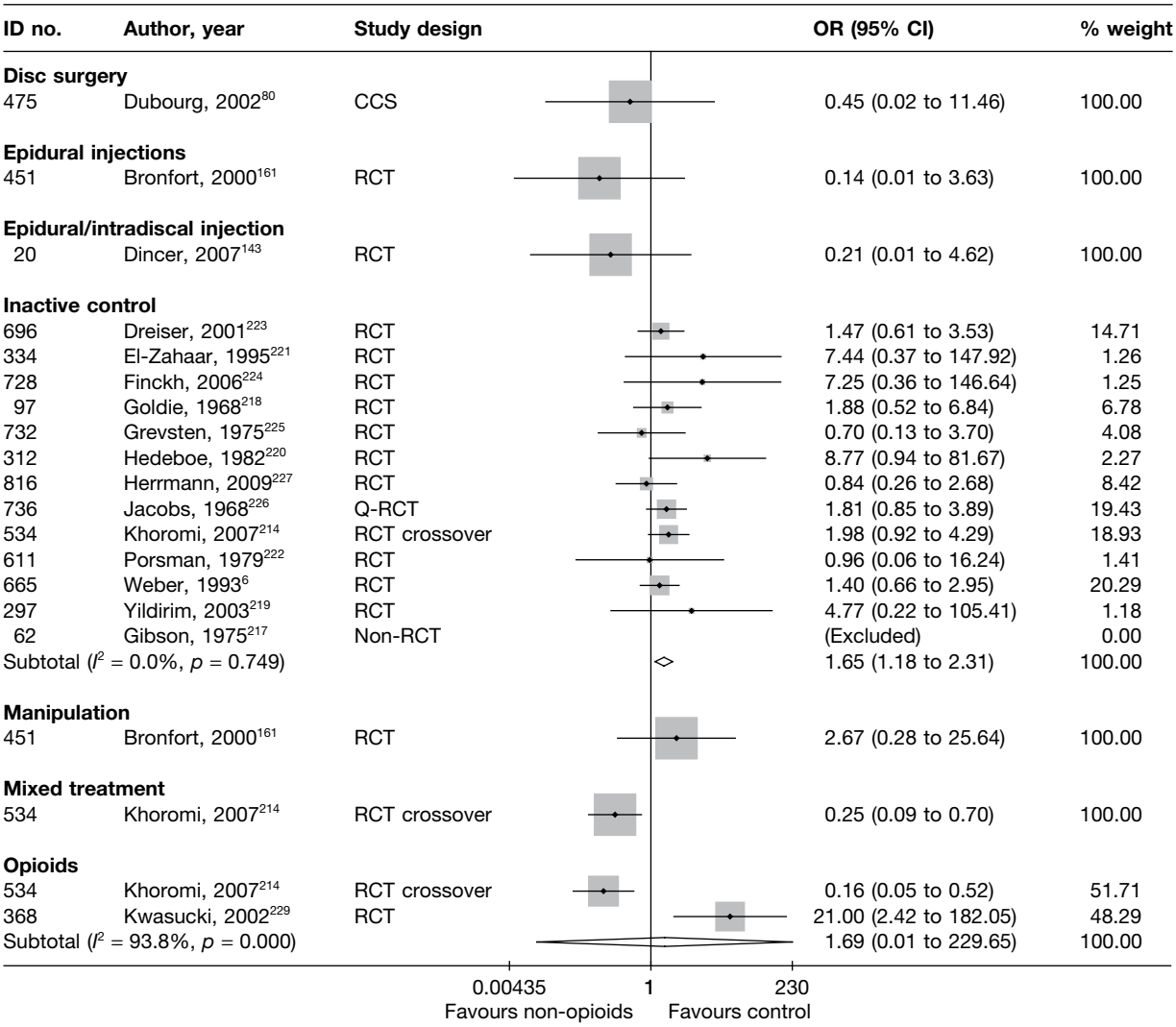

FIGURE 41 Summary of the findings of any adverse effect for studies comparing non-opioids with alternative interventions. Note: weights are from random effects analysis.

Non-opioids were less effective than epidural for reducing pain[143,156,175] and improving functional status[143] at short-term follow-up according to three poorly reported RCTs. There was no statistically significant difference between non-opioids and epidural for functional status at medium-term follow-up (RCT[143]).

Non-opioids were found to be statistically significantly better than opioids for reducing pain intensity at short-term follow-up,[229,230] but there was no significant difference between the intervention groups for global effect[229,230] or adverse effects (two poor-quality RCTs[214,229]).

One poor-quality RCT[215] found non-opioids to be significantly better than warming acupuncture for reducing pain intensity of chronic sciatica at short-term follow-up, but there was no significant difference between the intervention groups for the global effect at long-term follow-up.

One small historical CCS[216] found biological agents to be to be significantly better than non-opioids for reducing pain intensity and functional status at short-term follow-up.

TABLE 56 Summary of non-opioid studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Non-opioids vs alternative/non-traditional	1 (2)	90 (90)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Non-opioids vs biological agents	1 (1)	10 (10)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Non-opioids vs disc surgery	2 (3)	40–67 (54)	1/2 (50)	0/2 (0)	0/2 (0)	2/2 (100)	2/2 (100)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)
Non-opioids vs intradiscal injection	3 (3)	64–246 (93)	3/3 (100)	0/3 (0)	0/3 (0)	3/3 (100)	2/3 (67)	1/3 (33)	0/3 (0)	0/3 (0)	1/3 (33)	1/3 (33)
Non-opioids vs inactive control	13 (14)	29–532 (55)	10/13 (77)	1/13 (8)	8/13 (62)	13/13 (100)	4/13 (31)	0/13 (0)	0/13 (0)	1/13 (8)	5/13 (38)	0/13 (0)
Non-opioids vs mixed treatment	1 (1)	55 (55)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Non-opioids vs opioids	3 (4)	43–70 (55)	2/3 (67)	0/3 (0)	0/3 (0)	3/3 (100)	2/3 (67)	1/3 (33)	0/3 (0)	0/3 (0)	2/3 (67)	0/3 (0)
Total (for non-opioid studies)[a]	**22 (29)**	**10–532 (38)**	**17/22 (77)**	**0/22 (0)**	**9/22 (41)**	**22/22 (100)**	**9/22 (41)**	**2/22 (9)**	**0/22 (0)**	**1/22 (5)**	**8/22 (36)**	**2/22 (9)**

a These numbers are based on number of studies not the number of arms as above (e.g. study 534[214] includes three comparators, but has been counted only once here).
This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Traction

Description of traction studies

Summary of interventions

Twelve studies evaluated traction for sciatica.[176,242–252] Ten of these studies compared traction to an alternative intervention (three were multiple-arm studies).[176,242–250] One further study compared mixed treatment that included traction, with mixed treatments or with other comparators without traction (*Table 57a*).[253–256]

Three studies compared different types of traction (*Table 57b*).[248,251,252]

Summary of study participants for traction

Summary data for included participants are presented in *Table 58.* The number of participants included in the 10 studies that reported outcome data for global, pain or CSOMs ranged from 16 to 157 (median 60 participants). Five studies[176,243,245,246,249] (45%) included patients with acute sciatica, one study[242] (9%) included patients with chronic sciatica, one study[247] included patients with either acute or chronic sciatica and the remaining three studies[244,248,250] did not report this information. None of the studies included patients with spinal stenosis or sequestered or extruded discs. The diagnosis of sciatica, or the presence of herniated disc, was confirmed by imaging in four studies (40%). Two studies[243,246] included a mixture of patients with either recurrent or first episode of sciatica, whereas the remaining studies did not report this information. Two studies (one in which the comparator was activity restriction[243] and one in which the comparator was inactive control[247]) included patients who had already received previous treatment for their current episode of sciatica. This information was not stated for the remaining studies. One study,[243] which compared traction with activity restriction, included patients who had received previous disc surgery.

Summary of study quality for traction studies

Summary information on study details are presented in *Table 59.* Most of the traction studies were RCTs (9/10, 90%), but none was deemed to be good quality overall. Seven studies[176,242,243,245,246,248,249] were of moderate quality. Three studies[243,245,248] used adequate randomisation, but not allocation concealment, although two[243,245] used sealed envelopes. One study[243] had strong external validity.

Traction results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 60* and the accompanying forest plot (*Figure 42*). Traction was compared with inactive control, usual care/conservative treatment, activity restriction, exercise therapy and passive PT. Only one study[242] included patients with chronic sciatica; four studies[176,243,245,246] included patients with acute sciatica and the remaining study[250] did not report this information. The duration of follow-up ranged from 1 week[242] to 4 weeks.[245] Three further studies[254–256] combined the use of mixed treatments that incorporated traction with an alternative treatment.

Pooled analysis of two moderate-quality RCTs[245,246] showed non-statistically significant difference in favour of traction, compared with inactive control, for overall recovery from acute sciatica at 3 weeks[246] to 4 weeks.[245]

One poorly reported non-RCT[250] found a non-statistically significant difference in favour of pulse traction, compared with conservative treatment without traction, for overall improvement at 3 weeks. All patients were in bed for at least 18 hours a day in a position taking the strain off

TABLE 57a Summary of the interventions used when comparing traction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Treatment description	Control description
Traction vs activity restriction				
222	Moret, 1998[243]	RCT	Bed rest and traction (vertical traction using patient weight), 180 minutes daily for 1–2 weeks	Bed rest
Traction vs exercise therapy				
2	Ljunggren, 1992[242]	RCT	Manual traction	Isometric exercises
Traction vs inactive control				
553	Larsson, 1980[246]	RCT	Auto-traction, three treatments	Inactive corset
579	Mathews, 1975[247]	RCT	Traction (full traction) 5 days per week for 3 weeks	Sham traction (minimal traction) 5 days per week for 3 weeks
206	Pal, 1986[244]	RCT	Weighted traction: continuous lumbar traction of 5.5–8.2 kg according to body weight	Sham traction: continuous lumbar traction of 1.4–1.8 kg according to body weight
299	Rattanatharn, 2004[245]	RCT	Traction three times per week Traction force of 35–50% of the body weight performed intermittently	Sham traction three times per week Traction force of < 20% of body weight performed intermittently
746	Reust, 1988[248] (French language)	RCT	Normal traction (50 kg)	Placebo traction (5 kg)
746	Reust, 1988[248] (French language)	RCT	Light traction (15 kg)	Placebo traction (5 kg)
Traction vs passive PT				
9059	Mathews, 1987[176]	RCT	Lumbar traction of at least 45 kg, but sufficient to relieve pain sustained for 30 minutes	Control treatment. Infrared heat treatment to the low back area at 60 cm for 15 minutes, three times per week
148	Unlu, 2008[249]	RCT	Lumbar traction	Ultrasound treatment
148	Unlu, 2008[249]	RCT	Lumbar traction	Low-power laser
Traction vs usual/conventional care				
77	Styczynski, 1991[250] (Polish language)	Non-RCT	Antigravitational traction. Up to 15 treatments, mean 12.3	Conservative treatment without traction Up to 15 treatment sessions, mean 12.0
77	Styczynski, 1991[257] (Polish language)	Non-RCT	Chair traction. Up to 15 treatments, mean 11.7	Conservative treatment without traction Up to 15 treatment sessions, mean 12.0
77	Styczynski, 1991[257] (Polish language)	Non-RCT	Pulse traction. Up to 15 treatments, mean 11.3	Conservative treatment without traction Up to 15 treatment sessions, mean 12.0
Mixed treatment including traction vs mixed treatment without traction				
301	Harte, 2007[254]	RCT	Traction and/or manual therapy, exercise and/or advice to stay active	Manual therapy, exercise and/or advice to stay active

TABLE 57b Summary of the interventions used when comparing alternative forms of traction

ID no.	Author, year	Study design	Treatment description	Control description
161	Guvenol, 2000[251]	RCT	Conventional traction	Inverted traction
569	Ljunggren, 1984[252]	RCT	Autotraction	Manual traction
746	Reust, 1988[248] (French language)	RCT	Normal traction (50 kg)	Light traction (15 kg)

TABLE 58 Summary of sciatica type and study population details for studies comparing traction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Traction vs activity restriction													
222	Moret, 1998[243]	RCT	16	Mean 41.9 (SD 8.7)	12 (75)	Acute symptoms 50%	Nerve root pain	No	Recurrent and first episode	No	NR	Yes	Yes
Traction vs exercise therapy													
570	Ljunggren, 1992[242]	RCT	50	Mean 41.6 (range 19–62)	27 (54)	Mean 5 months	Nerve root pain	Yes	NR	No	No	NR	No
Traction vs inactive control													
553	Larsson, 1980[246]	RCT	84	Mean 37 (range 20–55)	51 (62)	Mean 6.7 weeks (range 2–14 weeks)	Nerve root pain	No	Recurrent and first episode	No	No	NR	NR
579	Mathews, 1975[247]	RCT	27	Range 20–60	NR	Mean 13 weeks	Nerve root pain and refereed pain	No	NR	No	No	Yes	NR
206	Pal, 1986[244]	RCT	41	Mean 39	23 (59)	Median 49 days	Nerve root pain and referred pain	NR	NR	No	No	NR	NR
299	Rattanatharn, 2004[245]	RCT	120	Mean 37.3	47 (46)	< 3 months	Nerve root pain	No	NR	No	No	Yes	No
746	Reust, 1988[248] (French language)	RCT	60	Mean 50.8 (SD 12.5)	35 (58)	NR	Nerve root pain and referred pain	No	NR	No	No	NR	NR

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Traction vs passive PT													
9059	Mathews, 1987[176]	RCT	143	Median 40 (range 20–60)	80 (56)	Median 3.5 weeks (range 0 days–3 months)	Nerve root pain	No	NR	NR	NR	NR	NR
148	Unlu, 2008[249]	RCT	60	Mean 44.5 (range 20–60)	18 (30)	< 3 months	Nerve root pain	Yes	NR	No	No	NR	No
Traction vs usual/conventional care													
77	Styczynski, 1991[250] (Polish language)	Non-RCT	157	Range 18–67	84 (54)	NR	Nerve root pain	Yes	NR	NR	NR	NR	NR
Mixed treatment including traction vs mixed treatment without traction													
301	Harte, 2007[254]	RCT	64	Mean 41.1 (SD 9.8)	28 (44)	Median 47.5 days (range 2–671 days)	Nerve root pain	No	Recurrent and first episode	No	No	Yes	Yes

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 59 Summary of the study details for studies comparing traction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Traction vs activity restriction										
222	Moret, 1998[243]	16	3 weeks	RCT	Yes	Partial	80–100	No	Moderate	Strong
Traction vs active PT/exercise therapy										
570	Ljunggren, 1992[242]	50	1 week	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
Traction vs inactive control										
553	Larsson, 1980[246]	84	3 months	RCT	Unclear	Unclear	80–100	Unclear	Moderate	Weak
579	Mathews, 1975[247]	27	3 months	RCT	Unclear	Unclear	Cannot tell	Unclear	Weak	Weak
206	Pal, 1986[244]	41	2 years	RCT	Unclear	Unclear	80–100	Yes	Weak	Weak
299	Rattanatharn, 2004[245]	120	4 weeks	RCT	Yes	Partial	60–79	NA	Moderate	Weak
746	Reust, 1988[248] (French language)	60	12 days	RCT	Yes	Unclear	<60	Yes	Moderate	Weak
Traction vs passive PT										
9059	Mathews, 1987[176]	143	12 months	RCT	Partial	Unclear	<60	Yes	Moderate	Moderate
148	Unlu, 2008[249]	60	3 months	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
Traction vs usual/conventional care										
77	Styczynski, 1991[250] (Polish language)	157	After treatment	Non-RCT	No	No	80–100	Unclear	Weak	Weak
Mixed treatment including traction vs mixed treatment without traction										
301	Harte, 2007[254]	30	6 months	RCT	Yes	Partial	60–79	Yes	Moderate	Strong

TABLE 60 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing traction with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
Traction vs activity restriction														
222	Moret, 1998[243]	A	RCT	3 weeks	Leg pain: recovered or strongly improved (vs little improved, no change, little worse, much worse or worse than ever)	Patient	8	4	0	8	4	0	1.00 (0.14 to 7.10)	
Traction vs exercise therapy														
570	Ljunggren, 1992[242]	C	RCT	1 week	Global evaluation: symptom-free or satisfactory improvement (vs unsatisfactory improvement or unchanged)	Physician	24	10	0	26	10	0	1.14 (0.37 to 3.55)	
Traction vs inactive control														
553	Larsson, 1980[246]	A	RCT	3 weeks	Completely recovered: free from back or leg pain (vs partially recovered 1 = no leg pain, partially recovered 2 = no back pain or no recovery)		41	7	0.05	41	3	0	2.61 (0.62 to 10.89)	
299	Rattanatharn, 2004[245]	A	RCT	4 weeks	Global improvement: complete recovery or much improved (vs little improved/unchanged or little/much worse)	Patient	54	38	0.10	48	34	0.20	0.98 (0.42 to 2.30)	

continued

TABLE 60 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing traction with alternative interventions (grouped by comparator then ordered by author) *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Traction vs passive PT														
9059	Mathews, 1987[176]	A	RCT	2 weeks	Recovered: pain score of 5 or 6 (vs not recovered = scores of 1–4)		77	40	0.07	54	27	0.10	1.08 (0.54 to 2.17)	Number of dropouts reported was different from the number missing from the analysis
Traction vs usual/conventional care														
77	Styczynski, 1991[250] (i) (antigravity)[a]	NR	Non-RCT	3 weeks	Overall improvement		38	26	0.10	29	17	0.03	1.53 (0.56 to 4.19)	
77	Styczynski, 1991[250] (ii) (chair)[a]	NR	Non-RCT	3 weeks	Overall improvement		41	28	0.05	29	17	0.03	1.52 (0.57 to 4.09)	
77	Styczynski, 1991[250] (iii) (pulse)[a]	NR	Non-RCT	3 weeks	Overall improvement		41	28	0.02	29	17	0.03	1.52 (0.57 to 4.09)	
Mixed treatment including traction vs mixed treatment without traction														
301	Harte, 2007[254]	A	RCT	Post-treatment	Median percentage overall improvement	Patient	16	Median 90% (IQR 24)	0.13	4	Median 90% (IQR 22.5) LT	0.14		ITT not used for dichotomous outcome Percentage improvement reported, not number of patients who improved

A, acute; A+C, acute and chronic; C, chronic; NR, not reported.

a Styczynski *et al.*[250] included four treatment groups: antigravitational traction (i), chair traction (ii), pulse traction (iiii) and conservative treatment without traction (iv). In order to prevent using the same comparator twice, only the first (i) and last (iv) treatment groups have been included in the meta-analysis (see *Figure 42*).

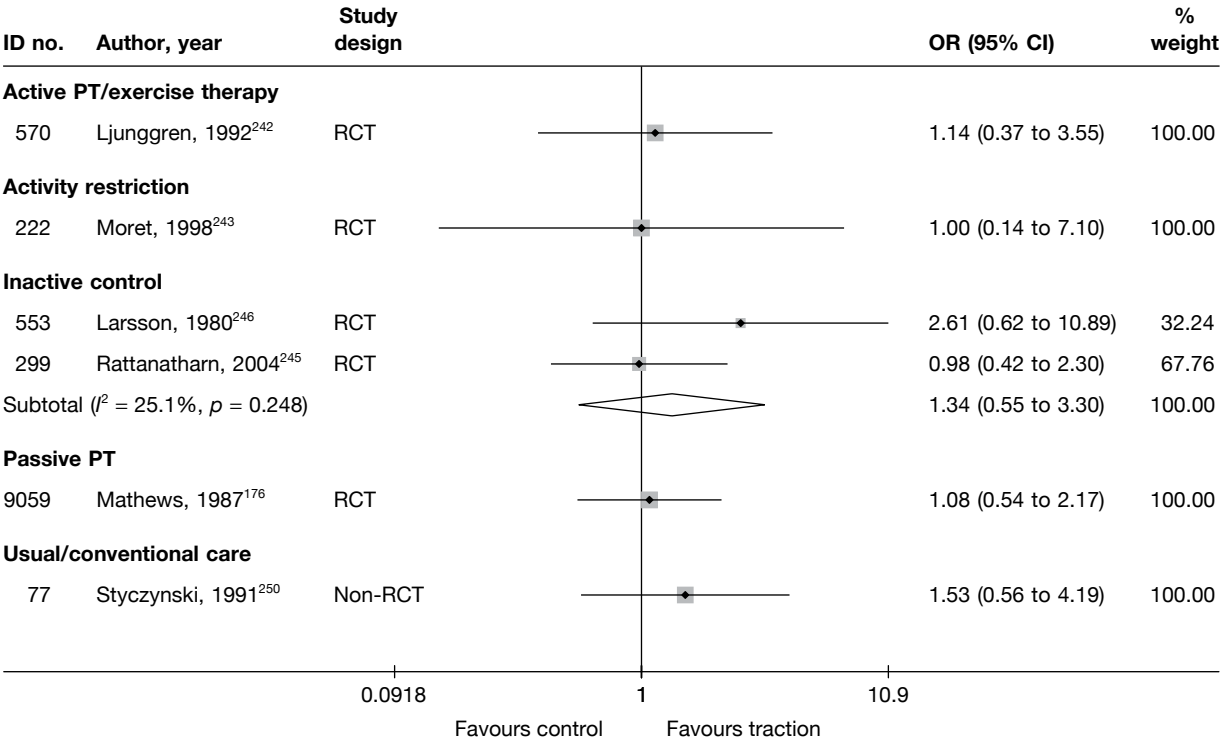

FIGURE 42 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

with legs bent at hips and knees for 3 weeks, and undertaking isometric exercises to strengthen muscles around the spine, hips, abdomen and limbs.

One small (n = 16), moderate-quality RCT[243] found no statistically significant difference between vertical traction using patient weight plus bed rest and bed rest alone (activity restriction) in terms of the proportion of patients with improvement in leg pain for acute sciatica at 3 weeks. Twelve patients (75%) were hospitalised.

One RCT[242] found no statistically significant difference between manual traction and isometric exercise (active PT) for overall improvement of chronic sciatica at 1 week. All patients were hospital inpatients and used crutches and elastic lumbar supports for any necessary out-of-bed activities. The study was of moderate quality, but the method of randomisation and allocation concealment was not stated.

One moderate-quality RCT[176] found no important difference between traction and infrared heat treatment (passive PT) for overall recovery from acute sciatica at 2 weeks. Patients were also given paracetamol to take when necessary and offered a corset. All patients attended a special outpatients clinic.

One small, moderate-quality, pilot RCT[254] reported the same median percentage improvement, as perceived by the patient, for mixed treatment (manual therapy, exercise and advice) with or without traction.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 61* and the accompanying forest plot (*Figure 43*). Traction was compared with inactive control, activity

TABLE 61 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing traction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Traction vs passive PT																
148	Unlu, 2008[249] (i)[d] (ultrasound)	A	RCT	1 month	Leg	VAS (0–100)	20	20	59.6 (15.4)	56 (15.3)	21.8 (15.4)	26.8 (18.36)			–5.00 (–15.58 to 5.58)	
148	Unlu, 2008[249] (ii)[d] (laser)	A	RCT	1 month	Leg	VAS (0–100)	20	20	59.6 (15.4)	53.1 (25.9)	21.8 (15.4)	25.6 (21.1)			–3.80 (–15.25 to 7.65)	
Traction vs inactive control																
206	Pal, 1986[244]	NR	RCT	3 weeks	Overall	VAS (0–100)	24	15	50	50	5	3			2.00 (–11.68 to 15.68)	Median used for mean; SD imputed from weighted average
746	Reust, 1988[248] (i)[e] (French language) (50 kg)	NR	RCT	12 days	Overall	VAS (0–100)	18	20	75.28 (23.85)	61.5 (23.63)	33.61 (29.55)	30.25 (26.23)			3.36 (–14.49 to 21.21)	ITT using LOCF Dropouts: intervention 3/18, control (placebo) 2/31
746	Reust, 1988[248] (ii)[e] (French language) (15 kg)	NR	RCT	12 days	Overall	VAS (0–100)	22	20	67.27 (23.74)	61.5 (23.63)	30.68 (26.83)	30.25 (26.23)			–0.43 (–15.63 to 16.49)	ITT using LOCF Dropouts: intervention 3/22, control (placebo) 2/31

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Traction vs activity restriction																
222	Moret, 1998[243]	A	RCT	3 weeks	Leg	NRS (0–10)	8	8	74 (12.0)	73 (10.0)	44 (12)	63 (10)	–30	–10	–19.00 (–29.82 to –8.18)	Final mean calculated from change score and baseline SD used
Mixed treatment including traction vs mixed treatment without traction																
301	Harte, 2007[254]	A	RCT	Post treatment	Overall	McGill	16	14	20.5 (6.67)	29 (14.81)	4 (11.33)	12 (12.22)	17.5 (9.48)	15.5 (19.11)	–8.00 (–16.47 to 0.47)	Small sample sizes Mean and SDs derived from median and IQR values ITT use LOCF Dropouts 3/30 (10%): intervention 2/16, control 1/14

A, acute; LOCF, last observation carried forward; NR, not reported; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the first (i) and last (iii) treatment groups have been included in the meta-analysis (see *Figure 43*).

e Reust *et al.*[248] included three treatment groups: light traction (15 kg) (ii), normal traction (50 kg) (i) and placebo traction (5 kg) (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 43*).

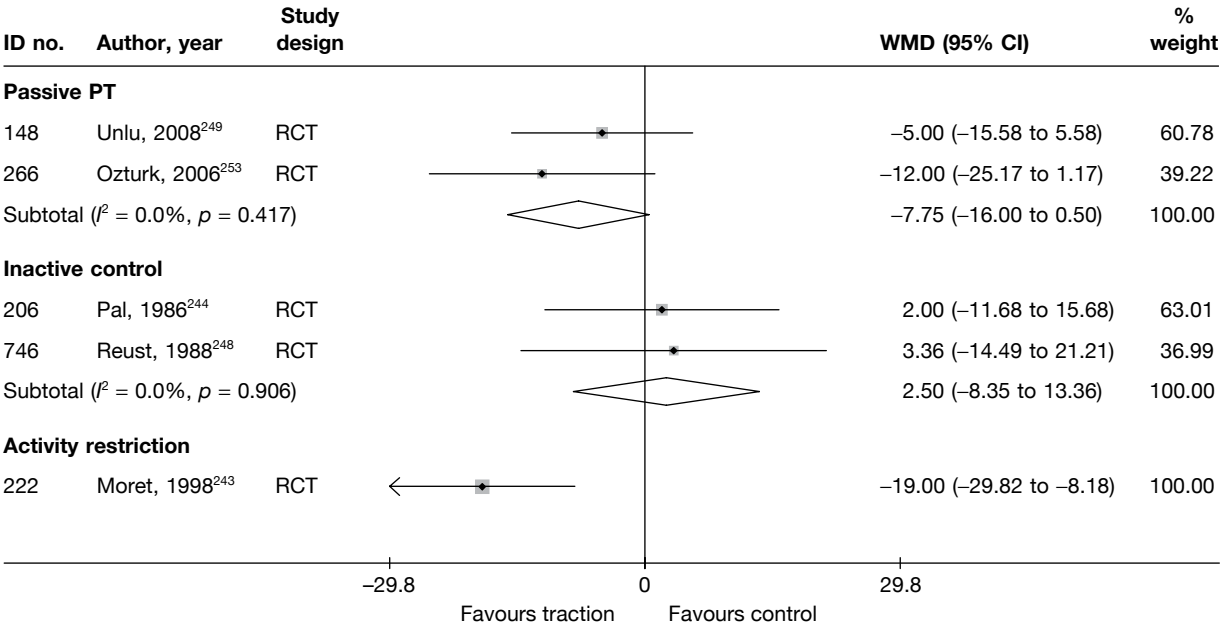

FIGURE 43 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

restriction and passive PT. Two studies[243,249] included patients with acute sciatica; the remaining two studies[244,248] did not report the duration of symptoms. The duration of follow-up ranged from 12 days[248] to 3 weeks.[243,244] Three further studies[253–255] compared the use of mixed treatments that incorporated traction with alternative interventions.

Two RCTs[247,248] compared the use of traction with inactive control; the pooled analysis showed a non-statistically significant difference in favour of inactive control for overall pain at 2 weeks[248] to 3 weeks.[244] The quality of the studies was poor in one case[244] and moderate in the other.[248] Only one of these used an adequate method of randomisation.[248] The method of randomisation was not stated in the second study and allocation concealment was not reported for either study. Inactive treatment included sham traction in both studies (1.4–1.8 kg according to body weight[244] or 20% of body weight[248]).

One small (n = 16), moderate-quality RCT[243] found vertical traction plus bed rest to be significantly better than bed rest alone (activity restriction) for reducing leg pain in patients with acute sciatica at 3 weeks. Twelve patients (75%) were hospitalised.

One moderate-quality RCT[249] compared the use of standard motorised traction with ultrasound (passive PT); there was an overall non-statistically significant finding in favour of ultrasound, for acute sciatica at 1 month. The method of randomisation and allocation concealment was not reported.

One small, moderate-quality pilot RCT[254] that compared manual exercise therapy, exercise and advice found that the traction combination resulted in a non-statistically significantly greater reduction in overall pain intensity that the control intervention.

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 62* and the accompanying forest plot (*Figure 44*). Traction was compared with inactive control, activity restriction and passive PT. All three studies[243,245,249] included patients with acute sciatica. The duration of

TABLE 62 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing traction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Traction vs activity restriction															
222	Moret, 1998[243]	A	RCT	3 weeks	RMDQ	8	8	18.1 (1.8)	18.5 (2.1)	14.5 (3.87)	17.1 (6.2)	–3.6	–1.4	–0.50 (–1.50 to 0.49)	Final mean calculated from change scores, final SD imputed from weighted mean of SDs from other studies
Traction vs inactive control															
299	Rattanatharn, 2004[245]	A	RCT	4 weeks	ODI	54	48	47.97 (15.32)	40.61 (13.94)	22.72 (18.61)	21.36 (17.27)	–25.25 (16.68)	–19.25 (15.9)	*ANCOVA for change scores showed no statistically significant difference,* p = *0.301* 0.08 (–0.31 to 0.46)	ITT not reported, no dropouts
Traction vs passive PT															
148	Unlu, 2008[249] (i)[c]	A	RCT	1 month	RMDQ	20	20	14.2 (4.3)	12.5 (5)	8.5 (3.5)	7.3 (4.3)	–5.7	–5.2	0.31 (–0.32 to 0.93)	
148	Unlu, 2008[249] (ii)[c]	A	RCT	1 month	RMDQ	20	20	14.2 (4.3)	13.4 (4.5)	8.5 (3.5)	8.2 (6)	–5.7	–5.2	0.06 (–0.56 to 0.68)	
Mixed treatment incorporating traction vs mixed treatment without traction															
301	Harte, 2007[254]	A	RCT	Post-treatment	RMDQ	16	14	10 (3.33)	11.5 (6.3)	4 (4.3)	4 (7.63)	–4.5 (5.41)	–3 (5.93)	0.0 (–0.72 to 0.72)	Medians used for means and SDs calculated from IQRs Small sample sizes – likely to be skewed ITT using LOCF

A, acute.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 44*).

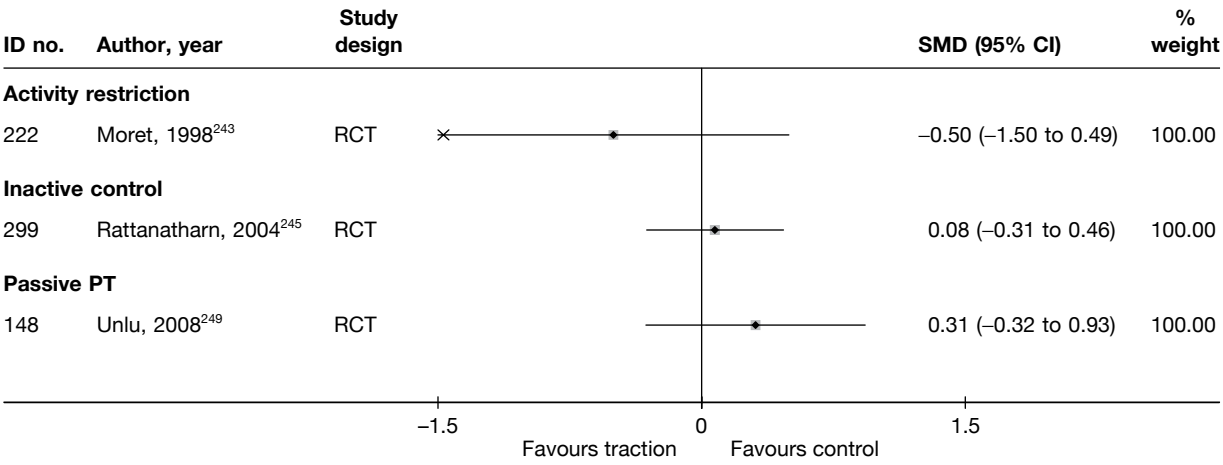

FIGURE 44 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

follow-up ranged from 12 days[248] to 3 weeks.[243,244] Two further studies[254,255] compared the use of mixed treatments that incorporated traction with alternative treatments.

One RCT,[245] of moderate quality, compared traction with inactive control and found a non-statistically significant difference, in favour of inactive control, in improved function in patients with acute sciatica at 4 weeks.

One small RCT,[243] of moderate quality, compared traction plus bed rest with bed rest alone (activity restriction) and found a non-statistically significant difference, in favour of traction, for improved function in patients with acute sciatica at 3 weeks.

One moderate-quality RCT[249] compared traction with ultrasound (passive PT); at 1 month, there was an overall non-statistically significant finding in favour of ultrasound for the treatment of acute sciatica. The methods of randomisation and allocation concealment were not reported.

One small, moderate-quality study[254] found no important difference between traction or no traction, with manual exercise therapy, exercise and advice for acute sciatica at treatment completion.

Traction results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 63* and the accompanying forest plot (*Figure 45*).

One moderate-quality RCT[246] compared the use of auto-traction with inactive control (inactive corset) in terms of the proportion of patients with acute sciatica who were symptom free at 3 months' follow-up. The methods of randomisation and allocation concealment used were not reported. There was a non-statistically significant difference between the groups in favour of inactive control. Most patients were treated as outpatients [20/84 (24%) were hospitalised] and patients in both groups were were supplied with a corset and advised to rest.

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 64* and the accompanying forest plot (*Figure 46*). Traction was compared with inactive control and passive

TABLE 63 Summary of the findings of the global effect at medium-term follow-up for studies comparing traction with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Traction vs inactive control														
553	Larsson, 1980[246]	A	RCT	3 months	Symptom free (vs persisting symptoms)		40	19	0.07	41	17	0	1.28 (0.53 to 3.07)	

A, acute.

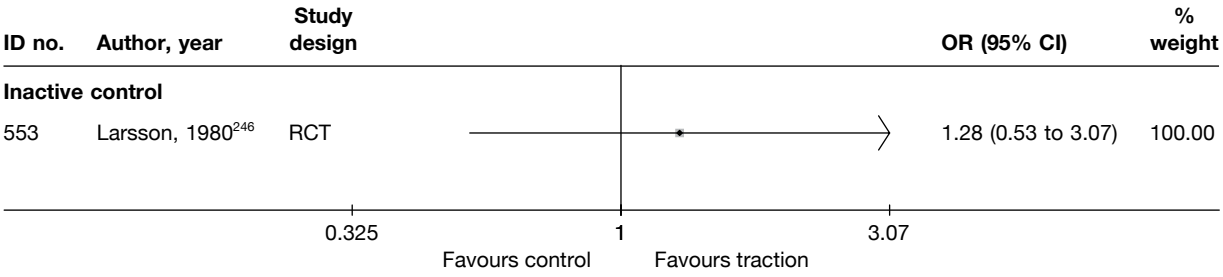

FIGURE 45 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

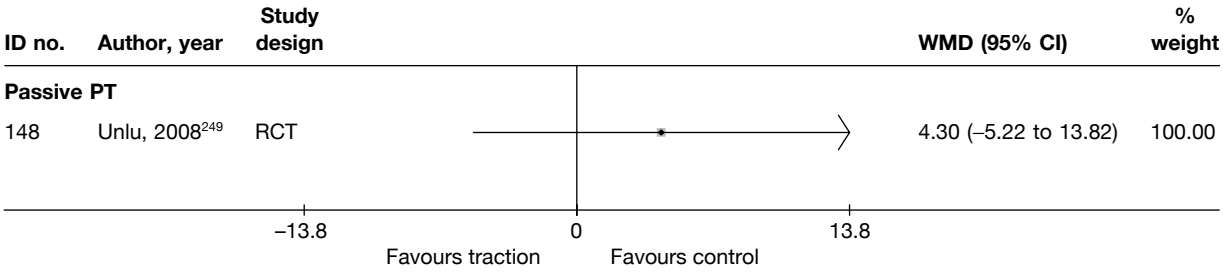

FIGURE 46 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

PT. One further study[254] compared the use of mixed treatments that incorporated traction with mixed treatments without traction for acute sciatica.

One small ($n = 27$), poor-quality and poorly reported RCT[247] compared traction with inactive control (sham traction using a maximum force of 9 kg). The study was published in 1975 and carried out by single physiotherapist. Patients were asked to judge by what percentage their pain had changed, assuming the level of pain at baseline to be 100%. The average improvement at 6 weeks was 28.8% in the traction group compared with 18.9% in the control group.

One moderate-quality RCT[249] compared traction with ultrasound (passive PT); at 3 months, there was a non-statistically significant improvement in acute sciatica, in favour of ultrasound. The methods of randomisation and allocation concealment were not reported.

One moderate-quality pilot study[254] compared the use of motorised lumbar traction combined with manual therapy, exercise and/or advice to stay active compared with manual therapy, exercise and/or advice to stay active without traction. There was no statistically significant difference between the intervention groups at 6 months' follow-up, but this may be due to the small sample size ($n = 30$).

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 65* and the accompanying forest plot (*Figure 47*). Traction was compared with passive PT for acute sciatica. One further study[254] compared the use of mixed treatments that incorporated traction with mixed treatments without traction for acute sciatica.

One moderate-quality RCT[249] compared traction with ultrasound (passive PT); at 3 months, there was an overall non-statistically significant improvement in acute sciatica, in favour of ultrasound.

TABLE 64 Summary of the findings of pain at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Traction vs passive PT																
148	Unlu, 2008[249] (i)[d] (ultrasound)	A	RCT	3 months	Leg	VAS (0–100)	20	20	59.6 (15.4)	56 (15.3)	29.5 (16.7)	25.2 (13.9)			4.30 (–5.22 to 13.82)	
148	Unlu, 2008[249] (ii)[d] (laser)	A	RCT	3 months	Leg	VAS (0–100)	20	20	59.6 (15.4)	53.1 (25.9)	29.5 (16.7)	23.6 (17.7)			5.90 (–4.76 to 16.56)	
Traction vs inactive control																
579	Mathews, 1975[247]	A + C	RCT	3 months	Overall	Improvement (0–100)	13	14					28.80	18.90		Average percentage improvement in pain since starting treatment All patients asked to judge by what percentage pain had changed assuming the level on entry to the trial to be 100%
Mixed treatment incorporating traction vs mixed treatment without traction																
301	Harte, 2007[254]	A	RCT	6 months	Overall	McGill	16	14	20.5 (6.67)	29 (14.8)	10 (15.9)	6.5 (15.56)	15.5 (12.81)	16.5 (22.81)	3.50 (–7.54 to 14.54)	Mean and SDs derived from median and IQR values

A, acute; A + C, acute and chronic.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the first and last treatment groups have been included in the meta-analysis (see *Figure 46*).

TABLE 65 Summary of the findings of CSOMs at medium-term follow-up (> 6 weeks to ≤ 6 months) for studies comparing disc surgery with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Traction (ultrasound) vs passive PT															
148	Unlu, 2008[249] (i)[c] (ultrasound)	A	RCT	3 months	RMDQ	20	20	14.2 (4.3)	12.5 (5)	8.9 (4)	6.7 (4.5)	–5.3	–5.8	0.52 (–0.11 to 1.15)	
148	Unlu, 2008[249] (ii)[c] (laser)	A	RCT	3 months	RMDQ	20	20	14.2 (4.3)	13.4 (4.5)	8.9 (4)	8.6 (6)	–5.3	–4.8	0.06 (–0.56 to 0.68)	
Mixed treatment incorporating manipulation vs mixed treatment without manipulation															
301	Harte, 2007[254]	A	RCT	6 months	RMDQ	16	14	10 (3.33)	11.5 (6.3)	4.5 (11.33)	11.5 (6.3)	–4 (9.11)	–3 (9.11)	–0.75 (–1.49 to –0.01)	IQR used to calculate SD, but small sample sizes – likely to be skewed ITT used LOCF

A, acute; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice only the first and last treatment groups have been included in the meta-analysis (see *Figure 47*).

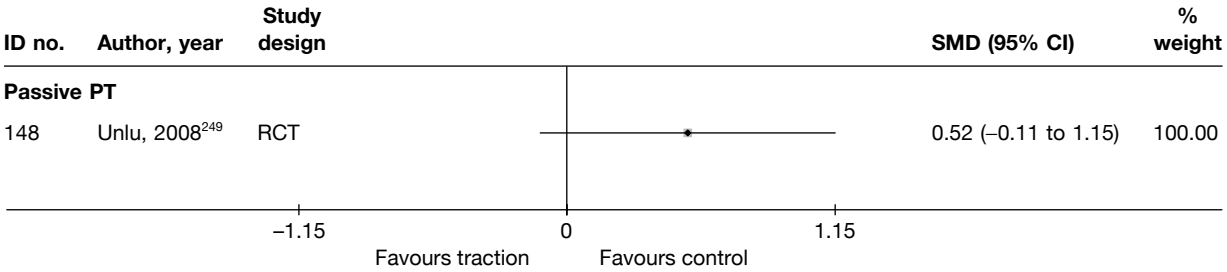

FIGURE 47 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

One moderate-quality pilot study[254] compared the use of motorised lumbar traction combined with manual therapy, exercise and/or advice to stay active with manual therapy, exercise and/or advice to stay active without traction. Improvement in functional status at 6 months' follow-up was marginally higher in the traction group and the difference was statistically significant.

Results at long-term follow-up (>6 months)

No long-term outcomes were reported for traction.

Analysis of adverse effects for traction

The results for the occurrence of any reported adverse effects are presented in *Table 66* and the accompanying forest plot (*Figure 48*).

The number of adverse effects associated with traction was significantly greater than the number associated with activity restriction. Pooled analyses showed no statistically significant differences for the number of adverse effects when comparing traction with inactive control, usual care or exercise therapy.

SUMMARY OF OVERALL FINDINGS FOR TRACTION COMPARED WITH ALTERNATIVE INTERVENTIONS

Half (5/10,[176,243,245,246,249] 50%) of the traction studies included patients with acute sciatica; 10% (1/10[242]) included patients with chronic sciatica. Most of the traction studies (90%) were RCTs,[176,242–249] but none was of a good quality (*Table 67*). One small, moderate-quality, pilot study evaluated mixed treatment (manual therapy, exercise and advice) with and without traction for patients with acute sciatica.[254]

There was no statistically significant difference between traction and inactive control for the treatment of acute sciatica in terms of the global effect (two moderate-quality RCTs[245,246]), reduction in pain intensity (two moderate-quality RCTs[244,248]) and improvement in functional status (one moderate-quality RCT[245]) at short-term follow-up, or in terms of the global effect at medium-term follow-up (one moderate-quality RCT[246]), or in adverse effects.[245]

One poorly reported non-RCT[250] found no statistically significant difference between traction and usual care in terms of the global effect at short-term follow-up or for adverse effects.

One small RCT[243] (moderate quality) found traction plus bed rest to be significantly better than bed rest alone (activity restriction) for reducing leg pain in patients with acute sciatica at short-term follow-up. Patients who received traction experienced significantly more adverse effects than those in the control group. There was no statistically significant difference

TABLE 66 Summary of the findings of any adverse effect for studies comparing traction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Traction vs active PT/exercise therapy							
570	Ljunggren, 1992[242]	RCT	8	24	8	26	1.13 (0.34 to 3.69)
Traction vs activity restriction							
222	Moret, 1998[243]	RCT	6	8	0	8	44.2 (1.8 to 1088.0)
Traction vs inactive control							
206	Pal, 1986[244]	RCT	NR	NR	NR	NR	
299	Rattanatharn, 2004[245]	RCT	4	54	2	48	1.84 (0.32 to 10.52)
553	Larsson, 1980[246]	RCT	NR	NR	NR	NR	
579	Mathews, 1975[247]	RCT	NR	NR	NR	NR	
746	Reust, 1988[248] (French language)	RCT	NR	NR	NR	NR	
746	Reust, 1988[248] (French language)	RCT	NR	NR	NR	NR	
Traction vs passive PT							
148	Unlu, 2008[249]	RCT	NR	NR	NR	NR	
148	Unlu, 2008[249]	RCT	NR	NR	NR	NR	
Traction vs usual care							
77	Styczynski, 1991[250]	Non-RCT	7	38	1	29	6.32 (0.73 to 54.64)
Mixed treatment including traction vs mixed treatment without traction							
301	Harte, 2007[254]	RCT	NR	NR	NR	NR	

NR, not reported.

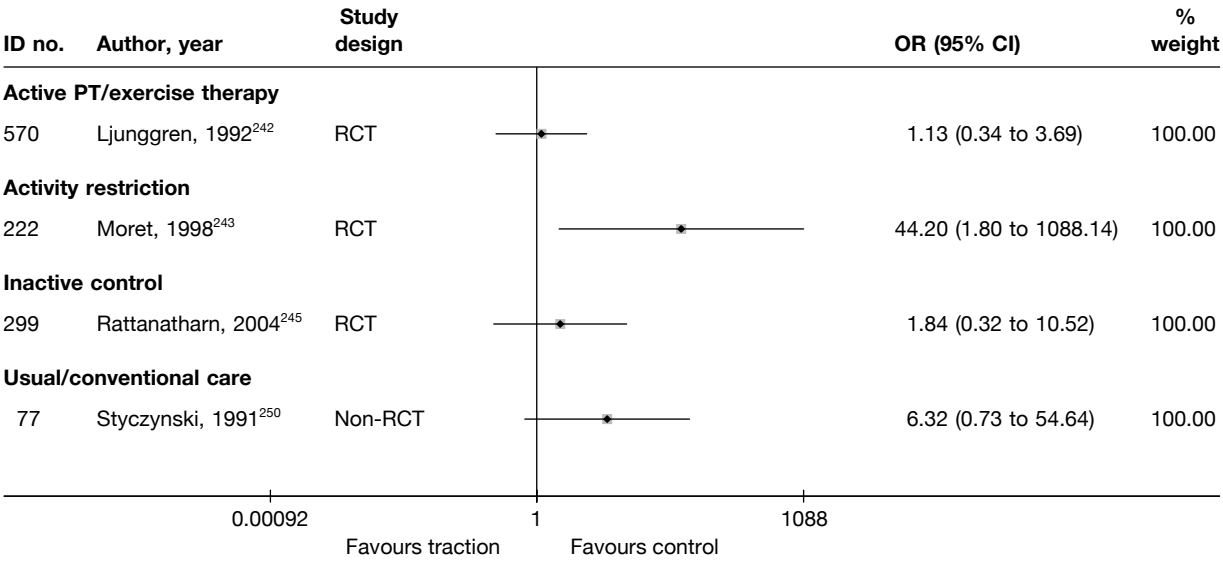

FIGURE 48 Summary of the findings of any adverse effect for studies comparing traction with alternative interventions. Note: weights are from random effects analysis.

TABLE 67 Summary of traction studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Traction vs activity restriction	1 (1)	16 (16)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
Traction vs exercise therapy	1 (1)	50 (50)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Traction vs inactive control	5 (6)	27–120 (60)	5/5 (100)	0/5 (0)	2/5 (40)	5/5 (100)	0/5 (0)	0/5 (0)	0/5 (0)	0/5 (0)	2/5 (40)	0/5 (0)
Traction vs passive PT	2 (3)	60–143 (102)	2/2 (100)	0/2 (0)	2/2 (100)	2/2 (100)	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
Traction vs usual/ conventional care	1 (3)	157 (157)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total (for traction studies)	**10 (14)**	**16–157 (60)**	**9/10 (90)**	**0/10 (0)**	**5/10 (50)**	**10/10 (100)**	**3/10 (30)**	**0/10 (0)**	**0/10 (0)**	**0/10 (0)**	**3/10 (30)**	**1/10 (10)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

between the treatment groups for global effect and CSOMs at short-term follow-up (one small, moderate-quality RCT[243]).

There was no statistically significant difference between traction and exercise therapy for the treatment of chronic sciatica in terms of the global effect at short-term follow-up or for adverse effects, according to one moderate-quality RCT.[242]

According to two moderate-quality RCTs,[176,249] there were no statistically significant difference between traction and passive PT for the treatment of acute sciatica in terms of global effect,[176] reduction in pain intensity[249] and improvement in functional status[249] at short-term follow-up, global effect[249] and functional status[249] at medium-term follow-up, or adverse effects.[249] There were no important differences between mixed treatments with or without traction for overall improvement, pain intensity or functional status at the end of the treatment (pilot RCT[254]).

Manipulation

Description of manipulation studies

Summary of interventions

Four studies compared spinal manipulation with an alternative type of intervention for sciatica.[169,208,258,259] Summary data of the interventions used are presented in *Table 68*. One RCT[258] compared chiropractic spinal manipulation with sham manipulation. One RCT[208] compared osteopathic spinal manipulation with chemonucleolysis. Two three-armed pilot RCTs compared chiropractic spinal manipulation with epidural corticosteroid injections, and also with either self-care education[169] or paracetamol, NSAIDs and activity modification.[161] Neither of these pilot RCTs reported outcomes at follow-up apart from adverse effects and cost data. One further non-RCT compared massage, traction and spinal manipulation (mixed treatment) with digital stimulation of acupuncture points and traction.[260]

Summary of study participants for manipulation

Summary data on the included participants are presented in *Table 69*. The two RCTs comparing manipulation with alternative interventions that reported follow-up results included 142 participants with mean ages between 42 and 43 years (48–63% men): one with acute symptom duration and one with chronic symptoms. One study included patients with recurrent episodes. Sciatica was confirmed by imaging in both. There were no patients with spinal stenosis or previous back surgery or sequestered discs.

Summary of study quality for manipulation studies

Study details are summarised in *Table 70*. All of the studies comparing manipulation with alternative interventions were RCTs and one was of good quality,[258] which was the only RCT with

TABLE 68 Summary of the interventions used when comparing manipulation with alternative interventions

ID no.	Author, year	Study design	Treatment description	Control description
Manipulation vs chemonucleolysis				
723	Burton, 2000[208]	RCT	Osteopathic spinal manipulation for up to 12 weeks	Chemonucleolysis with 400 U chymopapain
Manipulation vs education/advice				
722	Bronfort, 2004[169]	RCT	Chiropractic spinal manipulation	Self-care education
Manipulation vs epidural				
451	Bronfort, 2000[161]	RCT	Chiropractic spinal manipulation	Epidural corticosteroid injection (one to three times)
722	Bronfort, 2004[169]	RCT	Chiropractic spinal manipulation	Epidural corticosteroid injection (three times)
Manipulation vs inactive control				
52	Santilli, 2006[258]	RCT	Chiropractic manipulation up to 20 sessions	Sham manipulation up to 20 sessions
Manipulation vs non-opioids				
451	Bronfort, 2000[161]	RCT	Chiropractic spinal manipulation	Paracetamol, NSAIDs, activity modification
Mixed treatment including manipulation vs mixed treatment without manipulation				
687	Zhang, 2005[260]	Non-RCT	Massage, traction and spinal manipulation	Digital stimulation of acupuncture points and traction

U, units.

TABLE 69 Summary of sciatica type and study population details for studies comparing spinal manipulation with alternative interventions

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Manipulation vs chemonucleolysis													
723	Burton, 2000[208]	RCT	40	Mean 41.9 (SD 10.6)	19 (48)	Mean 31 (SD 35) weeks	Nerve root pain	Yes	Recurrent and first episode	No	No	NR	No
Manipulation vs education/advice													
722	Bronfort, 2004[169]	RCT	32	Mean 49.0 (SD 9.1)	18 (56)	1–3 months 19%; 4–6 months 6%; 7–12 months 9%; >12 months 66%	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	No previous spinal fusion
Manipulation vs epidural													
451	Bronfort, 2000[161]	RCT	20	Mean 44.5 (SD 10.6)	12 (60)	≤3 weeks $n=6$; 4–12 weeks $n=14$	Nerve root pain and referred pain	No	NR	No	No	Yes	No
722	Bronfort, 2004[169]	RCT	32	Mean 49.0 (SD 9.1)	18 (56)	1–3 months 19%; 4–6 months 6%; 7–12 months 9%; >12 months 66%	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	No previous spinal fusion
Manipulation vs inactive control													
52	Santilli, 2006[258]	RCT	102	Mean 43.1 (range 19–63)	64 (63)	<10 days	Nerve root pain and referred pain	Yes	NR	No	No	NR	No
Manipulation vs non-opioids													
451	Bronfort, 2000[161]	RCT	20	Mean 44.5 (SD 10.6)	12 (60)	≤3 weeks $n=6$; 4–12 weeks $n=14$	Nerve root pain and referred pain	No	NR	No	No	Yes	No
Mixed treatment including manipulation vs mixed treatment without manipulation													
687	Zhang, 2005[260]	Non-RCT	210	Mean 41.8	112 (53)	NR	Nerve root pain	Yes	NR	No	No	NR	NR

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 70 Summary of the study details for studies comparing manipulation with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Manipulation vs chemonucleolysis										
723	Burton, 2000[208]	40	12 months	RCT	No	No	60–79	Yes	Moderate	Weak
Manipulation vs education/advice										
722	Bronfort, 2004[169]	32	52 weeks	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Manipulation vs epidural										
451	Bronfort, 2000[161]	20	12 weeks	RCT	Unclear	Partial	80–100	NA	Moderate	Weak
722	Bronfort, 2004[169]	32	52 weeks	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Manipulation vs inactive control										
52	Santilli, 2006[258]	102	6 months	RCT	Yes	Yes	80–100	Yes	Strong	Strong
Manipulation vs non-opioids										
451	Bronfort, 2000[161]	20	12 weeks	RCT	Unclear	Partial	80–100	NA	Moderate	Weak
Mixed treatment including spinal manipulation vs mixed treatment without										
687	Zhang, 2005[260]	210	1 day	Non-RCT	No	No	80–100	Unclear	Weak	Weak

NA, not applicable.

an adequate method of random number generation, a secure method of allocation concealment and good external validity.

Manipulation results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 71* and the accompanying forest plot (*Figure 49*). There was no significant difference in the global effect in one good-quality RCT comparing chiropractic spinal manipulation with sham manipulation.[258] There was a significant improvement in global effect in one poor-quality non-RCT of massage, traction and spinal manipulation compared with digital stimulation of acupuncture points and traction.[260]

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 72* and the accompanying forest plot (*Figure 50*). There was no significant difference in pain intensity in one moderate-quality RCT comparing osteopathic spinal manipulation with chemonucleolysis.[208]

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 73* and the accompanying forest plot (*Figure 51*). There was no significant difference in CSOMs in one moderate-quality RCT comparing osteopathic spinal manipulation with chemonucleolysis.[208]

Manipulation results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 74* and the accompanying forest plot (*Figure 52*). There was significant improvement in global effect in one good-quality RCT comparing chiropractic spinal manipulation with sham manipulation.[258]

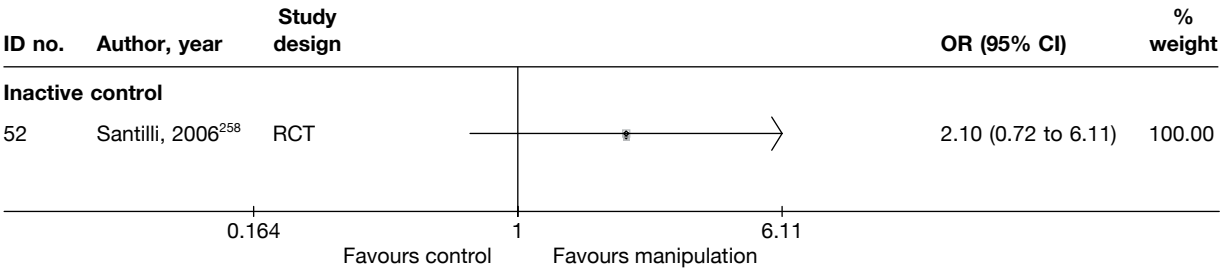

FIGURE 49 Summary of the findings of the global effect short-term follow-up (≤6 weeks) for studies comparing manipulation with alternative interventions. Note: weights are from random effects analysis.

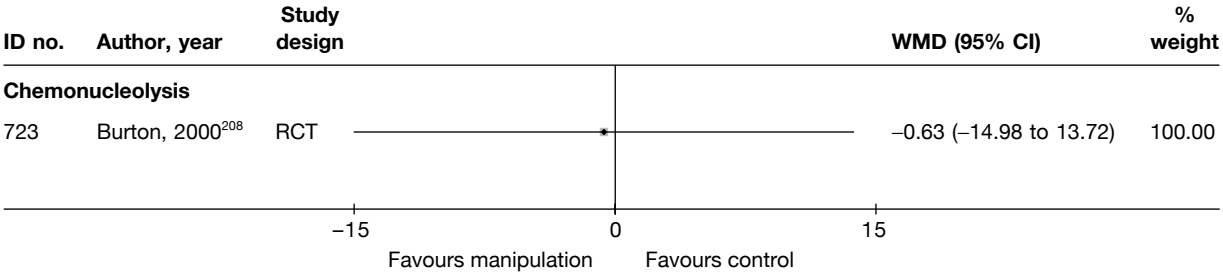

FIGURE 50 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing manipulation with alternative interventions. Note: weights are from random effects analysis.

TABLE 71 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing manipulation with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Manipulation vs inactive control														
52	Santilli, 2006[258]	A	RCT	30 days	Becoming pain free – radiating leg pain		53	12	0	49	6	0	2.10 (0.72 to 6.11)	Number randomised used as denominators by authors (two dropped out and four discontinued treatment)
Mixed treatment including spinal manipulation vs mixed treatment without														
687	Zhang, 2005[260]	C	Non-RCT	1 day	Remarkable effect on pain, SLR and analgesia score		108	56	0	102	35	0	0.40 (0.20 to 0.78)	

A, acute; C, chronic; SLR, straight leg raise.

TABLE 72 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing manipulation with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Manipulation vs chemonucleolysis																
723	Burton, 2000[208]	A + C	RCT	6 weeks	Leg	RMDQ annotated thermometer (0–6)	19	18	66.67 (14.17)	60.83 (26.5)	44.67 (26.7)	45.3 (17)			–0.63 (–14.98 to 13.72)	3/40 (8%) dropped out: intervention 1/20, control 2/20

A + C, acute and chronic.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 73 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing manipulation with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Manipulation vs chemonucleolysis														
723	Burton, 2000[208]	A+C	RCT	6 weeks	RMDQ	19	18	11.9 (5.48)	11.95 (5.83)	7.79 (6.65)	11 (5.69)	–4.11	–0.95	–0.52 (–1.17 to 0.14)

A+C, acute and chronic.
a Based on final means or change scores (with a preference given to change scores.

TABLE 74 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing manipulation with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)[a]	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Manipulation vs inactive control														
52	Santilli, 2006[258]	A	RCT	180 days	Becoming pain free – radiating leg pain		53	29	0	49	10	0	4.71 (1.95 to 11.37)	Number randomised used as denominators by authors (two dropped out and four discontinued treatment)

A, acute.

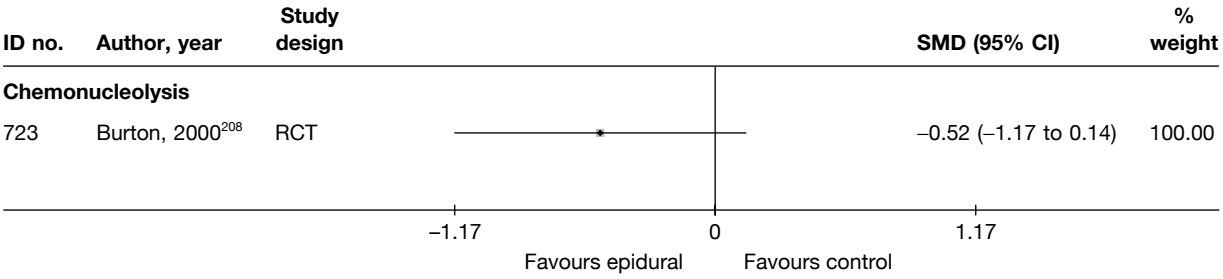

FIGURE 51 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing manipulation with alternative interventions. Note: weights are from random effects analysis.

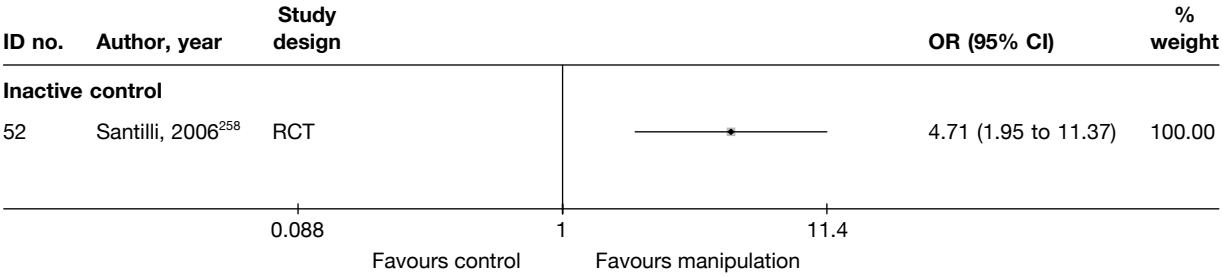

FIGURE 52 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing manipulation with alternative interventions. Note: weights are from random effects analysis.

Pain intensity at medium-term follow-up

No study reported medium-term outcomes for pain intensity.

Condition-specific outcome measures at medium-term follow-up

No study reported medium-term outcomes for CSOMs.

Results at long-term follow-up (>6 months)

Global effect at long-term follow-up

No study reported long-term outcomes for the global effect.

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 75* and the accompanying forest plot (*Figure 53*). There was no significant difference in pain intensity in one moderate-quality RCT comparing osteopathic spinal manipulation with chemonucleolysis.[208]

Condition-specific outcome measures at long-term

The results for CSOMs at long-term follow-up are presented in *Table 76* and the accompanying forest plot (*Figure 54*). There was no significant difference in CSOMs in one moderate-quality RCT comparing osteopathic spinal manipulation with chemonucleolysis.[208]

Analysis of adverse effects for spinal manipulation

The total number of adverse effects is presented in *Table 77* and the accompanying forest plot (*Figure 55*). Significantly more adverse effects were associated with manipulation than with self-care education,[169] but there was no significant difference compared with inactive control,[258] epidural injections[169] or chemonucleolysis.[208]

TABLE 75 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing manipulation with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Manipulation vs chemonucleolysis																
723	Burton, 2000[208]	A + C	RCT	12 months	Leg	RMDQ annotated thermometer (0–6)	15	15	66.67 (14.17)	60.83 (26.5)	35.5 (32)	37.8 (29.2)			–2.30 (–24.22 to 19.62)	10/40 (25%) dropped out: intervention 5/20, control 5/20

A + C, acute and chronic.
a The results have been converted to a scale of 0–100 for comparability.
b Based on final means or change scores (with a preference given to change scores).
c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 76 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing manipulation with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Manipulation vs chemonucleolysis														
723	Burton, 2000[208]	A + C	RCT	6 weeks	RMDQ	15	15	5.87 (5.96)	7.27 (6.65)	7.79 (6.65)	11 (5.69)			–0.22 (–0.94 to 0.50)

A + C, acute and chronic.
a Based on final means or change scores (with a preference given to change scores).

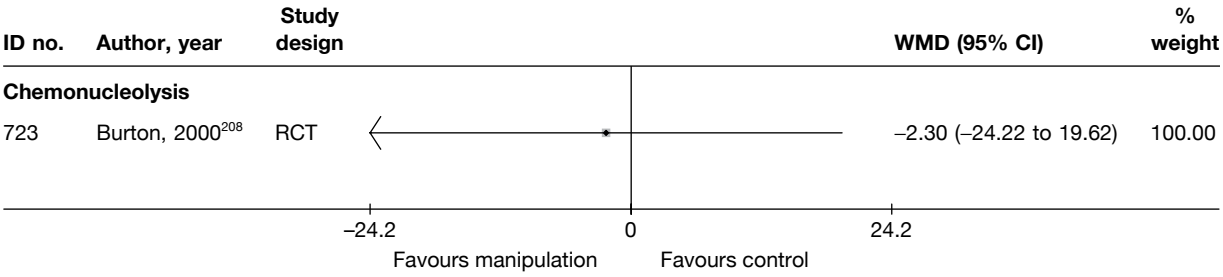

FIGURE 53 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing manipulation with alternative interventions. Note: weights are from random effects analysis.

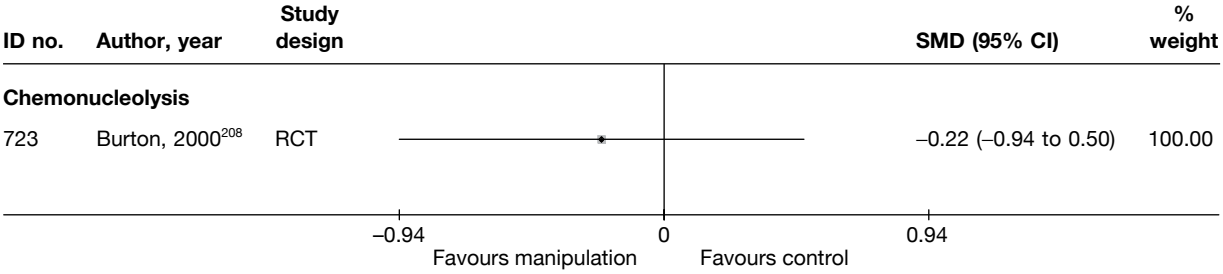

FIGURE 54 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing manipulation with alternative interventions. Note: weights are from random effects analysis.

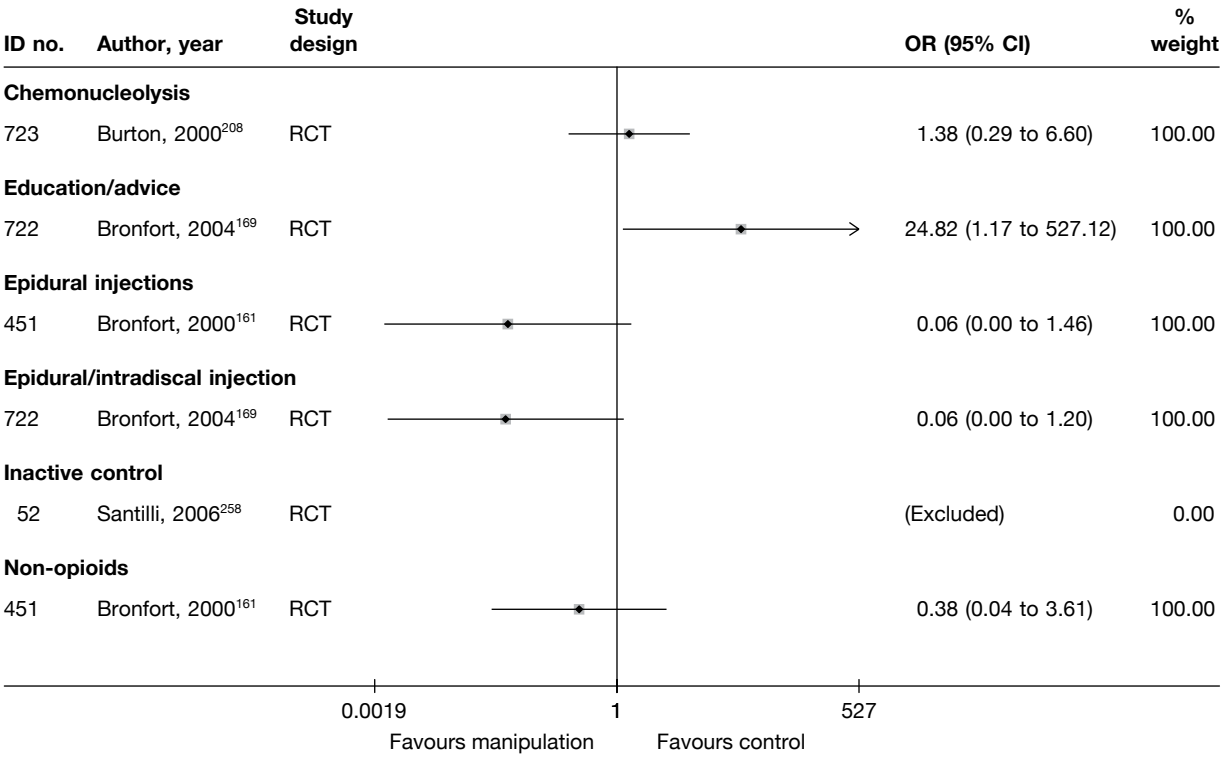

FIGURE 55 Summary of the findings of any adverse effect for studies comparing spinal manipulation with alternative interventions. Note: weights are from random effects analysis.

TABLE 77 Summary of the findings of any adverse effect for studies comparing spinal manipulation with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Manipulation vs chemonucleolysis							
723	Burton, 2000[208]	RCT	5	15	4	15	1.38 (0.29 to 6.60)
Manipulation vs education/advice							
722	Bronfort, 2004[169]	RCT	6	11	0	10	24.82 (1.17 to 527.00)
Manipulation vs epidural injection							
451	Bronfort, 2000[208]	RCT	3	7	6	6	0.60 (0.00 to 1.46)
722	Bronfort, 2004[169]	RCT	6	11	10	10	0.06 (0.00 to 1.20)
Manipulation vs inactive control							
52	Santilli, 2006[258]	RCT	0	53	0	49	
Manipulation vs non-opioids							
451	Bronfort, 2000[208]	RCT	3	7	4	6	0.38 (0.04 to 3.61)
Mixed treatment including spinal manipulation vs mixed treatment without							
687	Zhang, 2005[260]	Non-RCT	NR	NR	NR	NR	

NR, not reported.

SUMMARY OF OVERALL FINDINGS FOR MANIPULATION COMPARED WITH ALTERNATIVE INTERVENTIONS

Two RCTs[208,258] compared the use of manipulation with other interventions, one of which restricted inclusion to patients with acute sciatica (*Table 78*).

There was a statistically significant improvement in medium-term (but not short-term) global effect in a good-quality RCT[258] of chiropractic manipulation compared with sham manipulation. There was no significant difference in short- or long-term pain intensity, or in short-term CSOMs, in a moderate-quality RCT[208] comparing osteopathic manipulation with chemonucleolysis.

TABLE 78 Summary of manipulation studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Manipulation vs chemonucleolysis	1 (1)	40 (40)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Manipulation vs inactive control	1 (1)	102 (102)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total (for manipulation studies)	**2 (2)**	**40–102 (71)**	**2/2 (100)**	**1/2 (50)**	**1/2 (50)**	**2/2 (100)**	**2/2 (100)**	**0/2 (0)**	**0/2 (0)**	**0/2 (0)**	**0/2 (0)**	**0/2 (0)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Alternative therapies

Description of alternative therapy studies

Summary of interventions

Five studies evaluated alternative therapies for sciatica.[167,215,261–263] Three of these studies compared alternative therapy with an alternative intervention.[167,215,261] The types of interventions being compared are presented in *Table 79a*. One RCT compared acupuncture in correct acupuncture points with acupuncture in non-acupuncture points. One three-armed RCT[215] compared warming acupuncture by burning moxa with injections of an herbal preparation anisodamine, and with an oral NSAID nimesolide. One three-armed CCS[167] compared acupuncture and herbal medication with epidural injection of corticosteroid and local anaesthetic, and with epidural injection of local anaesthetic.

Two studies compared different types of alternative therapy.[262,263] The types of alternative therapy compared are listed in *Table 79b*, but the findings of these studies are not considered any further.

Summary of study participants for alternative therapy

Summary data on the included participants are presented in *Table 80*. The three studies that compared alternative therapies with comparator treatments included 398 participants with

TABLE 79a Summary of the interventions used when comparing alternative therapies with alternative interventions

ID no.	Author, year	Study design	Treatment description	Control description
Alternative vs epidural				
667	Wehling, 1997[167] (German language)	CCS	Acupuncture and herbal medication	Nerve root blockade with local anaesthetic 5 ml mepivacaine twice a week for 5 weeks
667	Wehling, 1997[167] (German language)	CCS	Acupuncture and herbal medication	Nerve root blockade with steroid triamcinolone 20 mg + local anaesthetic 5 ml mepivacaine twice a week for 5 weeks
Alternative vs inactive control				
476	Duplan, 1983[261] (French language)	RCT	Acupuncture	Placebo (same acupuncture procedure but in non-acupuncture points)
Alternative vs non-opioids				
801	Chen, 2009[215]	RCT	Warming acupuncture by burning moxa daily for 10 days (WAG)	Western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG)
801	Chen, 2009[215]	RCT	Anisodamine (2 mg) point injections into acupoints daily for 10 days (PIG)	Western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG)

PIG, point injection group; WAG, warming acupuncture group; WMG, western medicine group.

TABLE 79b Summary of the interventions used when comparing alternative forms of alternative therapy

ID no.	Author, year	Study design	Treatment description	Control description
533	Khoromi, 2007[262]	RCT (crossover)	Use of 200-g magnets in belts	Use of 50-g magnets in belts
72	Zhi, 1995[263]	Non-RCT	Scalp acupuncture combined with single body acupoint using scalp needles	Body acupuncture alone using stainless steel needles

TABLE 80 Summary of sciatica type and study population details for studies comparing alternative therapies with alternative interventions

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Alternative vs epidural/intradiscal injection													
667	Wehling, 1997[167] (German language)	CCS	278	NR	NR	≤ 3 months	Nerve root pain and referred pain	Clinical	NR	No	No	NR	NR
Alternative vs inactive control													
476	Duplan, 1983[261] (French language)	RCT	30	Mean 40 (SD 10)	21 (70)	Mean 34 days (SD 15 days)	Nerve root pain and referred pain	Clinical	NR	No	No	Yes	No
Alternative vs non-opioids													
801	Chen, 2009[215]	RCT	90	Mean 34.5 (SD 7.7)	63 (70)	Mean 5.3 years (SD 4.14 years)	Nerve root pain	Clinical	NR	NR	NR	NR	NR

NR, not reported; PIG, point injection group; WAG, warming acupuncture group; WMG, western medicine group.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

mean ages between 35 and 40 years (70% men): two with acute symptom duration and one with chronic symptoms. Recurrent episodes were not reported. Sciatica was not confirmed by imaging in any of the studies. There were no patients with spinal stenosis or previous back surgery or sequestered discs.

Summary of study quality for alternative therapy studies

Study details are summarised in *Table 81*. Two of the studies were RCTs[215,261] and none was of good quality. Neither an adequate method of random number generation nor a secure method of allocation concealment was recorded. No studies had good external validity.

Alternative therapy results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

No study reported short-term outcomes for global effect.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 82* and the accompanying forest plot (*Figure 56*). There was a significant improvement in pain intensity in a moderate-quality RCT of true acupuncture compared with needling non-acupuncture points[261] and in a poor-quality RCT of oral NSAID compared with warming acupuncture by burning moxa.[215] There was no significant difference in pain intensity in a poor-quality CCS of acupuncture and herbal medication compared with epidural injection.[264]

Condition-specific outcome measures at short-term follow-up

No study reported short-term CSOMs.

Alternative therapy results at medium-term follow-up (>6 weeks to ≤6 months)

No study reported medium-term outcomes for global effect, pain intensity or CSOMs.

Alternative therapy results at long-term follow-up (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 83* and the accompanying forest plot (*Figure 57*). There was no significant difference in the global effect in one poor-quality RCT comparing warming acupuncture by burning moxa, or injections of an herbal preparation anisodamine, with an oral NSAID.[215]

Pain intensity at long-term follow-up

No study reported long-term outcomes for pain intensity.

Condition-specific outcome measures at long-term follow-up

No study reported short-term CSOMs.

Analysis of adverse effects for alternative therapies

No adverse effects were reported in any of the studies (*Table 84*).

TABLE 81 Summary of the study details for studies comparing alternative therapies with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Alternative vs epidural/intradiscal injection										
667	Wehling, 1997[167] (German language)	278	5 weeks	CCS	No	No	80–100	No	Weak	Weak
Alternative vs inactive control										
476	Duplan, 1983[261] (French language)	30	5 days	RCT	Unclear	Unclear	80–100	Yes	Moderate	Moderate
Alternative vs non-opioids										
801	Chen, 2009[215]	90	1 year	RCT	Unclear	Unclear	80–100	Unclear	Weak	Moderate

TABLE 82 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing alternative therapies with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Alternative vs epidural/intradiscal injections																
667	Wehling, 1997[167] (German language) (i)[d] (steroid + LA)	C	CCS	5 weeks		VAS (0–100)	230	26					–62 (28)	–66 (24)	4.0 (10.18 to 18.18)	Results reported as percentage improvement (100% improvement = no pain; 0% pain reduction = pain the same as before treatment)
667	Wehling, 1997[167] (German language) (ii)[d] (LA)	C	CCS	5 weeks		VAS (0–100)	230	22					–62 (28)	–48 (31)	–14.00 (–27.45 to –0.55)	Results reported as percentage improvement (100% improvement = no pain; 0% pain reduction = pain the same as before treatment)
Alternative vs inactive control																
476	Duplan, 1983[261] (French language)	A	RCT	5 days	Overall	VAS (0–100)	15	15	48	45	19 (21.51)	44 (23.67)			–25.00 (–41.19 to –8.81)	Mean percentage VAS score SD imputed from weighted average Dropouts not stated
Alternative vs non-opioids																
801	Chen, 2009[215] (i)[e] (WAG)	C	RCT	36 days (end of treatment)	Leg	Not stated	30	30	1.56 (0.35)	1.42 (0.37)	5.74 (0.25)	2.42 (0.33)			3.32 (3.17 to 3.47)	Outcome = improvement in clinical symptoms (scale and range not stated) Reported separately for: sciatica, lumbago, aggravated pain on coughing, aggravated pain on sneezing and aggravated pain on defecation

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
801	Chen, 2009[215] (ii)[e] (PIG)	C	RCT	36 days (end of treatment)	Leg	Not stated	30	30	1.75 (0.32)	1.42 (0.37)	2.75 (0.32)	2.42 (0.33)			0.33 (0.17 to 0.49)	Outcome = improvement in clinical symptoms (scale and range not stated) Reported separately for: sciatica, lumbago, aggravated pain on coughing, aggravated pain on sneezing and aggravated pain on defecation

A, acute; C, chronic; LA, local anaesthetic; PIG, point injection group; WAG, warming acupuncture group; WMG, western medicine group.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Wehling and Reinecke[167] included three treatment groups: nerve root blockade with steroid (triamcinolone) + LA (mepivacaine) (i), nerve root blockade with local anaesthetic (mepivacaine) (ii) and acupuncture and herbal medication (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 56*).

e Chen *et al.*[215] included three treatment groups: warming acupuncture group with needles warmed by burning moxa (WAG) (i), point injections of anisodamine (2 mg) into acupoints (PIG) (ii) and western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG) (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 56*).

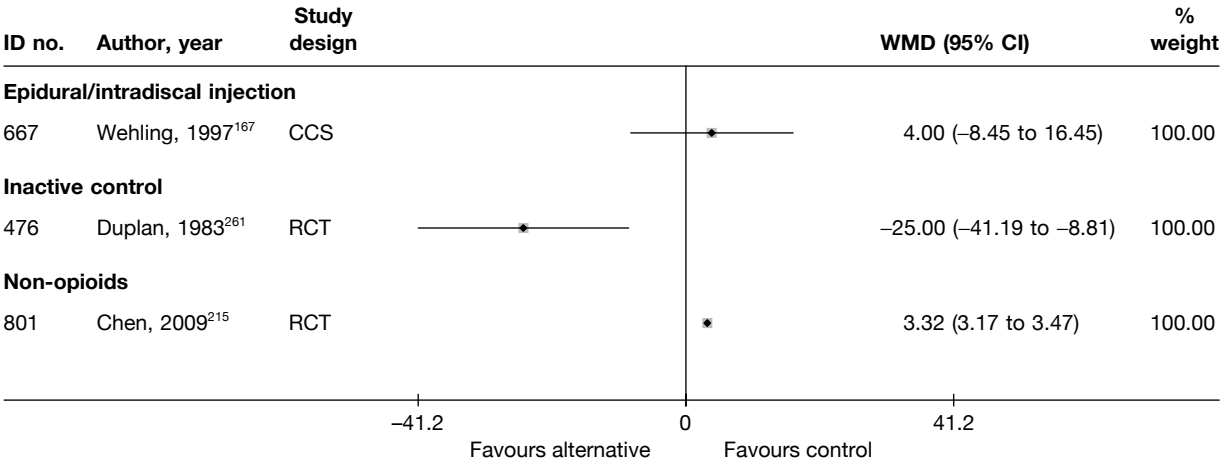

FIGURE 56 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing alternative therapies with alternative interventions. Note: weights are from random effects analysis.

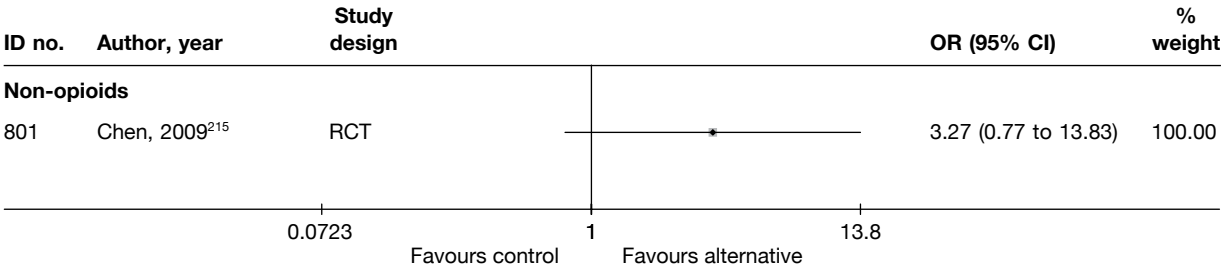

FIGURE 57 Summary of the findings of the global effect at long-term follow-up (>6 months) for studies comparing alternative therapies with alternative interventions. Note: weights are from random effects analysis.

SUMMARY OF OVERALL FINDINGS FOR ALTERNATIVE INTERVENTIONS COMPARED WITH COMPARATOR INTERVENTIONS

Three studies,[167,215,261] two of which were RCTs,[215,261] compared the use of acupuncture with other interventions (*Table 85*).

There was a significant improvement in pain intensity in a moderate-quality RCT of true acupuncture compared with needling non-acupuncture points,[261] but pain intensity was significantly worse in another poor-quality RCT[215] comparing warming acupuncture by burning moxa, or injecting a herbal preparation into acupuncture points, with an oral NSAID. There was no significant difference in pain intensity in a poor-quality CCS[167] of acupuncture and herbal medication compared with epidural injection.

TABLE 83 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing alternative therapies with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Alternative vs non-opioids														
801	Chen, 2009[215] (i)[a] (WAG)	C	RCT	1 year	Success: cured or improved (vs no improvement)	Patient	30	27	0	30	22	0	3.27 (0.77 to 13.83)	Data inferred from graphs reporting percentages ITT using worst-case analysis (with non-opioids as the control group)
801	Chen, 2009[215] (ii)[a] (PIG)	C	RCT	1 year	Success: cured or improved (vs no improvement)	Patient	30	19	0	30	22	0	0.63 (0.21 to 1.88)	Data inferred from graphs reporting percentages ITT using worst-case analysis (with non-opioids as the control group)

C, chronic; PIG, point injection group; WAG, warming acupuncture group; WMG, western medicine group.

a Chen *et al.*[215] included three treatment groups: point injections of anisodamine (2 mg) into acupoints (PIG) (ii), warming acupuncture group with needles warmed by burning moxa (WAG) (i) and western medicine – oral nimesolide (NSAIDs) 2 g daily for 10 days (WMG) (iii). In order to prevent using the same comparator twice, only the first and third treatment groups have been included in the meta-analysis (see *Figure 57*).

TABLE 84 Summary of the findings of any adverse effect for studies comparing alternative therapies with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group
Alternative vs epidural injections						
667	Wehling, 1997[167]	RCT	NR	NR	NR	NR
667	Wehling, 1997[167]	RCT	NR	NR	NR	NR
Alternative vs inactive control						
476	Duplan, 1983[261]	RCT	NR	NR	NR	NR
Alternative vs non-opioid						
801	Chen, 2009[215]	RCT	NR	NR	NR	NR
801	Chen, 2009[215]	RCT	NR	NR	NR	NR

NR, not reported.

TABLE 85 Summary of alternative therapies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Alternative vs epidural/intradiscal injection	1 (2)	278 (278)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Alternative vs inactive control	1 (1)	30 (30)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Alternative vs non-opioids	1 (2)	90 (90)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total (for alternative therapies)	**3 (4)**	**30–278 (90)**	**2/3 (67)**	**0/3 (0)**	**1/3 (33)**	**3/3 (100)**	**0/3 (0)**	**0/3 (0)**	**0/3 (0)**	**0/3 (0)**	**1/3 (33)**	**0/3 (0)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Active physical therapy/exercise therapy

Description of exercise therapy studies

Summary of interventions

Six studies compared active physical/exercise therapy with an alternative type of intervention for sciatica.[68,242,255,256,264,265] Summary data of the interventions used are presented in *Table 86*. One crossover RCT[265] compared a 4-week course of lumbar-stabilising exercise with no exercise. One three-arm RCT[256] compared massage, hot packs and exercise with hot packs and rest or with pelvic traction and strengthening exercises. One RCT[68] compared exercise therapy alone with disc surgery plus exercise therapy. One RCT[255] compared an extension-orientated treatment including exercise, mobilisation and education with lumbar traction plus the extension-orientated treatment approach. One RCT[242] compared isometric exercises with manual traction. One RCT[266] compared physiotherapy plus GP care with GP care alone.

Summary of study participants for active physical therapy/exercise therapy

Summary data on the included participants are presented in *Table 87*. The six trials included 305 participants with mean ages between 32 and 42 years; between 44% and 61% were men; and, three with acute and chronic symptom duration and three with chronic symptoms. Two RCTs included participants with first and recurrent episodes of sciatica, but this was not reported in the remainder. Sciatica was confirmed by imaging in three trials. There were no patients with spinal stenosis, or previous back surgery, and one RCT included patients with sequestered discs.

Summary of study quality for active physical therapy/exercise therapy

Study details are summarised in *Table 88*. All of the studies were RCTs and one was of good quality.[266] Four had an adequate method of random number generation and two documented a secure method of allocation concealment. One study had good external validity.[266]

Active physical therapy/exercise therapy results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 89* and the accompanying forest plot (*Figure 58*). There was no significant difference in global effect in a moderate-quality RCT comparing isometric exercises with manual traction;[242] a moderate-quality RCT comparing exercise therapy alone with disc surgery plus exercise therapy;[68] a poor-quality RCT comparing massage, hot packs and exercise with hot packs and rest;[256] a moderate-quality RCT comparing exercise, mobilisation and education with extension-orientated approach and traction;[255] and a good-quality RCT comparing general practitioner care and PT with GP care.[266] In a poor-quality RCT, there was a significant improvement in global effect with pelvic traction and strengthening exercises compared with massage, hot packs and exercise.[256]

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 90* and the accompanying forest plot (*Figure 59*). There was a significant improvement in pain intensity in a moderate-quality crossover RCT of exercise therapy compared with inactive control,[265] and in a moderate-quality RCT of disc surgery plus exercise therapy compared with exercise therapy alone.[68] In a good-quality RCT there was no significant difference in pain intensity with GP care and PT compared with GP care alone,[266] or in a moderate-quality RCT of exercise, mobilisation and education compared with extension-orientated approach and traction.[255]

TABLE 86 Summary of the interventions used when comparing exercise therapy with alternative interventions (ordered by control group then author)

ID no.	Author, year	Study design	Treatment description	Control description
Exercise therapy vs activity restriction				
564	Lidstrom, 1970[256]	RCT	Massage, hot packs and exercise (conventional treatment)	Hot packs and rest (control group)
Exercise therapy vs disc surgery				
300	Osterman, 2006[68]	RCT	Exercise therapy (conservative treatment)	Microdiscectomy and exercise therapy (surgery)
Exercise therapy vs inactive control				
429	Bakhtiary, 2005[265]	RCT (crossover)	4 weeks of lumbar-stabilising exercise followed by a 4 weeks of no exercise (group A) *Only 4-week outcomes used*	4 weeks of no exercise followed by 4 weeks of lumbar-stabilising exercise (group B) *Only 4-week outcomes used*
Exercise therapy vs mixed treatment				
395	Fritz, 2007[255]	RCT	Extension-oriented treatment approach (exercises, mobilisation and education) only	Traction and extension-oriented treatment approach
564	Lidstrom, 1970[256]	RCT	Hot packs, massage, mobilising exercise and strengthening exercises	Traction and strengthening exercises
Exercise therapy vs traction				
570	Ljunggren, 1992[242]	RCT	Isometric exercises	Manual traction
Exercise therapy vs usual/conventional care				
742	Luijsterburg, 2008[264]	RCT	General practitioner care plus PT	General practitioner care

Condition-specific outcomes at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 91* and the accompanying forest plot (*Figure 60*). There was no significant difference in CSOMs in a moderate-quality RCT of exercise therapy alone compared with disc surgery plus exercise therapy[68] or in a moderate-quality RCT of exercise, mobilisation and education compared with extension-orientated approach and traction.[255] There was a marginal statistically significant improvement in a good-quality RCT of pain intensity for GP care alone compared with PT and GP care.[266]

Active physical therapy/exercise therapy results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 92* and the accompanying forest plot (*Figure 61*). In a moderate-quality RCT there was no significant difference in global effect with exercise therapy alone compared with disc surgery plus exercise therapy,[68] or in a good-quality RCT of GP care and PT compared with GP care alone.[266]

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 93* and the accompanying forest plot (*Figure 62*). There was no significant difference in pain intensity in a moderate-quality RCT of exercise therapy alone compared with disc surgery plus exercise therapy[68] or in a good-quality RCT of GP care and PT compared with GP care alone.[266]

TABLE 87 Summary of sciatica type and study population details for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Exercise therapy vs activity restriction													
564	Lidstrom, 1970[256]	RCT	62	Range 21–61	29 (47)	>1 year 52%	Nerve root pain and referred pain	No	NR	No	No	NR	NR
Exercise therapy vs disc surgery													
300	Osterman, 2006[68]	RCT	57	Mean 38 (SD 7)	34 (61)	Mean 68.5 days (SD 27 days)	Nerve root pain	Yes	Recurrent and First episode	No	Yes	NR	No
Exercise therapy vs inactive control													
429	Bakhtiary, 2005[265]	RCT (crossover)	60	Mean 32 (SD 5.79)	Not reported	Mean 3.95 months (SD 1.30 months)	NR	Yes	NR	No	No	NR	NR
Exercise therapy vs mixed treatment													
395	Fritz, 2007[255]	RCT	64	Mean 41.1 (SD 9.8; range 18–60)	28 (44)	Median 47.5 days (range 2–761 days)	Nerve root pain	No	49 (77%) had prior history of low back pain	No	No	NR	No
564	Lidstrom, 1970[256]	RCT	62	Range 21–61	29 (47)	>1 year 52%	Nerve root pain and referred pain	No	NR	No	No	NR	NR
Exercise therapy vs traction													
570	Ljunggren, 1992[242]	RCT	50	Mean 41.6 (range 19–62)	27 (54)	Mean 5 months	Nerve root pain	Yes	NR	No	No	NR	No
Exercise therapy vs usual/conventional care													
742	Luijsterburg, 2008[264]	RCT	135	Mean 43 (SD 11)	70 (52)	>6 weeks	Nerve root pain	No	NR	No	No	NR	No

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 88 Summary of the study details for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Exercise therapy vs activity restriction										
564	Lidstrom, 1970[256]	62	1 month	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Exercise therapy vs disc surgery										
300	Osterman, 2006[68]	57	2 years	RCT	Yes	Yes	80–100	NA	Moderate	Weak
Exercise therapy vs inactive control										
429	Bakhtiary, 2005[265]	60	8 weeks	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
Exercise therapy vs mixed treatments										
395	Fritz, 2007[255]	64	6 weeks	RCT	Yes	Partial	80–100	Partial	Moderate	Weak
564	Lidstrom, 1970[256]	62	1 month	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Exercise therapy vs traction										
570	Ljunggren, 1992[242]	50	1 week	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak
Exercise therapy vs usual/conventional care										
742	Luijsterburg, 2008[264]	135	12 months	RCT	Yes	Yes	80–100	NA	Strong	Strong

NA, not applicable.

TABLE 89 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing exercise therapy with alternative interventions (grouped by comparator then ordered by author)

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
Exercise therapy vs activity restriction														
564	Lidstrom, 1970[256] (ii)[a] (Rest)	A + C	RCT	1 month	Noticeable improvement (vs no change or worse)	Patient	21	10	0	21	14	0	0.45 (0.13 to 1.58)	
Exercise therapy vs disc surgery														
300	Osterman, 2006[68]	A	RCT	6 weeks	Full recovery	Patient	28	0	0	28	5	0.03	0.07 (0.00 to 1.43)	
Exercise therapy vs mixed treatments														
395	Fritz, 2007[255]	A	RCT	6 weeks	Improved: Likert-type scale rating > 2 (scale range −7 to + 7: worsened < −2; unchanged −2 to + 2)	Patient	33	21	0	31	21	0	0.83 (0.30 to 2.34)	ITT using LOCF Dropouts 13%: intervention 3/33, control 5/31
564	Lidstrom, 1970[256] (i)[a] (traction + excercise)	A + C	RCT	1 month	Noticeable improvement (vs no change or worse)	Patient	21	10	0	20	18	0	0.10 (0.02 to 0.55)	

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Exercise therapy vs traction														
570	Ljunggren, 1992[242]	C	RCT	1 week	Global evaluation: symptom-free or satisfactory improvement (vs unsatisfactory improvement or unchanged)	Patient	26	10	0	24	1	0	0.88 (0.28 to 2.72)	
Exercise therapy vs usual/conventional care														
742	Luijsterburg, 2008[264]	A	RCT	6 weeks	Improved (on seven-point Likert scale): 'completely recovered' and 'much improved' (vs 'slightly improved', 'not changed', 'slightly worsened', 'much worsened' and 'worse than ever')	Patient	67	38	0	68	30	0	1.66 (0.84 to 3.28)	ITT using LOCF Dropouts 4%: intervention 2/67, control 4/68

A, acute; A + C, acute and chronic; C, chronic; LOCF, last observation carried forward.

a Lidstrom and Zachrisson[256] included three treatment groups: traction + strengthening exercises (i), rest + hot packs (ii) and massage, mobilising exercises, strengthening exercises + hot packs (iii).

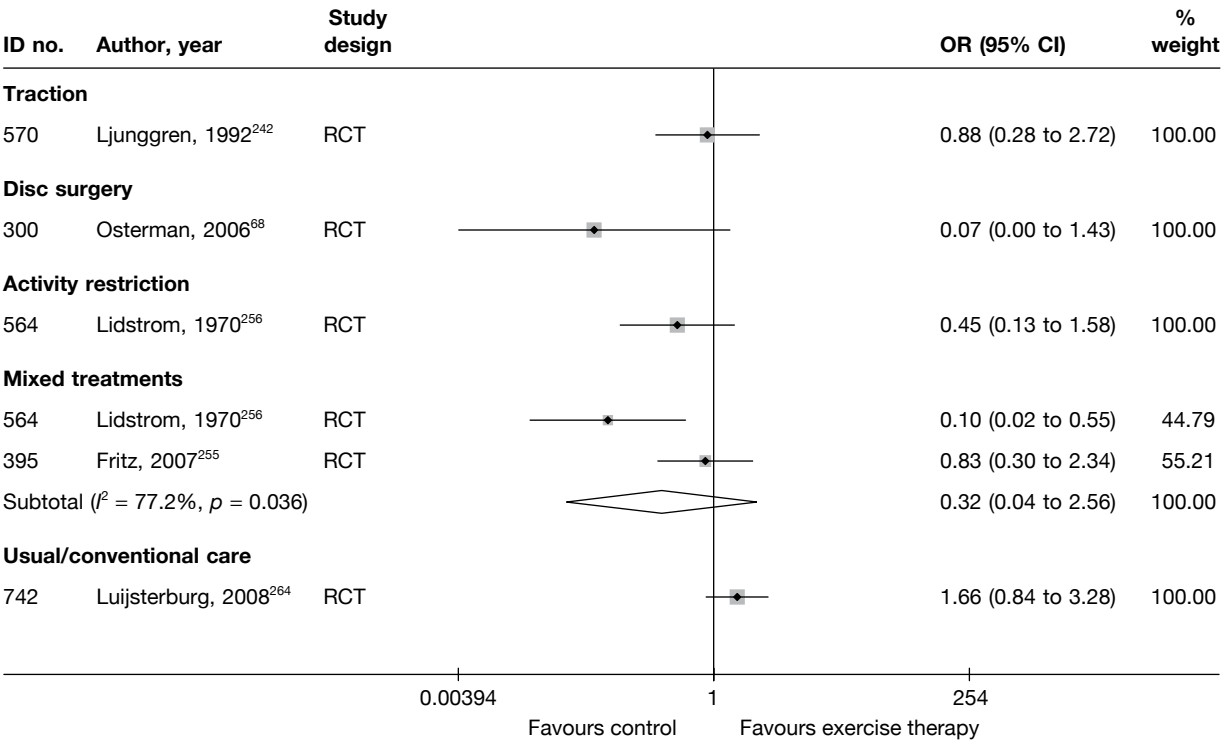

FIGURE 58 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

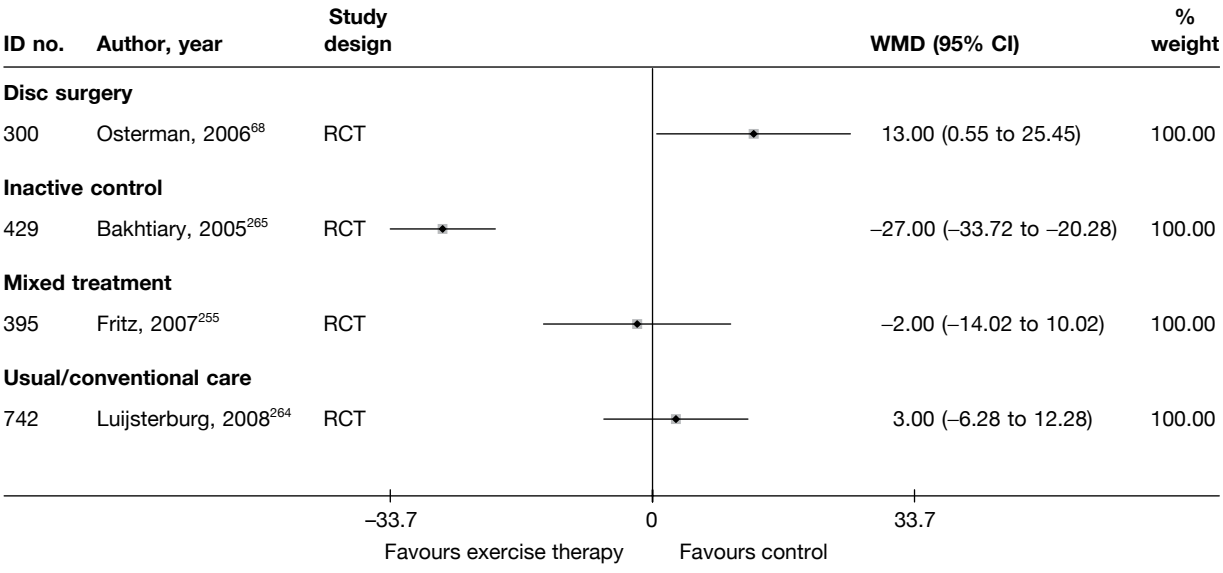

FIGURE 59 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

TABLE 90 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Exercise therapy vs disc surgery																
300	Osterman, 2006[68]	A	RCT	6 weeks	Leg	VAS (0–100)	28	28	57 (21)	61 (20)	25 (27)	12 (20)			13.00 (0.55 to 25.45)	Dropouts 2%: surgery 1/29 (did not meet inclusion criteria, excluded from analysis), exercise 0/28
Exercise therapy vs inactive control																
429	Bakhtiary, 2005[265]	A + C	RCT (crossover)	4 weeks	Overall	VAS (0–10)	30	30	42.9 (9)	45 (11)			–32 (14.7)	–5 (11.7)	–27.00 (–33.72 to –20.28) *Mean difference –2.7 (–3.5 to –1.9), p < 0.0001 (two-way ANOVA)*	ITT, method not stated Dropouts 1%: intervention 3/30, control 3/30 This was a crossover study, where all patients received LSE or no exercise; however, the authors compared the outcomes of group A (LSE followed by no exercise) vs group B (no exercise followed by LSE) not LSE vs no exercise
Exercise therapy vs mixed treatments																
395	Fritz, 2007[255]	A	RCT	6 weeks	Overall	NRS (0–10)	33	31	53.0 (15.0)	50.0 (18.0)	30.0 (24.0)	32.0 (25.0)			–2.00 (–14.02 to 10.02) *Adjusted mean difference, ANCOVA –0.17 (95% CI –1.4 to 1.1)*	ITT using LOCF Dropouts 13%: intervention 3/33, control 5/31

continued

TABLE 90 Summary of the findings of pain intensity at short-term follow-up (≤ 6 weeks) for studies comparing exercise therapy with alternative interventions *(continued)*

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Exercise therapy vs usual/conventional care																
742	Luijsterburg, 2008[264]	A	RCT	6 weeks	Leg	NRS (0–10)	67	68	63 (22)	63 (22)			–30 (27)	–33 (28)	3.00 (–6.28 to 12.28) *Unadjusted mean difference 3 (95% CI –6 to 12)*	ITT using LOCF Dropouts 4%: intervention 2/67, control 4/68

A, acute; A + C, acute and chronic; LOCF, last observation carried forward; LSE, lumbar stabilising exercise; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 91 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Active PT/exercise therapy vs disc surgery															
300	Osterman, 2006[68]	A	RCT	6 weeks	ODI	28	28	39 (14)	39 (15)	22 (16)	16 (16)	–17	–23	0.38 (–0.15 to 0.90)	ITT used LOCF, but one patient that did not meet inclusion criteria excluded from analysis
Active PT/exercise therapy vs mixed treatment															
395	Fritz, 2007[255]	A	RCT	6 weeks	Modified ODI	33	31	41.5 (10.7)	46.1 (14.9)	25.6 (19.9)	28.3 (19.3)			–0.14 (–0.63 to 0.35) *Adjusted mean difference, ANCOVA: 1.8 (95% CI –6.4 to 10.1)*	ITT used LOCF Dropouts 13%: intervention 3/33, control 5/31
Active PT/exercise therapy vs usual/conventional care															
742	Luijsterburg, 2008[264]	A	RCT	6 weeks	RMDQ	67	68	15.9 (4.1)	15.4 (5)	10.6 (4.1)	8.8 (6.1)	–5.3 (7)	–6.6 (6.1)	0.35 (0.01 to 0.69)	Final mean calculated from change score, final SD missing so baseline SD used

A, acute; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

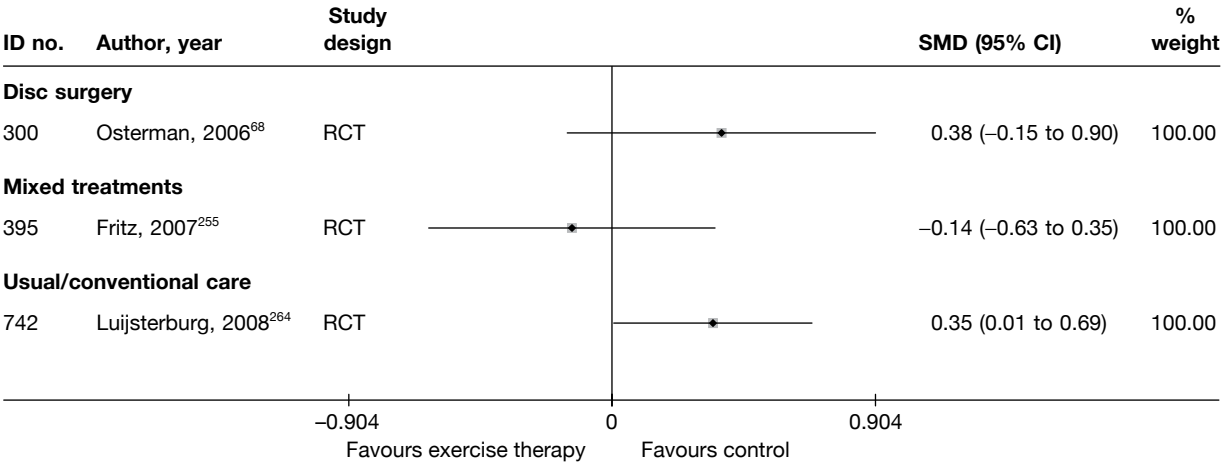

FIGURE 60 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

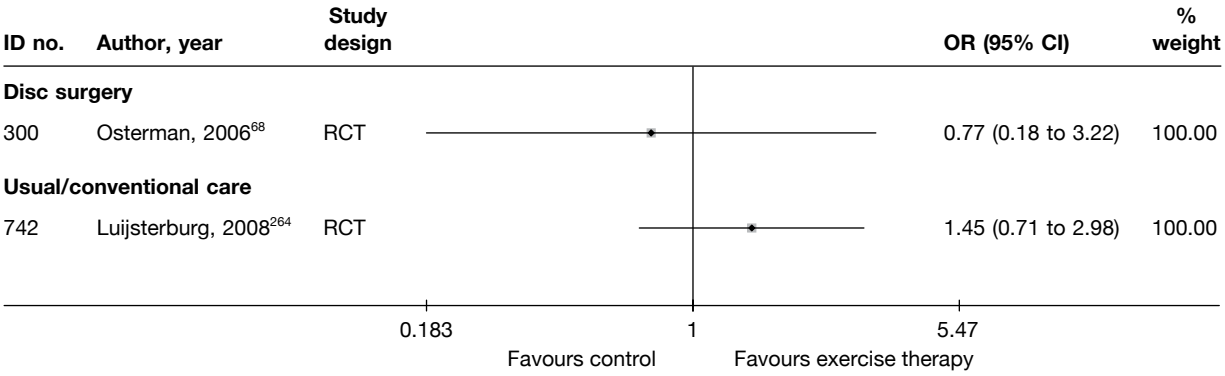

FIGURE 61 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 94* and the accompanying forest plot (*Figure 63*). There was no significant difference in CSOMs in a moderate-quality RCT of exercise therapy alone compared with disc surgery plus exercise therapy[68] or in a good-quality RCT of GP care and PT compared with GP care alone.[266]

Active physical therapy results at long-term follow-up (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 95* and the accompanying forest plot (*Figure 64*). There was no significant difference in CSOMs in a moderate-quality RCT of exercise therapy alone compared with disc surgery plus exercise therapy.[68] There was a significant improvement for the global effect in a good-quality RCT of GP care and PT compared with GP care alone.[266]

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 96* and the accompanying forest plot (*Figure 65*). There was no significant difference in pain intensity with exercise therapy alone compared with disc surgery plus exercise therapy[68] or with GP care and PT compared with GP care alone.[266]

TABLE 92 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Exercise therapy vs disc surgery														
300	Osterman, 2006[68]	A	RCT	6 months	Full recovery	Patient	28	4	0	28	5	0	0.77 (0.18 to 3.22)	ITT using LOCF Dropouts 12%: surgery 3/29 (one patient did not meet inclusion criteria, excluded from analysis), exercise 4/28
Exercise therapy vs usual/conventional care														
742	Luijsterburg, 2008[264]	A	RCT	12 weeks	Improved (seven-point Likert scale): 'completely recovered' and 'much improved' (vs 'slightly improved', 'not changed', 'slightly worsened', 'much worsened' and 'worse than ever')	Patient	67	47	0	68	42	0	1.45 (0.71 to 2.98)	ITT using LOCF Dropouts 7%: intervention 3/67, control 6/68

A, acute; LOCF, last observation carried forward.

TABLE 93 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Exercise therapy vs disc surgery																
300	Osterman, 2006[68]	A	RCT	6 months	Leg	VAS (0–100)	28	28	57 (21)	61 (20)	18 (29)	9 (20)			9.00 (–4.05 to 22.05)	ITT using LOCF Dropouts 12%: surgery 3/29 (one patient did not meet inclusion criteria, excluded from analysis), exercise 4/28
Exercise therapy vs usual/conventional care																
742	Luijsterburg, 2008[264]	A	RCT	12 weeks	Leg	NRS (0–10)	67	68	63 (22)	63 (22)			–39 (28)	–37 (31)	–2.00 (–11.96 to 7.96) *Mean difference –0.2 (95% CI –1.2 to 0.8)*	ITT using LOCF Dropouts 7%: intervention 3/67, control 6/68

A, acute; LOCF, last observation carried forward; NRS, numerical rating scale.
a The results have been converted to a scale of 0–100 for comparability.
b Based on final means or change scores (with a preference given to change scores); results reported by study in italics.
c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.
Bakhtiary *et al.*[265] also reported 8-week outcome data, but these data do not represent exercise therapy vs alternative and therefore are not included here. The intervention was 4 weeks of lumbar-stabilising exercise followed by a 4 weeks of no exercise (group A) compared with 4 weeks of no exercise followed by 4 weeks of lumbar-stabilising exercise (group B).

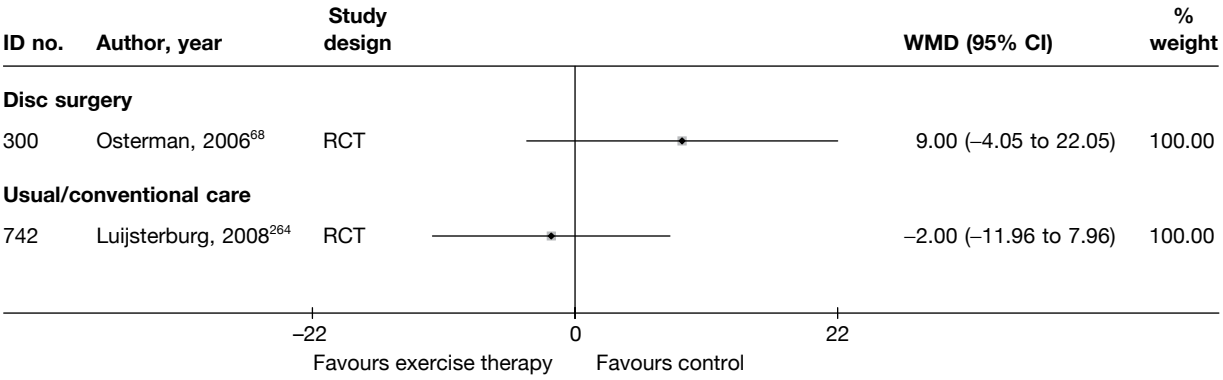

FIGURE 62 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

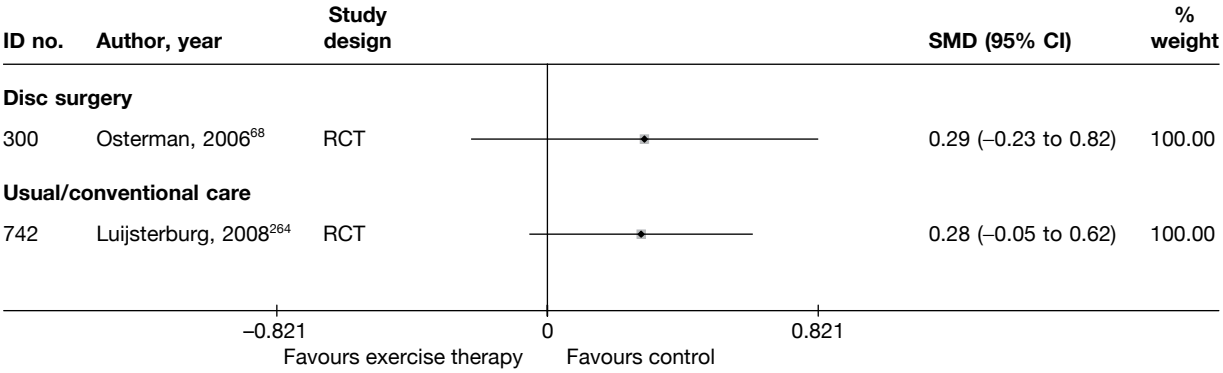

FIGURE 63 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

Condition-specific outcome measures at long-term follow-up

The results for CSOMs at long-term follow-up are presented in *Table 97* and the accompanying forest plot (*Figure 66*). There was no significant difference in CSOMs in a moderate-quality RCT of exercise therapy alone compared with disc surgery plus exercise therapy,[68] or in a good-quality RCT of GP care and PT compared with GP care alone.[266]

Adverse effects

The total number of adverse effects is presented in *Table 98* and the accompanying forest plot (*Figure 67*). There was no significant difference between exercise therapy and disc surgery with exercise therapy,[68] or between isometric exercises and manual traction.[242]

SUMMARY OF OVERALL FINDINGS FOR ACTIVE PHYSICAL/EXERCISE THERAPY COMPARED WITH ALTERNATIVE INTERVENTIONS

Six RCTs,[68,242,255,256,264,265] one of which was a crossover trial,[265] compared the use of active physical therapy with other interventions (*Table 99*).

One moderate-quality crossover RCT[265] found that lumbar-stabilising exercises, compared with no exercise, resulted in a significant improvement in pain intensity in the short term. However, in another poor-quality RCT,[256] massage, hot packs and exercise resulted in no significant difference in short-term global effect compared with hot packs and rest. In this same RCT, short-term

TABLE 94 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Exercise therapy vs disc surgery															
300	Osterman, 2006[68]	A	RCT	6 months	ODI	28	28	39 (14)	39 (15)	12 (15)	8 (12)	–27	–31	0.29 (–0.23 to 0.82)	ITT used LOCF, but one patient that did not meet inclusion criteria excluded from analysis
Exercise therapy vs usual/conventional care															
742	Luijsterburg, 2008[264]	A	RCT	12 weeks	RMDQ	67	68	15.9 (4.1)	15.4 (5)	8.2 (4.10)	6.9 (5)	–7.7 (7.3)	–8.5 (6.7)	0.28 (–0.05 to 0.62)	Baseline SD used for final mean SD ITT used LOCF

A, acute; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 95 Summary of the findings of the global effect at long-term follow-up (> 6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Exercise therapy vs disc surgery														
300	Osterman, 2006[68]	A	RCT	2 years	Full recovery	Patient	28	5	0	28	7	0.03	0.66 (0.18 to 2.37)	ITT using LOCF Dropouts 12%: surgery 3/29 (one patient did not meet inclusion criteria, excluded from analysis), exercise 4/28
Exercise therapy vs usual/conventional care														
742	Luijsterburg, 2008[264]	A	RCT	52 weeks	Improved (seven-point Likert scale): 'completely recovered' or 'much improved' (vs 'slightly improved', 'not changed', 'slightly worsened', 'much worsened' or 'worse than ever')	Patient	67	53	0	68	38	0	2.99 (1.40 to 6.38)	ITT using LOCF Dropouts 13%: intervention 7/67, control 11/68

A, acute; LOCF, last observation carried forward.

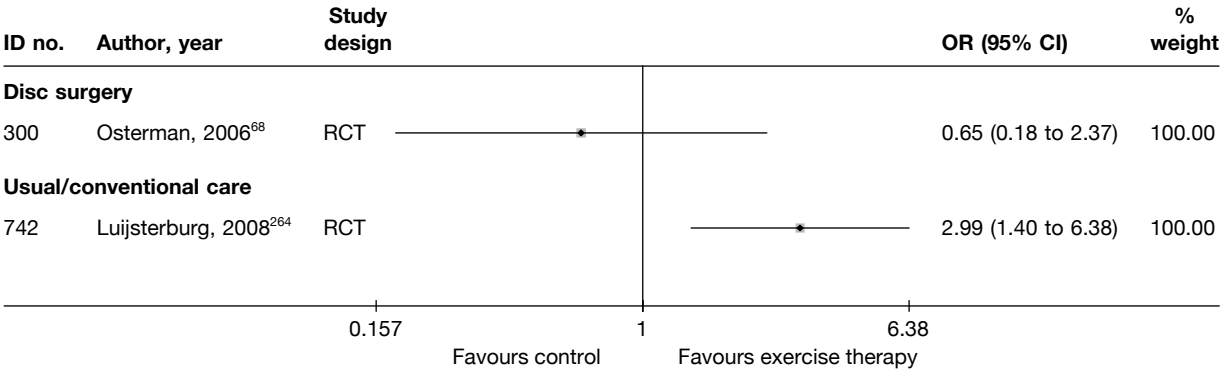

FIGURE 64 Summary of the findings of the global effect at long-term follow-up (>6 months) for studies comparing exercise therapy to alternative interventions. Note: weights are from random effects analysis.

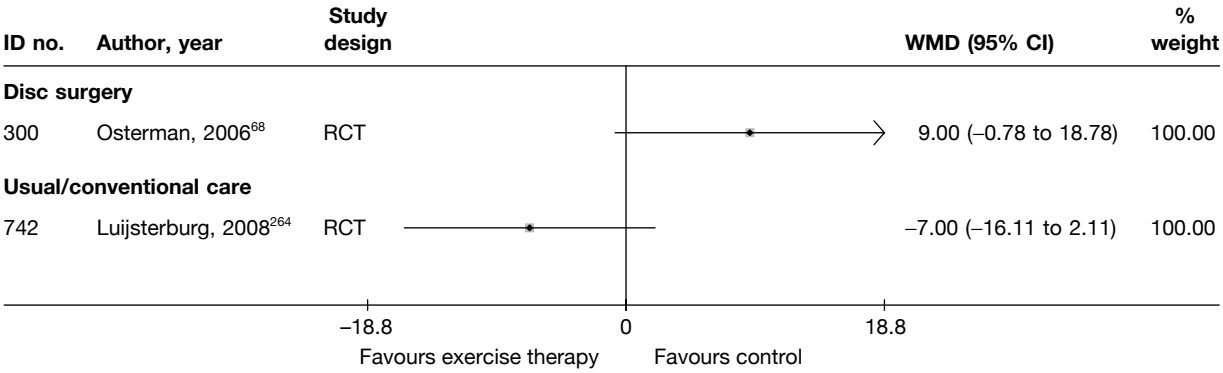

FIGURE 65 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

global effect of massage, hot packs and exercise were worse than those of pelvic traction and strengthening exercises, but two other moderate-quality RCTs[242,255] found no significant difference in short-term global effect between isometric exercises and traction, and no significant difference in short-term global effect, pain intensity or CSOMs between an extension-orientated treatment approach consisting of exercise, mobilisation and exercises and the extension-orientated treatment approach plus traction. In one good-quality RCT,[266] PT plus GP care, compared with GP care alone, resulted in significantly worse short-term CSOMs and significantly better long-term global effect, but there was no significant difference at other follow-up periods or in pain intensity at any of the three follow-up periods. In one moderate-quality RCT,[68] short-term pain intensity was significantly worse in the group that received exercise therapy than in the group treated with exercise therapy plus microdiscectomy, but there was no significant difference in pain intensity at medium- and long-term follow-up, or in the global effect or CSOMs at any of the three follow-up periods.

TABLE 96 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Exercise therapy vs disc surgery																
300	Osterman, 2006[68]	A	RCT	2 years	Leg	VAS (0–100)	28	28	57 (21)	61 (20)	15 (24)	6 (11)			9.00 (–0.78 to 18.78)	ITT using LOCF Dropouts 12%: surgery 4/29 (one patient did not meet inclusion criteria, excluded from analysis), exercise 4/28
Exercise therapy vs usual/conventional care																
742	Luijsterburg, 2008[264]	A	RCT	52 weeks	Leg	NRS (0–10)	67	68	63 (22)	63 (22)			–44 (27)	–37 (27)	–7.00 (–16.11 to 2.11) *Mean difference –0.7 (95% CI –1.7 to 0.2)*	ITT using LOCF Dropouts 13%: intervention 7/67, control 11/68

A, acute; LOCF, last observation carried forward; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores.

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 97 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing exercise therapy to alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/ conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Exercise therapy vs disc surgery															
300	Osterman, 2006[68]	A	RCT	2 years	ODI	28	28	39 (14)	39 (15)	11 (16)	6 (9)	–28	–33	0.39 (–0.14 to 0.91)	ITT used LOCF, but one patient that did not meet inclusion criteria excluded from analysis
Exercise therapy vs usual/conventional care															
742	Luijsterburg, 2008[264]	A	RCT	52 weeks	RMDQ	67	68	15.9 (4.1)	15.4 (5)	5.9 (4.1)	6.3 (5)	–10 (6.5)	–9.1 (6.1)	0.09 (–0.42 to 0.25)	Final score calculated from change score No final SD, so baseline SD used ITT used LOCF

A, acute; LOCF, last observation carried forward.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

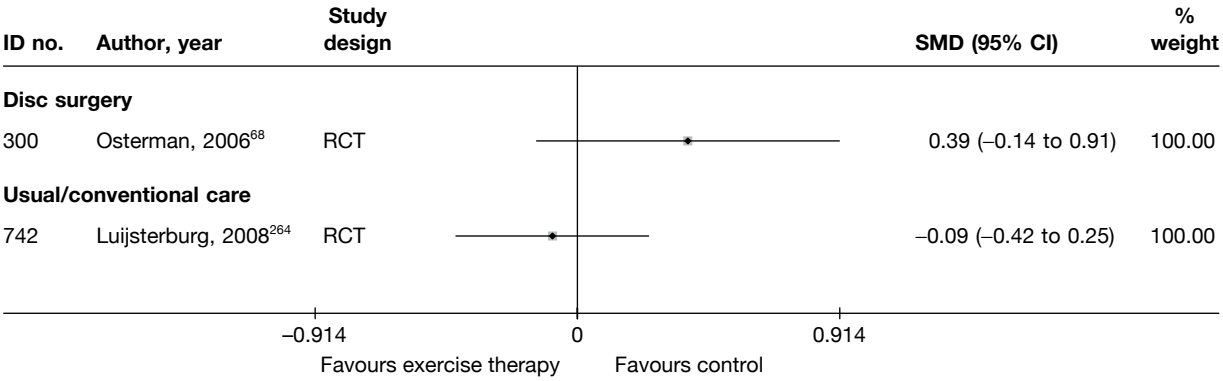

FIGURE 66 Summary of the findings of CSOMs at long-term follow-up (> 6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

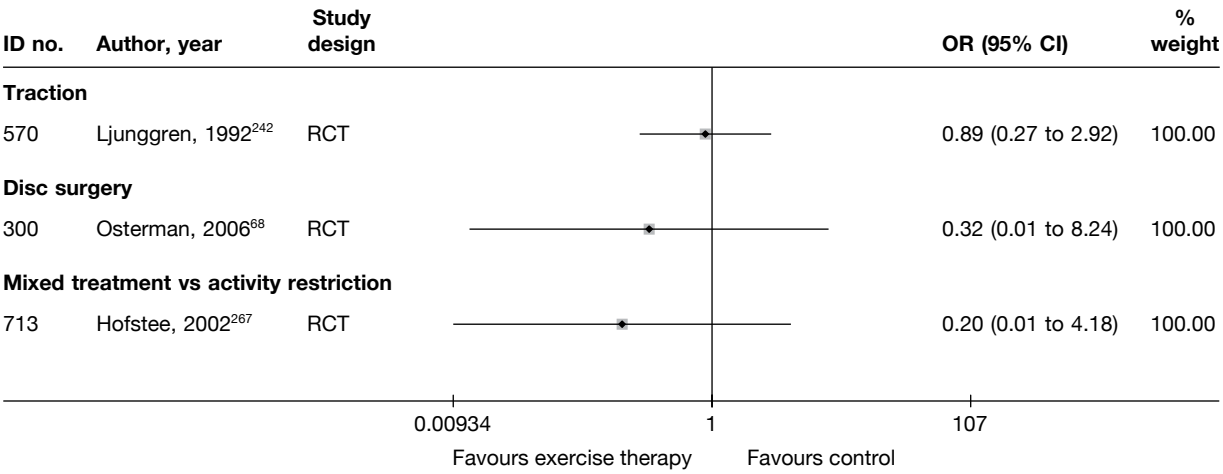

FIGURE 67 Summary of the findings of any adverse effect for studies comparing active PT with alternative interventions. Note: weights are from random effects analysis.

TABLE 98 Summary of the findings of any adverse effects for studies comparing active PT with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Exercise therapy vs activity restriction							
429	Bakhtiary, 2005[265]	RCT (crossover)	NR	NR	NR	NR	
564	Lidstrom, 1970[256]	RCT	NR	NR	NR	NR	
Exercise therapy vs activity restriction							
713	Hofstee, 2002[267]	RCT	0	83	2	84	5.00 (0.24 to 100.00)
Exercise therapy vs disc surgery							
300	Osterman, 2006[68]	RCT	0	28	1	28	0.32 (0.01 to 8.24)
Exercise therapy vs mixed treatment							
564	Lidstrom, 1970[256]	RCT	NR	NR	NR	NR	
Exercise therapy vs traction							
570	Ljunggren, 1992[242]	RCT	8	26	8	24	0.89 (0.27 to 2.92)
Exercise therapy vs usual care							
742	Luijsterburg, 2008[264]	RCT	NR	NR	NR	NR	

NR, not reported.

TABLE 99 Summary of exercise therapy studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Exercise therapy vs activity restriction	1 (1)	62 (62)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Exercise therapy vs disc surgery	1 (1)	57 (57)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)
Exercise therapy vs inactive control	1 (1)	60 (60)	1/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Exercise therapy vs mixed treatment	1 (1)	62 (63)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Exercise therapy vs traction	1 (1)	50 (50)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Exercise therapy vs usual/ conventional care	1 (1)	135 (135)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total (for exercise therapy studies)	**(6) (7)**	**50–135 (62)**	**6/6 (100)**	**1/6 (17)**	**3/6 (50)**	**5/6 (83)**	**3/6 (50)**	**0/6 (0)**	**1/6 (17)**	**0/6 (0)**	**0/6 (0)**	**0/6 (0)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Passive physical therapy

Description of passive physical therapy studies

Summary of interventions

Six studies compared passive PT with an alternative type of intervention for sciatica.[155,176,249,253,268,269] Summary data of the interventions used are presented in *Table 100a*. Two of these studies also included more than two arms and both compared different types of passive PT (*Table 100b*).[249,268] One three-armed crossover RCT[268] compared transcutaneous electrical nerve stimulation (TENS) with percutaneous electrical nerve stimulation (PENS) and with sham PENS. One three-armed RCT[249] compared ultrasound treatment with a low-power laser and with lumbar traction. One RCT[253] compared a PT programme (consisting of hot packs, ultrasound and diadynamic electric currents) with the PT programme and traction. One RCT[176] compared infrared heat treatment with lumbar traction. One RCT[155] compared conservative physiotherapy (no further details given) with epidural steroid and local anaesthetic injection. One non-RCT[269] compared physiotherapy (no further details given) with ESI and active or passive PT.

TABLE 100a Summary of the interventions used when comparing passive PT with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	Treatment description	Control description
Passive PT vs epidural/intradiscal injection				
359	Veihelmann, 2006[155]	RCT	Conservative physiotherapy	Epidural injection via epidural catheter (neuroplasty) of steroid triamcinolone 40 mg and ropivacaine
Passive PT vs inactive control				
496	Ghoname, 1999[268]	RCT (crossover)	PENS	Sham PENS
496	Ghoname, 1999[268]	RCT (crossover)	TENS	Sham PENS
Passive PT vs mixed treatment				
354	Bokonjic, 1975[269] (German language)	Non-RCT	Physiotherapy alone	Three epidural injection of steroid dexa-neurobion every 4 days + active or passive PT
266	Ozturk, 2006[253] (traction vs passive PT)	RCT	PT programme (control group)	Traction and PT programme (traction group)
Passive PT vs traction				
9059	Mathews, 1987[176]	RCT	Infrared heat treatment	Lumbar traction
148	Unlu, 2008[249]	RCT	Ultrasound treatment	Lumbar traction
148	Unlu, 2008[249]	RCT	Low-power laser	Lumbar traction

PENS, percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation.

TABLE 100b Summary of the interventions used when comparing alternative forms of passive PT

ID no.	Author, year	Study design	Treatment description	Control description
496	Ghoname, 1999[268]	RCT (crossover)	TENS	Sham PENS
148	Unlu, 2008[249]	RCT	Low-power laser	Ultrasound treatment

PENS, percutaneous electrical nerve stimulation; TENS, transcutaneous electrical nerve stimulation.

Summary of study participants in passive physical therapy studies

Summary data on the included participants are presented in *Table 101*. The six trials included 468 participants with mean ages between 31 and 46 years (30–60% men): one with acute symptom duration, three with chronic symptoms and two that did not report length of symptoms. One non-RCT included participants with first and recurrent episodes of sciatica, but this was not reported in the remainder. Sciatica was confirmed by imaging in five trials. There were no patients with spinal stenosis or sequestered discs and previous back surgery was excluded in two trials.

Summary of study quality for passive physical therapy

Study details are summarised in *Table 102*. Five of the studies were RCTs (5/6, 83%) and none was of good quality. None had an adequate method of random number generation and only one documented a secure method of allocation concealment.[155] No studies had good external validity.

Passive physical therapy results at short-term follow-up (≤ 6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 103* and the accompanying forest plot (*Figure 68*). There was a significant improvement in the global effect in the TENS or PENS group compared with inactive control in one poor-quality crossover RCT.[268] However, one poor-quality non-RCT found a significant improvement in the global effect when ESI was combined with active or passive PT compared with physiotherapy alone.[269] There was no significant difference in the global effect in one moderate-quality RCT comparing heat treatment with traction.[176]

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 104* and the accompanying forest plot (*Figure 69*). There was a significant improvement in pain intensity in the groups receiving TENS or PENS compared with inactive control in one poor-quality non-RCT.[268] There was no significant difference in pain intensity in two moderate- or poor-quality RCTs comparing ultrasound or laser with traction[249] or unspecified PT with PT and traction.[253]

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 105* and the accompanying forest plot (*Figure 70*). There was no significant difference in CSOMs in one moderate-quality RCT comparing ultrasound or laser with traction.[249]

Passive physical therapy results at medium-term follow-up (> 6 weeks to ≤ 6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 106* and the accompanying forest plot (*Figure 71*). In one moderate-quality RCT there was a significant improvement in global effect in a group receiving epidural steroids compared with conservative physiotherapy.[155]

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 107* and the accompanying forest plot (*Figure 72*). There was no significant difference in pain intensity in one moderate-quality RCT comparing ultrasound or laser with traction[249] or in another moderate-quality RCT that compared epidural steroids with conservative physiotherapy.[155]

TABLE 101 Summary of sciatica type and study population details for studies comparing passive PT with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Passive PT vs epidural/intradiscal injection													
359	Veihelmann, 2006[155]	RCT	99	Mean 44.5 (SD 24)	45 (45)	NR	Nerve root pain	Yes	NR	No	No	Yes	Yes
Passive PT vs inactive control													
496	Ghoname, 1999[268]	RCT (crossover)	64	Mean 43 (range ± 19)	30 (47)	Mean 21 months (SD 9; range 6–28 months)	Nerve root pain and referred pain	Yes	NR	No	No	Yes	Yes
Passive PT vs mixed treatments													
354	Bokonjic, 1975[269] (German language)	Non-RCT	56	Mean 31.1	23 (64)	NR	Nerve root pain and referred pain	Yes	Recurrent and first episode	No	No	NR	NR
266	Ozturk, 2005[253]	RCT	46	Mean 46.2 (SD 10.2); range 16–70)	22 (48)	Inclusion criteria ≥ 6 months	Nerve root pain	Yes	NR	No	No	NR	No
Passive PT vs traction													
9059	Mathews, 1987[176]	RCT	143	Median 40 (range 20–60)	80 (56)	Median 3.5 weeks (range 0 days–3 months)	Nerve root pain	No	NR	No	No	NR	NR
148	Unlu, 2008[249]	RCT	60	Mean 44.5 (range 20–60)	18 (30)	> 3 months	Nerve root pain	Yes	NR	No	No	NR	No

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 102 Summary of the study details for studies comparing passive PT with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Passive PT vs epidural/intradiscal injection										
359	Veihelmann, 2006[155]	99	12 months	RCT	Partial	Yes	<60	Yes	Moderate	Weak
Passive PT vs inactive control										
496	Ghoname, 1999[268]	64	11 weeks	RCT	Unclear	Unclear	Can't tell	NA	Weak	Weak
Passive PT vs mixed treatments										
354	Bokonjic, 1975[269] (German language)	56	12 days	Non-RCT	No	No	80–100	Unclear	Weak	Weak
266	Ozturk, 2006[253]	46	2 weeks	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Passive PT vs traction										
9059	Mathews, 1987[176]	143	12 months	RCT	Partial	Unclear	<60	Yes	Moderate	Moderate
148	Unlu, 2008[249]	60	3 months	RCT	Unclear	Unclear	80–100	Yes	Moderate	Weak

TABLE 103 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing passive PT with alternative interventions

							Intervention			Control				
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)	Comments
Passive PT vs inactive control														
496	Ghoname, 1999[268] (i)[a] (PENS)	A + C	RCT (crossover)	72 hours	'Improved sense of well being' selected out of four subheadings (asked about treatment preference in crossover trial)	Patient	64	42	0	64	5	0	22.53 (7.89 to 64.28)	
496	Ghoname, 1999[268] (ii)[a] (TENS)	A + C	RCT (crossover)	72 hours	'Improved sense of well being' selected out of four subheadings (asked about treatment preference in crossover trial)	Patient	64	17	0	64	5	0	4.27 (1.47 to 12.42)	
Passive PT vs mixed treatments														
354	Bokonjic, 1975[269] (German language)	NR	Non-RCT	12 days	Improved = excellent or good (vs no change = moderate or poor)		20	4	0	34	17	0.06	0.25 (0.07 to 0.90)	
Passive PT vs traction														
9059	Mathews, 1987[176]	A	RCT	2 weeks	Number of patients recovered (percentage). Pain score of 5 or 6 represented definite improvement and designated 'recovered', scores of 1–4 designated 'not recovered'		54	27	0.10	77	40	0.07	0.93 (0.46 to 1.86)	Number of dropouts reported were different to the number missing from the analysis

A, acute; A + C, acute and chronic; NR, not reported.

a Ghoname *et al.*[268] included three treatment groups: PENS (i), TENS (ii) and sham PENS (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 68*).

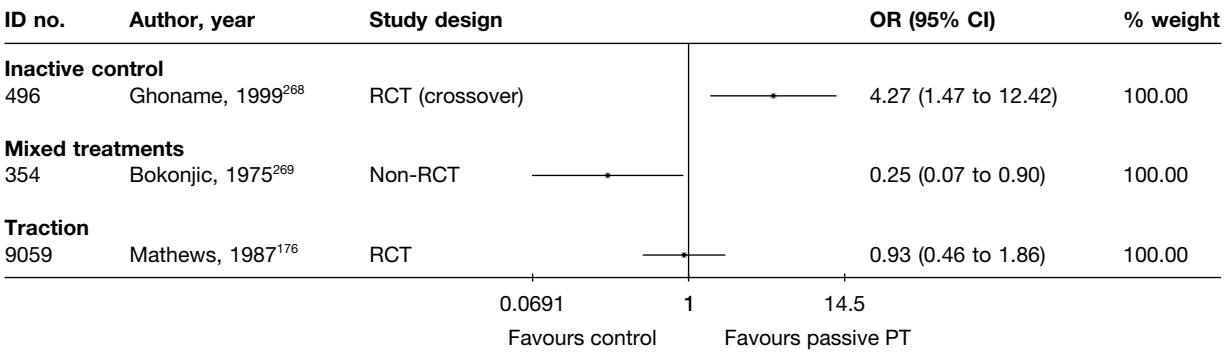

FIGURE 68 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing passive PT with alternative interventions. Note: weights are from random effects analysis.

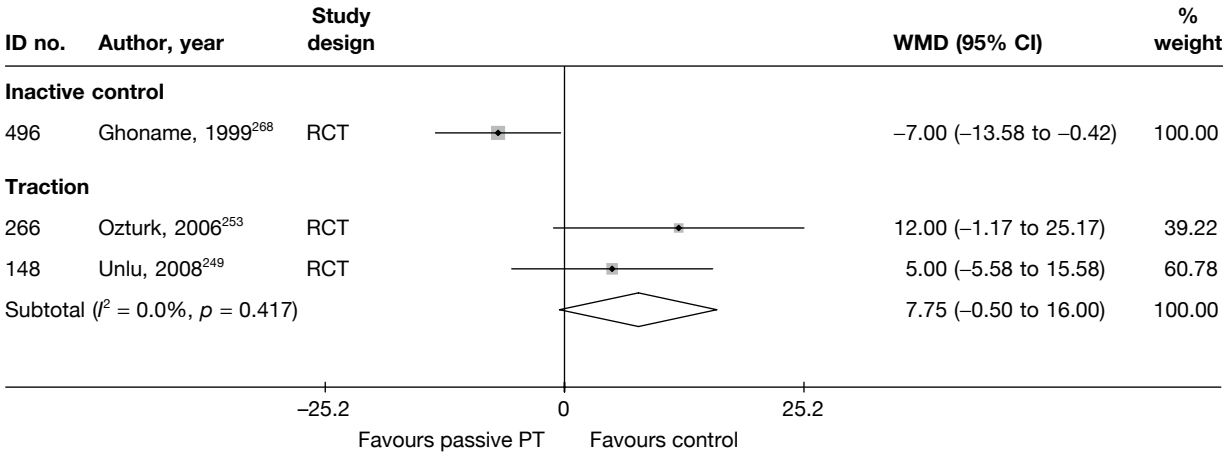

FIGURE 69 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing passive PT with alternative interventions. Note: weights are from random effects analysis.

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 108* and the accompanying forest plot (*Figure 73*). There was no significant difference in CSOMs in one moderate-quality RCT comparing ultrasound or laser with traction,[249] or in another moderate-quality RCT that compared epidural steroids with conservative physiotherapy.[155]

Passive physical therapy results at long-term follow-up (>6 months)

Global effect at long-term follow-up

The results for the global effect at long-term follow-up are presented in *Table 109* and the accompanying forest plot (*Figure 74*). In one moderate-quality RCT, there was a significant improvement in global effect in a group receiving epidural steroids compared with a group receiving conservative physiotherapy.[155]

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 110* and the accompanying forest plot (*Figure 75*). There was no significant difference in pain intensity in one moderate-quality RCT that compared conservative physiotherapy with epidural steroids.[155]

Condition-specific outcome measures at long-term follow-up

The results for CSOMs at long-term follow-up are presented in *Table 111* and the accompanying forest plot (*Figure 76*). In one moderate-quality RCT, there was a significant improvement in CSOMs in a group receiving epidural steroids compared with conservative physiotherapy.[155]

TABLE 104 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing passive PT with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Passive PT vs inactive control															
496	Ghoname, 1999[268] (i)[c] (PENS)	A + C	RCT (crossover)	72 hours		VAS (0–10)	64	64	72 (18)	66 (19)	41 (14)	61 (19)			–20.00 (–25.78 to –14.22)
496	Ghoname, 1999[268] (ii)[c] (TENS)	A + C	RCT (crossover)	72 hours	Leg	VAS (0–10)	28	28	70 (19)	66 (19)	54 (19)	61 (19)			–7.00 (–13.58 to –0.42)
Passive PT vs traction															
148	Unlu, 2008[249] (i)[d] (ultrasound)	A	RCT	1 month	Leg	VAS (0–100)	20	20	56.0 (15.3)	59.6 (15.4)	26.8 (18.6)	21.8 (15.4)			5.00 (–5.58 to 15.58)
148	Unlu, 2008[249] (ii)[d] (laser)	A	RCT	1 month	Leg	VAS (0–100)	20	20	53.1 (25.9)	59.6 (15.4)	25.6 (21.1)	21.8 (15.4)			3.80 (–7.65 to 15.25)
Passive PT vs mixed treatments															
266	Ozturk, 2006[253] (traction + PT vs PT)	NR	RCT	15 days	Overall	VAS (0–10)	22	24	68 (11)	63 (14)	36 (27)	24 (17)			12.00 (–1.17 to 25.17)

A, acute; A + C, acute and chronic; NR, not reported.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c Ghoname *et al.*[268] included three treatment groups: PENS (i), TENS (ii) and sham PENS (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 69*).

d Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the first and last treatment groups have been included in the meta-analysis (see *Figure 69*).

TABLE 105 Summary of the findings of CSOMs at short-term follow-up (≤ 6 weeks) for studies comparing passive PT with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Passive PT vs traction														
148	Unlu, 2008[249] (i)[b] (ultrasound)	A	RCT	1 month	RMDQ	20	20	13.4 (4.5)	14.2 (4.3)	8.2 (6)	8.5 (3.5)	–5.2	–5.7	–0.06 (–0.68 to 0.56)
148	Unlu, 2008[249] (ii)[b] (laser)	A	RCT	1 month	RMDQ	20	20	12.5 (5)	14.2 (4.3)	7.3 (4.3)	8.5 (3.5)	–5.2	–5.7	–0.31 (–0.93 to 0.32)

A, acute.

a Based on final means or change scores (with a preference given to change scores).

c Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the first and last treatment groups have been included in the meta-analysis (see *Figure 70*).

TABLE 106 Summary of the findings of the global effect at medium-term follow-up (> 6 weeks to ≤ 6 months) for studies comparing passive therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	
Passive PT vs epidural/intradiscal injection													
359	Veihelmann, 2006[155]	C	RCT	6 months	Gerbershagen score (Chronification Index), GHS I (vs GHS II, III)		27	8	0.48	46	31	0.02	0.19 (0.07 to 0.54)

C, chronic.

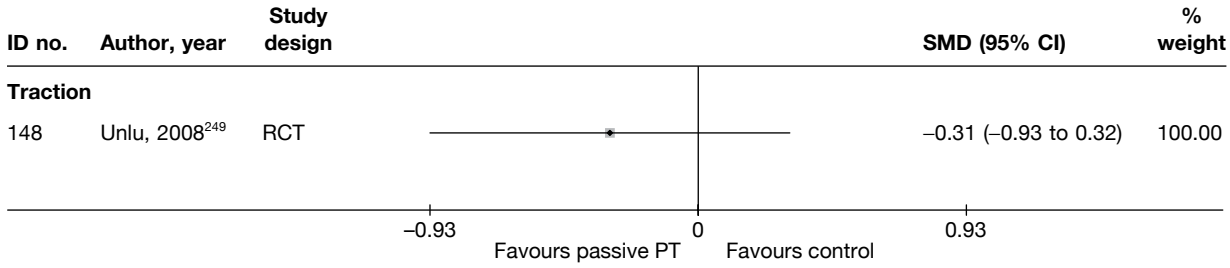

FIGURE 70 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing passive PT with alternative interventions. Note: weights are from random effects analysis.

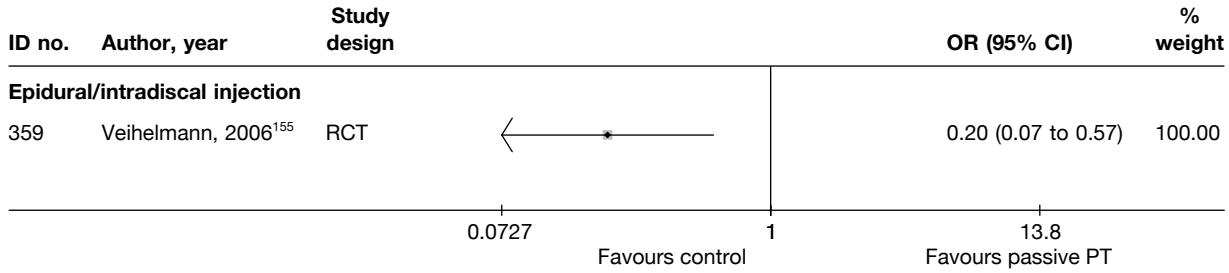

FIGURE 71 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing passive therapy with alternative interventions. Note: weights are from random effects analysis.

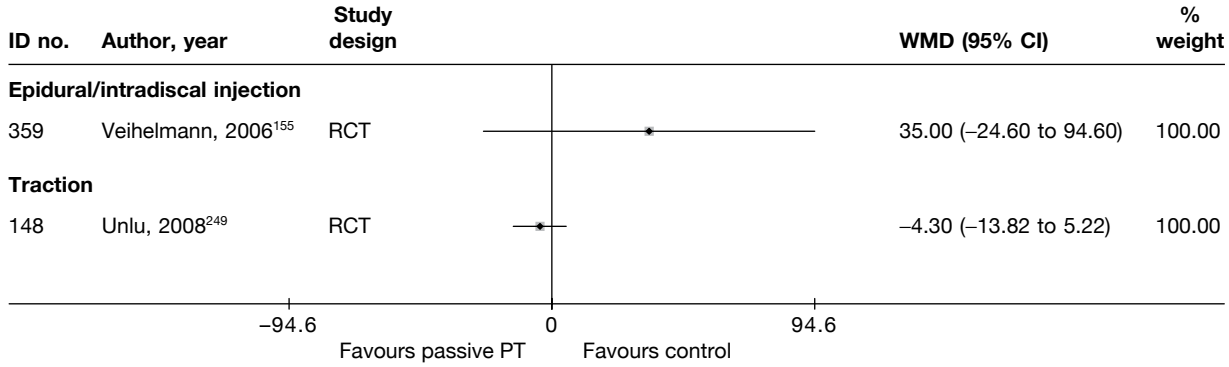

FIGURE 72 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing passive PT with alternative interventions. Note: weights are from random effects analysis.

Adverse effects

The total number of adverse effects is presented in *Table 112* and the accompanying forest plot (*Figure 77*). Adverse effects were reported in only one RCT, which found significantly more adverse events in the group receiving epidural steroids than in the group receiving conservative physiotherapy.[155]

SUMMARY OF OVERALL FINDINGS FOR PASSIVE PHYSICAL THERAPY COMPARED WITH ALTERNATIVE INTERVENTIONS

Six studies, five of which were RCTs[155,176,249,253,269] (one was a crossover trial[268]), compared the use of passive physical therapy with other interventions. Two RCTs[176,249] restricted inclusion to patients with acute sciatica (*Table 113*).

TABLE 107 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing passive PT with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/ conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Passive PT vs epidural																
359	Veihelmann, 2006[155]	C	RCT	6 months	Leg	VAS (0–10)	27	46	67 (103.9)	72 (135.6)	58 (114.3)	23 (142.4)			35.00 (–24.60 to 94.60)	SD derived from SE
Passive PT vs traction																
148	Unlu, 2008[249] (i)[d] (ultrasound)	A	RCT	3 months	Leg	VAS (0–100)	20	20	56.0 (15.3)	59.6 (15.4)	25.2 (13.9)	29.5 (16.7)			–4.30 (–13.82 to 5.22)	
148	Unlu, 2008[249] (ii)[d] (laser)	A	RCT	3 months	Leg	VAS (0–100)	20	20	53.1 (25.9)	59.6 (15.4)	23.6 (17.7)	29.5 (16.7)			–5.90 (–16.56 to 4.76)	

A, acute; C, chronic.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

d Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the first and last treatment groups have been included in the meta-analysis (see *Figure 72*).

TABLE 108 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing passive PT with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Passive PT vs epidural															
359	Veihelmann, 2006[155]	C	RCT	6 months	ODI	27	46	23.1	21.4	22.5 (46.25)	10.8 (50.19)			–0.22 (–0.70 to 0.25)	SD based on weighted average Dropouts 26 (26%): control (epidural) 1/47, intervention (PT) 25/52
Passive PT vs traction															
148	Unlu, 2008[249] (i)[c] (laser)	A	RCT	3 months	RMDQ	20	20	13.4 (4.5)	14.2 (4.3)	8.6 (6)	8.94 (4)	–4.8	–5.3	–0.06 (–0.68 to 0.56)	
148	Unlu, 2008[249] (ii)[c] (ultrasound)	A	RCT	3 months	RMDQ	20	20	12.5 (5)	14.2 (4.3)	6.7 (4.5)	8.9 (4)	–5.8	–5.3	–0.52 (–1.15 to 0.11)	

A, acute; C, chronic.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Unlu *et al.*[249] included three treatment groups: ultrasound treatment (i), low-power laser (ii) and lumbar traction (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 73*).

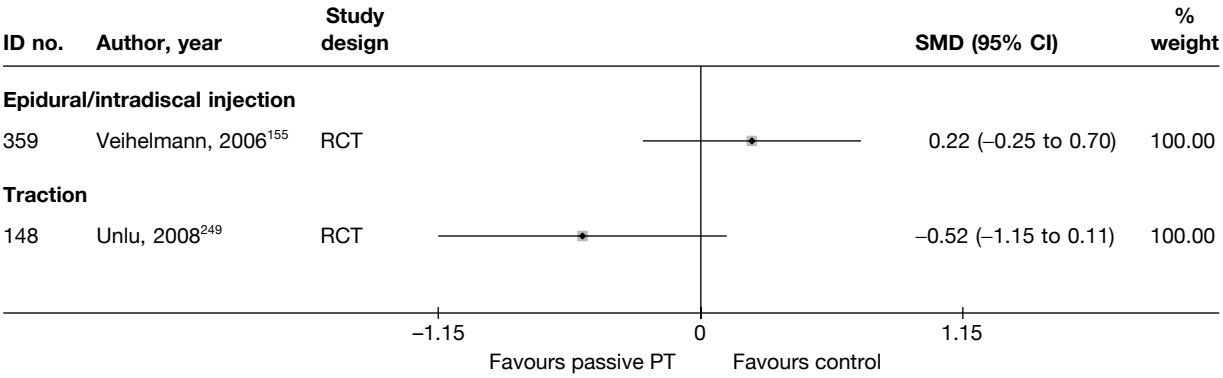

FIGURE 73 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing passive PT with alternative interventions. Note: weights are from random effects analysis.

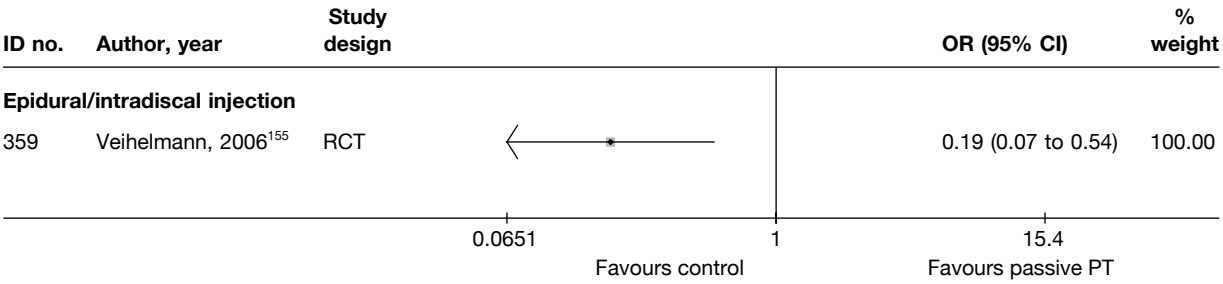

FIGURE 74 Summary of the findings of the global effect at long-term (>6 months) follow-up for studies comparing passive PT with alternative interventions. Note: weights are from random effects analysis.

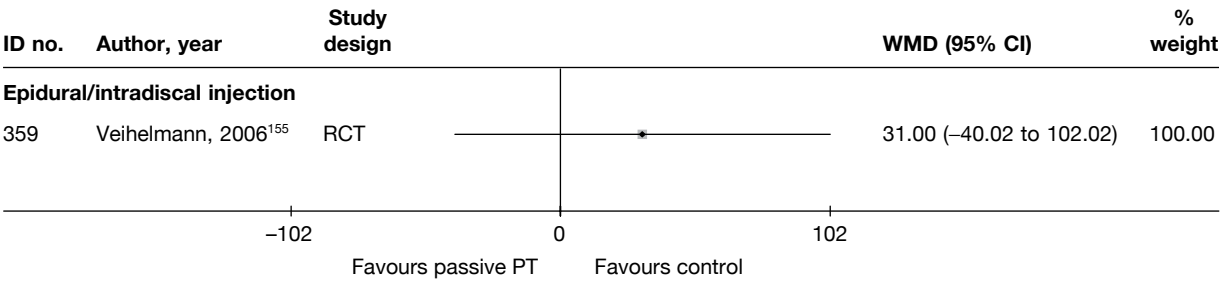

FIGURE 75 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

In one poor-quality crossover RCT[268] there was a significant improvement in global effect and pain intensity in the short term with TENS or PENS compared with inactive control. There was no significant difference in terms of global effect, pain intensity or CSOMs at short-, medium- or long-term follow-up in three moderate- or poor-quality RCTs[176,249,253] that compared heat, ultrasound, laser or an unspecified PT programme with traction. Physiotherapy programmes were less effective than epidural corticosteroid injections in terms of short-term global effect in one poor-quality non-RCT[269] and in terms of medium- and long-term global effect, pain intensity and CSOMs in one moderate-quality RCT.[155] Adverse effects were less common with physiotherapy than with epidural injection of corticosteroid in this latter RCT.

TABLE 109 Summary of the findings of the global effect at long-term (>6 months) follow-up for studies comparing passive PT with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Out come (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Passive PT vs epidural/intradiscal injection														
359	Veihelmann, 2006[155]	C	RCT	12 months	Gerbershagen score (Chronification Index), GHS I (vs GHS II, III)	–	27	7	0.48	46	30	0.02	0.20 (0.07 to 0.57)	Twelve patients moved over to epidural group and excluded from analysis

C, chronic.

TABLE 110 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Passive PT vs epidural/intradiscal injection																
359	Veihelmann, 2006[155]	C	RCT	12 months	Leg	VAS (0–10)	27	46	67 (103.9)	72 (135.6)	59 (119.51)	28 (189.91)			35.00 (–24.60 to 94.60)	SD derived from SE Dropouts 26/99 (26%): intervention 22/52 (48%), control (epidural) 1/47 (2%) Twelve patients in PT group moved over to epidural and excluded from analysis

C, chronic.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 111 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing exercise therapy with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Passive PT vs epidural/intradiscal injection															
359	Veihelmann, 2006[155]	C	RCT	12 months	ODI	27	46	23.1	21.4	21.6 (54.2)	11.6 (67.82)			–0.77 (–1.26 to –0.28)	SD based on weighted average Dropouts 26/99 (26%): intervention 22/52 (48%), control (epidural) 1/47 (2%) Twelve patients in PT group moved over to epidural and excluded from analysis

C, chronic.

a Based on final means or change scores (with a preference given to change scores).

b Dropouts have been used for missing data as well as patients lost to follow-up.

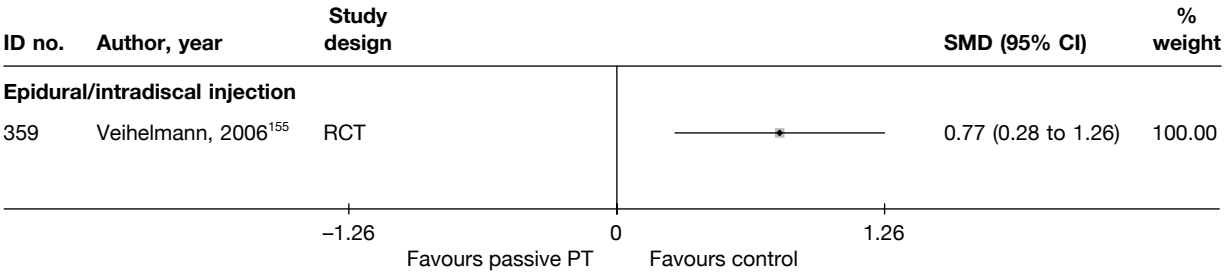

FIGURE 76 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing exercise therapy with alternative interventions. Note: weights are from random effects analysis.

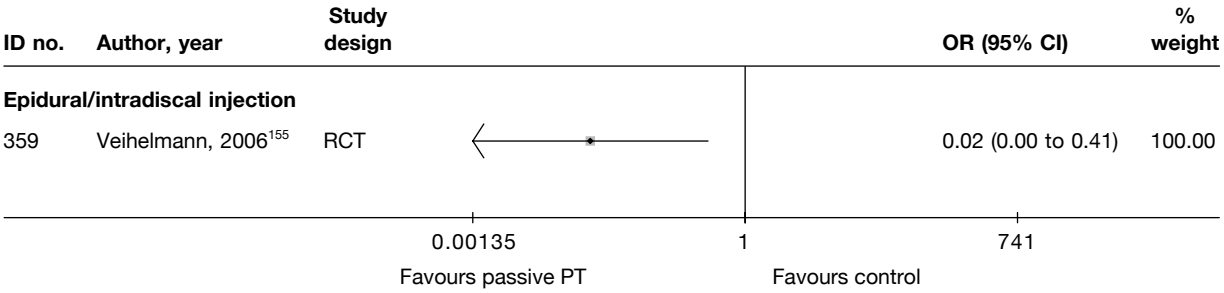

FIGURE 77 Summary of the findings of any adverse effect for studies comparing passive PT with alternative treatment. Note: weights are from random effects analysis.

TABLE 112 Summary of the findings of any adverse effect for studies comparing passive PT with alternative treatment

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Passive PT vs epidural							
359	Veihelmann, 2006[155]	RCT	0	39	16	46	0.02 (0.00 to 0.40)
Passive PT vs inactive control							
496	Ghoname, 1999[268] (PENS)	RCT	NR	NR	NR	NR	
496	Ghoname, 1999[268] (TENS)	RCT	NR	NR	NR	NR	
Passive PT vs mixed treatment							
354	Bokonjic, 1975[269]	Non-RCT	NR	NR	NR	NR	
266	Ozturk, 2006[253] (traction vs passive PT)	RCT	NR	NR	NR	NR	
Passive PT vs traction							
9059	Mathews, 1987[176]	RCT	NR	NR	NR	NR	
148	Unlu, 2008[249] (laser)	RCT	NR	NR	NR	NR	
148	Unlu, 2008[249] (ultrasound)	RCT	NR	NR	NR	NR	

NR, not reported.

TABLE 113 Summary of passive PT studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Passive PT vs epidural/ intradiscal injection	1 (1)	99 (99)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
Passive PT vs inactive control	1 (2)	64 (64)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
Passive PT vs mixed treatment	2 (2)	46–56 (51)	1/2 (50)	0/2 (0)	0/2 (0)	2/2 (100)	2/2 (100)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
Passive PT vs traction	2 (2)	60–143 (102)	2/2 (100)	0/2 (0)	2/2 (100)	2/2 (100)	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
Total (for passive PT studies)	**6 (6)**	**46–143 (62)**	**5/6 (83)**	**0/6 (0)**	**2/6 (33)**	**6/6 (100)**	**5/6 (83)**	**0/6 (0)**	**0/6 (0)**	**0/6 (0)**	**2/6 (33)**	**2/6 (33)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Biological agents

Biological agents are derived from living material and have a highly complex chemical structure. They are being used increasingly in rheumatological practice to control inflammatory disease. Tumour necrosis factor-alpha (TNF-α) is one of the proinflammatory factors released from prolapsed intervertebral discs that is responsible for inflammation of the affected nerve root in sciatica and may be amenable to treatment by these biological therapies. Biological agents that inhibit TNF-α include etanercept, infliximab (Remicade®, Schering-Plough Ltd) and adalimumab (Humira®, Abbott).

Description of biological agents studies

Summary of interventions

Five studies evaluated biological agents for sciatica.[149,216,270–272] Four of these studies compared biological agents with an alternative type of intervention.[149,216,270,271] Summary data of the interventions used are presented in *Table 114a*. Two RCTs,[149,271] one non-RCT[270] and one HCS[216] compared biological agents with alternative treatments. One RCT[270] and one non-RCT[271] compared intravenous infusions of infliximab with placebo injections of saline. One RCT[149] compared epidural injections of autologous conditioned serum, rich in anti-inflammatory cytokines, with epidural injections of corticosteroid and local anaesthetic. One CCS[216] compared subcutaneous injections of etanercept with intravenous injections of corticosteroid.

One three-armed study compared different doses of the same biological agent with each other.[272] The doses and biological agent being compared are presented in *Table 114b*, but this study is not considered any further.

TABLE 114a Summary of the interventions used when comparing biological agents with alternative interventions

ID no.	Author, year	Study design	Treatment description	Control description
Biological agents vs epidural/intradiscal injection				
321	Becker, 2007[149]	RCT	Epidural injection of autologous conditioned serum (group 1)	Epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (group 3)
321	Becker, 2007[149]	RCT	Epidural injection of autologous conditioned serum (group 1)	Epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (group 2)
Biological agents vs inactive control				
398	Karppinen, 2003[270]	Non-RCT	Intravenous infusion of infliximab 3 mg/kg (anti-TNF-α)	Periradicular saline injection
741	Korhonen, 2005[271]	RCT	Intravenous infliximab 5 mg/kg	Intravenous saline (placebo)
Biological agents vs non-opioids				
323	Genevay, 2004[216]	HCS	Three subcutaneous injections of etanercept 25 mg (anti-TNF-α)	Three intravenous injection of methylprednisolone 250 mg

TABLE 114b Summary of the interventions used when comparing alternative forms of biological agents

ID no.	Author, year	Study design	Treatment description	Control description
804	Cohen, 2009[272]	RCT	Transforaminal epidural injections of etanercept (4 mg)	Transforaminal epidural injections of etanercept (2 mg)
804	Cohen, 2009[272]	RCT	Transforaminal epidural injections of etanercept (6 mg)	Transforaminal epidural injections of etanercept (2 mg)

Summary of study participants in biological agent studies

Summary data on the included participants are presented in *Table 115*. The four studies that compared biological agents with alternative treatments included 213 participants with mean ages between 39 and 54 years (50–80% men), all with acute symptom duration. One non-RCT included only participants with the first episode of sciatica, one RCT also included recurrent symptoms, but symptom duration was not reported in two studies. Sciatica was confirmed by imaging in three trials. There were no patients with spinal stenosis or sequestered discs and previous back surgery was excluded in two trials.[270,271]

Summary of study quality for biological agents

Study details are summarised in *Table 116*. Half of the studies were RCTs (2/4, 50%) and none was of good quality. Only two had an adequate method of random number generation,[149,271] and none documented a secure method of allocation concealment. No studies had good external validity.

Biological agent results at short-term follow-up (≤ 6 weeks)

Global effect at short-term follow-up

No studies reported global effect data at short-term follow-up.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 117* and the accompanying forest plot (*Figure 78*). There was a significant improvement in pain intensity in the infliximab group compared with the inactive control group in one poor-quality non-RCT,[270] and also in the etanercept group compared with the intravenous corticosteroid injection group in a poor-quality HCS.[216]

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 118* and the accompanying forest plot (*Figure 79*). There was a significant improvement in CSOMs with infliximab compared with placebo injection in one poor-quality non-RCT,[270] and also with etanercept compared with intravenous corticosteroid in one poor-quality HCS.[216] There was no significant difference in CSOMs in the group receiving an epidural injection of autologous conditioned serum compared with epidural injection of corticosteroid and local anaesthetic in one moderate-quality RCT.[149]

Biological agents results at medium-term follow-up (> 6 weeks to ≤ 6 months)

Global effect at medium-term follow-up

No studies reported global effect data at long-term follow-up.

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 119* and the accompanying forest plot (*Figure 80*). There was a significant improvement in pain intensity in one poor-quality non-RCT of infliximab compared with placebo injection,[270] but not in another moderate-quality RCT,[271] and there was no significant difference when these results were combined in a meta-analysis. There was no significant difference in pain intensity in a group receiving an epidural injection of autologous conditioned serum compared with epidural injection of corticosteroid and local anaesthetic in one moderate-quality RCT.[149]

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 120* and the accompanying forest plot (*Figure 81*). There was a significant improvement in CSOMs in one poor-quality non-RCT of infliximab compared with placebo injection.[270] There was no significant difference in CSOMs in a group receiving an epidural injection of autologous conditioned

TABLE 115 Summary of sciatica and study population details for studies comparing biological agents with alternative interventions

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Biological agents vs epidural/intradiscal injection													
321	Becker, 2007[149]	RCT	90	Mean 53.9 (range 29–81)	52 (62)	At least 6 weeks	Nerve root pain	Yes	NR	No	No	NR	NR
Biological agents vs inactive control													
398	Karppinen, 2003[270]	Non-RCT	72	TNF-α group: mean 38.5	TNF-α group: 8 (80)	TNF-α group: mean 7.2 weeks (range 2–12 weeks); no data for saline group	Nerve root pain	Yes	First episode	No	No	NR	No
741	Korhonen, 2005[271]	RCT	41	Mean 40.7 (SD 8.4)	24 (60)	Median 61 days (range 20–102 days)	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	No
Biological agents vs non-opioids													
323	Genevay, 2004[216]	HCS	10	Mean 47.3 (SD 13.3, range > 18)	10 (50)	Mean 3.2 weeks (SD 3.7 weeks)	Nerve root pain	No	NR	No	No	NR	NR

NR, not reported.
a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

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TABLE 116 Summary of the study details for studies comparing biological agents with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Biological agents vs epidural/intradiscal injection										
321	Becker, 2007[149]	90	22 weeks	RCT	Yes	Partial	80–100	Yes	Moderate	Weak
Biological agents vs inactive control										
398	Karppinen, 2003[270]	72	3 months	Non-RCT	No	No	Cannot tell	No	Weak	Weak
741	Korhonen, 2005[271]	41	1 year	RCT	Yes	Unclear	80–100	Unclear	Moderate	Weak
Biological agents vs non-opioids										
323	Genevay, 2004[216]	10	6 weeks	HCS	No	No	80–100	No	Weak	Moderate

TABLE 117 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing biological agents with alternative interventions

							Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)			
ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Mean difference (95% CI)[b]	Comment/ conversion[c]
Biological agents vs inactive control																
398	Karppinen, 2003[270]	A	Non-RCT	1 month	Leg	VAS (0–100)	10	62	80 (18)	76 (19)	18 (19)	47 (32)	–62	–29	–40.50 (–43.22 to –14.78)	Change scores presented as percentages
Biological agents vs non-opioids																
323	Genevay, 2004[216]	A	HCS	6 weeks	Leg	VAS (0–100)	10	10	74.4 (12.9)	75.1 (14.2)	12.4 (13.2)	52.9 (25.1)			–40.50 (–58.08 to –22.92)	

A, acute.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

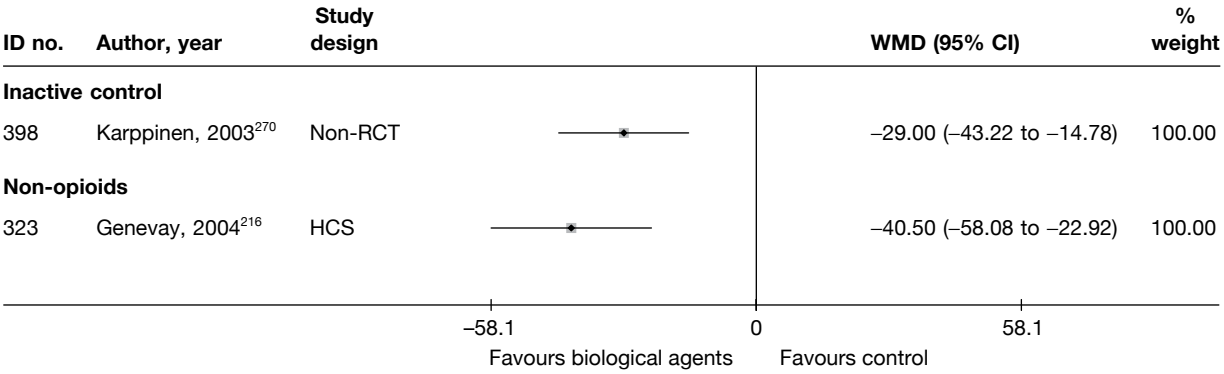

FIGURE 78 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

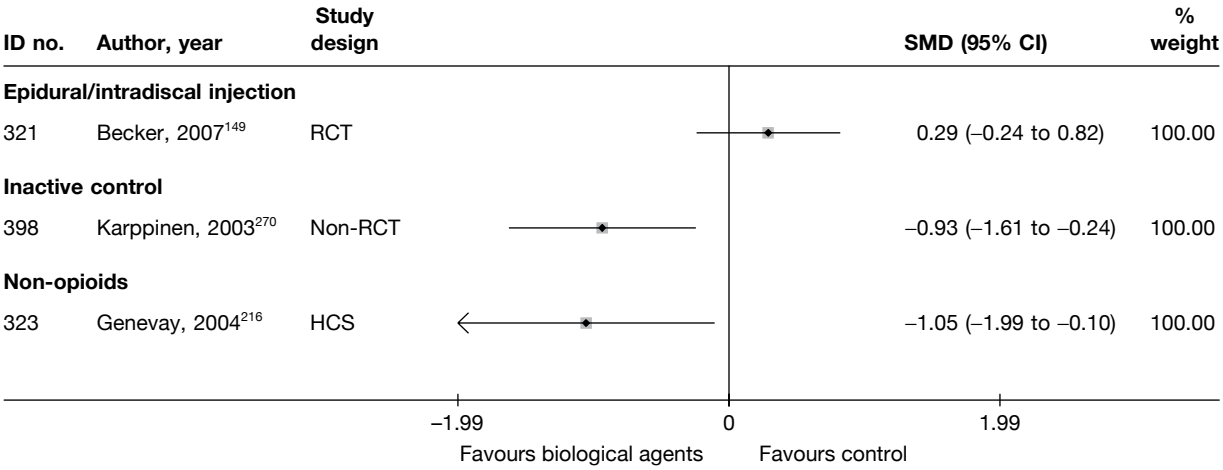

FIGURE 79 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

serum compared with epidural injection of corticosteroid and local anaesthetic in one moderate-quality RCT.[149]

Biological agent results at long-term follow-up (>6 months)

Global effect at long-term follow-up

No studies reported the global effect data at long-term follow-up.

Pain intensity at long-term follow-up

The results for pain intensity at long-term follow-up are presented in *Table 121* and the accompanying forest plot (*Figure 82*). There was no significant difference in pain intensity in one moderate-quality RCT of infliximab compared with placebo injection.[271]

Condition-specific outcome measures at long-term follow-up

The results for CSOMs at long-term follow-up are presented in *Table 122* and the accompanying forest plot (*Figure 83*). There was no significant difference in CSOMs in one moderate-quality RCT of infliximab compared with placebo injection.[271]

Adverse effects

The total number of adverse effects are presented in *Table 123* and the accompanying forest plot (*Figure 84*). There was no significant difference in the number of adverse events between

TABLE 118 Summary of the findings of CSOMs at short-term follow-up (≤ 6 weeks) for studies comparing biological agents with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Biological agents vs epidural															
321	Becker, 2007[149] (i)[c] (5 mg)	A + C	RCT	6 weeks	ODI	32	27	22.0 (8.3)	20.6 (8.1)	13.8 (9.8)	12.1 (9.0)			0.18 (–0.33 to 0.69)	ITT not used Dropouts 6 (7%); number originally randomised to each group not stated
321	Becker, 2007[149] (ii)[c] (10 mg)	A + C	RCT	6 weeks	ODI	32	25	22.0 (8.3)	19.4 (9.9)	13.8 (9.8)	11.0 (9.5)			0.29 (–0.24 to 0.82)	ITT not used Dropouts 6 (7%); number originally randomised to each group not stated
Biological agents vs inactive control															
398	Karppinen, 2003[270]	A	Non-RCT	1 month	ODI	10	62	43 (21)	44 (15)	15 (9)	30 (17)	–28	–14	–0.93 (–1.61 to –0.24)	Percentage change scores from baseline and adjusted difference between groups Percentage change converted
Biological agents vs non-opioids															
323	Genevay, 2004[216]	A	HCS	6 weeks	RMDQ	10	10	17.8 (3.3)	15.5 (2.9)	5.8 (5.5)	11.1 (4.6)			–1.05 (–1.99 to –0.10)	

A, acute; A + C, acute and chronic.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Becker *et al.*[149] included three treatment groups: epidural injection of autologous conditioned serum (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (iii). In order to prevent using the same comparator twice, only the first and last treatment groups have been included in the meta-analysis.

TABLE 119 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing biological agents with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Biological agents vs epidural																
321	[c]Becker, 2007[149] (5 mg)	A + C	RCT	22 weeks	Overall	VAS (0–100)	32	24	78	85					*Adjusted mean difference between groups (i) and (ii): –9.3 (95% CI –23.5 to 4.9)*	Seven participants (8%) dropped out; number originally randomised to each group not stated
321	[c]Becker, 2007[149] (10 mg)	A + C	RCT	22 weeks	Overall	VAS (0–100)	32	27	78	82					*Adjusted mean difference between groups (i) and (iii): –13.5 (95% CI –27.4 to 0.4); repeated measures analysis of variance*	Seven participants (8%) dropped out; number originally randomised to each group not stated
Biological agents vs inactive control																
398	Karppinen, 2003[270]	A	Non-RCT	3 months	Leg	VAS (0–100)	10	62	80 (18)	76 (19)	10 (16)	37 (35)	–70	–39	–27.00 (–40.20 to –13.80)	Change scores presented as percentages
741	Korhonen, 2005[271]	A + C	RCT	12 weeks	Leg	VAS (0–100)	21	19	73	73	30 (15.31)	23 (30.1)	–43	–50	7.00 (–8.04 to 22.04)	Median reported for baseline, reduction in pain and range Median used form means and final score derived form change SD imputed from weighted average

A, acute; A + C, acute and chronic.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Becker *et al.*[149] included three treatment groups: epidural injection of autologous conditioned serum (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (iii). In order to prevent using the same comparator twice, only the first and second treatment groups have been included in the meta-analysis.

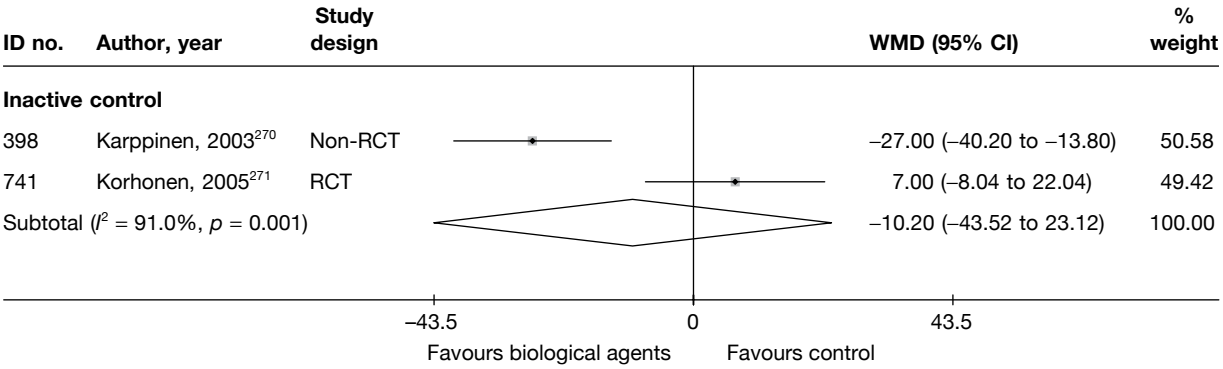

FIGURE 80 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

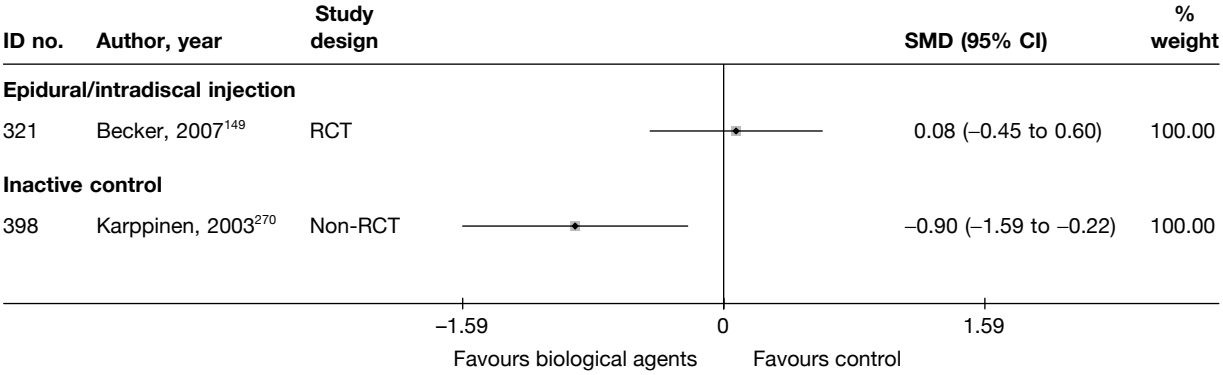

FIGURE 81 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

infliximab and placebo in two RCTs,[270,271] or between epidural injections of autologous conditioned serum compared with corticosteroid and local anaesthetic in one RCT.[149]

SUMMARY OF OVERALL FINDINGS FOR BIOLOGICAL AGENT COMPARED WITH ALTERNATIVE INTERVENTIONS

Four studies,[149,216,270,271] three of which were RCTs,[149,216,271] compared the use of biological agents with other interventions (*Table 124*).

There was conflicting evidence for the efficacy of intravenous infliximab as one poor-quality non-RCT found significant improvement in global effect and pain intensity at short- and medium-term follow-up,[270] but one moderate-quality RCT did not.[271] A poor-quality HCS found significant improvement in short-term pain intensity and CSOMs with etanercept compared with intravenous corticosteroids.[216] There was no significant difference in pain intensity or CSOMs in the short or medium term with epidural injection of autologous conditioned serum compared with epidural injection of corticosteroid and local anaesthetic in one moderate-quality RCT.[149] There was no difference in the number of adverse effects.

TABLE 120 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing biological agents with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Biological agents vs epidural															
321	Becker, 2007[149] (i)[c] (5 mg)	A + C	RCT	6 weeks	ODI	32	27	22.0 (8.3)	11.1 (7.1)	11.7 (9.2)	11.1 (7.1)			0.07 (–0.44 to 0.58)	ITT not used Dropouts: 7 (8%) Number originally randomised to each group not stated
321	Becker, 2007[149] (ii)[c] (10 mg)	A + C	RCT	6 weeks	ODI	32	25	22.0 (8.3)	11.0 (9.5)	11.7 (9.2)	11.0 (9.5)			0.08 (–0.45 to 0.60)	ITT not used Dropouts: 7 (8%) Number originally randomised to each group not stated
Biological agents vs inactive control															
398	Karppinen, 2003[270]	A	Non-RCT	1 month	ODI	10	62	43 (21)	24 (20)	7 (6)	24 (20)	–36	–20	–0.90 (–1.59 to –0.22) *Adjusted mean difference 13% (95% CI 4 to 22); ANOVA (poor-quality study)*	Percentage change scores from baseline and adjusted difference between groups – not based on summary score (repeated ANCOVA)
741	Korhonen, 2005[271]	A + C	RCT	12 weeks	ODI (%)	21	19								Only medians reported; *p*-values reported based on Mann–Whitney *U*-test or Fisher's exact-test ITT not used but all patients included in analysis except one who did not meet including criteria

A, acute; A + C, acute and chronic.

a Based on final means or change scores (with a preference given to change scores); results reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

c Becker *et al.*[149] included three treatment groups: epidural injection of autologous conditioned serum (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (iii). In order to prevent using the same comparator twice, only the first and second treatment groups have been included in the meta-analysis.

TABLE 121 Summary of the findings of pain intensity at long-term follow-up (> 6 months) for studies comparing biological agents with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Biological agents vs inactive control																
741	Korhonen, 2005[271]	A + C	RCT	12 weeks	Leg	VAS (0–100)	21	19	73	73	23 (15.31)	12 (23.67)	–43	–50	11.00 (–1.50 to 23.50)	Median reported for baseline, reduction in pain and range Median used form means and final score derived form change SD imputed from weighted average Dropouts 1/41 (2%): group allocation not stated

A + C, acute and chronic.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

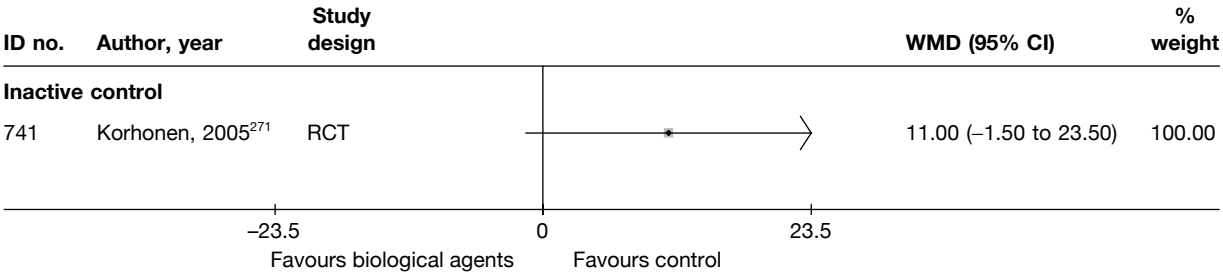

FIGURE 82 Summary of the findings of pain intensity at long-term follow-up (>6 months) for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

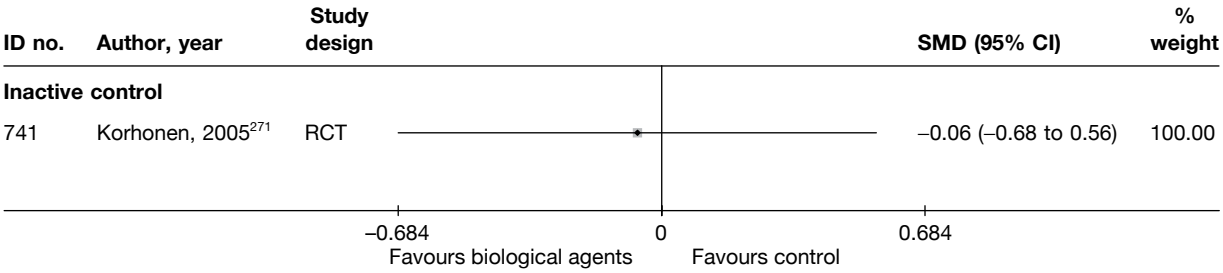

FIGURE 83 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

TABLE 122 Summary of the findings of CSOMs at long-term follow-up (>6 months) for studies comparing biological agents with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Biological agents vs inactive control															
741	Korhonen, 2005[271]	A + C	RCT	12 months	ODI (%)	21	19	45	48	9 (10.71)	10 (20)	–28	–23	–0.06 (–0.68 to 0.56)	Only median reported – used as mean *p*-values reported based on Mann–Whitney *U*-test or Fisher's exact test Final SD imputed from WMD of SDs for ODI medium-term follow-up ITT not used, but all patients included in analysis except one who did not meet inclusion criteria

A + C, acute and chronic.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 123 Summary of the findings of any adverse effects for studies comparing biological agents with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Biological agent vs epidural							
321	Becker, 2007[149] (i)[a] (5 mg)	RCT	1	32	1	27	0.84 (0.05 to 14.08)
321	Becker, 2007[149] (ii)[a] (10 mg)	RCT	1	32	1	25	0.77 (0.05 to 13.02)
Biological agent vs inactive control							
398	Karppinen, 2003[270]	Non-RCT	0	10	0	62	
741	Korhonen, 2005[271]	RCT	0	21	0	19	
Biological agent vs non-opioids							
323	Genevay, 2004[216]	HCS	NR	NR	NR	NR	

NR, not reported.

a Becker *et al.*[149] included three treatment groups: epidural injection of autologous conditioned serum (i), epidural injection of steroid triamcinolone 10 mg + local anaesthetic 1 ml (ii) and epidural injection of steroid triamcinolone 5 mg + local anaesthetic 1 ml (iii). In order to prevent using the same comparator twice, only the first and second treatment groups have been included in *Figure 84*..

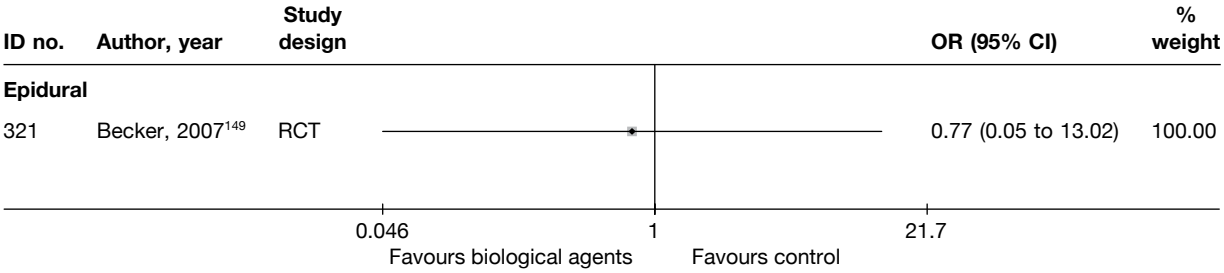

FIGURE 84 Summary of the findings of any adverse effects for studies comparing biological agents with alternative interventions. Note: weights are from random effects analysis.

TABLE 124 Summary of biological agent studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Biological agents vs epidural/intradiscal injection	1 (2)	90 (90)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Biological agents vs inactive control	2 (2)	41–72 (57)	1/2 (50)	0/2 (0)	1/2 (50)	2/2 (100)	2/2 (100)	0/2 (0)	0/2 (0)	1/2 (50)	1/2 (50)	0/2 (0)
Biological agents vs non-opioids	1 (1)	10 (10)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total (for biological agent studies)	**4 (5)**	**10–90 (57)**	**2/4 (50)**	**0/4 (0)**	**2/4 (50)**	**4/4 (100)**	**3/4 (75)**	**0/4 (0)**	**0/4 (0)**	**1/4 (25)**	**1/4 (25)**	**0/4 (0)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

Activity restriction

Description of activity restriction studies

Summary of interventions

Five studies compared passive PT with an alternative type of intervention.[14,145,243,256,267] Summary data of the interventions used are presented in *Table 125*. Two RCTs compared bed rest for 1 or 2 weeks with advice to keep active,[14] or continue activities of daily living.[267] This last RCT[267] was a three-arm study which also compared bed rest with twice weekly hospital physiotherapy for at least 4 weeks, consisting of segmental mobilisation, exercises and hydrotherapy. Another three-arm RCT[256] compared rest and hot packs with hot packs, massage, mobilising and isotonic strengthening exercise, and also with intermittent pelvic traction and isometric strengthening exercises. Another RCT[243] compared bed rest at home with bed rest and vertical traction. A non-RCT[145] compared 1–2 weeks of bed rest with a sacral epidural injection of local anaesthetic.

Summary of study participants in activity restriction studies

Summary data on the included participants are presented in *Table 126*. The five studies included 551 participants with mean ages between 39 and 46 years (47–76% men). Symptom duration was acute in two studies, chronic in one and a mixture of acute and chronic in the other. Three studies included patients with recurrent symptoms, and not recorded in two. Sciatica was confirmed by imaging in one RCT.[267] There were no patients with spinal stenosis or sequestered discs, and previous back surgery was excluded in one RCT.[14]

Summary of study quality for activity restriction studies

Study details are summarised in *Table 127*. Most studies were RCTs (4/5, 80%); however, the proportion that were of good quality was low (1/5, 20%). Only three had an adequate method of random number generation[14,243,267] and none documented a secure method of allocation concealment. Two studies had good external validity.[14,243]

TABLE 125 Summary of the interventions used when comparing activity restriction with alternative interventions

ID no.	Author, year	Study design	Treatment description	Control description
Activity restriction vs exercise therapy				
564	Lidstrom, 1970[256]	RCT	Rest	Massage + mobilising and strengthening exercises
Activity restriction vs education/advice				
713	Hofstee, 2002[267]	RCT	Bed rest	Advised to continue activities of daily living
658	Vroomen, 1999[14]	RCT	Bed rest	Advice to keep active
Activity restriction vs epidural/intradiscal injection				
140	Coomes, 1961[145]	Non-RCT	Bed rest at home on fracture boards	Sacral epidural injection local anaesthetic 50–60 ml procaine
Activity restriction vs mixed treatment				
713	Hofstee, 2002[267]	RCT	Bed rest	Hospital physiotherapy: segmental mobilisation + exercises + hydrotherapy
564	Lidstrom, 1970[256]	RCT	Rest	Traction + strengthening exercises
Activity restriction vs traction				
222	Moret, 1998[243]	RCT	Bed rest	Bed rest and traction (vertical traction using patient weight), 180 minutes daily for 1–2 weeks

TABLE 126 Summary of sciatica type and study population details for studies comparing activity restriction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Activity restriction vs education/advice													
713	Hofstee, 2002[267]	RCT	250	Mean 39 (SD 10)	150 (60)	Mean 2 weeks	Nerve root pain and referred pain	Yes	Recurrent	No	No	NR	Yes
658	Vroomen, 1999[14]	RCT	183	Mean 46 (SD 12)	103 (56)	Median 16 days	Nerve root pain	No	Recurrent and first episode	No	No	NR	No
Activity restriction vs epidural													
140	Coomes, 1961[145]	Non-RCT	40	Mean 43 (range 16–70)	26 (65)	Mean of 34 days	Nerve root pain	No	NR	No	No	Yes	NR
Activity restriction vs exercise therapy													
564	Lidstrom, 1970[256]	RCT	62	Range 21–61	29 (47)	>1 year 52%	Nerve root pain and referred pain	No	NR	No	No	NR	NR
Activity restriction vs mixed treatments													
713	Hofstee, 2002[267]	RCT	250	Mean 39 (SD 10)	150 (60)	Mean 2 weeks	Nerve root pain and referred pain	Yes	Recurrent	No	No	NR	Yes
564	Lidstrom, 1970[256]	RCT	62	Range 21–61	29 (47)	>1 year 52%	Nerve root pain and referred pain	No	NR	No	No	NR	NR
Activity restriction vs traction													
222	Moret, 1998[243]	RCT	16	Mean 41.9 (SD 8.7)	12 (75)	Acute symptoms 50%	Nerve root pain	No	Recurrent and first episode	No	NR	Yes	Yes

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 127 Summary of the study details for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Activity restriction vs education/advice										
713	Hofstee, 2002[267]	250	6 months	RCT	Yes	No	80–100	No	Moderate	Moderate
658	Vroomen, 1999[14]	183	12 weeks	RCT	Yes	No	80–100	Yes	Moderate	Strong
Activity restriction vs epidural/intradiscal injection										
140	Coomes, 1961[145]	40	9 weeks	Non-RCT	No	No	80–100	No	Weak	Weak
Activity restriction vs exercise therapy										
564	Lidstrom, 1970[256]	62	1 month	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Activity restriction vs mixed treatments										
713	Hofstee, 2002[267]	250	6 months	RCT	Yes	No	80–100	No	Moderate	Moderate
564	Lidstrom, 1970[256]	62	1 month	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
Activity restriction vs traction										
222	Moret, 1998[243]	16	3 weeks	RCT	Yes	Partial	80–100	No	Moderate	Strong

Activity restriction results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 128* and the accompanying forest plot (*Figure 85*). There was no significant difference between bed rest and advice to keep active in two RCTs.[14,267] There was no significant difference between bed rest and mobilisation with exercises carried out in a hospital physiotherapy department,[267] between rest and spinal manipulation with exercises, pelvic traction and exercises,[137] or between bed rest and bed rest with vertical traction.[243]

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 129* and the accompanying forest plot (*Figure 86*). There was a significant improvement in pain intensity in the bed rest group compared with advice to keep active in one RCT,[14] but no significant difference in another RCT,[267] and none when these results were combined in a meta-analysis. There was no significant difference in pain intensity between bed rest and mobilisation with exercises carried out in a hospital physiotherapy department.[267] There was a significant improvement in pain intensity in the bed rest with vertical traction group compared with the group treated with bed rest alone.[243]

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 130* and the accompanying forest plot (*Figure 87*). There was a significant improvement in CSOMs with advice to keep active compared with bed rest when the two RCTs were combined in a meta-analysis.[14,267] There was a significant improvement in CSOMs in the group receiving mobilisation with exercises carried out in a hospital physiotherapy department compared with the bed rest group in one RCT.[267] There was no significant difference in CSOMs in the bed rest with vertical traction group compared with the group treated with bed rest alone.[243]

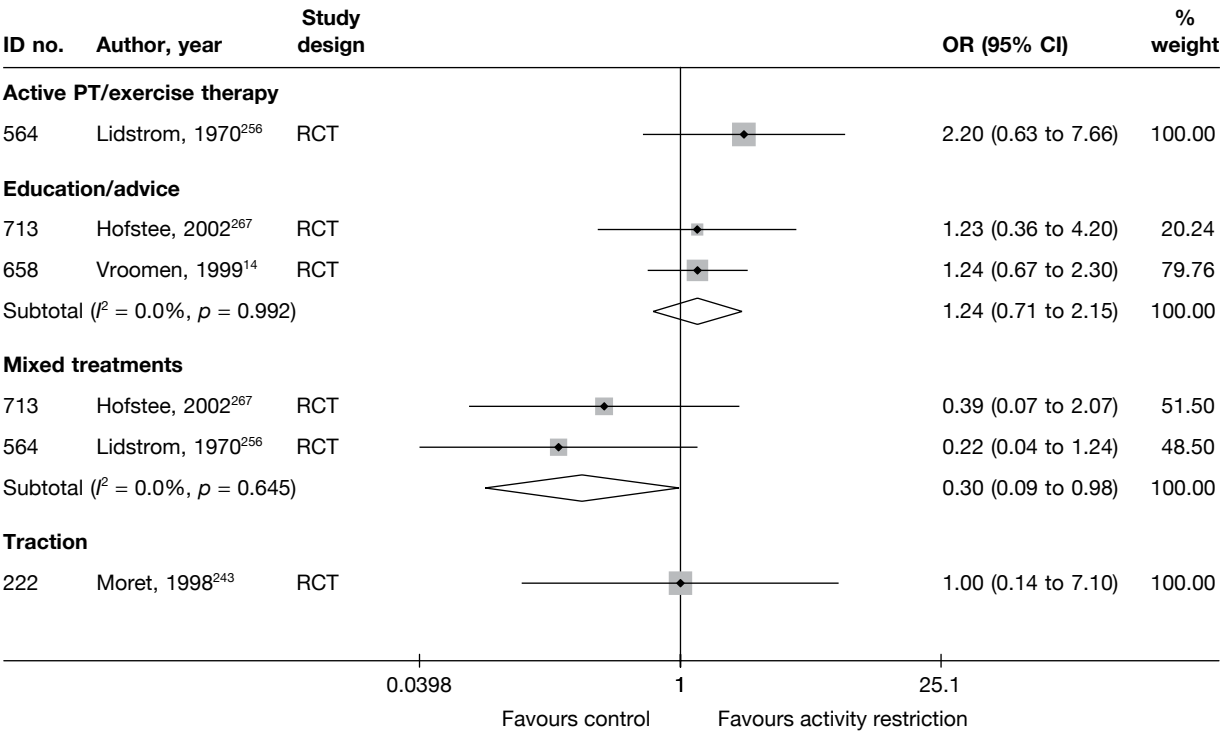

FIGURE 85 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

TABLE 128 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	
Activity restriction vs education/advice													
713	Hofstee, 2002[267]	A	RCT	1 month	Treatment failure. Opposite extracted	Physician	84	79	0.00	83	77	0.00	1.23 (0.36 to 4.20)
658	Vroomen, 1999[14]	A	RCT	2 weeks	Assessment of improvement	Patient	92	64	0.00	91	59	0.00	1.24 (0.67 to 2.30)
Activity restriction vs exercise therapy													
564	Lidstrom, 1970[256]	A + C	RCT	1 month	Patient's ability to function socially was a decisive factor for both evaluations (no change or worse)	Patient	21	14	0.00	21	10	0.00	2.20 (0.63 to 7.66)
Activity restriction vs mixed treatments													
713	Hofstee, 2002[267]	A	RCT	1 month	Treatment failure. Opposite extracted	Physician	84	79	0.00	83	81	0.00	0.39 (0.07 to 2.07)
564	Lidstrom, 1970[256]	A + C	RCT	1 month	Patient's ability to function socially was a decisive factor for both evaluations (no change or worse)	Patient	21	14	0.00	20	18	0.00	0.22 (0.04 to 1.24)
Activity restriction vs traction													
222	Moret, 1998[243]	A	RCT	3 weeks	Leg pain: recovered or strongly improved (vs little improved, no change, little worse, much worse or worse than ever)	Patient	8	4	0.00	8	4	0.00	1.00 (0.14 to 7.10)

A, acute; A + C, acute and chronic.

TABLE 129 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Activity restriction vs education/advice															
713	Hofstee, 2002[267]	A	RCT	1 month	Leg	VAS (0–100)	82	83	65.5 (18.5)	60.7 (21.4)			–25.9 (29.16)	–23.4 (29.16)	–2.50 (–11.40 to 6.40)
658	Vroomen, 1999[14]	A	RCT	2 weeks	Leg	VAS (0–100)	92	91	62 (22)	68 (21)	36 (28)	44 (27)			–8.00 (–15.97 to –0.03)
Activity restriction vs mixed treatment															
713	Hofstee, 2002[267] (manipulation + exercise therapy	A	RCT	1 month	Leg	VAS (0–100)	82	80	65.5 (18.5)	60.9 (20.1)			–25.9 (29.16)	–24.2 (29.31)	–1.70 (–10.70 to 7.30)
Activity restriction vs traction															
222	Moret, 1998[243]	A	RCT	3 weeks	Leg	NRS (0–10)	8	8	73 (10.0)	74 (12.0)	63 (10)	44 (12)	–10.0	–30.0	19.00 (8.18 to 29.82)

A, acute.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

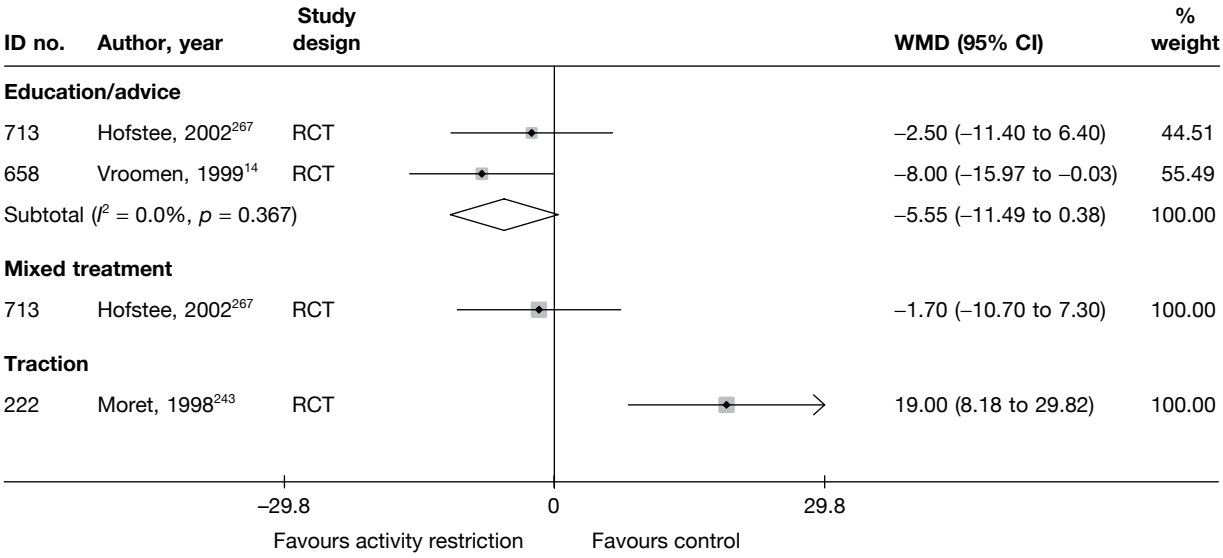

FIGURE 86 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

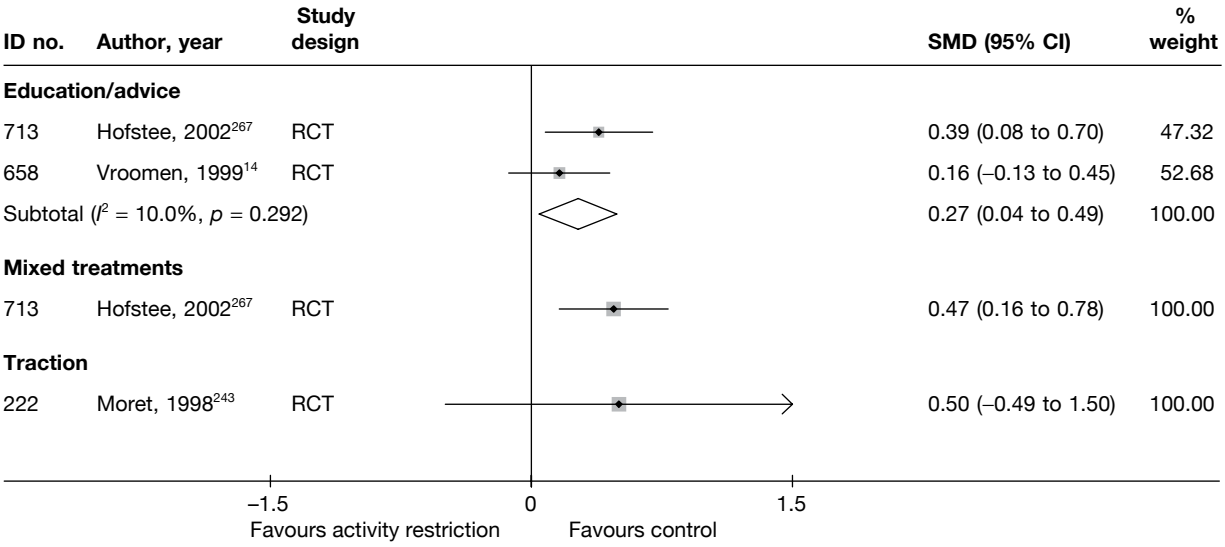

FIGURE 87 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

Activity restriction results at long-term follow-up

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 131* and the accompanying forest plot (*Figure 88*). There was no significant difference between bed rest and advice to keep active in two RCTs.[14,267] There was no significant difference in one RCT between bed rest and mobilisation with exercises carried out in a hospital physiotherapy department.[267] There was a significant improvement in global effect for epidural injections compared with bed rest in one RCT.[145]

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 132* and the accompanying forest plot (*Figure 89*). There was no significant difference between bed rest and

TABLE 130 Summary of the findings of CSOMs at short-term follow-up (≤ 6 weeks) for studies comparing activity restriction with alternative interventions (grouped by comparator then ordered by author)

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Activity restriction vs education/advice															
713	Hofstee, 2002[267]	A	RCT	1 month	QDS	82	83	58.6 (14.6)	57.4 (16.3)	47.2 (14.6)	41.2 (16.3)	–11.4 (18.84)	–16.2 (18.84)	0.39 (0.08 to 0.70)	Final means calculated from change scores Distribution at follow-up reported to be skewed ITT used (incorporating treatment compliance and dropouts), but dropouts excluded the results reported Dropouts: intervention 2/84, control 0/83
658	Vroomen, 1999[14]	A	RCT	3 weeks	Revised RMDQ	92	91	5.5 (3.9)	5.2 (3.8)	14.8 (6.2)	13.8 (6.3)	–2.7	–4.0	0.16 (–0.13 to 0.45) *Adjusted mean difference –1.6 (95% CI –3.7 to 0.4)*	ITT used For baseline and mean, high score = good outcome; sign of change score altered so that negative indicates improvement Adjusted difference between groups not based on change scores
Activity restriction vs traction															
222	Moret, 1998[243]	A	RCT	3 weeks	RMDQ	8	8	18.5 (2.1)	18.1 (1.8)	17.1 (6.2)	14.5 (3.87)	–1.4	–3.6	0.50 (1.50 to –0.49)	Final mean based on change score with SD imputed from weighted average
Activity restriction vs mixed treatment															
713	Hofstee, 2002[267]	A	RCT	1 month	QDS	82	80	58.6 (14.6)	56 (17.6)	47.2 (14.6)	40.3 (14.6)	–11.4 (18.84)	–45.7 (18.89)	0.47 (0.16 to 0.78)	Final means calculated from change scores Distribution at follow-up reported to be skewed ITT used (incorporating treatment compliance and dropouts), but dropouts excluded in the results reported Dropouts: intervention 2/84, control 3/83

A, acute; QDS, Quebec Disability Scale.

a Based on final means or change scores (with a preference given to change scores); results as reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 131 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	
Activity restriction vs education/advice													
713	Hofstee, 2002[267]	A	RCT	6 months	Treatment failure. Opposite extracted	Physician	84	63	0.00	83	69	0.00	0.16 (0.29 to 1.30)
658	Vroomen, 1999[14]	A	RCT	12 weeks	Assessment of improvement	Patient	92	80	0.00	91	79	0.00	1.01 (0.43 to 2.39)
Activity restriction vs epidural/intradiscal injection													
140	Coomes, 1961[145]	A	Non-RCT	9 weeks	Neurological state: completely relieved or improved (vs not changed or worse)	Physician	20	5	0.00	20	12	0.00	0.22 (0.06 to 0.86)
Activity restriction vs mixed treatments													
713	Hofstee, 2002[267]	A	RCT	6 months	Treatment failure. Opposite extracted	Physician	84	63	0.00	83	64	0.00	0.89 (0.44 to 1.81)

A, acute.

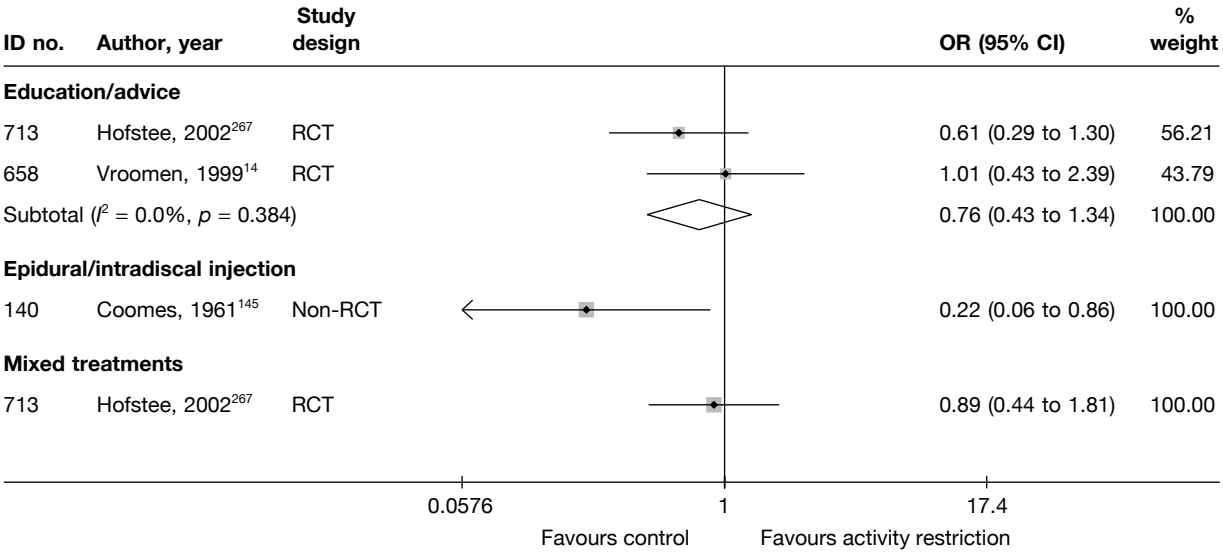

FIGURE 88 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

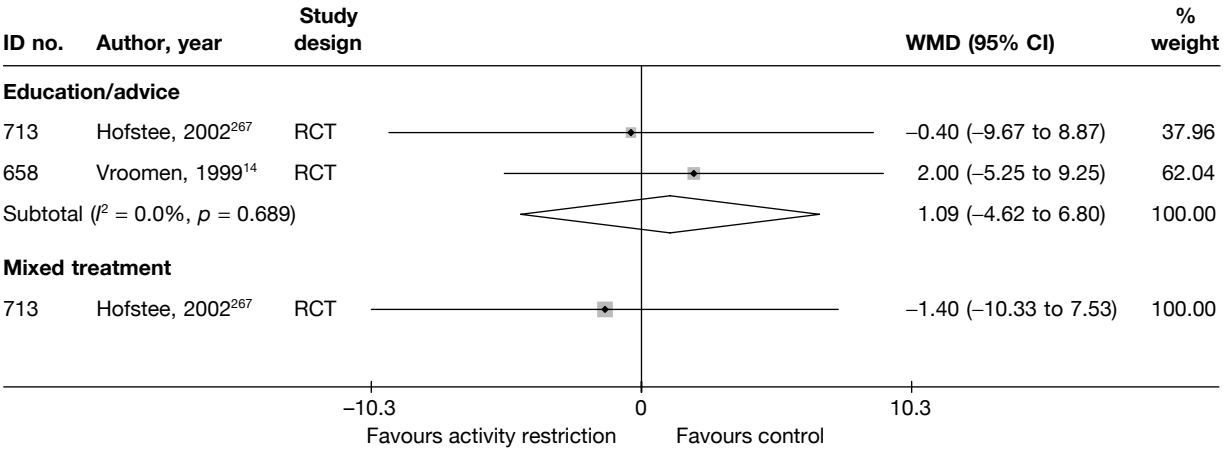

FIGURE 89 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

advice to keep active in two RCTs.[14,267] There was no significant difference in one RCT between bed rest and mobilisation with exercises carried out in a hospital physiotherapy department.[267]

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 133* and the accompanying forest plot (*Figure 90*). There was no significant difference between bed rest and advice to keep active in two RCTs.[14,267] There was no significant difference in one RCT between bed rest and mobilisation with exercises carried out in a hospital physiotherapy department.[267]

Activity restriction results at long-term follow-up (>6 months)

No long-term outcomes were reported for global effect, pain intensity or CSOMs.

Adverse effects

The total number of adverse effects are presented in *Table 134* and the accompanying forest plot (*Figure 91*). There was no significant difference between bed rest and advice to keep active in two

TABLE 132 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Activity restriction vs education/advice															
713	Hofstee, 2002[267]	A	RCT	6 months	Leg	VAS (0–100)	78	75	65.5 (18.5)	60.7 (21.4)			–48.2 (27.92)	–47.8 (30.45)	–0.40 (–9.67 to 8.87)
658	Vroomen, 1999[14]	A	RCT	12 weeks	Leg	VAS (0–100)	92	91	62 (22)	68 (21)	16 (26)	14 (24)			2.00 (–5.25 to 9.25)
Activity restriction vs mixed treatment															
713	Hofstee, 2002[267]	A	RCT	6 months	Leg	VAS (0–100)	78	72	65.5 (18.5)	60.9 (20.1)			–48.2 (27.92)	–46.8 (27.83)	–1.40 (–10.33 to 7.53)

A, acute.
a The results have been converted to a scale of 0–100 for comparability.
b Based on final means or change scores (with a preference given to change scores).

TABLE 133 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Activity restriction vs education/advice															
713	Hofstee, 2002[267]	A	RCT	6 months	QDS	78	75	58.6 (14.6)	57.4 (16.3)	25.9 (14.6)	22 (16.3)	–32.7 (23.66)	–35.4 (23.66)	0.25 (–0.07 to 0.57)	
658	Vroomen, 1999[14]	A	RCT	12 weeks	Revised RMDQ	92	91	5.5 (3.9)	5.2 (3.8)	7.8 (7)	7.3 (7)	–9.7	–10.5	0.07 (–0.22 to 0.36) *Adjusted mean difference –0.5 (95% CI –2.6 to 1.6)*	ITT used For baseline and mean, high score = good outcome; sign of change score altered so that negative indicates improvement in our analysis
Activity restriction vs mixed treatment															
713	Hofstee, 2002[267]	A	RCT	6 months	QDS	78	75	58.6 (14.6)	56 (17.6)	25.9 (14.6)	21.4 (17.6)	–32.7 (23.66)	–34.6 (23.9)	0.28 (–0.04 to 0.60)	

A, acute; QDS, Quebec Disability Scale.

a Based on final means or change scores (with a preference given to change scores); results as reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

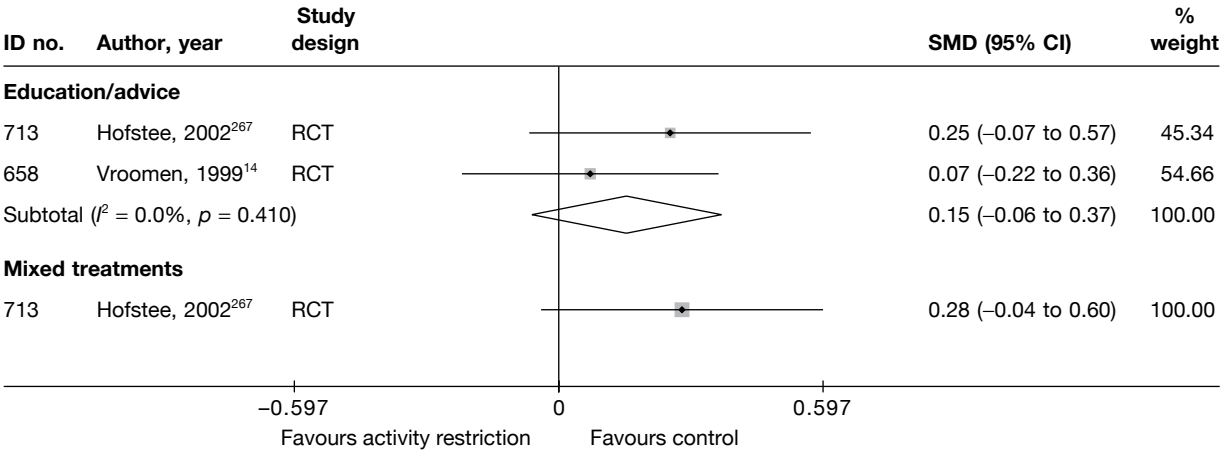

FIGURE 90 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

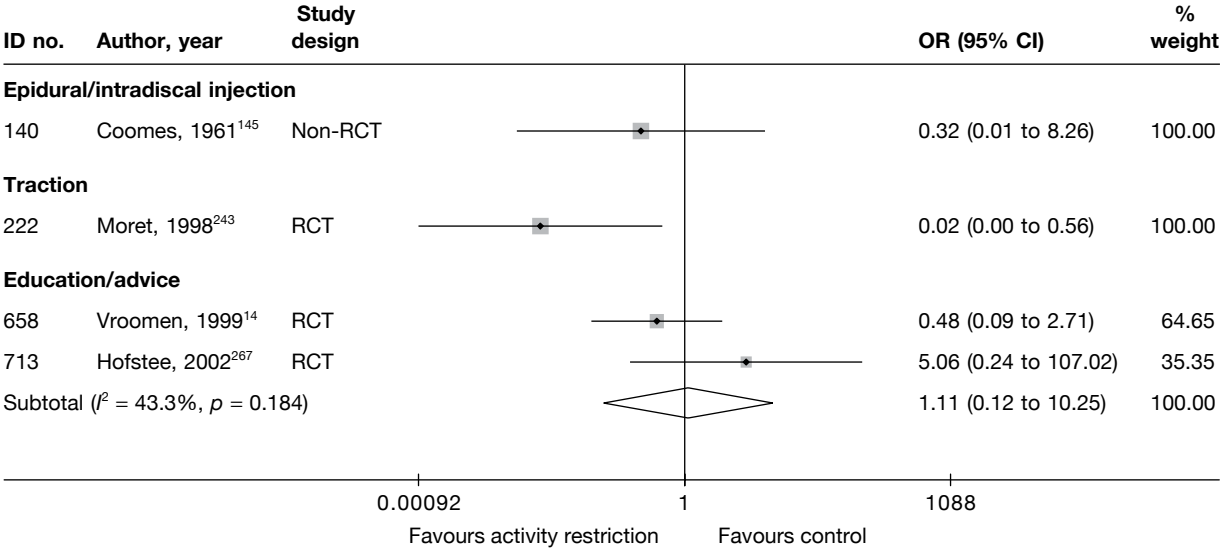

FIGURE 91 Summary of the findings of any adverse effect for studies comparing activity restriction with alternative interventions. Note: weights are from random effects analysis.

RCTs,[14,267] or between bed rest and epidural injection.[145] However, there were significantly fewer adverse effects in the bed rest group compared with the traction group in one RCT.[243]

SUMMARY OF OVERALL FINDINGS FOR ACTIVITY RESTRICTION COMPARED WITH ALTERNATIVE INTERVENTIONS

Five studies,[14,145,243,256,267] four of which were RCTs,[14,243,256,267] compared the use of activity restriction with other interventions. Four RCTs restricted inclusion to patients with acute sciatica (*Table 135*).[14,243,256,267]

There was no significant difference between bed rest and advice to keep active, or between bed rest and mobilisation with exercises carried out in a hospital physiotherapy department, in terms of global effect or pain intensity at short- and medium-term follow-up. However, CSOMs at short-term follow-up were significantly better in the active groups, although there

TABLE 134 Summary of the findings of any adverse effect for studies comparing activity restriction with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Activity restriction vs education/advice							
658	Vroomen, 1999[14]	RCT	2	92	4	91	
713	Hofstee, 2002[267]	RCT	2	84	0	83	0.20 (0.01 to 4.18)
Activity restriction vs epidural							
140	Coomes, 1961[145]	Non-RCT	0	20	1	20	0.32 (0.01 to 8.33)
Activity restriction vs exercise therapy							
564	Lidstrom, 1970[256]	RCT	NR	NR	NR	NR	
Activity restriction vs mixed treatment							
564	Lidstrom, 1970[256]	RCT	NR	NR	NR	NR	
713	Hofstee, 2002[267]	RCT	2	84	0	83	0.20 (0.01 to 4.18)
Activity restriction vs traction							
222	Moret, 1998[243]	RCT	0	8	6	8	0.02 (0.00 to 0.56)

NR, not reported.

was no significant difference at medium-term follow-up. There was no significant difference between rest and spinal manipulation with exercises, or between pelvic traction and exercises, in terms of global effect or pain intensity at short-term follow-up. Nor was there a significant difference between bed rest and bed rest with vertical traction, in terms of short-term global effect or CSOMs, but there was a significant reduction in pain intensity in the short term in the traction group. There was a significant improvement in medium-term global effect following epidural injections compared with bed rest, with a significantly greater number of adverse effects (*Table 135*).

TABLE 135 Summary of activity restriction results

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Activity restriction vs education/advice	2 (2)	183–250 (217)	2/2 (100)	0/2 (0)	2/2 (100)	2/2 (100)	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)
Activity restriction vs epidural/intradiscal injection	1 (1)	40 (40)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Activity restriction vs exercise therapy	1 (1)	62 (62)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Activity restriction vs mixed treatment	2 (2)	183–250 (217)	2/2 (100)	0/2 (0)	1/2 (50)	2/2 (100)	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)
Activity restriction vs traction	1 (1)	16 (16)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)
Total (for activity restriction studies)[a]	**5 (7)**	**16–250 (62)**	**4/5 (80)**	**1/5 (20)**	**4/5 (80)**	**5/5 (100)**	**1/5 (20)**	**0/5 (0)**	**0/5 (0)**	**0/5 (0)**	**2/5 (40)**	**2/5 (40)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

a These numbers are based on number of studies not number of arms as above (e.g. study 713 includes two comparators, but has been counted only once here).

Opioids

Description of opioid studies

Summary of interventions

Three studies compared opioids with alternative types of intervention for sciatica.[214,229,230] Summary data of the interventions used are presented in *Table 136*. One three-arm RCT[229] compared 10-day courses of intramuscular injections of a moderate-strength opioid tramadol with two oral antidepressants: imipramine or fluvoxamine. One RCT[230] compared a 7-day course of oral tramadol with a tapering dose of the oral corticosteroid dexamethasone. The third was a four-arm crossover trial[214] comparing 7-week courses of a potent opioid (morphine), an antidepressant (nortriptyline), a combination of morphine and nortriptyline and a placebo (benztropine).

Summary of study participants in opioid studies

The three RCTs[214,229,230] included 168 participants with mean ages ranging from 43 to 53 years, a majority of men, acute and chronic symptom duration and all included recurrent episodes. Sciatica was confirmed by imaging in two out of three studies. One RCT included patients with spinal stenosis. Previous back surgery was either excluded or not reported (*Table 137*).

Summary of study quality for opioid studies

Study details are summarised in *Table 138*. The full results of the quality assessment are presented in the appendices. None of the RCTs was of good quality, but one[214] had an adequate method of random number generation, a secure method of allocation concealment and good external validity.

TABLE 136 Summary of the interventions used when comparing opioids with alternative interventions

ID no.	Author, year	Study design	Treatment description	Control description
Opioids vs inactive control				
534	Khoromi, 2007[214]	RCT (crossover)	Sustained-release morphine plus inert placebo (oral, ≤ 90 mg/day for 8.5 weeks)	Benztropine (active placebo) plus inert placebo (oral, 0.25–1.00 mg/day for 8.5 weeks)
Opioids vs mixed treatments (opioids and non-opioids)				
534	Khoromi, 2007[214]	RCT (crossover)	Sustained-release morphine plus inert placebo (oral, ≤ 90 mg/day for 8.5 weeks)	Morphine plus nortriptyline (oral morphine, ≤ 90 mg/day for 8.5 weeks; oral nortriptyline, ≤ 100 mg/day for 7.5 weeks)
Opioids vs non-opioids				
534	Khoromi, 2007[214]	RCT (crossover)	Sustained-release morphine plus inert placebo (oral, ≤ 90 mg/day for 8.5 weeks)	Nortriptyline plus inert placebo (oral, ≤ 100 mg/day for 7.5 weeks)
547	Kwasucki, 1993[230] (Polish language)	RCT	Tramadol. First 5 days of 100 mg twice daily; sixth and seventh days 100 mg once daily	Dexamethasone. First and second days 24 mg (16 mg at 7AM, 8 mg at 7PM); third day 8 mg twice daily; fourth and fifth days 4 mg twice daily; sixth and seventh days 4 mg once daily
368	Kwasucki, 2002[229] (Polish language)	RCT	Tramadol (100 mg intramuscular injection)	Fluvoxamine (10 mg oral)
368	Kwasucki, 2002[229] (Polish language)	RCT	Tramadol (100 mg intramuscular injection)	Imipramine (25 mg oral)

TABLE 137 Summary of sciatica and study population details for studies comparing opioids with alternative interventions

ID no.	Author, year	Study design	No. of patients	Age (years)	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Opioids vs inactive control													
534	Khoromi, 2007[214]	RCT (crossover)	55	Median 53 (range 19–65)	30 (55)	Median 5 years (range 0.3–37 years)	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	No
Opioids vs mixed treatments (opioids and non-opioids)													
534	Khoromi, 2007[214]	RCT (crossover)	55	Median 53 (range 19–65)	30 (55)	Median 5 years (range 0.3–37 years)	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	No
Opioids vs non-opioids													
534	Khoromi, 2007[214]	RCT (crossover)	55	Median 53 (range 19–65)	30 (55)	Median 5 years (range 0.3–37 years)	Nerve root pain	Yes	Recurrent and first episode	No	No	Yes	No
368	Kwasucki, 2002[229] (Polish language)	RCT	70	Mean 42.8 (range 23–68)	51 (73)	Range 1 week–8 months	Nerve root pain	Yes	Recurrent and first episode	Yes	No	Yes	No
547	Kwasucki, 1993[230] (Polish language)	RCT	43	Mean 43.2 (range 27–69)	37 (86)	Mean 6.3 weeks (range 1 week–8 months)	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	NR

NR, not reported.
a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 138 Summary of the study details for studies comparing opioids with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Opioids vs inactive control										
534	Khoromi, 2007[214]	55	36 weeks	RCT (crossover)	Yes	Yes	<60	Yes	Moderate	Strong
Opioids vs mixed treatment (opioids and non-opioids)										
534	Khoromi, 2007[214]	55	36 weeks	RCT (crossover)	Yes	Yes	<60	Yes	Moderate	Strong
Opioids vs non-opioids										
534	Khoromi, 2007[214]	55	36 weeks	RCT (crossover)	Yes	Yes	<60	Yes	Moderate	Strong
368	Kwasucki, 2002[229] (Polish language)	70	19 days	RCT	Unclear	Unclear	80–100	Unclear	Weak	Weak
547	Kwasucki, 1993[230] (Polish language)	43	2 weeks	RCT	Unclear	Unclear	80–100	Unclear	Wear	Weak

Opioid results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 139* and the accompanying forest plot (*Figure 92*). Short courses of opioids were compared with short courses of antidepressants or oral corticosteroids. One poor-quality RCT[229] found that a course of intramuscular injections of tramadol was not significantly different from oral antidepressants, and one poor-quality RCT[230] found that oral tramadol was significantly worse than a course of oral corticosteroid.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 140* and the accompanying forest plot (*Figure 93*). Short courses of opioids were compared with short courses of antidepressants or oral corticosteroids. One poor-quality RCT[229] found that a course of intramuscular injections of tramadol was not significantly different from oral antidepressants, and one moderate-quality RCT[230] found that oral tramadol was significantly worse than a course of oral corticosteroid.

Condition-specific outcome measures at short-term follow-up

There were no CSOMs at short-term follow-up.

Opioid results at medium-term follow-up (>6 weeks to ≤6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 141* and the accompanying forest plot (*Figure 94*). One moderate-quality, four-arm crossover RCT[214] found that a 7-week course of oral morphine had similar effects to 7-week courses of oral nortriptyline, a combination of morphine and nortriptyline or a placebo (benztropine).

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 142* and the accompanying forest plot (*Figure 95*). One moderate-quality, four-arm crossover RCT[214] found that a 7-week course of oral morphine had similar effects to 7-week courses of oral nortriptyline, a combination of morphine and nortriptyline or a placebo (benztropine).

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 143* and the accompanying forest plot (*Figure 96*). One moderate-quality, four-arm crossover RCT[214] found that a 7-week course of oral morphine had similar effects to 7-week courses of oral nortriptyline, a combination of morphine and nortriptyline or a placebo (benztropine).

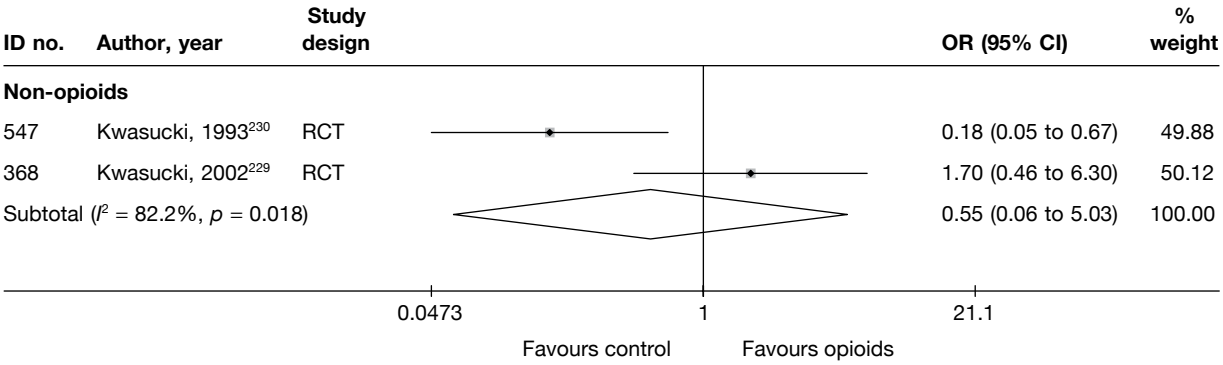

FIGURE 92 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing opioids with alternative interventions. Note: weights are from random effects analysis.

TABLE 139 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing opioids with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Opioids vs non-opioids														
547	Kwasucki, 1993[230] (Polish language)	A + C	RCT	2 weeks	Improvement in pain: cessation of symptoms or clear improvement (vs no improvement or mild improvement)		22	8	0.00	21	16	0.00	22.50 (10.48 to 34.52)	Data extracted from histograms of raw pain scores
368	Kwasucki, 2002[229] (Polish language) (i)[a] (fluvoxamine)	A + C	RCT	19 days (end of treatment)	Overall improvement: complete relief or improvement (vs no improvement)	Patient	22	17	0.00	24	18	0.00	20.00 (6.84 to 33.16)	
368	Kwasucki, 2002[229] (Polish language) (ii)[a] (imipramine)	A + C	RCT	19 days (end of treatment)	Overall improvement: complete relief or improvement (vs no improvement)	Patient	22	17	0.00	24	16	0.00	21.36 (12.49 to 30.24)	

A + C, acute and chronic.

a Kwasucki *et al.*[229] included three treatment groups: fluvoxamine (10 mg oral) (i), imipramine (25 mg oral) (ii) and tramadol (100 mg intramuscular injection) (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 92*).

TABLE 140 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing opioids with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Opioids vs non-opioids															
547	Kwasucki, 1993[230] (Polish language)	A + C	RCT	2 weeks	Overall	NRS (0–4)	22	21	77.5 (15)	77.5 (12.5)	50.0 (22.5)	27.5 (17.5)			22.50 (10.48 to 34.52)
368	Kwasucki, 2002[229] (Polish language) (i)[c] (fluvoxamine)	A + C	RCT	19 days	Overall	NRS (0–4)	22	24	70 (17.5)	67.5 (15)	50.0 (25.0)	30 (20)			20.00 (6.84 to 33.16)
368	Kwasucki, 2002[229] (Polish language) (ii)[c] (imipramine)	A + C	RCT	19 days	Overall	NRS (0–4)	22	24	70 (17.5)	75 (25)	50.0 (25.0)	37.5 (25.0)			12.50 (–1.96 to 26.96)

A + C, acute and chronic; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c Kwasucki *et al.*[229] included three treatment groups: fluvoxamine (10 mg oral) (i), imipramine (25 mg oral) (ii) and tramadol (100 mg intramuscular injection) (iii). In order to prevent using the same comparator twice, only the last two treatment groups have been included in the meta-analysis (see *Figure 93*).

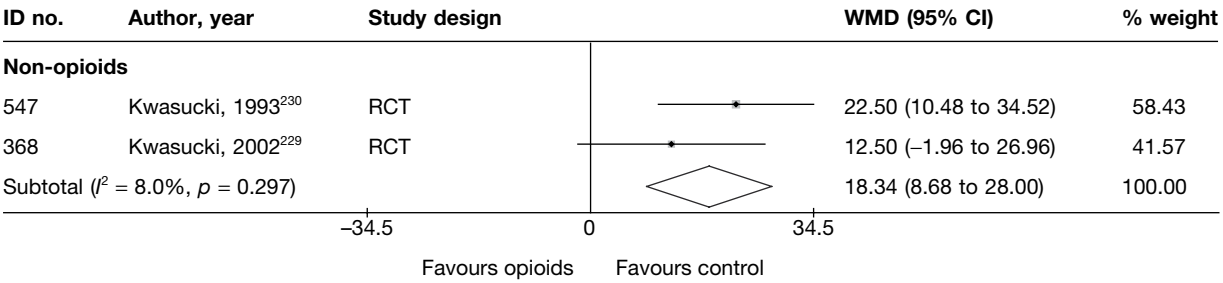

FIGURE 93 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing opioids with alternative interventions. Note: weights are from random effects analysis.

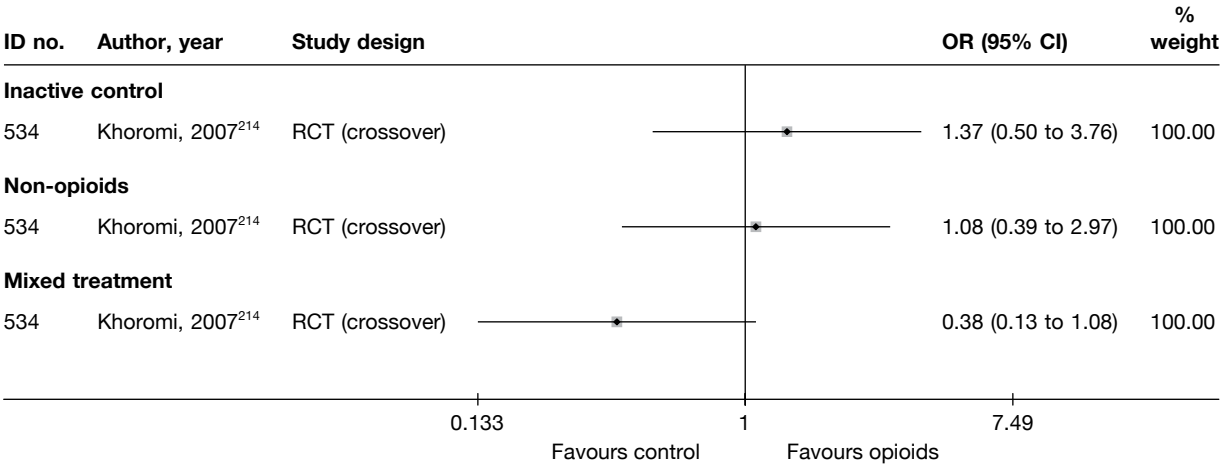

FIGURE 94 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing opioids with alternative interventions. Note: weights are from random effects analysis.

Opioid results at long-term follow-up (>6 months)

No studies with long-term global effect, pain intensity or CSOMs were identified.

Adverse effects

Adverse effects were very poorly reported in most studies. *Table 144* and the accompanying forest plot (*Figure 97*) present the overall number of any adverse event that occurred. More detailed description of these are presented in the appendices. There was evidence from one RCT[214] that opioids had more adverse effects than placebo, but there was conflicting evidence from two RCTs[229,214] about the number of adverse effects associated with placebo compared with antidepressants.

SUMMARY OF OVERALL FINDINGS FOR OPIOIDS COMPARED WITH ALTERNATIVE INTERVENTIONS

Three RCTs compared the use of opioids with other interventions (*Table 145*).[214,229,230]

At short-term follow-up opioids were more efficacious than placebo in one moderate-quality crossover RCT[214] in terms of global effect, but not pain intensity. There was no significant difference in effectiveness compared with antidepressants in terms of the global effect or pain intensity at short-term and medium-term follow-up in two moderate- or poor-quality RCTs.[229,214]

TABLE 141 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing opioids with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)	Comments
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate		
Opioids vs inactive control														
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Global pain relief (GPR): worse pain, no pain relief		32	13	0.42	33	11	0.40	1.37 (0.50 to 3.76)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Opioids vs non-opioids														
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Global pain relief (GPR): worse pain, no pain relief		32	13	0.42	31	12	0.44	1.08 (0.39 to 2.97)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Opioids vs mixed treatment (opioids and non-opioids)														
534	Khoromi, 2007[214] (opioids + non-opioids)	C	RCT (crossover)	9 weeks (end of treatment)	Global pain relief (GPR): worse pain, no pain relief		32	13	0.42	28	18	0.49	0.38 (0.13 to 1.08)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

C, chronic.

TABLE 142 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing opioids with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]	Comment/conversion[c]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Opioids vs inactive control																
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Leg	NRS (0–10)	28	28	49 (24.3)	49 (24.3)	34 (28)	37.0 (27)			–3.00 (–17.41 to 11.41)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Opioids vs non-opioid																
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Leg	NRS (0–10)	28	28	49 (24.3)	49 (24.3)	34 (28)	30.0 (27)			4.00 (–10.41 to 18.41)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Opioids vs mixed treatment (opioids and non-opioids)																
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	Leg	NRS (0–10)	28	28	49 (24.3)	49 (24.3)	34 (28)	38.0 (24)			–4.00 (–17.66 to 9.66)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

C, chronic; NRS, numerical rating scale.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

c The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

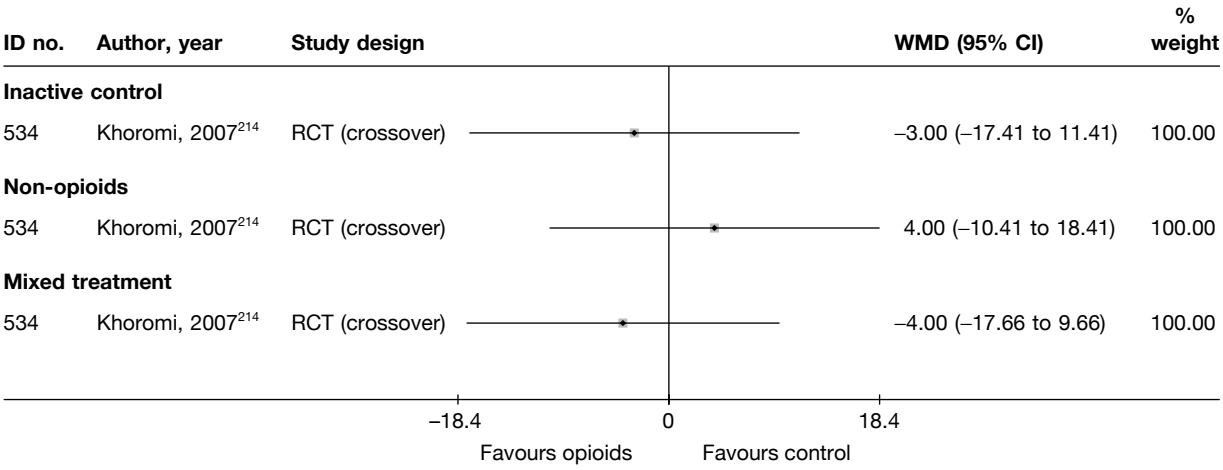

FIGURE 95 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing opioids with alternative interventions. Note: weights are from random effects analysis.

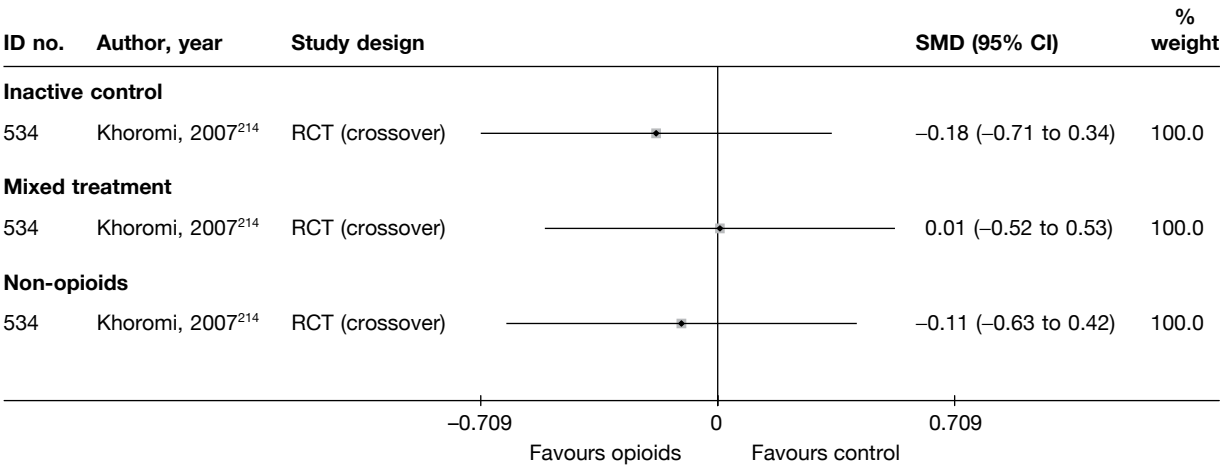

FIGURE 96 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing opioids with alternative interventions. Note: weights are from random effects analysis.

Opioids were significantly less effective than a course of corticosteroids in one moderate-quality RCT.[230] Opioids had more adverse effects than placebo in one RCT, but there was conflicting evidence from two RCTs about the number of adverse effects associated with placebo compared with antidepressants.

TABLE 143 Summary of the findings of CSOMs at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing opioids with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/ conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Opioids vs inactive control															
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	NRS (0–10)	28	28	30 (15)	30 (15)	27.5 (16.7)	30.5 (15.9)			–0.18 (–0.71 to 0.35)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Opioids vs non-opioid															
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	NRS (0–10)	28	28	30 (15)	30 (15)	25.7 (16.5)	27.5 (16.7)			0.01 (–0.52 to 0.53)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)
Opioids vs mixed treatment (opioids and non-opioids)															
534	Khoromi, 2007[214]	C	RCT (crossover)	9 weeks (end of treatment)	NRS (0–10)	28	28	30 (15)	30 (15)	27.5 (16.7)	27.4 (15.4)			–0.11 (–0.63 to 0.42)	Pain reported only for 28/50 patients (56%) who completed study (all treatments)

C, chronic; NRS, numerical rating scale.

a Based on final means or change scores (with a preference given to change scores).

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 144 Summary of the findings of any adverse effect for studies comparing opioids with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Opioids vs inactive control							
534	Khoromi, 2007[214]	RCT (crossover)	51	55	28	55	12.29 (3.91 to 38.7)
Opioids vs mixed treatment (opioids and non-opioids)							
534	Khoromi, 2007[214]	RCT (crossover)	51	55	49	55	1.56 (0.42 to 5.87)
Opioids vs non-opioids							
534	Khoromi, 2007[214]	RCT (crossover)	51	55	37	55	6.20 (1.94 to 19.85)
547	Kwasucki, 1993[230]	RCT	NR	NR	NR	NR	
368	Kwasucki, 2002[229] (fluvoxamine)	RCT	1	22	2	24	0.52 (0.04 to 6.22)
368	Kwasucki, 2002[229] (imipramine)	RCT	1	22	12	24	0.05 (0.01 to 0.41)

NR, not reported.

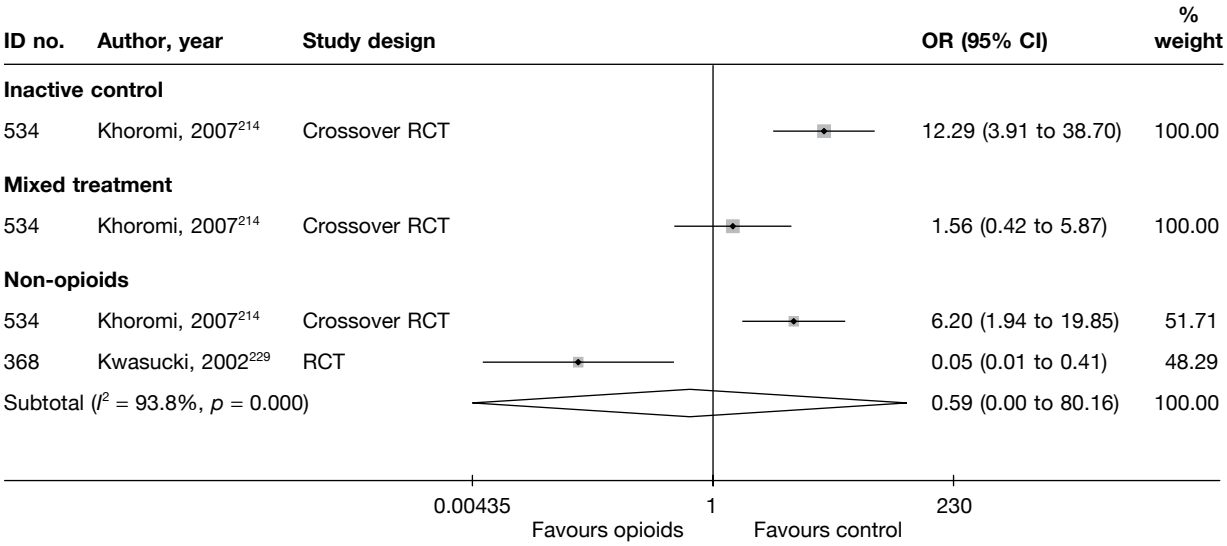

FIGURE 97 Summary of the findings of any adverse effect for studies comparing opioids with alternative interventions. Note: weights are from random effects analysis.

TABLE 145 Summary of opioid studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Opioids vs inactive control	1 (1)	55 (55)	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Opioids vs mixed treatment	1 (1)	55 (55)	1/1 (100)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)
Opioids vs non-opioids	3 (4)	43–70 (55)	2/3 (67)	1/3 (33)	0/3 (0)	3/3 (100)	2/3 (67)	1/3 (33)	0/3 (0)	0/3 (0)	2/3 (67)	0/3 (0)
Total (for opioid studies)[a]	**3 (6)**	**43–70 (55)**	**3/3 (100)**	**1/3 (33)**	**0/3 (0)**	**3/3 (100)**	**2/3 (67)**	**1/3 (33)**	**0/3 (0)**	**0/3 (0)**	**2/3 (67)**	**0/3 (0)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

a These numbers are based on number of studies not number of arms as above (e.g. study 534 includes three comparators, but has been counted only once here).

Education/advice

Description of education/advice studies

Summary of interventions

Three studies compared educational interventions or advice with alternative treatments.[14,169,267] Summary data for the interventions are presented in *Table 146*. One RCT[14] compared advice to keep active with bed rest for 2 weeks. One three-arm RCT[267] compared bed rest for 7 days with advice to continue activities of daily living, or with hospital physiotherapy twice weekly for at least 4 weeks. Another three-arm pilot study[169] compared two 60-minute educational sessions about postural advice and an educational booklet with a course of chiropractic spinal manipulation or three epidural injections of corticosteroid. This pilot RCT[169] did not compare outcome measures between groups.

Summary of study participants in education/advice studies

The two RCTs that compared outcomes included 433 participants with mean ages between 39 and 46 years, mostly men, with acute symptom duration, and including recurrent symptoms. Sciatica was confirmed by imaging in one RCT.[267] There were no patients with spinal stenosis or sequestered discs and previous back surgery was excluded in one RCT (*Table 147*).[14]

Summary of study quality for education/advice studies

Study details are summarised in *Table 148*. The full results of the quality assessment are presented in the appendices. All of the studies were RCTs and one was of good quality.[14] Two had used an adequate method of random number generation,[14,267] but none had a secure method of allocation concealment, and only one had good external validity.[14]

Education/advice results at short-term follow-up (≤6 weeks)

Global effect at short-term follow-up

The results for the global effect at short-term follow-up are presented in *Table 149* and the accompanying forest plot (*Figure 98*). There was no significant difference between advice to keep active and bed rest in two moderate- or good-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in one RCT.[267]

TABLE 146 Summary of the interventions used when comparing education/advice with alternative interventions

ID no.	Author, year	Study design	Treatment description	Control description
Education/advice vs activity restriction				
713	Hofstee, 2002[267]	RCT	Advised to continue activities of daily living (ADL)	Bed rest (BR)
658	Vroomen, 1999[14]	RCT	Advice to keep active	Bed rest
Education/advice vs epidural/intradiscal injection				
722	Bronfort, 2004[169]	RCT	Self-care education	Three ESIs over 12 weeks
Education/advice vs manipulation				
722	Bronfort, 2004[169]	RCT	Self-care education	Chiropractic spinal manipulation
Education/advice vs mixed treatments				
713	Hofstee, 2002[267]	RCT	Advised to continue activities of daily living (ADL)	Hospital physiotherapy (Ph) – manipulation + exercises

TABLE 147 Summary of sciatica type and study population details for studies comparing education/advice with alternative interventions

ID no.	Author, year	Study design	No. of patients	Age	No. of men (%)	Symptom duration	Type of sciatica	Confirmed by imaging?	Recurrent episode	Included patients with stenosis?[a]	Included patients with sequestered disc (or extruded)?[a]	Any previous treatment for sciatica?	Any previous back surgery for sciatica?
Education/advice vs activity restriction													
713	Hofstee, 2002[267]	RCT	250	Mean 39 (SD 10)	150 (60)	Mean 2 weeks	Nerve root pain and referred pain	Yes	Recurrent	No	No	NR	Yes
658	Vroomen, 1999[14]	RCT	183	Mean 46 (SD 12)	103 (56)	Median 16 days	Nerve root pain	No	Recurrent and first episode	No	No	NR	No
Education/advice vs epidural/intradiscal injection													
722	Bronfort, 2004[169]	RCT	32	Mean 49.0 (SD 9.1)	18 (56)	1–3 months 19%, 4–6 months 6%, 7–12 months 9%, >12 months 66%	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	No
Education/advice vs manipulation													
722	Bronfort, 2004[169]	RCT	32	Mean 49.0 (SD 9.1)	18 (56)	1–3 months 19%, 4–6 months 6%, 7–12 months 9%, >12 months 66%	Nerve root pain and referred pain	No	Recurrent and first episode	No	No	NR	No
Education/advice vs mixed treatments													
713	Hofstee, 2002[267]	RCT	250	Mean 39 (SD 10)	150 (60)	Mean 2 weeks	Nerve root pain and referred pain	Yes	Recurrent	No	No	NR	Yes

NR, not reported.

a Marked yes if patient population or inclusion criteria specifically reported that patient with sequestered disc, extruded disc or stenosis were included; otherwise reported as no.

TABLE 148 Summary of the study details for studies comparing education/advice with alternative interventions

ID no.	Author, year	Study size	Overall follow-up	Study design	Adequate randomisation?	Allocation concealment?	Follow-up (%)	Blind outcome assessment?	Overall quality rating	Overall external validity rating
Education/advice vs activity restriction										
658	Vroomen, 1999[14]	183	12 weeks	RCT	Yes	No	80–100	Yes	Moderate	Strong
713	Hofstee, 2002[267]	250	6 months	RCT	Yes	No	80–100	No	Moderate	Moderate
Education/advice vs epidural/intradiscal injection										
722	Bronfort, 2004[169]	32	52 weeks	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Education/advice vs manipulation										
722	Bronfort, 2004[169]	32	52 weeks	RCT	Unclear	Partial	80–100	Unclear	Weak	Weak
Education/advice vs mixed treatments										
713	Hofstee, 2002[267]	250	6 months	RCT	Yes	No	80–100	No	Moderate	Moderate

TABLE 149 Summary of the findings of the global effect at short-term follow-up (≤6 weeks) for studies comparing education/advice with alternative interventions

							Intervention			Control			
ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	OR (95% CI)
Education/advice vs activity restriction													
713	Hofstee, 2002[267]	A	RCT	1 month	Treatment failure Opposite extracted	Physician	83	77	0.00	84	79	0.00	0.81 (0.24 to 2.77)
658	Vroomen, 1999[14]	A	RCT	2 weeks	Assessment of improvement	Patient	91	59	0.00	92	64	0.00	0.81 (0.43 to 1.50)
Education/advice vs mixed treatments													
713	Hofstee, 2002[267]	A	RCT	1 month	Treatment failure Opposite extracted	Physician	83	77	0.00	83	81	0.00	0.32 (0.06 to 1.62)

A, acute.

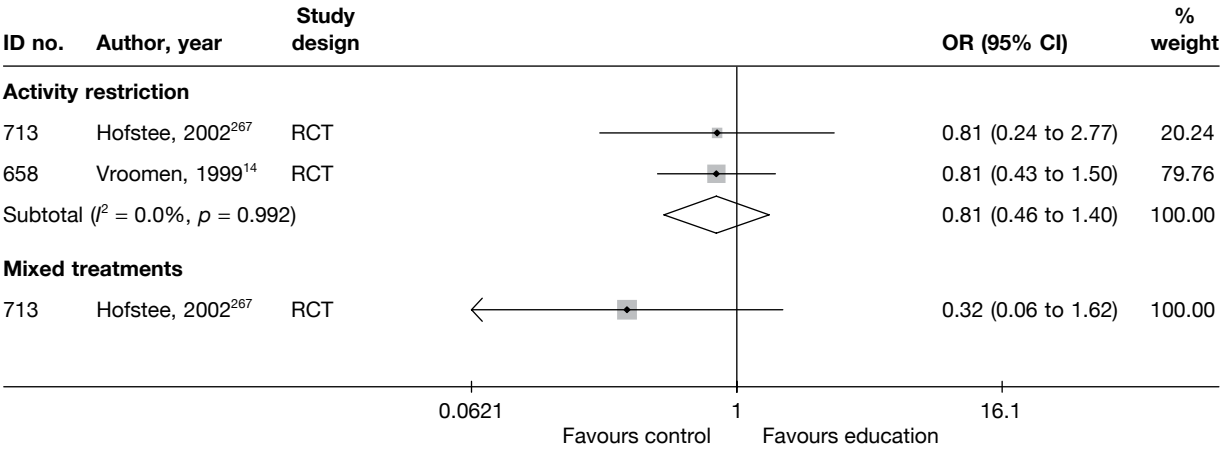

FIGURE 98 Summary of the findings of the global effect at short-term follow-up (≤ 6 weeks) for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

Pain intensity at short-term follow-up

The results for pain intensity at short-term follow-up are presented in *Table 150* and the accompanying forest plot (*Figure 99*). There was no significant difference between advice to keep active and bed rest in two good- or moderate-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in one moderate-quality RCT.[267]

Condition-specific outcome measures at short-term follow-up

The results for CSOMs at short-term follow-up are presented in *Table 151* and the accompanying forest plot (*Figure 100*). There was no significant difference between advice to keep active and bed rest in two good- or moderate-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in one moderate-quality RCT.[267]

Education/advice results at medium-term follow-up (> 6 weeks to ≤ 6 months)

Global effect at medium-term follow-up

The results for the global effect at medium-term follow-up are presented in *Table 152* and the accompanying forest plot (*Figure 101*). There was no significant difference between advice to keep active and bed rest in two good- or moderate-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in one moderate-quality RCT.[267]

Pain intensity at medium-term follow-up

The results for pain intensity at medium-term follow-up are presented in *Table 153* and the accompanying forest plot (*Figure 102*). There was no significant difference between advice to keep active and bed rest in two good- or moderate-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in one moderate-quality RCT.[267]

Condition-specific outcome measures at medium-term follow-up

The results for CSOMs at medium-term follow-up are presented in *Table 154* and the accompanying forest plot (*Figure 103*). There was no significant difference between advice to keep active and bed rest in two good- or moderate-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in one moderate-quality RCT.[267]

TABLE 150 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing education/advice with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Education/advice vs activity restriction															
713	Hofstee, 2002[267]	A	RCT	1 month	Leg	VAS (0–100)	83	82	60.7 (21.4)	65.5 (18.5)			–23.4 (29.16)	–25.9 (29.16)	2.50 (–6.40 to 11.40)
658	Vroomen, 1999[14]	A	RCT	2 weeks	Leg	VAS (0–100)	91	92	68 (21)	62 (22)	44 (27)	36 (28)			8.00 (0.03 to 15.97)
Education/advice vs mixed treatment															
713	Hofstee, 2002[267]	A	RCT	1 month	Leg	VAS (0–100)	83	80	60.7 (21.4)	60.9 (20.1)			–23.4 (29.31)	–24.2 (29.31)	0.80 (–8.20 to 9.80)

A, acute.
a The results have been converted to a scale of 0–100 for comparability.
b Based on final means or change scores (with a preference given to change scores).

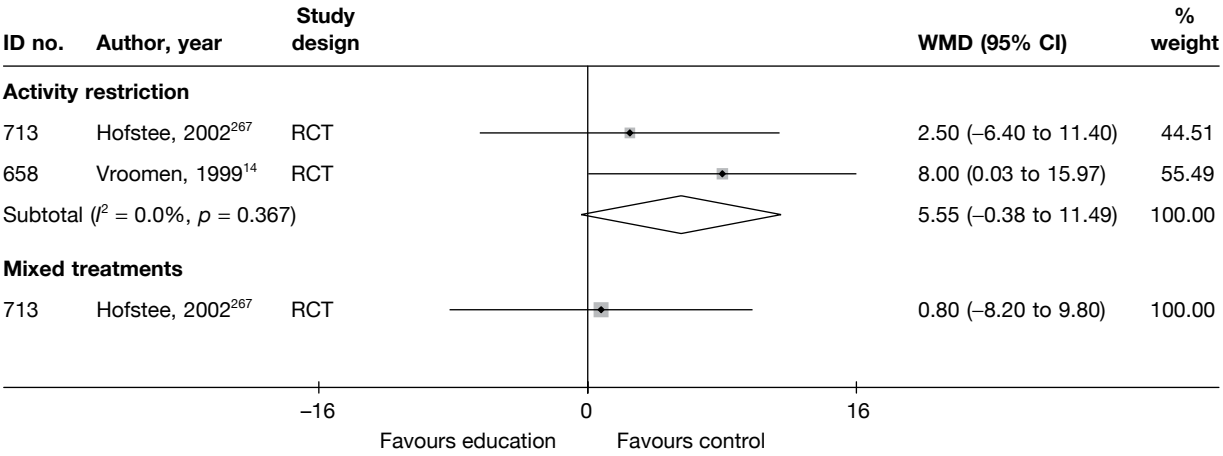

FIGURE 99 Summary of the findings of pain intensity at short-term follow-up (≤6 weeks) for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

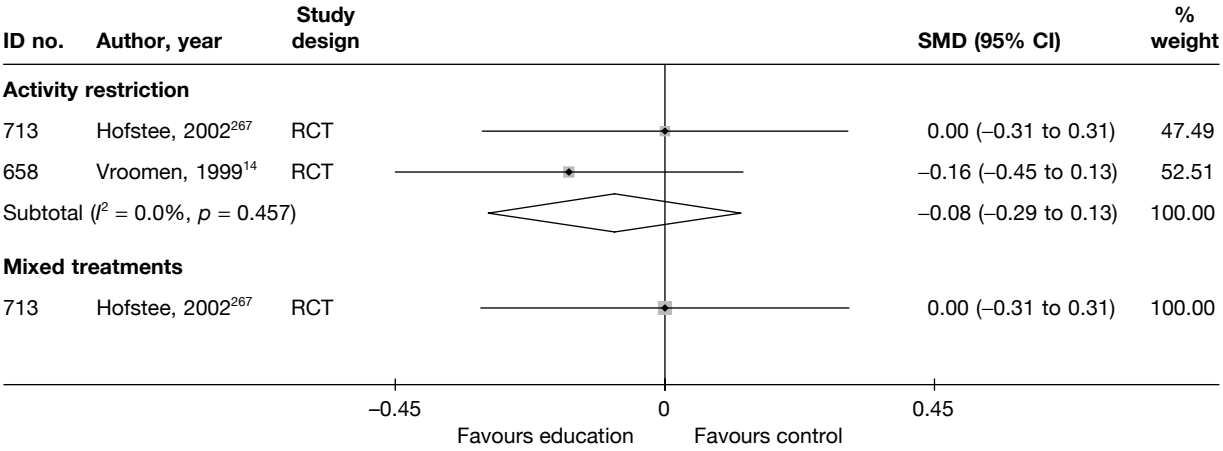

FIGURE 100 Summary of the findings of CSOMs at short-term follow-up (≤6 weeks) for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

Education/advice at long-term follow-up (>6 months)

No long-term outcomes were reported for global effect, pain intensity or CSOMs.

Adverse effects

Adverse effects were very poorly reported in most studies. *Table 155* and the accompanying forest plot (*Figure 104*) present the overall number of any adverse event that occurred. More detailed descriptions of these are presented in the appendices. Education or advice interventions were associated with significantly fewer adverse events, in single RCTs, than epidural injections or spinal manipulation. There was no significant difference between the number of adverse events associated with education or advice compared with activity restriction in two RCTs.

SUMMARY OF OVERALL FINDINGS FOR EDUCATION/ADVICE COMPARED WITH ALTERNATIVE INTERVENTIONS

Two moderate- or good-quality RCTs compared the use of opioids with other interventions (*Table 156*).[14,267]

TABLE 151 Summary of the findings of CSOMs at short-term follow-up (≤ 6 weeks) for studies comparing education/advice with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Education/advice vs activity restriction															
713	Hofstee, 2002[267]	A	RCT	1 month	QDS	83	82	57.4 (16.3)	58.6 (14.6)	41.2 (16.3)	41.2 (16.3)	–16.2 (18.84)	–16.2 (18.84)	0.00 (–0.3 to 0.31)	Final means calculated from change scores Distribution at follow-up reported to be skewed ITT analyses reported (incorporating treatment compliance and dropouts), but dropouts excluded the results reported Number randomised: BR 84, Ph 83, ADL (control) 83
658	Vroomen, 1999[14]	A	RCT	3 weeks	Revised RMDQ	91	92	5.2 (3.8)	5.5 (3.9)	9.2 (6.3)	9.2 (6.3)	–4	–4	–0.16 (–0.43 to 0.13) *Adjusted mean difference 1.6 (95% CI –0.4 to 3.7)*	ITT used For baseline and mean, high score = good outcome; sign of change score altered so that negative indicates improvement Adjusted difference between groups not based change scores
Education/advice vs mixed treatments															
713	Hofstee, 2002[267]	A	RCT	1 month	QDS	83	80	57.4 (16.3)	56 (17.6)	41.2 (16.3)	41.2 (16.3)	–16.2 (18.89)	–16.2 (18.89)	0.00 (–0.31 to 0.31)	Final means calculated from change scores Distribution at follow-up reported to be skewed ITT analyses reported (incorporating treatment compliance and dropouts), but dropouts excluded the results reported Number randomised: BR 84, Ph 83, ADL (control) 83

A, acute; ADL, activities of daily living; BR, bed rest; Ph, physiotherapy; QDS, Quebec Disability Scale.

a Based on final means or change scores (with a preference given to change scores); results as reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

TABLE 152 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing education/advice with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Outcome measure	Perspective	Intervention			Control			OR (95% CI)
							Total (*n*)	Outcome (*n*)	Withdrawal rate	Total (*n*)	Outcome (*n*)	Withdrawal rate	
Education/advice vs activity restriction													
713	Hofstee, 2002[267]	A	RCT	6 months	Treatment failure. Opposite extracted	Physician	83	69	0.00	84	63	0.00	1.46 (0.77 to 3.50)
658	Vroomen, 1999[14]	A	RCT	12 weeks	Assessment of improvement	Patient	91	79	0.00	92	80	0.00	0.99 (0.42 to 2.33)
Education/advice vs mixed treatments													
713	Hofstee, 2002[267]	A	RCT	6 months	Treatment failure. Opposite extracted	Physician	83	69	0.00	83	64	0.00	1.46 (0.68 to 3.16)

A, acute.

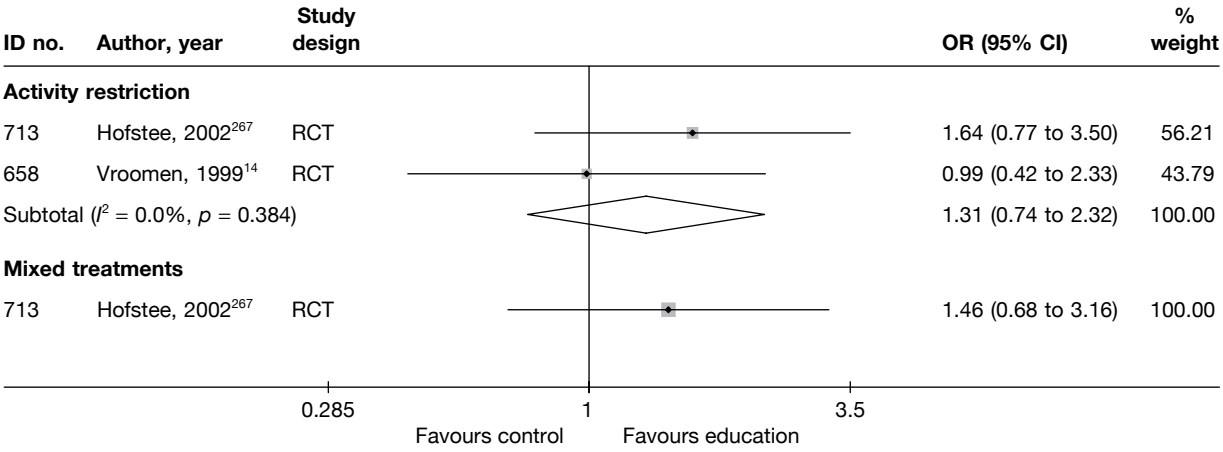

FIGURE 101 Summary of the findings of the global effect at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

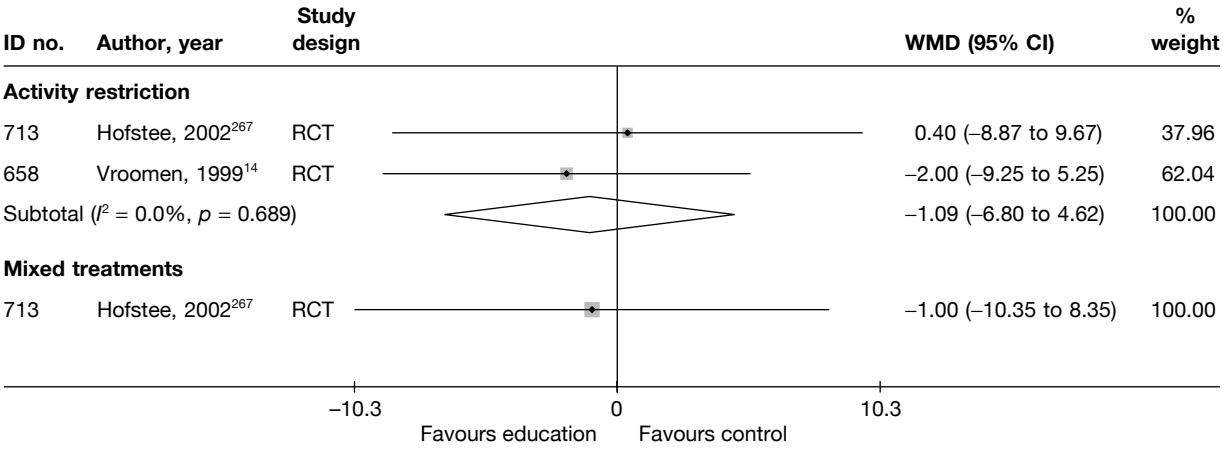

FIGURE 102 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

In two moderate- or good-quality RCTs there was no significant difference between advice to keep active and bed rest, in terms of the global effect, pain intensity and CSOMs at short- and medium-term follow-up, in two good- or moderate-quality RCTs.[14,267] There was no significant difference between advice to keep active and mobilisation with exercises carried out in a hospital physiotherapy department in terms of the global effect, pain intensity and CSOMs at short- and medium-term follow-up in a moderate-quality RCT.[267]

TABLE 153 Summary of the findings of pain intensity at medium-term follow-up (>6 weeks to ≤6 months) for studies comparing education/advice with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Location	Scale (range)[a]	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[b]
							Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Education/advice vs activity restriction															
713	Hofstee, 2002[267]	A	RCT	6 months	Leg	VAS (0–100)	75	78	60.7 (21.4)	65.5 (18.5)			–47.8 (30.45)	–48.2 (27.92)	0.40 (–8.87 to 9.67)
658	Vroomen, 1999[14]	A	RCT	12 weeks	Leg	VAS (0–100)	91	92	68 (21)	62 (22)	14 (24)	16 (26)			–2.00 (–9.25 to 5.25)
Education/advice vs mixed treatment															
713	Hofstee, 2002[267]	A	RCT	6 months	Leg	VAS (0–100)	75	72	60.7 (21.4)	60.9 (20.1)			–47.8 (29.99)	–46.8 (27.83)	–1.00 (–10.35 to 8.35)

A, acute.

a The results have been converted to a scale of 0–100 for comparability.

b Based on final means or change scores (with a preference given to change scores).

TABLE 154 Summary of the findings of CSOMs at medium-term (>6 weeks to ≤6 months) follow-up for studies comparing education/advice with alternative interventions

ID no.	Author, year	Chronicity	Study design	Follow-up	Scale	Total (*n*)		Baseline mean (SD)		Final mean (SD)		Change scores (SD)		Mean difference (95% CI)[a]	Comment/conversion[b]
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control		
Education/advice vs activity restriction															
713	Hofstee, 2002[267]	A	RCT	2 months	QDS	75	78	57.4 (16.3)	58.6 (14.6)	22 (16.3)	25.9 (14.6)	–35.4 (23.66)	–32.7 (23.66)	–0.25 (–0.57 to 0.07)	Final means calculated from change scores Distribution at follow-up reported to be skewed ITT analyses reported (incorporating treatment compliance and dropouts), but dropouts excluded the results reported Number randomised: BR 84, Ph 83, ADL (control) 83
658	Vroomen, 1999[14]	A	RCT	12 weeks	Revised RMDQ	91	92	5.2 (3.8)	5.5 (3.9)	7.3 (7)	7.8 (7)	–10.5	–9.7	–0.07 (–0.36 to 0.22) *Adjusted mean difference 0.5 (95% CI –1.6 to 2.6)*	For baseline and mean, high score = good outcome; sign of change score altered so that negative indicates improvement ITT used, method not stated
Education/advice vs mixed treatment															
713	Hofstee, 2002[267]	A	RCT	2 months	QDS	75	75	57.4 (16.3)	56 (17.6)	22 (16.3)	21.4 (17.6)	–35.4 (23.9)	–34.6 (23.9)	0.04 (0.28 to 0.36)	Final means calculated from change scores Distribution at follow-up reported to be skewed ITT analyses reported (incorporating treatment compliance and dropouts), but dropouts excluded the results reported Number randomised: BR 84, Ph 83, ADL (control) 83

A, acute; ADL, advised to continue activities of daily living; BR, bed rest; Ph, physiotherapy; QDS, Quebec Disability Scale.

a Based on final means or change scores (with a preference given to change scores); results as reported by study in italics.

b The term 'dropouts' has been used for missing data, post-baseline exclusions and patients lost to follow-up.

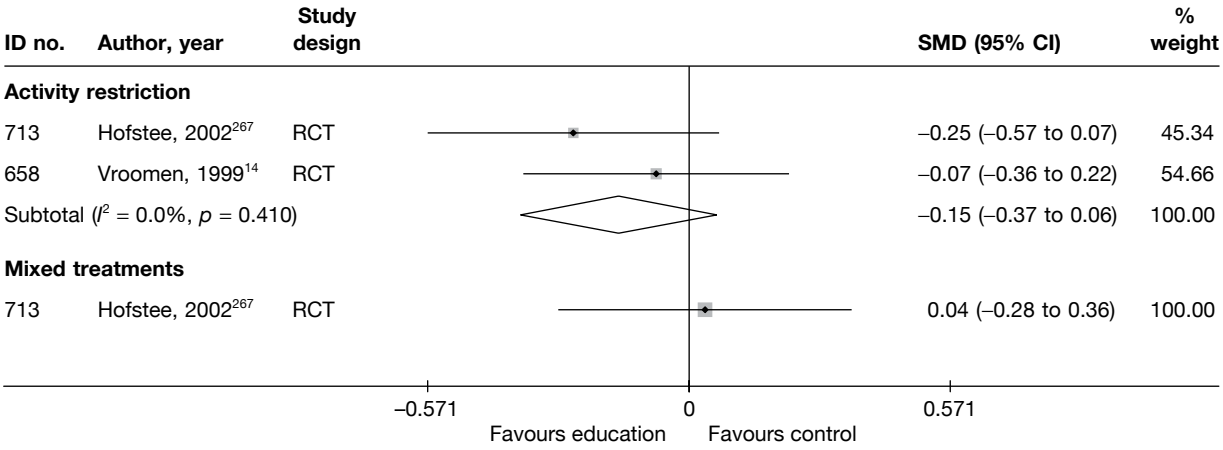

FIGURE 103 Summary of the findings of CSOMs at medium-term (>6 weeks to ≤6 months) follow-up for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

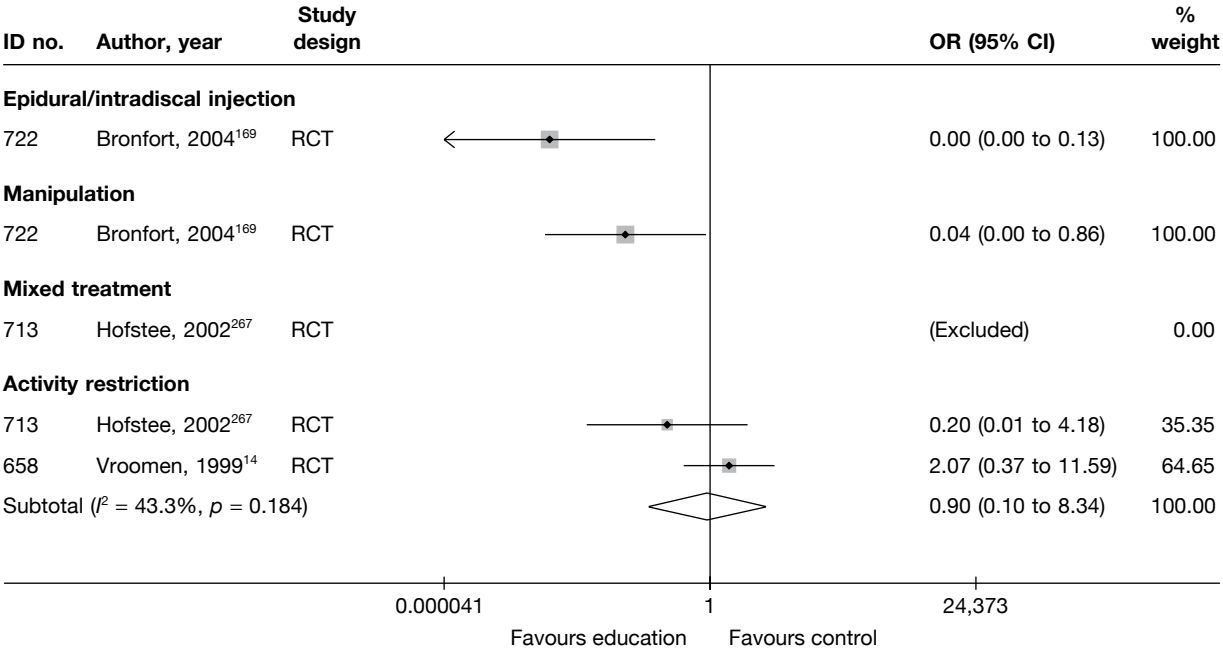

FIGURE 104 Summary of the findings of any adverse effect for studies comparing education/advice with alternative interventions. Note: weights are from random effects analysis.

TABLE 155 Summary of the findings of any adverse effect for studies comparing education/advice with alternative interventions

ID no.	Author, year	Study design	No. of events in intervention group	No. of participants in intervention group	No. of events in control group	No. of participants in control group	OR (95% CI)
Education/advice vs activity restriction							
713	Hofstee, 2002[267]	RCT	0	83	2	84	0.20 (0.00 to 4.18)
658	Vroomen, 1999[14]	RCT	4	91	2	92	2.07 (0.37 to 11.59)
Education/advice vs epidural							
722	Bronfort, 2004[169]	RCT	0	10	10	10	0.00 (0.00 to 0.13)
Education/advice vs manipulation							
722	Bronfort, 2004[169]	RCT	0	10	6	11	0.04 (0.00 to 0.86)
Education/advice vs mixed treatment							
713	Hofstee, 2002[267]	RCT	0	83	0	83	

TABLE 156 Summary of education/advice studies

Control category	No. of studies (arms)	Sample size range (median)	Proportion of studies that were RCTs (%)	Proportion of studies that were deemed good quality (%)	Proportion of studies that only included acute sciatica (%)	Proportion of studies that included patients with nerve root pain (%)	Proportion of studies that reported diagnosis confirmed by imaging (%)	Proportion of studies that included patients with stenosis (%)	Proportion of studies that included patients with extruded/ sequestered discs (%)	Proportion of studies that only included patients with first episode (%)	Proportion of studies that included patients who had received previous treatment (%)	Proportion of studies that included patients who had received previous surgery (%)
Education/advice vs activity restriction	2 (2)	183–250 (217)	2/2 (100)	0/2 (0)	2/2 (100)	2/2 (100)	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)
Education/advice vs mixed treatment	1 (1)	250 (250)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)
Total (for education/ advice studies)[a]	**2 (3)**	**183–250 (217)**	**2/2 (100)**	**0/2 (0)**	**2/2 (100)**	**2/2 (100)**	**1/2 (50)**	**0/2 (0)**	**0/2 (0)**	**0/2 (0)**	**0/2 (0)**	**1/2 (50)**

This table shows only studies that reported outcomes for global effect, pain intensity or CSOMs.

a These numbers are based on number of studies not number of arms as above (e.g. Hofstee *et al.*[267] includes two comparators, but has been counted only once here).

Chapter 7

Mixed treatment comparisons: results

Description of mixed treatment comparison models

The network for studies reporting the outcome global effect is presented in *Figure 105*. In total, six MTC analyses were conducted for the three types of outcome (global effect, pain intensity and CSOMs) for all study designs and for RCTs and Q-RCTs only. The network diagrams for pain intensity and CSOMs are presented in *Appendix 6*, as well as the network diagram for global effect that only includes RCTs and Q-RCTs.

The MTC analyses rely on the key assumption that the relative treatment effect of one treatment versus another is the same across the entire set of studies.[273,274] We used a random effects model, which means that we assumed that the common distribution of effects is the same across all sets of studies. A further assumption that was made in the analyses was that the relative efficacy of different treatments is the same at different stages in the care pathway.

Convergence was assessed using the Gelman–Rubin statistic (R) monitored over iteration–time. ($R = B/W$, where B represents the within-chain variability and W the between-chain variability.) Convergence occurred at around 6000–8000 iterations for all three outcome measures (global effect, pain intensity and CSOMs), as demonstrated in the random selection of plots presented in *Appendix 7*. The auto-correlation and history plots also showed good convergence. The goodness of fit of the models to the data, measured by the residual deviance, was found to be high (data presented in *Appendix 8*).

The results of the evaluation of between-study heterogeneity, presented in *Appendix 8*, showed a moderate-to-high level of statistical heterogeneity for many of the pair-wise comparisons, as well as across all studies as a whole.

The mean pain scores (scale 0–100) at baseline for each treatment category, according to the studies included in the MTC, were fairly similar and are presented in *Table 157*. With the exception of biological agents, most ranged from 60 to 69.

The MTC method enables us to estimate the probability that each treatment category is best (or most effective), the findings of which are presented in *Tables 159–164*, along with the summary effect estimates for comparisons of each intervention category with inactive control. The credible intervals (or the CIs presented in *Figures 106–111*) provide an indication of the uncertainty surrounding the effect sizes, which needs to be taken into account. For example, for global effect the estimates of the medians for biological agents and alternative therapy are associated with a great deal of uncertainty. Although they had the highest probability of being the best interventions, their 95% credible intervals were very wide and included unity, so were not statistically significant. Although the estimates of the median effect size for disc surgery and epidural injections were smaller, the 95% credible intervals were narrower and their findings were statistically significant (the direction of benefit in the forest plot is different for pain and CSOM is different from the direction for global effect).

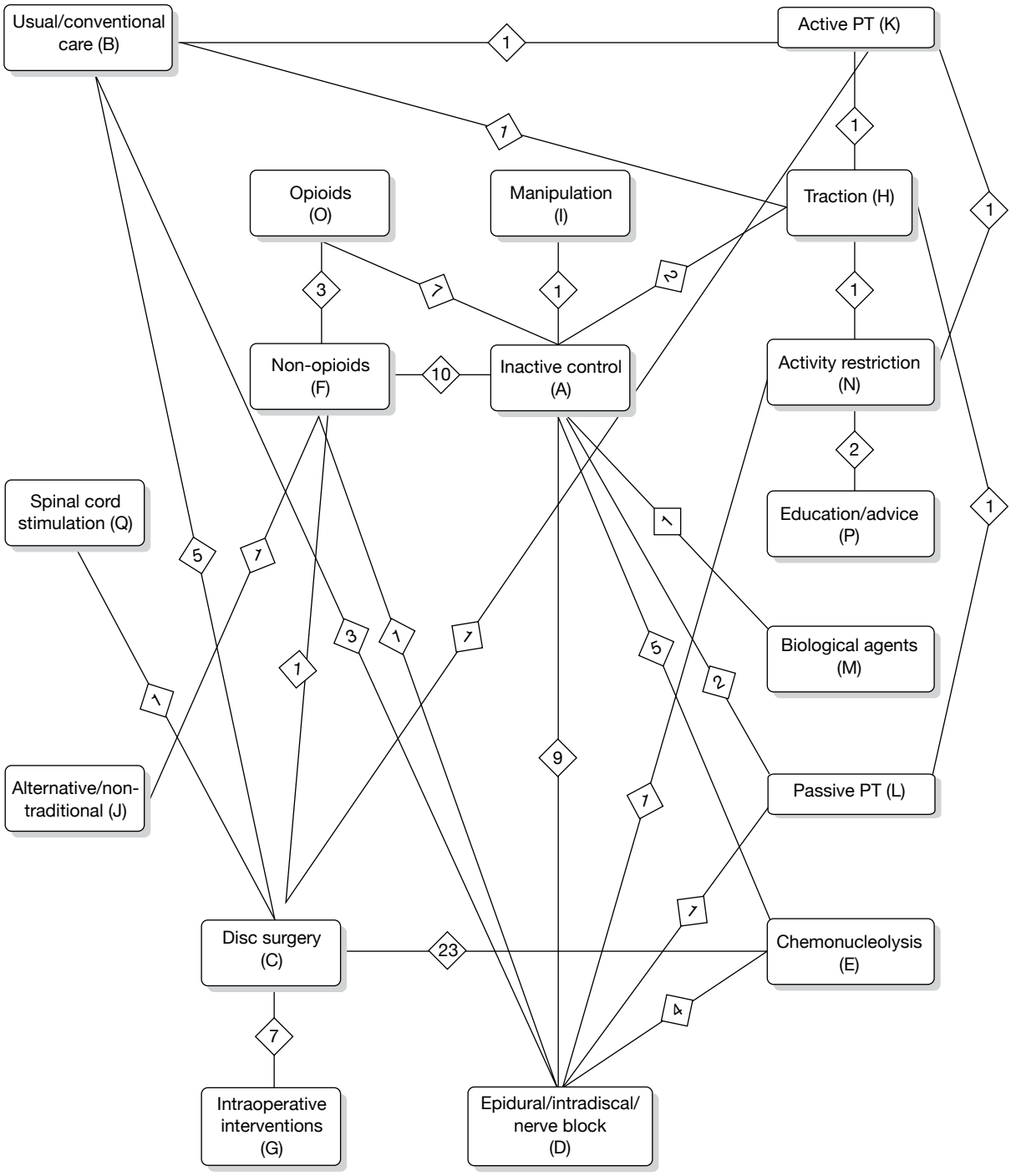

FIGURE 105 Mixed treatment comparison network for global effect, including all studies.

The indirect comparison, as part of the MTC analysis, provides a full set of comparisons for all treatment groups. The summary estimates of effect (with 95% credible intervals) for each treatment comparison in the network for the analysis of global effect, which included all study designs is presented in *Table 158*. The results of each treatment comparison in the MTC analyses for all the networks are also presented in *Appendix 9*. The MTC findings can be directly compared with summaries of the pair-wise meta-analysis (with 95% CIs) derived from STATA, which are also presented in the same matrices (top right-hand corner). For example, when

TABLE 157 Mean baseline pain for each treatment category (based on arm level data for studies included in the MTC analyses)

Treatment category	No. of studies (no. of RCTs/Q-RCTs)	Mean baseline pain
Alternative/non-traditional	Not reported	
Intraoperative interventions	7 (7)	59.8
Active PT/exercise therapy	2 (2)	60.0
Chemonucleolysis	5 (3)	60.2
Education/advice	1 (1)	60.7
Inactive control	18 (17)	63.3
Opioids	2 (2)	63.3
Non-opioids	12 (10)	64.4
Usual/conventional care	4 (3)	65.8
Activity restriction	3 (3)	66.8
Epidural/intradiscal injection	11 (11)	67.6
Traction	4 (4)	68.0
Passive PT	3 (3)	68.3
Disc surgery	15 (11)	68.7
Biological agents	2 (1)	76.5

considering all study types, pair-wise data from nine studies show epidural to be significantly better than the inactive control for global effect (OR 2.58; 95% CI 1.25 to 5.29), and the indirect data show a similar result (OR 3.10; 95% credible interval 1.79 to 5.46). An example of where there is no direct comparison of interventions is that between disc surgery and epidural injections for global effect, but the indirect comparison shows a non-statistically significant finding in favour of surgery (OR 1.11; 95% credible interval 0.55 to 2.25).

The results of the mixed treatment comparison of each intervention category with inactive control

Comparisons of the findings of the pair-wise meta-analysis for each intervention category with inactive control are presented in *Tables 159–164* and *Figures 106–111*. When these direct comparisons are compared with those obtained from the MTC analysis, it can be seen that there is a broad agreement for the global effect, but there are more discrepancies for pain intensity and for CSOMs. These discrepancies are greatest for comparisons for which there is very little direct evidence, such as biological agents versus inactive control (one study[271]).

For global effect, interventions that resulted in a statistically significant improvement compared with inactive control were, in order of effect size, intraoperative interventions, epidural injections, disc surgery, non-opioids and chemonucleolysis. For pain intensity these included alternative, biological agents and epidural. Opioids were found to be significantly less effective than inactive control for reducing pain. For CSOMs, biological agents resulted in statistically significant improvement compared with inactive control. When the analyses were limited to RCTs/Q-RCTs, the only interventions that remained significantly better than inactive control were intraoperative interventions, epidural injections, disc surgery and non-opioids for global effect and epidural for pain intensity.

Results when observational studies were excluded were broadly similar.

TABLE 158 Results of MTC analysis for all comparative studies reporting global effect

A			*n*=9, 2.58 (1.3 to 5.3)	*n*=5, 2.56 (1.6 to 4.1)	*n*=10, 2.16 (1.1 to 4.5)		*n*=2 to 1.11 (0.6 to 2.1)	*n*=1, 4.71 (2.0 to 11.4)			*n*=2, 1.57 (0.2 to 11.3)	*n*=1, 10.0 (0.7 to 167)		*n*=1, 1.37 (0.5 to 3.8)			
0.83 (0.4 to 1.9)	B	*n*=5, 2.60 (1.6 to 4.3)	*n*=3, 5.46 (0.8 to 38.5)				*n*=1, 1.53 (0.6 to 4.2)			*n*=1, 1.45 (0.7 to 3.0)							
2.78 (1.4 to 5.6)	3.37 (1.7 to 6.8)	C		*n*=23, 0.65 (0.5 to 0.9)	*n*=1, 6.72 (0.8 to 58.8)	*n*=7, 1.49 (1.0 to 2.2)				*n*=1, 0.77 (0.2 to 3.2)						*n*=1, 1.13 (0.4 to 3.6)	
3.10 (1.8 to 5.5)	3.75 (1.7 to 8.4)	1.11 (0.6 to 2.3)	D	*n*=4, 1.13 (0.4 to 3.6)	*n*=1, 0.45 (0.2 to 1.4)						*n*=1, 0.20 (0.1 to 0.6)		*n*=1, 0.22 (0.1 to 0.9)				
2.00 (1.1 to 3.8)	2.42 (1.2 to 5.1)	0.72 (0.5 to 1.1)	0.65 (0.3 to 1.2)	E													
2.55 (1.4 to 4.7)	3.09 (1.2 to 8.4)	0.92 (0.4 to 2.2)	0.82 (0.4 to 1.8)	1.27 (0.6 to 2.9)	F				*n*=1, 3.27 (0.8 to 13.8)					*n*=2, 0.55 (0.1 to 5.0)			
4.73 (1.6 to 14.0)	5.72 (2.0 to 16.8)	1.70 (0.8 to 3.9)	1.52 (0.5 to 4.5)	2.35 (1.0 to 5.8)	1.85 (0.6 to 6.1)	G											
1.20 (0.5 to 3.1)	1.46 (0.5 to 4.2)	0.44 (0.2 to 1.2)	0.39 (0.1 to 1.1)	0.60 (0.2 to 1.7)	0.47 (0.2 to 1.4)	0.26 (0.1 to 1.0)	H			*n*=1, 0.88 (0.3 to 2.7)	*n*=1, 0.93 (0.5 to 1.9)		*n*=1, 1.00 (0.1 to 7.0)				
4.88 (0.7 to 33.2)	5.91 (0.7 to 47.1)	1.76 (0.2 to 13.4)	1.57 (0.2 to 11.4)	2.45 (0.3 to 18.3)	1.91 (0.3 to 14.0)	1.03 (0.1 to 9.1)	4.06 (0.5 to 33.8)	I									

9.32 (1.0 to 104.5)	11.27 (1.0 to 144.5)	3.35 (0.3 to 40.9)	2.99 (0.3 to 35.6)	4.64 (0.4 to 56.2)	3.65 (0.4 to 38.0)	1.98 (0.2 to 27.5)	7.73 (0.7 to 102)	1.91 (0.1 to 41.7)	J							
1.10 (0.3 to 3.8)	1.33 (0.4 to 4.4)	0.40 (0.1 to 1.3)	0.35 (0.1 to 1.2)	0.55 (0.2 to 1.9)	0.43 (0.1 to 1.6)	0.23 (0.1 to 1.0)	0.90 (0.3 to 3.2)	0.22 (0.0 to 2.2)	0.12 (0.0 to 1.6)	K			*n*=1, 2.2 (0.6 to 7.7)			
1.14 (0.4 to 3.2)	1.38 (0.4 to 4.7)	0.41 (0.1 to 1.3)	0.37 (0.1 to 1.1)	0.57 (0.2 to 1.8)	0.45 (0.1 to 1.4)	0.24 (0.1 to 1.0)	0.94 (0.3 to 3.1)	0.23 (0.0 to 2.0)	0.13 (0.0 to 1.5)	1.04 (0.2 to 4.7)	L					
15.77 (0.6 to 1002)	19.26 (0.7 to 1357)	5.68 (0.2 to 396)	5.10 (0.2 to 335)	7.90 (0.3 to 545)	6.19 (0.2 to 409)	3.38 (0.1 to 249)	13.2 (0.4 to 943)	3.36 (0.1 to 306)	1.75 (0.0 to 180)	14.6 (0.4 to 1085)	14.03 (0.5 to 974)	M				
1.28 (0.3 to 5.5)	1.54 (0.3 to 7.1)	0.46 (0.1 to 2.0)	0.41 (0.1 to 1.7)	0.64 (0.1 to 2.8)	0.50 (0.1 to 2.4)	0.27 (0.1 to 1.5)	1.05 (0.2 to 4.7)	0.26 (0.0 to 2.9)	0.14 (0.0 to 2.0)	1.16 (0.3 to 5.1)	1.12 (0.2 to 6.0)	0.08 (0.0 to 2.9)	N		*n*=2, 1.32 (0.8 to 2.3)	
1.60 (0.5 to 5.4)	1.95 (0.5 to 8.4)	0.58 (0.2 to 2.3)	0.52 (0.1 to 1.9)	0.80 (0.2 to 3.1)	0.63 (0.2 to 2.0)	0.34 (0.1 to 1.7)	1.33 (0.3 to 6.2)	0.33 (0.0 to 3.3)	0.17 (0.0 to 2.1)	1.46 (0.3 to 8.3)	1.41 (0.3 to 6.8)	0.10 (0.0 to 3.3)	1.26 (0.2 to 8.7)	O		
1.63 (0.2 to 12.1)	1.98 (0.3 to 14.7)	0.59 (0.1 to 4.3)	0.53 (0.1 to 3.7)	0.81 (0.1 to 6.0)	0.64 (0.1 to 5.0)	0.34 (0.0 to 3.0)	1.35 (0.2 to 10.0)	0.33 (0.0 to 5.3)	0.17 (0.0 to 3.5)	1.48 (0.2 to 10.9)	1.43 (0.2 to 12.5)	0.10 (0.0 to 4.9)	1.28 (0.3 to 4.9)	1.02 (0.1 to 10.2)	P	
3.19 (0.4 to 27.6)	3.84 (0.4 to 33.7)	1.14 (0.2 to 8.9)	1.03 (0.1 to 8.9)	1.59 (0.2 to 12.8)	1.25 (0.1 to 11.6)	0.67 (0.1 to 5.9)	2.66 (0.3 to 26.0)	0.65 (0.0 to 12.2)	0.34 (0.0 to 8.0)	2.90 (0.3 to 30.8)	2.80 (0.3 to 28.9)	0.19 (0.0 to 10.1)	2.54 (0.2 to 31.9)	2.0 (0.2 to 23.5)	1.97 (0.1 to 34.8)	Q

A, inactive control; B, usual care; C, disc surgery; D, epidural/nerve block; E, chemonucleolysis; F, non-opioids; G, intraoperative interventions; H, traction; I, manipulation; J, alternative/non-traditional; K, active PT; L, passive PT; M, biological agents; N, activity restriction; O, opioids; P, education/advice; Q, spinal cord stimulation; *n*, number of studies included in conventional pair-wise meta-analysis.
Results of direct standard pairwise meta-analyses (OR plus 95% CI rounded to one decimal place) are reported in the top right-hand triangle and the results of the MTC analyses (odds ratio plus 95% credible interval rounded up to one decimal place) are reported in the bottom left-hand triangle.
Statistically significant findings have been highlighted using shading.
OR > 1.0 favours intervention compared with control.

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TABLE 159 Odds ratios for global effect of the different treatment categories for all studies compared with the inactive control from the MTC analysis and standard pair-wise meta-analyses (treatments ordered according to the probability of being the best)

Treatment category	Code	Probability of being 'best' (mean)	Median OR (95% credible interval)	Results of standard pair-wise meta-analysis	
				No. of studies	ORs (95% CI)
Biological agents	M	0.5062	15.77 (0.61 to 1002.00)	1	10.00 (0.65 to 100.00)
Alternative/non-traditional	J	0.2764	9.32 (0.95 to 104.50)		
Manipulation	I	0.0990	4.88 (0.73 to 33.20)	1	4.76 (11.11 to 1.96)
Spinal cord stimulation	Q	0.0604	3.19 (0.36 to 27.57)		
Intraoperative interventions	G	0.0389	4.72 (1.61 to 13.99)		
Education/advice	P	0.0142	1.63 (0.22 to 12.05)		
Opioids	O	0.0018	1.60 (0.48 to 5.41)	1	1.37 (0.50 to 3.70)
Epidural/nerve block	D	0.0017	3.09 (1.79 to 5.46)	9	2.63 (1.27 to 5.56)
Usual care	B	0.0000	0.83 (0.35 to 1.91)		
Chemonucleolysis	E	0.0000	2.00 (1.05 to 3.82)	5	2.56 (1.59 to 4.17)
Activity restriction	N	7.2×10^{-4}	1.28 (0.29 to 5.51)		
Non-opioids	F	4.4×10^{-4}	2.55 (1.42 to 4.65)	10	2.71 (1.05 to 4.55)
Disc surgery	C	2.4×10^{-4}	2.78 (1.37 to 5.59)		
Active PT	K	1.4×10^{-4}	1.09 (0.32 to 3.78)		
Passive PT	L	1.0×10^{-4}	1.14 (0.41 to 3.17)	2	1.56 (0.22 to 11.11)
Traction	H	4.0×10^{-5}	1.20 (0.47 to 3.07)	2	1.11 (0.60 to 2.04)
Inactive control	A	0.0000			

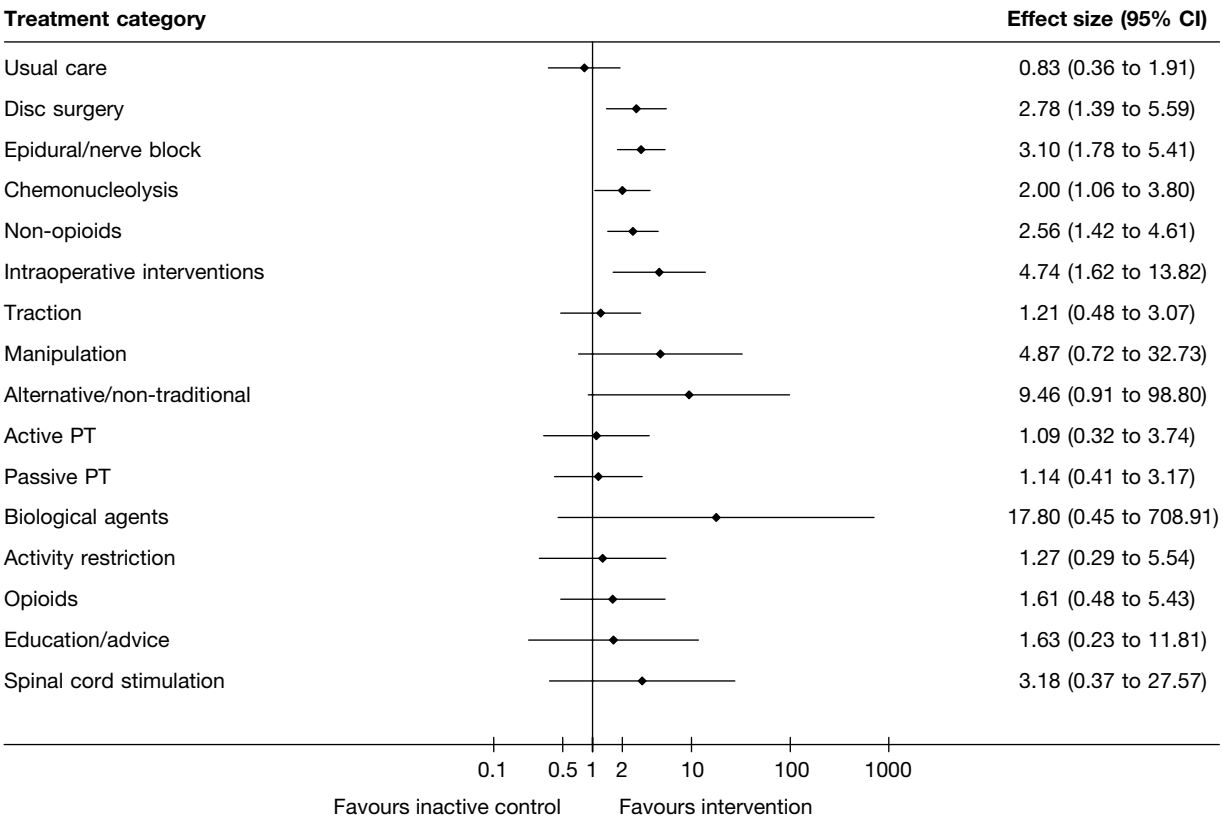

FIGURE 106 Odds ratios for the global effect of the different treatment categories for all studies compared with the inactive control from the MTC analysis. Note: weights are from random effects analysis.

TABLE 160 Odds ratios for the global effect of the different treatment categories for RCTs and Q-RCTs compared with the inactive control from the MTC analysis and standard pair-wise meta-analyses (treatments ordered according to the probability of being the best)

Treatment category	Code	Probability of being 'best' (mean)	Median OR (95% credible interval)	Results of standard meta-analysis	
				No. of studies	ORs (95% CI)
Biological agents	M	0.4847	16.04 (0.60 to 1138.00)	1	10.00 (0.65 to 100.00)
Intraoperative interventions	G	0.3930	4.99 (1.50 to 17.47)		
Alternative/non-traditional	J	0.2568	9.25 (0.90 to 107.70)		
Manipulation	I	0.0882	4.90 (0.70 to 34.48)	1	4.76 (1.96 to 11.11)
Education/advice	P	0.0593	3.12 (0.29 to 34.36)		
Spinal cord stimulation	Q	0.0582	3.30 (0.34 to 32.70)		
Activity restriction	N	0.00944	2.43 (0.35 to 17.52)		
Epidural/nerve block	D	0.00164	3.14 (1.77 to 5.65)	9	2.63 (1.27 to 5.56)
Opioids	O	0.00112	1.62 (0.46 to 5.66)	1	1.37 (0.50 to 3.70)
Traction	H	1.0×10^{-4}	1.36 (0.47 to 3.94)	2	1.12 (0.60 to 2.04)
Non-opioids	F	2.6×10^{-4}	2.59 (1.37 to 4.96)	9	2.56 (1.16 to 5.26)
Disc surgery	C	3.0×10^{-4}	2.94 (1.18 to 7.49)		
Usual care	B	4.0×10^{-5}	1.14 (0.38 to 3.46)		
Active PT	K	4.2×10^{-4}	1.46 (0.38 to 5.75)		
Chemonucleolysis	E	6.0×10^{-5}	2.38 (1.19 to 4.81)	5	2.56 (1.59 to 4.17)
Passive PT	L	6.0×10^{-6}	1.19 (0.42 to 3.42)	2	1.56 (0.22 to 11.11)
Inactive control	A	0.0000			

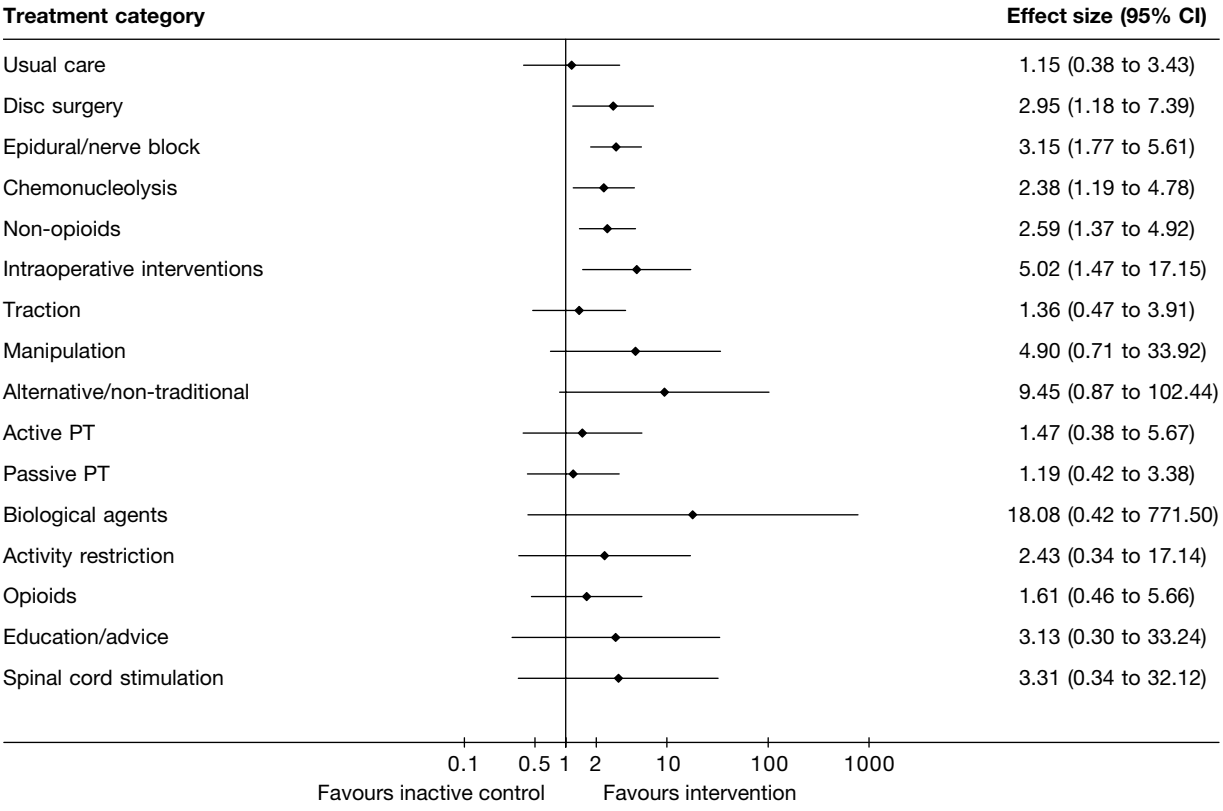

FIGURE 107 Odds ratios for the global effect of the different treatment categories for RCTs and Q-RCTs compared with the inactive control from the MTC analysis. Note: weights are from random effects analysis.

TABLE 161 Weighted mean difference for pain intensity of the different treatment categories for all studies compared with the inactive control from the MTC analysis and standard pair-wise meta-analyses (treatments ordered according to the probability of being the best)

Treatment category	Code	Probability of being 'best' (mean)	Median of the posterior (95% credible interval)	Results of standard meta-analysis	
				No. of studies	WMD (95% CI)
Alternative/non-traditional	J	0.4397	–26.08 (–46.65 to –6.06)	1	–25.00 (–41.75 to –8.24)
Biological agents	M	0.2344	–21.80 (–35.95 to –7.95)	2	–9.91 (–43.23 to 23.41)
Manipulation	I	0.1474	–11.72 (–44.97 to 21.59)		
Intraoperative interventions	G	0.0688	–14.88 (–34.05 to 4.02)		
Chemonucleolysis	E	0.01566	–11.24 (–29.76 to 7.20)	1	–5.40 (–23.66 to 12.86)
Active PT	K	0.014	–3.04 (–27.35 to 20.94)		
Education/advice	P	0.0083	17.04 (–20.80 to 54.62)		
Traction	H	0.00716	–1.21 (–22.07 to 20.04)	1	3.36 (–14.49 to 21.21)
Passive PT	L	0.0039	–0.40 (–19.33 to 19.00)	1	–7.00 (–13.58 to –0.42)
Epidural/nerve block	D	0.00306	–12.85 (–20.91 to –5.14)	8	–12.31 (–23.90 to –0.72)
Radiofrequency lesioning	S	0.00222	12.94 (–13.38 to 39.01)	1	13.00 (2.04 to 23.96)
Activity restriction	N	0.0015	18.00 (–15.57 to 51.16)		
Disc surgery	C	0.0011	–9.78 (–26.51 to 6.81)		
Usual care	B	7.2×10^{-4}	–3.184 (–19.45 to 13.18)		
Non-opioids	F	8×10^{-5}	–4.07 (–13.57 to 5.11)	5	–10.70 (–21.21 to –0.19)
Opioids	O	6×10^{-5}	9.34 (–9.15 to 27.40)		
Inactive control	A	0.0			

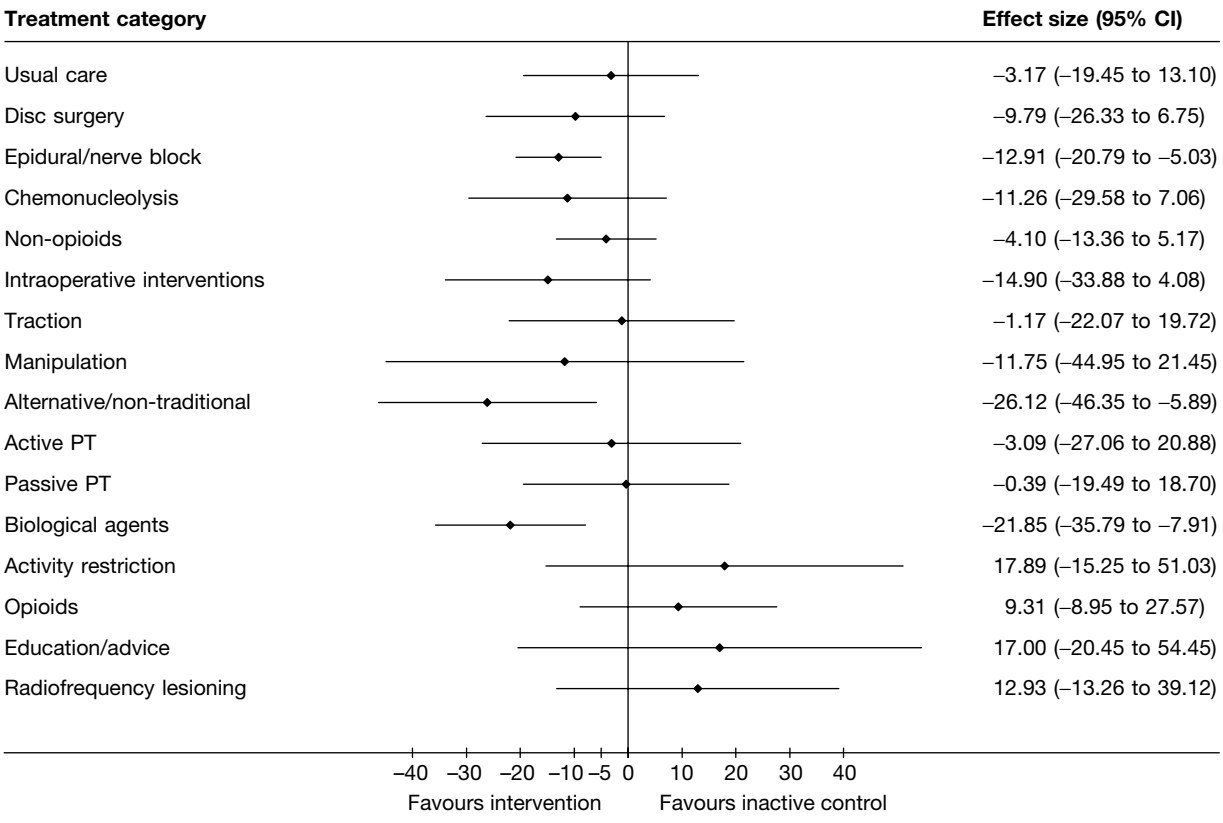

FIGURE 108 Weighted mean difference for pain intensity of the different treatment categories for all studies compared with the inactive control from the MTC analysis. Note: weights are from random effects analysis.

TABLE 162 Weighted mean difference for pain intensity of the different treatment categories for RCTs and Q-RCTs compared with the inactive control from the MTC analysis and standard pair-wise meta-analyses (treatments ordered according to the probability of being the best)

Treatment category	Code	Probability of being 'best' (mean)	Median of the posterior (95% credible interval)	Results of standard meta-analysis	
				No. of studies	WMD (95% CI)
Alternative/non-traditional	J	0.4945	–24.89 (–55.67 to 5.35)	1	–25.00 (–41.75 to –8.24)
Manipulation	I	0.1859	–12.79 (–50.28 to 24.55)		
Intraoperative interventions	G	0.1016	–13.94 (–39.47 to 11.56)		
Biological agents	M	0.07186	–11.18 (–30.77 to 8.83)	1	7.00 (–5.25 to 19.25)
Chemonucleolysis	E	0.04438	–12.28 (–35.85 to 11.38)	1	–5.40 (–23.66 to 12.89)
Epidural/nerve block	D	0.02446	–12.66 (–21.47 to –4.11)	8	–12.31 (–23.90 to –0.72)
Active PT	K	0.02244	–3.39 (–30.69 to 23.94)		
Traction	H	0.01374	–1.32 (–23.17 to 20.91)	1	3.36 (–14.49 to 21.21)
Education/advice	P	0.0115	16.62 (–22.42 to 26.93)		
Passive PT	L	0.00792	–0.23 (–20.29 to 20.33)	1	–7.00 (–13.58 to –0.42)
Disc surgery	C	0.00516	–8.87 (–32.27 to 14.47)		
Usual care	B	0.00464	–4.45 (–23.49 to 14.63)		
Radiofrequency lesioning	S	0.00408	13.01 (–14.41 to 40.77)	1	13.00 (2.04 to 23.96)
Non-opioids	F	0.00408	–5.84 (–16.65 to 4.47)	5	–10.70 (–20.21 to –0.19)
Activity restriction	N	0.0025	17.44 (–16.86 to 52.78)		
Opioids	O	0.00122	7.41 (–12.54 to 26.94)		
Inactive control	A	0.0			

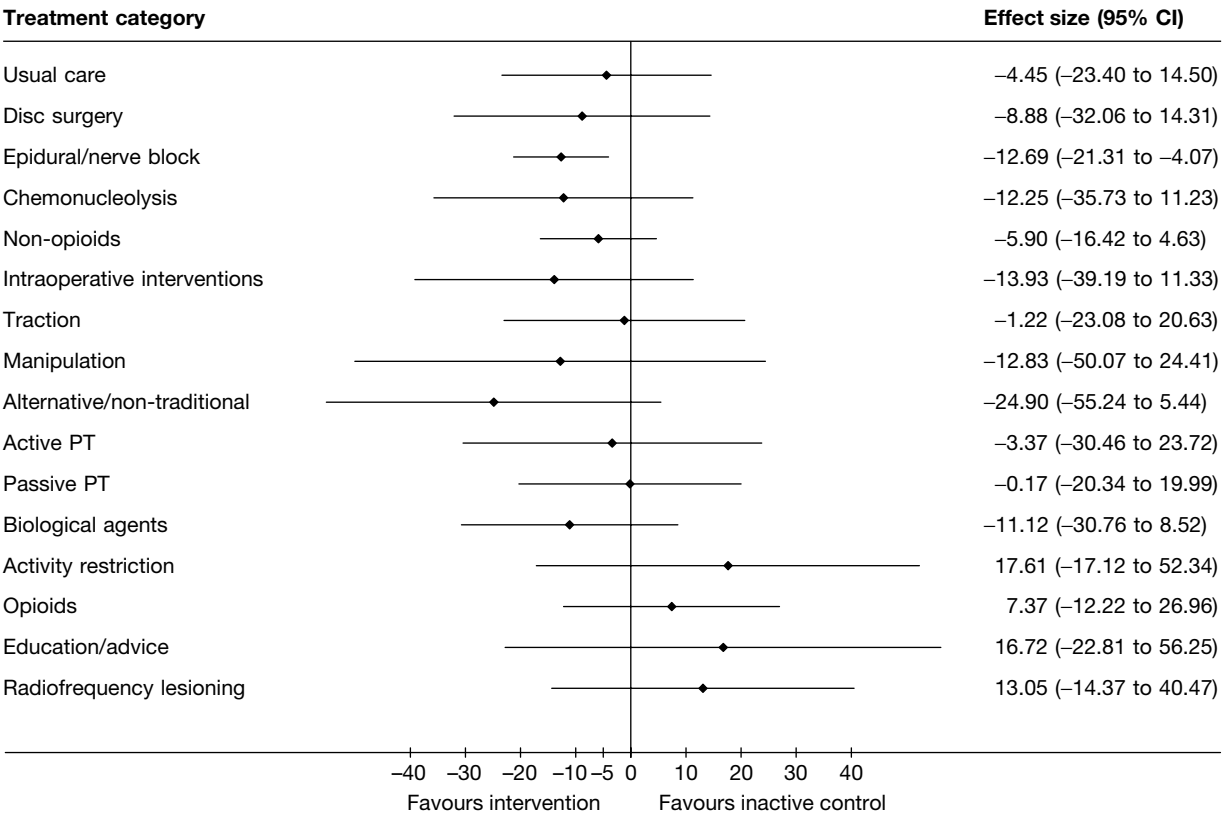

FIGURE 109 Weighted mean difference for pain intensity of the different treatment categories for RCTs and Q-RCTs compared with the inactive control from the MTC analysis. Note: weights are from random effects analysis.

TABLE 163 Standardised mean difference for CSOMs of the different treatment categories for all studies compared with the inactive control from the MTC analysis and standard pair-wise meta-analyses (treatments ordered according to the probability of being the best)

Treatment category	Code	Probability of being 'best' (mean)	Median SMD (95% credible interval)	Results of standard meta-analysis	
				No. of studies	SMD (95% CI)
Activity restriction	N	0.3223	–0.82 (–2.58 to 0.74)		
Biological agents	M	0.2393	–0.67 (–1.27 to –0.08)	3	–0.90 (–1.52 to –0.18)
Education/advice	P	0.1741	–0.66 (–2.59 to 1.00)		
Passive PT	L	0.1186	–0.47 (–1.36 to 0.43)		
Intraoperative interventions	G	0.05489	–0.06 (–1.38 to 1.29)		
Active PT	K	0.0393	0.18 (–1.26 to 1.61)		
Traction	H	0.03458	–0.35 (–1.21 to 0.46)	1	0.08 (–0.31 to 0.47)
Chemonucleolysis	E	0.00496	0.38 (–0.99 to 1.80)		
Usual care	B	0.00365	0.16 (–1.07 to 1.42)		
Disc surgery	C	0.00341	0.10 (–1.17 to 1.39)		
Epidural/nerve block	D	0.00324	–0.16 (–0.53 to 0.20)	5	0.34 (–0.81 to 0.13)
Non-opioids	F	0.00162	0.08 (–0.48 to 0.66)	2	0.30 (–0.14 to 0.74)
Inactive control	A	9.0×10^{5}			

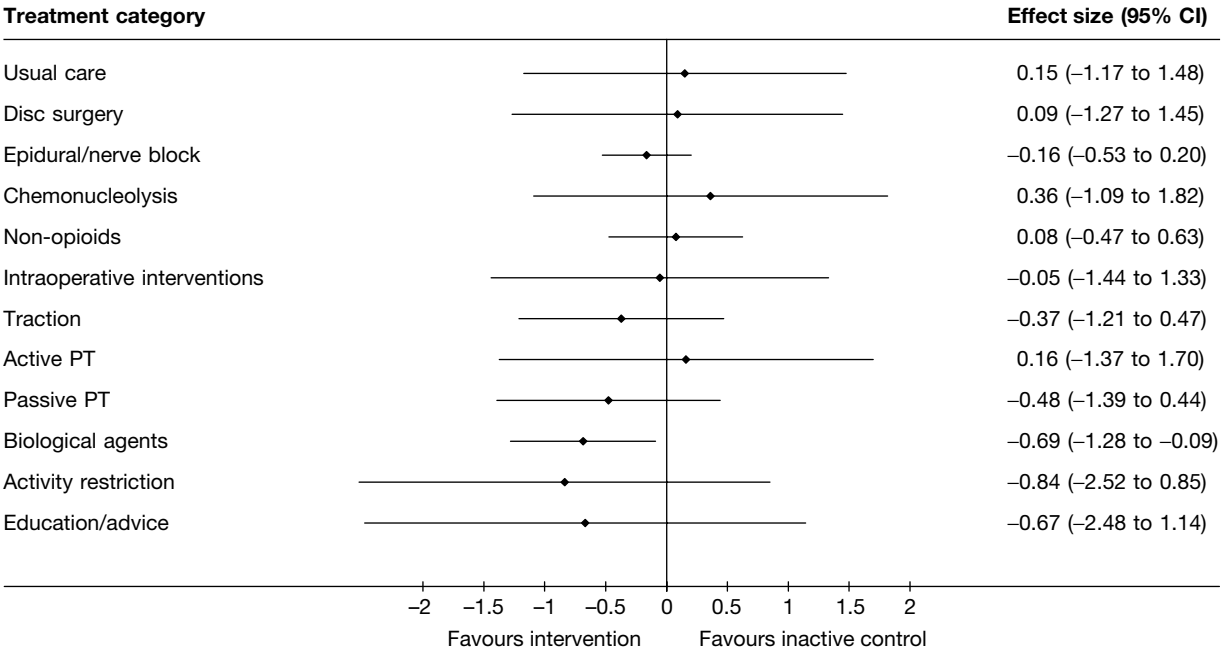

FIGURE 110 Standardised mean difference for CSOMs of the different treatment categories for all studies compared with the inactive control from the MTC analysis. Note: weights are from random effects analysis.

TABLE 164 Standardised mean difference for CSOMs of the different treatment categories for RCTs and Q-RCTs compared with the inactive control from the MTC analysis and standard pair-wise meta-analyses (treatments ordered according to the probability of being the best)

Treatment category	Code	Probability of being 'best' (mean)	Median SMD (95% credible interval)	Results of standard meta-analysis	
				No. of studies	SMD (95% CI)
Activity restriction	N	0.3562	–0.75 (–2.47 to 1.03)		
Education/advice	P	0.1825	–0.61 (–2.40 to 1.31)		
Biological agents	M	0.1786	–0.41 (–1.18 to 0.37)	2	–1.07 (–2.64 to 0.50)
Passive PT	L	0.1285	–0.34 (–1.26 to 0.57)		
Intraoperative interventions	G	0.05476	0.15 (–1.29 to 1.58)		
Traction	H	0.05209	–0.30 (–1.15 to 0.54)	1	0.08 (–0.31 to 0.47)
Active PT	K	0.01826	0.39 (–1.05 to 1.87)		
Non-opioids	F	0.01192	0.08 (–0.49 to 0.66)	2	0.30 (–0.141 to 0.74)
Usual care	B	0.00661	0.35 (–0.94 to 1.62)		
Chemonucleolysis	E	0.00341	0.62 (–0.86 to 2.13)		
Disc surgery	C	0.00326	0.29 (–1.07 to 1.70)		
Epidural/nerve block	D	0.00165	0.04 (–0.35 to 0.43)	4	–0.03 (–0.18 to 0.13)
Inactive control	A	0.00222			

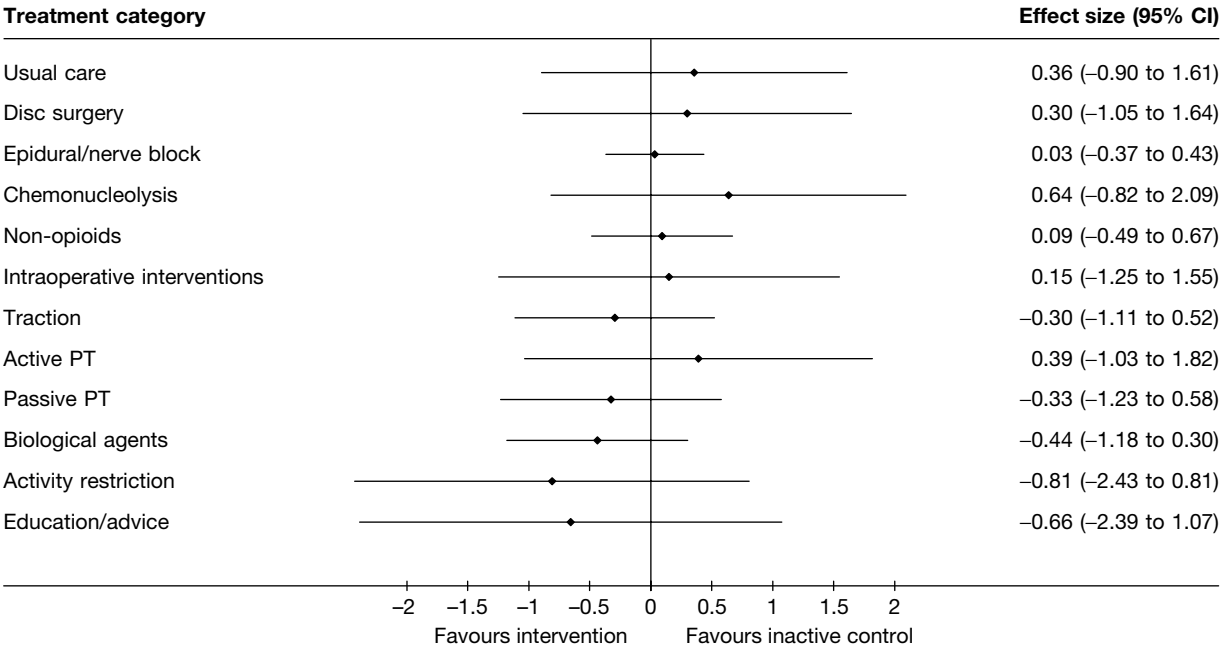

FIGURE 111 Standardised mean difference for CSOMs of the different treatment categories for RCTs and Q-RCTs compared with the inactive control from the MTC analysis. Note: weights are from random effects analysis.

Results of the mixed treatment comparison comparing all interventions that formed a connected network

The following is a summary of the remaining results without the inactive control, for global effect, pain intensity or CSOMs, according to whether or not there was a statistically significant difference between the intervention groups.

For disc surgery, the MTC analysis that included all study types showed a significant improvement in global effect when compared with usual care (OR 3.4, 95% credible interval 1.7 to 6.8). Following intra-operative intervention there was also significant improvement in the global effect for the comparison with usual care (OR 5.7, 95% credible interval 2.0 to 16.8). These comparisons remained statistically significant when the observational studies were excluded from the MTC analyses.

For epidural injection, the MTC analysis that included all study types found a significant improvement in global effect for the comparison with usual care (OR 3.8, 95% credible interval 1.7 to 8.4), and for pain intensity when compared with opioid medication (WMD –22.2, 95% credible interval –3.3 to –41.1). When observational studies were excluded from the MTC analysis there was no longer a significant difference for either of these outcomes.

For chemonucleolysis, the MTC analysis that included all study types found a significant improvement in the global effect compared with usual care (OR 2.4, 95% credible interval 1.2 to 5.1). When observational studies were excluded from the MTC analysis these findings were no longer significant.

For non-opioid medication, the MTC analysis that included all study types found a significant improvement in the global effect compared with usual care (OR 3.1, 95% credible interval 1.2 to 8.4). There was a significantly worse result in pain intensity compared with alternative therapy (mainly acupuncture) (WMD 22.1, 95% credible interval 0.1 to 43.8) or biological agents (OR 17.8, 95% credible interval 2.5 to 33.0). When observational studies were excluded from the MTC analysis these findings were no longer significant.

For alternative therapies (mainly acupuncture), the MTC analysis that included all study types found a significant improvement in pain intensity compared with activity restriction (WMD –44.1, 95% credible interval –82.9 to –4.9), opioids (WMD –35.5, 95% credible interval –62.3 to –8.3), non-opioid medication (WMD –22.1, 95% credible interval –43.8 to –0.1), or education/advice (WMD –44.2, 95% credible interval –85.5 to –0.2). When observational studies were excluded from the MTC analysis these findings were no longer significant.

For passive PT, the MTC analysis that included all study types found a significantly worse result in pain intensity for the comparison with biological agents (WMD 21.3, 95% credible interval 1.9 to 45.5). This finding was no longer a significant when observational studies were excluded from the MTC analysis.

For biological agents, the MTC analysis that included all study types found a significant improvement in pain intensity compared with activity restriction (WMD –39.7, 95% credible interval –75.8 to –3.6), opioids (WMD –31.2, 95% credible interval –53.0 to –9.2), non-opioid medication (WMD –17.8, 95% credible interval –2.46 to –33.0), or passive PT (WMD –21.3, 95% credible interval –45.5 to –1.9), and CSOMs compared with non-opioid medication (SMD –0.8, 95% credible interval –1.5 to –0.0). When observational studies were excluded from the MTC analysis these findings were no longer significant.

For activity restriction, the MTC analysis that included all study types found a significantly worse result in pain intensity compared with biological agents (WMD 39.7, 95% credible interval 3.6 to 75.8) or alternative therapies (WMD 44.1, 95% credible interval 4.9 to 82.9). When observational studies were excluded from the MTC analysis these findings were no longer significant.

For opioid medication, the MTC analysis that included all study types found a significantly worse result in terms of pain intensity compared with epidural injections (WMD 22.2, 95% credible interval 3.3 to 41.1), alternative therapy (mainly acupuncture) (WMD 35.5, 95% credible interval 8.3 to 62.3) or biological agents (WMD 31.2, 95% credible interval 9.2 to 53.0). When observational studies were excluded from the MTC analysis these findings were no longer significant.

For education/advice, the MTC analysis that included all study types found a significantly worse result in terms of pain intensity compared with alternative therapy (WMD 43.2, 95% credible interval 0.2 to 85.5). This finding was no longer significant when observational studies were excluded from the MTC analysis.

Chapter 8

Review of existing economic evaluations: results

Introduction

It was anticipated that the existing evidence relating to the cost-effectiveness of treatments would have a number of limitations that would make it insufficient to inform decision-making regarding the most appropriate management strategy for patients with sciatica. The findings from this review, alongside the review of clinical effectiveness, are intended to assist in informing the basis for the economic model.

Summary of results

Twelve studies were reviewed, data extracted and appraised.[62,100,173,275–283] A brief summary of these studies is presented in *Table 164*. A full summary is presented in *Appendix 10*. Studies evaluated the cost-effectiveness of single interventions for the treatment of sciatica (i.e. pair-wise comparisons) rather than mixed treatment effects. There was significant variation in the quality of studies presented as economic evaluations.

The majority of studies (9/12) were conducted primarily from a health-care or payer perspective. Several studies considered employment-related losses related to work days lost owing to sciatica; with three studies conducted from a societal perspective. The studies covered a diverse range of population settings, with some variation in age range and gender within the studies. Most studies considered a relatively short time horizon. One of the limitations of all studies was the lack of data relating to the longer-term outcome of sciatica. There was little distinction made in most studies between acute and chronic sciatica.

With the exception of one earlier study which employed a decision tree to represent potential pathways, all studies were based on individual patient data derived from RCTs and observational studies. As the majority of identified studies focused on intermediate or surgical interventions, resource utilisation and costs were commonly evaluated with respect to secondary care contacts and associated resource usage. Only one study focused specifically on primary care. Outcomes varied across studies, but the majority considered a global outcome and condition-specific or health-related quality of life (HRQoL). The measures used varied considerably from instruments designed specifically for the study to the use of established generic measures.

Of considerable importance to the review was the quality and robustness of the cost-effectiveness analysis (CEA). Only five studies were considered as full economic evaluations, i.e. reported incremental cost-effectiveness ratios (ICERs), when reviewed against established guidelines.[29,31] The other seven studies reported costs per adjusted outcome,[62] unsuccessful outcome,[281] cost per response[276] or costs per extra success,[275] with no ICERs presented. One study, published 16 years previously,[277] reported a decision-analytic model to compare chemonucleolysis with surgical disctectomy. Again, this study did not present ICERs.

TABLE 165 Summary of cost-effectiveness studies

No.	Study	Country	Perspective	Source	Intervention and comparator(s)		Outcomes	ICER
					Intervention	Control		
1	Dullerud, 1999[275]	Norway	Health provider	Prospective cohort	Surgical macrodiscectomy	Nucleotomy	Marginal cost per extra success choosing surgery as primary outcome	
2	Hansson, 2007[100]	Sweden	Societal	Prospective cohort	Disc surgery	Conservative treatment	Cost per QALY	
3	Karppinen, 2001[276]	Finland	Health provider	RCT	Methylprednisolone-bupivacaine	Saline	Cost per response	
4	Launois, 1994[277]	France	Health provider	Published studies + prospective survey	Chemonucleolysis	Surgical discectomy	Cost per QALY	
5	Luijsterburg, 2007[278]	Netherlands	Societal	RCT	PT + GP care	GP care	Cost per global perceived effect gain	Direct costs: €837 (95% CI –€732 to €3186) Total costs: €6224 (95% CI –€10,419 to €27,551)
6	Malter, 1996[279]	USA	Health purchaser perspective	RCT, published studies	Lumbar discectomy	Conservative management	Cost per QALY	Non discounted: US$29,200 5% discounted: US$33,900 Based on HMO data: US$12,000
7	Manca, 2008[280]	Canada, UK and Europe	Health-care provider (Canada and UK)	RCT	Spinal cord stimulation + non surgical conservative medical management	Non-surgical conservative medical management	Costs and HRQoL outcomes considered separately	

No.	Study	Country	Perspective	Source	Intervention and comparator(s)		Outcomes	ICER
					Intervention	Control		
8	Price, 2005[173]	UK	Health provider and purchaser (NHS)	RCT	Epidural steroid (ESI) + local anaesthetic	Normal saline (placebo)	Cost per QALY	Provider: £44,701 Purchaser: £354,171 *If only one ESI* Provider: £25,745 Purchaser: £167,145
9	Shvartzman, 1992[62]	USA	Health payer (insurance)	Retrospective chart review	Surgery	Conservative treatment	Cost per adjusted outcome	
10	Stevenson, 1995[281]	UK	Health provider	RCT	Automated percutaneous disctectomy	Microdistectomy	Costs per successful outcome	
11	Tosteson, 2008[282]	USA	Societal	RCT + observational cohort	Standard open aminectomy/ laminectomy with removal of herniation + examination of involved nerve route	Non-operative (usual care decided by physician and patient)	Cost per QALY	US$69,404 (95% CI US$49,523 to US$94,999) using general adult surgery costs US$34,355 (95% CI US$20,419 to US$52,512) using Medicare costs
12	van den Hout, 2008[283]	Netherlands	Health-care and societal perspective	RCT	6 months of prolonged conservative care	Early surgery	Cost per QALY	Health-care perspective: €41,000 (95% CI €14,000 to €430,000) Societal: –€12 (95% CI –€4029 to €4006)

HMO, health maintenance organisation; ICER, incremental cost–effectiveness ratio (e.g. incremental cost per QALY gained).

Economic evaluation conducted alongside trials, modelling studies and analyses of administrative databases were included if they compared two or more treatments, and considered both costs and consequences (including cost-effectiveness, cost–utility, cost–benefit and cost-consequences analysis). Some comparative studies included in the effectiveness section of the review also reported cost data, but the data on costs and consequences were not combined. Although not conforming to a full economic evaluation under our definition, two studies warrant specific attention as providing useful information on the cost–utility of interventions for sciatica.

Hansson and Hansson[100] undertook a cost–utility analysis (CUA) of 92 individuals who underwent surgery for lumbar disc herniation in a cohort of 1822 individuals aged between 18 and 59 years and selected consecutively in five regions of Sweden between 1994 and 1995. All participants had been off work for at least 28 days as a result of either low back pain or neck problems. The intervention was surgery with conservative treatment as the comparator. Outcome measures were HRQoL using European Quality of Life-5 Dimensions (EQ-5D); functional restrictions because of back problems using the Hannover Activities of Daily Living questionnaire; and pain experienced during the previous 6 months using the Von Korff pain scale. Medical costs for back pain were estimated (appointments, admission, examination and treatment) over a 2-year study period. Cost of work absenteeism was also estimated. A 5% discount rate and an assumed annual increase in productivity of 1.5% were used to convert future years' production loss to present values. Costs of illness, HRQoL and cost–utility (presented as difference in utility between 28 days and 2 years) were used as the gain in QALY.

The findings showed that the total cost of surgical treatment of lumbar disc herniation during a 2-year period was lower than the cost of non-surgical treatment. The direct cost of surgery was much higher than the direct cost of non-surgical treatment, whereas the indirect cost was lower. Lower indirect costs were the effect of lower rates of recurrence of work absence episodes and permanent disability benefits. Surgery reduced pain and improved back function and HRQoL to a greater extent than non-surgical treatments. The effects on HRQoL in combination with lower costs for surgery resulted in a better cost–utility for surgical treatment. The authors concluded that surgery for lumbar disc herniation is quite cost-effective.

Patients were drawn from a cohort study[100] with explicit selection criteria in place, although the well-reported difficulties of selecting appropriate controls was acknowledged. The EQ-5D was used with utility values derived from a time trade-off (TTO) method, although a UK (rather than Swedish) population was used. Resource costs appear limited and methods to collect cost information were not fully described. Discounting was applied, but not at comparable NHS rates. Costs of illness were reported based on mean costs over 2 years (no CIs were presented). Cost per QALY were then calculated by calculating the difference between 28 days and 2 years. It is not clear why baseline values were not used. In addition, no ICERs were presented to explore QALY gain/loss over a longer time period. No sensitivity analysis was presented, with the authors stating that the Swedish cohort had a lower frequency of disc surgery within the starting 3 months than other national cohorts.

Manca *et al.*[280] reported HRQoL, resource consumption and costs of spinal cord stimulation compared with conventional medical management in 100 patients aged ≥ 18 years participating in the PROCESS (prospective, randomised controlled multicentre study of patients with failed back surgery syndrome) trial. Conservative medical management included oral medications, nerve blocks, epidural corticosteroids, physical and psychological rehabilitative therapy, or chiropractic care. HRQoL using the Short Form questionnaire-36 items (SF-36) and EQ-5D was measured at baseline and 3 months and 6 months after initiation of treatment. Unit costs were calculated using UK and Canadian figures. Health resource-data were prospective and

collected over a comprehensive range of resources. Because of the time line, discounting was not performed.

The 6-month mean total costs were significantly higher (£15,081) in the spinal cord stimulation group than in the conservative management group (£3573), with a statistically significant adjusted differential mean cost of £11,373. However, the gain in HRQoL with spinal cord stimulation over the same period was considerably greater in this group, with a mean EQ-5D score difference of 0.25 ($p < 0.001$) and 0.21 ($p < 0.001$), respectively, at 3 and 6 months after adjustment for baseline characteristics. The authors concluded that the addition of spinal cord stimulation to conservative medical management in patients resulted in higher costs to health-care systems, but generated important improvements in patients EQ-5D over the same period.

Resource data were collected in detail and unit costs were undertaken using Canadian and UK figures, although patient resource data were derived from eight countries participating in the study. However, analysis of 'country effect' suggested that the differences in the total cost for UK and Canada did not appear to be statistically significantly different from the trial overall mean. The study did not take into account the patients' perspective in the economic evaluation. EQ-5D data were collected and utilities were derived from a UK sample. The analysis of cost and HRQoL were presented separately. The limited follow-up period was the main limitation of this study and the authors acknowledged that a full CEA would need to consider how costs and HRQoL difference developed beyond the 6-month period.

With significant heterogeneity across these studies, it was difficult for any reliable conclusions from the results to be drawn from the existing economic evaluation evidence base.

A summary of the main issues identified include:

- studies were undertaken across different countries
- variability in the population settings across studies
- lack of information on the clinical management pathways with many studies not indicating the previous treatment strategies or the timing of the intervention since diagnosis (e.g. patients who received conservative management for longer periods may be less likely to receive surgery which could lead to differences in costs and QALYs)
- different perspectives were adopted (a significant limitation; of particular relevance for this review was the lack of a NHS and personal social services perspective in the studies)
- unclear distinctions between acute and chronic sciatica
- different comparators were used across studies
- usual care was often poorly defined and variable across studies
- short time horizons for studies with little consideration for the longer-term outcomes of sciatica
- lack of discounting
- the difficulty in blinding patients in the RCTs reported (patients' preferences for treatment may have influenced the reported utilities and costs)
- different approaches to measuring resource utilisation and unit costs
- different outcome measures used across studies
- limited data (particularly in earlier studies) of preference-based valuations
- lack of information on the overall duration of symptoms and how these varied across different patient groups and treatments in order to adjust for these durations in any estimation of QALYs
- the potential for crossover between interventions and additional co-interventions (e.g. owing to recurring or worsening symptoms/relapse/complications over time) has been overlooked in the majority of economic evaluations

- variability in the CEA presented, with nearly 60% of studies not presenting an ICER
- lack of sensitivity analysis in these evaluations (where sensitivity analysis is performed, there was considerable variability in the parameters used for changing the base-case analysis).

A recognised limitation in reporting this review is the relevance of these studies and data to current decision-making in the UK NHS. However, even with the significant heterogeneity precluding any formal comparison or conclusions from the results, the ICER estimates reported in *Table 165* suggest marked differences between treatments. The approaches, assumptions and results of these five studies are reviewed in detail to identify possible key differences and issues in order to assist in the development of the new model. Five studies were reviewed. One study compared PT with GP care,[278] one study compared an intermediate intervention (ESI with placebo)[173] and three studies compared surgery with conservative treatment,[283] usual care[282] or chemonucleolysis.[279]

Review of full economic evaluations

Primary care

Luijsterburg *et al.*

Luijsterburg *et al.*[278] undertook an economic evaluation as part of an RCT with 112 GPs in Rotterdam. One hundred and thirty-five patients aged between 18 and 65 years with duration of symptoms of < 6 weeks were randomised to PT and GP care compared with GP care alone. PT consisted of exercise therapy with information and advice provided by physical therapists. Passive therapies were not allowed. GP care was defined as care according to GP clinical guidelines and included information, advice and, if necessary, prescribed analgesia. A societal perspective was taken to the economic evaluation.

Source of effectiveness data

The primary outcome measure was global perceived effect (GPE) measured on a seven-point scale, dichotomised to improved and much improved versus not improved. GPE was rated as the percentage of patients who reported improvement. The EQ-5D was a secondary outcome measure that measured health utilities in order to calculate QALYs. Outcome measures and costs were assessed at baseline and at 3, 6, 12 and 52 weeks. Longer time horizons were not examined and discounting was not applied.

Source of cost data

Direct health-care costs included the costs of PT, GP care, medication, additional visits to other health-care providers and hospitalisations. Prices were obtained from Dutch guidelines[284] or from the Professional Association.[285] The currency was euros (€), but the year was not reported. Indirect costs outside the health-care system included the costs of production losses caused by absence from work. Costs for paid work were calculated by using the friction cost approach (period 154 days) based on the overall mean income of the Dutch population.

Summary of cost-effectiveness analysis

Analysis was undertaken using the ITT principle. Difference in resource utilisation between the two groups was assessed using non-parametric methods because of the skewed nature of the cost data. For the CEA, GPE and EQ-5D were used to calculate benefits. Utilities derived from the EQ-5D allowed a CUA to be performed, although this was not reported. ICERs were constructed and CIs were calculated using Fieller's methods using bootstrapping methods with the construction of cost-effectiveness acceptability curves. No sensitivity analysis was undertaken

because it was claimed that most variations in cost or health effects were included in the bootstrap estimates of the ICER.

Summary of the findings

Total costs (direct and indirect) at 3, 6, 12 and 52 weeks consisted mainly of production losses with significant differences between groups for PT visits in favour of the control groups. Total direct costs were also significantly different at the four follow-up time points in favour of the control group. At baseline and 6 and 12 weeks, the mean utility score was higher in the control group (0.41, 0.70 and 0.73 compared with 0.39, 0.34 and 0.65), but the difference was statistically significant only at 6 weeks. At 52 weeks, the utility in the intervention group was higher (0.76 compared with 0.73).

The ICERs were: for direct costs €837 (95% CI –€732 to €3186) per improved patient gained and for total costs €6224 (95% CI €10,419 to €27,551) per patient improvement gained. The ICERs and CIs estimated by bootstrap and Fieller's methods were similar. The cost-effectiveness acceptability curve constructed for direct costs showed, for a threshold of €600 per patient improved, an ICER acceptable with 35% certainty and, for a threshold of €1200 per patient improved, an ICER acceptable with 69% certainty. For total costs, the curve showed, for a threshold of €4000 per patient improved, an ICER acceptable at 37%, and for a threshold of €12,000 per patient improved, an ICER acceptable at 68%.

The authors concluded that treatment of patients with lumbar radicular syndrome (LRS) with PT and GP care was not more cost-effective than GP care alone.

Critique of Luijsterburg et al.

The study research question was justified because there was a lack of knowledge concerning the cost-effectiveness of PT in sciatica. The economic evaluation has been conducted alongside a RCT which appeared to have good internal validity.

However, some clear issues were identified. The data collection methods used to collect resource utilisation and cost data were not well explained and the reliability of this information could be questioned. For example, the authors recognised that some aspects that may have affected absence from work and productivity costs (e.g. waiting times) were ignore . The authors conceded that future studies should pay more attention to analysing the effect of these factors on absence from work and costs. Costs were cumulative so recall bias from patients may have occurred, but the authors did state that differences between the groups would be minimised by the randomisation process. The authors did not clarify why only a 1-year time horizon was considered, apart from the implicit reason of length of follow-up for the RCT. The collection of outcome measures was also highlighted as a possible limitation, with the EQ-5D criticised as not being sensitive enough to capture the health effects of the additional PT, but no information was given about how benefits were valued. A CUA was not undertaken as there was no effect on QoL between the two groups with higher costs for the intervention group, and in the case of no effect the authors suggested that interventions with the lowest cost were the preferred option. However, despite no significant differences reported, the authors could have estimated an ICER based on best information available, and this highlights the continued criticism that few studies are adequately powered to detect a difference in QoL outcomes.

The issue of uncertainty around the ICER was assessed using the bootstrap method. However, although this allowed CIs to be estimated, and reliability confirmed by comparison with the results of the parametric Fieller's method, it did not allow changes in the base-case assumptions to be explicitly examined (e.g. to take into account increased waiting time).

Surgery

Malter and Weinstein

Malter *et al.*[286] undertook a review of published studies and estimated the cost-effectiveness of lumbar discectomy for herniated intervertral disc. The study was of 126 patients randomly assigned to medical or surgical treatment for radicular pain unresponsive to conservative therapy and was supplemented by data from a second trial to account for early surgery. Estimates of effectiveness were derived from a survey of 42 surgeons. This US-based study took the perspective of the health payer.

Source of effectiveness data

Effectiveness was defined as the number of QALYs gained with surgical treatment versus medical treatment. The comparator was chemonucleolysis. To determine effectiveness, results from the two trials were adjusted by QoL values obtained in a separate study of 83 subjects reporting an episode of severe back pain. A TTO utility measure was administered to estimate QoL. Mean TTO values were calculated and self-assessed outcomes reported in the trials were weighted by corresponding QoL values. For discectomy, a 2-week postoperative period was included in the base-case model. Benefits were discounted by an annual 5% rate.

Source of resource utilisation and costs

Rates of service utilisations were obtained, from a commercially available database, using data from 2175 patients diagnosed with a herniated disc. Demographic details of these patients were reported as similar to the trial participants. From this database, patients operated within 6 weeks of treatment were defined as surgically treated. Those patients who never underwent surgery and those operated on after 6 weeks were categorised as medically treated. Operation costs for medical patients requiring late surgery were counted as costs of initially choosing medical treatment. Direct costs were not discounted. Direct costs reflected costs for all services related to disc herniation (patient visits, diagnostic tests, procedures and hospitalisations). The quantity–cost boundary adopted was that of the hospital. The estimation of quantities and costs was based on actual data. Costs and rates of service utilisation were derived from MEDSTAT (January 1987–December 1989) and data on 78 patients diagnosed at a health maintenance organisation (HMO). Costs were adjusted to 1993 prices using the medical component of the Consumer Price Index and presented in US dollars ($). A 10-year time horizon was undertaken.

Summary of cost-effectiveness analysis

A model-based cost-effectiveness analysis was undertaken. Sensitivity analyses were conducted on efficacy (±25%), QoL (±50%) and costs. Additional estimates were obtained from a survey of spine surgeons, who were presented with case scenarios and asked to estimate the probabilities of excellent to poor outcome after surgical or medical treatment. However, these estimates were not reported, but were available on request from the authors. Additional cost estimates were undertaken from 78 patients diagnosed at a HMO. The authors stated that these were designed to estimate the true resource cost and may have reflected the actual costs more accurately than those used in the base-case analysis.

Summary of the findings

Patients treated with surgical discectomy or chemonucleolysis experienced faster improvement than patients treated medically. The probability of a good outcome varied between 0.36 and 0.56 after medical treatment and between 0.64 and 0.70 after discectomy. For a poor outcome, the probability varied between 0.06 and 0.20 after medical treatment and between 0.07 and 0.14 after discectomy. QoL values associated with a good outcome were 0.95, with a fair outcome 0.77, with a poor outcome 0.62 and with a bad outcome 0.5.

During the 10 years after surgery the average surgical patient experienced 8.7 QALYs whereas the average medical patient experienced 8.27 QALYs, with the difference of 0.43 representing the non-discounted improvement in QALYs associated with surgery. Total costs for the 18-month period beginning 6 months before diagnosis, were $17,020 for the surgical group compared with $4470 for the medical group. The non-discounted cost-effectiveness ratio of surgical over medical therapy was $29,200 per QALY. The discounted cost-effectiveness was $33,900 per QALY. Cost-effectiveness of discectomy remained < $100,000 as long as surgery produced an incremental quality-adjusted benefit of at least 0.125 years. The authors concluded that, for carefully selected patients with herniated discs, surgical discectomy was a cost-effective treatment with favourable cost-effectiveness results obtained from its effect on QoL coupled with moderate costs.

Critique of Malter and Weinstein

There are key limitations of Malter and Weinstein's study which limit its relevance to current practice. It is a US study, involving a comparator not currently available to the UK NHS. In addition, the effectiveness data were from the 1970s and 1980s; improvements in surgical management may be important, so caution would be needed if attempting to generalise these findings to current management.

Although not reported in accordance with accepted current guidelines, the paper reasonably reported the economic evaluation undertaken. One possible issue was the robustness of the review undertaken, with effectiveness estimates derived from a qualitative synthesis. Effectiveness data were collected from different subjects, combined, then the estimation of benefits was modelled. The reporting of this process was limited; however, the TTO method used to derive the measure of benefits appears to be appropriate.

All costs relevant to the perspective adopted appeared to have been included in the analysis. The authors were unable to assess costs incurred more than 1-year after diagnosis from the MEDSTAT database. A sensitivity analysis was conducted on prices, but not on costs. The authors did make appropriate comparisons of their findings with those from other studies at the time of publication.

van den Hout *et al.*

van den Hout *et al.*[283] examined the cost-effectiveness of early surgery compared with 6 months of prolonged conservative care, for patients aged 18–65 years with sciatica for 6–12 weeks because of lumbar disc herniation. Economic evaluation was conducted alongside a RCT.

Source of effectiveness data

The source of clinical effectiveness data was a RCT undertaken in nine hospitals in the Netherlands.[87] Two hundred and eighty-three patients were randomised with 142 patients (mean age 43 ± 10 years; 68% men). Patients were followed up in the trial for 12 months. A CUA was undertaken from the perspectives of the health-care system and society.

Source of resource utilisation and cost data

Costs included the costs of hospital stay, visits to health-care professionals, home care, paid domestic help, informal care, drugs and aids, out-of-pocket expenses as a result of the disc hernia (e.g. swimming) and hours of absenteeism from work. Resource-use data were collected using patient-completed diaries and collected at several time-points over the study period. Nine per cent of patients who did not return resource diaries were equally distributed across the two comparator groups and less likely to have undergone surgery. Correction for selected non-response was made by multiple imputation of data on costs from patients in the same group with same surgical status who returned diaries. This did not substantially change the results compared

with excluding these patients. For patients who did return cost diaries, the diaries covered 97%, 91%, 83% and 84% at 3, 6, 9 and 12 months respectively. For periods that were not covered, data were imputed from the closest available diary from the same patient.

Hospital costs were obtained following diagnosis using treatment prices available from 75 different centres, excluding the two highest and two lowest prices. Other health-care costs were based on Dutch standard prices. The costs of absenteeism were valued using the human capital approach. All costs were presented in euros and at 2008 Dutch consumer index prices. As a 1-year time horizon was used, costs were not discounted.

Summary of cost-effectiveness analysis

Utilities were obtained from the same patients participating in the RCT, through the administration of the EQ-5D (US and UK), the SF-6D (derived from the SF-36) and the VAS. Utilities were derived at several time points from baselines to 52 weeks after randomisation. Missing data were present in 4%, 5% and 5% of the EQ-5D, SF-36 and VAS, respectively, and inputted using the rounded average within the same randomisation group at the same time. QALYs were derived, using the area under the curve (AUC) method, for each separate quarter of the year after randomisation and during the entire year as the summary benefit measure.

Uncertainty was addressed by calculating CIs around the cost–utility ratios. Cost-effective acceptability curves were presented. Sensitivity analysis was carried out on the different utility measures and on the included cost categories using a health-care or societal perspective.

Summary of the findings

Over 12 months, the differences in QALYs and all four utility measures during all four quarters were consistently more favourable after early surgery. The differences in QALYs reported according to the utility measure used were UK EQ-5D 0.044 (95% CI 0.0005 to 0.083), US EQ-5D 0.032 (95% CI 0.005 to 0.059), SF-6D 0.024 (95% CI 0.003 to 0.046) and VAS 0.032 (95% CI –0.003 to 0.066).

From the perspective of the health-care system, total health-care costs remained significantly higher than the costs of prolonged conservative care, with a difference in costs of €1819 (95% CI €842 to €2790) per patient. Total societal costs were –€12 (95% CI –€4029 to €4006): slightly in favour of early surgery. The probability that early surgery is cost-effective compared with conservative care varies with willingness to pay. From a societal perspective it was 76% at €40,000 per QALY and was 87% at €80,000 per QALY. Smaller differences were seen with other utility measures.

From the health-care perspective, according to the UK EQ-5D and US EQ-5D, the incremental cost per QALY gained with early surgery was estimated at €41,000 (95% CI €14,000 to €430,000) and €57,000 (95% CI €19,000 to €436,000), respectively.

The authors concluded that faster recovery from sciatica makes early surgery more cost-effective than prolonged conservative care. The estimated differences in health-care costs were acceptable and were compensated for by the difference in absenteeism from work. For a 'willingness-to-pay' ceiling ratio of €40,000 or more per QALY, early surgery need not be withheld for economic reasons.

Critique of van den Hout et al.

The source of economic data, methodology and interpretation of findings from this study were generally of good quality in this well-presented paper.

The economic evaluation was performed alongside a RCT, so selection bias was unlikely with comparable clinical, demographic and economic characteristics at baseline. The comparators were well defined and justified on the basis that prolonged conservative care is often advocated with no evidence available on the optimal timing of disc surgery.

There were clear inclusion criteria, robust power calculation and analysis undertaken using ITT principles. The internal validity of the study underpinning the economic evaluation was good. One of the strengths of the paper was the considered approach taken to the instruments used to derive utilities. In the absence of a condition-specific measure of health utility, three different generic instruments were used to measure patient preferences, which were compared in a sensitivity analysis.

Costs were considered within the two perspectives. Although there are inherent difficulties associated with the collection of resource data using patient diaries, adherence was high and, where necessary, appropriate analysis was undertaken to account for missing data. A detailed breakdown of costs was presented in the paper including sources of data, price year and statistical analysis. A limitation of the paper, which was clearly acknowledged by the authors, was the considerable variation depending on the method used for assigning costs.

Cost and benefits were appropriately analysed using an ICER. These were clearly presented. Uncertainty was addressed by calculating CIs; however, these were extremely wide. The authors did caution about the limitation of this study owing to the particular characteristics of the Dutch health-care system, citing a high rate of surgery, quicker waiting times and legislation which protects employees resulting in higher absenteeism, but not necessarily lower productivity.

Other limitations acknowledged were the 1-year time horizon for the study; a longer time horizon would have reduced statistical power and the clinical evaluation showed no differences after year 1. Another limitation was that patients were inevitably aware of the randomised group they were in; their reported utilities and costs may have been influenced by their preference for treatment. A final limitation identified was that 40% of patients randomised to receive prolonged conservative care underwent disc surgery at some time, although this was similar to other reported studies. The authors stated that this was an expected clinical consequence, as the study compared two different management strategies and that persistent or increasing symptoms that caused some patients to cross over should be part of the economic evaluation.

Tosteson *et al.*

Tosteson *et al.*[282] reported a cost-effectiveness analysis based on data derived from the pooled analysis of the SPORT randomised and observational cohorts, based in the USA. The interventions compared were standard open laminectomy, laminectomy with removal of herniation and examination of the involved nerve root, and non-operative treatment, defined as usual care chosen individually by patients and physicians. Participants were aged ≥ 18 years, diagnosed with herniated intervertebral disc and confirmed as surgical candidates with a symptom history of at least 6 weeks.

Source of effectiveness data

Cost-effectiveness analysis was based on data from 1191 participants, including 775 who underwent surgery and 416 who were treated non-operatively for the entire follow-up period of 2 years. Clinical effectiveness was evaluated using QALYs at baseline, 6 weeks and 3, 6, 12 and 24 months. Health-utility values were obtained using the EQ-5D with US scoring. Time-weighted sums of EQ-5D values, adjusted to the overall mean baseline health-state value, provided the estimate of QALYs for each treatment group. CEA was based on the perspective of the health insurer and society.

At baseline, differences in patient demographic and clinical status were noted. Surgical patients were significantly younger, more likely to work full-time and to receive or be in receipt of social security compensation. Clinically, surgical patients were more likely to have L5–S1 (lumbar segment 5 to sacral segment 1) herniation, worse bodily pain, physical function, mental health and ODI and EQ-5D scores compared with non-operative patients.

Source of resource utilisation and cost data

Costs were collected on health-care costs (visits to health-care professionals, diagnostic tests, other health-care services, medications and surgery, including repeat surgery costs). Other costs included lost productivity, measured as missed work, unpaid caregiving time and missed housekeeping. Resource-use data were collected at each follow-up visit for health-care costs. A nurse-administered survey collected detail on medication usage. Recall time for self-reports of resource utilisation and time away from work/usual activities were 6 weeks for the 6-week and 3-month visits. For all other times a 1-month recall was used. Participants were provided with a diary to assist in tracking resource utilisation and missed work/housekeeping days.

Direct medical costs were estimated by multiplying patient-reported medical resource use by unit costs for each cost component. These were presented in the paper. Unit costs for office visits, hospitalisation, diagnostic test and procedures are based on 2004 Medicare national allowable payment amounts and medication prices on 2004 Red Book prices.[287] Costs were adjusted for inflation, expressed in 2004 US dollars with a 3% annual discount rate used in the analysis of costs and QALYs. The differences in surgical costs were considered in terms of the procedure performed and the cost of intraoperative complications, which determined their diagnostic-related group (DRG). This was handled in the following manner: (1) a cost approximating the value paid by non-Medicare insurers was estimated to be 70% of the mean amount billed to Medicare in 2004; and (2) the observed 2004 Medicare mean total DRG price was used to reflect hospital-related surgery costs population aged > 65 years. Surgeons' costs were based on 2004 Medicare amounts; anaesthesiology costs were estimated using operative time with a fixed amount added if an intraoperative complications occurred. For non-spine-related hospitalisations, costs were based on the DRG and priced using mean observed Medicare prices in 2004 for each admission.

Loss of productivity costs due to spine-related problems were calculated by recording missed days of work (for those employed) and missed homemaking days. Use of unpaid caregivers (including spousal care given) were obtained and costs were estimated using the standard human capital approach; for work days lost this was estimated by multiplying change in hours worked by the gross of tax wage rate on self-reported wages at study entry. For homemaking and caregiving these were valued using the average wage plus non-health benefits for individuals aged ≤ 35 years.

Summary of cost-effectiveness

Owing to the high rates of non-adherence in the original randomised and observational cohorts, the two cohorts were combined and analysed according to treatment received using regression modelling of longitudinal data via generalised estimating equations. Separate models were fitted for EQ-5D and 30-day cost rates; measured at 6 weeks and 3, 6, 12 and 24 months. Cost rates were based on reported utilisation rates at each time period taking into account the recall period used.

Outcomes were assigned to the surgical group with follow-up times measured from the surgery date. To take into account the windows for scheduled visits and crossover, the actual time of the outcome assessment varied. This was included as adjusting variables in the longitudinal variables. To adjust for potential confounding baselines, variables associated with missing data or treatment received were included as covariates.

Based on the adjusted mean differences in EQ-5D from the longitudinal regression, an AUC/time-weighted average was undertaken to estimate QALY differences between surgical and non-operative costs, adjusted to a common baseline value. ICER CIs were estimated using bootstrapping methods. Sensitivity analyses were undertaken to consider the impact of limiting costs included in the analysis to direct medical cost or direct medical costs plus costs of work loss for those employed.

Summary of the findings

Mean health scores improved over time for both groups of patients. Total mean discounted QALYs were 1.64 (95% CI 1.62 to 1.67) for surgical patients and 1.44 (95% CI 1.40 to 1.47) for non-operative patients, a difference of 0.21 (95% CI 0.16 to 0.25).

Ninety-six per cent of surgical procedures were back and neck without complications (DRG 500) with a mean cost of $12,754 (95% CI $12,740 to $12,760). Three per cent had complications (DRG 499) with mean costs estimated at $19,063 (95% CI $18,960 to $19,160). Repeat surgery occurred in 6.8% of surgical patients with a mean cost of $28,019 (95% CI $19,950 to $26,730).* Total mean costs were $27,273 (95% CI $26,009 to $28,644) for surgical patients and $13,135 (95% CI $11,244 to $14,902) for non-operative patients. Total direct costs were $20,237 (95% CI $19,314 to $21,160) for surgery and $5804 (95% CI $4639 to $6969) for non-operative patients. Total loss of productivity costs were $7089 (95% CI $6155 to $8022) for surgical patients and $7399 (95% CI $6221 to $8577) for non-operative costs. Over the 2-year period, indirect costs contented for 26% of costs for surgical patients and 57% of non-operative patients. The distribution of non-surgical direct costs was similar across both groups. Both types of cost were highest following the first 6 weeks among those undergoing surgery. Mean indirect costs for non-operative patients were higher over time than for surgically treated patients.

When all costs were considered, the cost per QALY gained for surgical treatment relative to non-operative care in the general population was $69,403 (95% CI $4923 to $94,999). For those aged ≥ 65 years, the cost per QALY gained decreased to $34,355 (95% CI $20,419 to $25,512).* Limiting costs to direct costs alone for general population ($72,181, 95% CI $56,473 to $92,394) and Medicare ($37,285, 95% CI $28,364 to $48,993) or direct costs with lost work days (general population $77,300, 95% CI $60,009 to $99,544) or Medicare ($42,111, 95% CI $30,976 to $56,284) had little change. This also had little impact on the ICER, which was estimated at $33,176 (95% CI $18,348 to $54,157) under Medicare pricing.

The authors concluded that surgery for intervertabral disc herniation was moderately cost-effective over 2 years, but expressed caution about the different values for surgery according to the method used for assigning surgical costs.

*There was obviously an error in the published paper for the figures, but no erratum could be found; therefore, we do not know whether it is the mean estimate or the CI that is correct.

Critique of Tosteson et al.

The approach and interpretation of the data and findings in the paper appeared to be of good quality. Efforts were made by the authors to capture the different resource costs associated with different surgery, and also indirect costs. The justifications for taking into account the high non-adherence rates and the variations encountered during follow-up (e.g. missed visits, delaying surgery, timing of assessment and confounding variables) were well explained.

The rationale for the study is based upon critiquing the findings from Malter and Weinstein's study.[286] In this paper, the comparators could be better described. The type of surgical technique

was not controlled for. There is also little description of what constituted non-operative care beyond 'usual care chosen individually by patients and physicians'.

The data were derived from two cohorts of patients: randomised and observational. The demographics of the cohorts showed significant differences. Although these were considered in the analysis, there was little interpretation beyond a descriptive analysis of these differences. Possible reasons for the decision to have surgery (e.g. surgical patients were younger, less likely to be working full-time or to be receiving or have applied for compensation, and generally had worse clinical signs and symptoms) may have resulted in worse outcomes, which in turn influenced QALYs.

The authors considered resource usage. However, the limitations of using patients' self-reporting of resource use are referred to. The paper mentions the data collection approaches to obtain patient-reported data, but provides little information on how reliable or valid the data were. Recall bias is a potential concern, and the authors attempted to minimise this by limiting the recall window to 6 weeks after early visits and 1 month after annual visits. The authors expressed reasonable confidence that chronic problems were captured as they incurred ongoing costs, and that large costs including hospitalisation and repeat surgery were not limited by the recall period. However, some acute costs could have been missed and the small but important biases when reporting indirect costs may be a factor to take into account. However, it would seem likely this bias was applicable to both groups. The authors considered better ways of capturing resource costs, e.g. linking with electronic billing records, but this would have been likely to have biased cost ascertainment with near-complete capture of surgery compared with non-operative care.

Epidural steroids

Price *et al.*

Price *et al.*[173] undertook a multicentre, double-blinded RCT of ESIs versus placebo in 228 patients with clinically diagnosed unilateral sciatica aged between 18 and 70 years who had duration of symptoms between 4 weeks and 18 months. The justification for the study was that, although 45,938 ESIs were performed in the NHS in 2002–3, there was a lack of evidence of their benefit, with safety and cost-effectiveness not previously evaluated.

Source of effectiveness data

The intervention was up to three ESIs compared with normal saline. The primary outcome was the ODI with measures of pain, physical and psychological function collected alongside objective measures of sciatic root irritation, neurological deficit and procedural side effects. QoL was determined using the SF-36.

Source of resource utilisation and cost data

A pilot was undertaken to inform the data collection method. Resource-use data were collected using an instrument completed by all clinical staff which recorded their time spent on patient consultation, aiding the patient before or after the consultation, the time associated with patient administration for all patients presenting with sciatica not included in the trial, pathology tests and imaging. Data were collected across all three centres during July–October 2000. Costs of initial radiology and pathology, if not already performed by the referring centre, were included. Analgesic costs were examined and assumed not to differ between the two groups, so were not considered in the economic analysis.

Cost data were used to calculate a cost per patient for treating sciatica with epidural injections from the perspective of health provider and purchaser. An average cost per patient was based on two management practices. Under each management practice it was assumed that patients had an

initial consultation and follow-up. Owing to the short time horizon when costs and benefits were incurred, discounting was not performed.

Summary of cost-effectiveness analysis

Cost-effectiveness was undertaken from the perspective of the health provider and purchaser (NHS).

QALYS were derived from SF-6D health-utility scores using SF-36 raw data by the Brazier *et al.*[288] technique. CUA was undertaken using the standard gamble (SG) method to derive incremental cost per QALY ratios for managing a patient with an ESI. Sensitivity analysis was undertaken to explore how cost estimates changed, given the assumptions that underlay resources, resource-base costs were relaxed. Sensitivity analysis was not undertaken for purchaser costs.

Summary of the findings

The study found ESIs conferred a short-term benefit only. The resource savings could be substantial even with a modest change to treatment. For example (from the purchasers' perspective), the saving from moving from an assumed model of current pragmatic practice (maximum of three ESIs) to a patient management strategy suggested by the trial (one ESI) would represent a saving of £16,505,700 in the sector.

The estimated average cost per patient treated from the provider's perspective was £265.30 per patient for the trial protocol and £152.80 per patient assuming a management strategy based on trial costs. Using NHS recharge cost from the purchaser's perspective, the estimated average cost was £2102 per patient to deliver treatment based on the trial protocol and £992 per patient for one epidural injection, based on the trial results.

The incremental analysis is shown in *Table 166*.

To obtain an improvement at 3 weeks in one patient based on the trial protocol is £16,816–23,963 [depending on number needed to treat (NNT) assumed (8–11.4)], or one epidural to improvement in one patient at 3 weeks is £936–11,306.

In the sensitivity analysis, relaxation of the base-case assumptions of labour time, using the maximum recorded time for nurses and clinicians, more than doubled the average patient cost under each management strategy. Changing from day case to overnight stay also increased average patient costs. Assuming that QALYs remain unchanged, the effect would be to increase the cost–utility ratio further. The authors concluded that although ESIs are relatively safe, they confer only transient benefits in symptoms and self-reported function in a small group of patients

TABLE 166 Incremental analysis from Price *et al.*[173]

Perspective	Trial protocol (up to three ESIs)	Strategy based on trial results (one ESI)
Provider		
Incremental cost (£)	265.30	152.80
Incremental QALY	0.0059350	25,745.68
Cost per benefit gain (£)	44,701.11	
Purchaser		
Incremental cost (£)	2102	992
Cost per benefit gain (£)	354,171.65	167,144.76

with sciatica at substantial costs. ESIs failed the QALY threshold recommended by NICE and do not represent good value for money if NICE recommendations are followed.

Critique of Price et al.

Reporting of the economic evaluation conforms to accepted guidelines and is presented in detail. The authors recognised the limitations of the pragmatic study design and attempted to overcome this through their recruitment strategy. The intention was to compare epidural corticosteroid injections with placebo. The duration of symptoms varied from 4 weeks to 18 months, with patients who had previous back surgery excluded. There was a clear acknowledgement that the intention was to consider only patients who presented with sciatica at the point of referral to secondary care, and for the economic analysis a standard package of care was assumed. Costs associated with this package were not considered, as it was assumed that these would be incurred regardless of whether or not the patient received an epidural. Costs of health-service utilisation after week 52 were not included as no significant difference was found. There was a variability in resource usage across the three centres, reflecting the persistent limitation of a lack of clinical consensus in the management of sciatica.

The perspective taken in the economic evaluation was clearly defined and resource data appeared to have been systematically collected across the three centres. Direct costs were appropriately collected based on the perspective chosen. Indirect costs were not obtained, as it was argued that inclusion of indirect costs could overstate potential costs savings and that such savings were not relevant to resource allocation decisions. The authors clearly stated that resource data did not reflect resources expended in the trial per se, but represented the costs to normal practice.

Where differences occurred, these have been highlighted in the study. One of the most notable differences was the difference in clinicians' and nurses' time across the three centres, which probably reflected differences in practice and culture rather than marked differences in the quality of patient care. Although the justification of staff costs were made explicit, several resource costs appeared to have been generalised across several categories.

Cost–utility analysis was clearly presented. SF-6D scores were derived from the SF-36 using an established technique with SG scores calculated, assuming the trial protocol of three injections. The authors note the variability in the number in each sample, so average SG score were derived for patients with observations for all visits up to week 12 to correct for possible sample bias. One of the possible issues was the lack of sensitivity of this generic measure to detect small but important changes that may have affected the findings of limited changes in QoL. QALYs were derived and benefits were appropriately analysed using an incremental analysis.

Cost per QALY gained to the provider using a patient management strategy administering only one epidural injection. These results assumed that gain in QALY calculated would approximate that under a patient management strategy based on the trial results (one ESI). This was not considered an unreasonable assumption by the authors as change in SG score after week 3 was lower in the active group than the placebo group. However, only 21 patients received one injection to confirm this from the clinical data. Costs derived using NNT recognised the fact that ESI was compared with placebo and may therefore increase NNT and subsequent costs.

Sensitivity analysis was appropriately carried out to take into account how costs would change if base-case assumptions were relaxed. These examined changes in variation of clinical labour practices and resource use. The base-case assumption had implied that patients would be treated as day cases, so this assumption was changed. However, in practice this was felt to be too extreme, as in reality there was more likely to be a mix of day-case care and inpatient stay. In both cases,

the cost increases. Assuming that QALYs remained unchanged, the effect of this would be to increase the cost–utility ratio further.

As noted by the authors, indirect costs and return to work were not considered. This was justified in terms of the recognised difficulties in using such an outcome measure owing to its definition and collection in a population of mixed age, gender and socioeconomic groups, and that there are many risk factors associated with chronic work disability apart from the level of pain. The study clearly acknowledges that the UK NHS charges differ from the actual resource used. In addition, some strategies for sciatica can be purchased from the private sector. Although these are not true resource costs (in terms of a UK NHS perspective), these may still have an opportunity cost attached. Such costs are substantial for a short period of pain relief. The lack of an individual perspective might limit the interpretation of findings, as a small chance of short-term pain relief (1 in 8 to 1 in 11) based on NNT might be welcomed by some patients. As would be expected, these findings cannot be translated into private clinical practice.

Summary

Although some economic evaluations identified in the systematic review were of reasonable to good quality, they 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 favourable benefit such as with disc surgery, robust findings could not be reliably drawn. Although an evidence base is emerging, there remains a lack of well-designed economic evaluations. The majority of evaluations were undertaken in conjunction with clinical trials, with a lack of published decisions models. There was considerable variation with each of the studies to the management of patients with sciatica, thus limiting the lessons that can be drawn from current evidence in order to understand the relative cost-effectiveness of current management strategies that reflect current practice. Of particular note is the relevance of these studies to the UK NHS setting.

Chapter 9

Economic evaluation

Introduction

The aim of the economic evaluation was to determine the relative cost-effectiveness of the treatment regimens for managing patients with sciatica. The existing evidence relating to the cost-effectiveness of treatments had a number of limitations, which made it insufficient to inform decision-making regarding the most appropriate management strategy for patients with sciatica. The majority of evaluations were undertaken in conjunction with clinical trials with a lack of published decisions models. There was considerable variation with each of the studies to the management of patients with sciatica, thus limiting the lessons that can be drawn from current evidence in order to understand the relative cost-effectiveness of current management strategies that reflect current practice. Hence, it was necessary to construct a decision-analytic model to address a number of these issues more formally. The model provided a framework for the synthesis of data from the clinical effectiveness, economic reviews and other relevant sources. It was developed to estimate costs from the perspective of the UK NHS[289,290] and health outcomes in terms of successful treatment and utility gain for all the relevant treatment strategies.

Development of the economic model

The limitations associated with the economic evaluation studies reviewed resulted in a decision-analytic model being developed to estimate the relative cost-effectiveness of management strategies for patients with sciatica. The heterogeneous nature of the condition, the lack of recognised guidelines for the management of patients with sciatica and considerable variation within practice all made it extremely difficult to develop a model that reflected current practice. Further, the considerable levels of uncertainty surrounding the outcomes from the MTCs restricted the development of a probabilistic model and, therefore, a deterministic model structure was constructed based on information from some of the studies reviewed, the findings from the review of effectiveness and MTCs undertaken, published sources of unit costs and expert opinion from clinicians and other health-care professionals. The decision tree model, highlighted in *Figure 112*, was used to estimate the expected costs and number of successful treatments over a 12-month period. The perspective employed was that of the UK NHS and out-of-pocket expenditures on over-the-counter (OTC) medications and alternative therapies, for example, have not been included. This has important ramifications as it is assumed that ultimate treatment failures will resort to alternative therapies outside the conventional health-care system, at zero cost to the NHS.

The number of appropriate and relevant health states was informed by the results of the service provider survey (see *Chapter 10, Summary of economic evaluation*), the literature review and from advice within the research team. The cost of managing patients within each state was reflected in the model, although it was not envisaged that patient progression will be seamless, or indeed linear and uni-directional. The structure of the model will reflect this and the probability of movement between health states will be based on the evidence from the literature review, including the distribution around the point estimates. In addition, a sensitivity analysis was

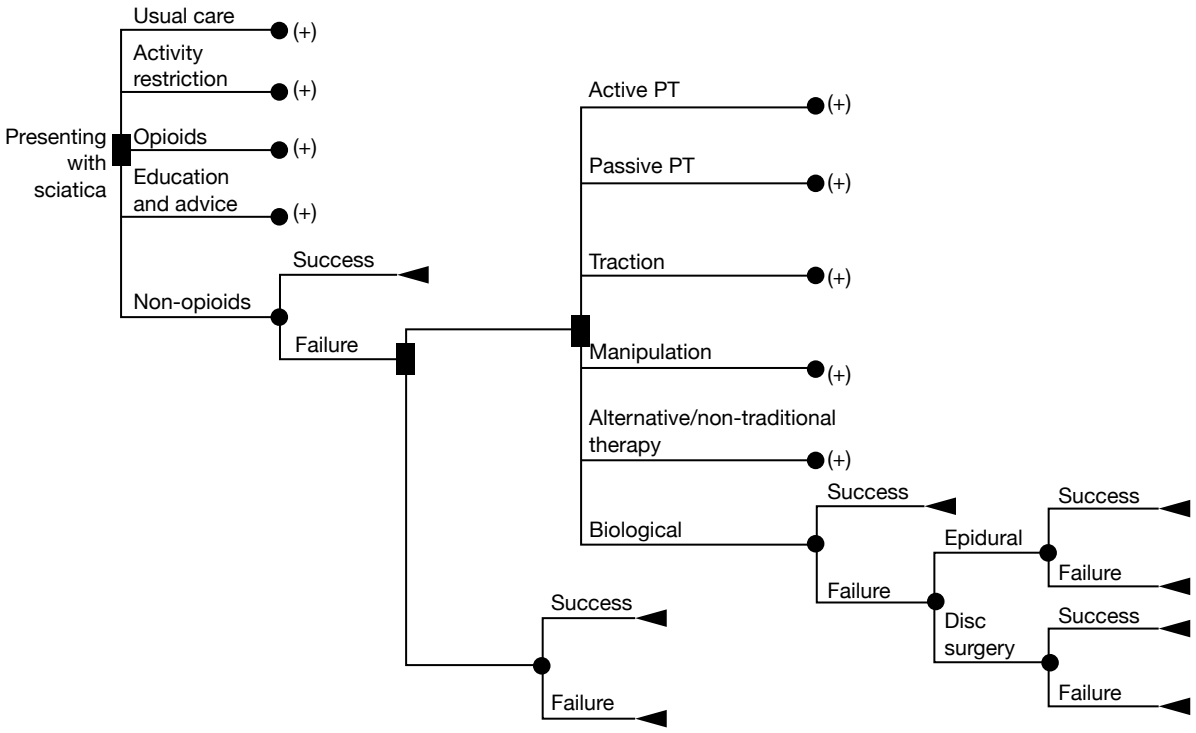

FIGURE 112 Decision tree.

used to assess the impact of 'changes' in the variable estimates, and identify potential areas for future research.

Telephone survey of service providers

A panel of service providers known to the advisory group members were contacted by telephone to determine their usual clinical practice, the usual treatment pathways and whether or not they use a stepped-care approach. This information was used to inform which sequence of treatments to include in the economic model.

Recruitment and access for the telephone survey was undertaken between June 2009 and September 2009. Three local health boards in Wales and six primary care trusts and hospital trusts in England were contacted. As required under the Research Governance Frameworks for England and Wales, permission was sought from each relevant research and development department prior to seeking and recruiting a range of service providers (e.g. spinal surgeons, physiotherapists, service commissioners). The response rate was poor from England, with only three contacts established, predominantly because of difficulty in locating the suitable person with research governance responsibility (e.g. web-based contacts out of date, lack of clarity of specific research governance procedures in primary care trusts). Of these three, two primary care trusts request evidence of NHS Ethical Committee review, despite confirmation from Cardiff University Research Governance Officer that this was deemed audit/service evaluation.

Preliminary informal interviews were conducted with four service providers. However, these generated wide disparities in services (e.g. whether or not an intermediate care service was provided) and interventions offered (e.g. biologicals were not licensed for use and so would not

be considered), resulting in difficulty in using individual service providers to contextualise a generic 'sequence of treatments' in relation to the findings emerging from the systematic review for the purposes of developing the structure for the economic model base case. On review of these difficulties, the economic team felt that the provider survey would be better placed once the MTC analysis was completed in order to 'validate' the interventions/care approaches drawn from the review findings. However, owing to time constraints, these initial interviews were used along with input from the steering group (clinicians on the review team) to build up a staged treatment approach through the assumption of patient progression through primary, intermediate and specialist care.

Previously conducted systematic reviews were used to generate a list of potential treatments for sciatica. During the telephone interviews, clinicians were asked initially what treatments (including combination and sequence of treatments) they usually use, and, afterwards, if prominent treatments identified from previous reviews were not mentioned, they were asked if they have ever considered using these.

Model description

The model 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 use of analgesics and other medications if considered appropriate, to attempt to secure symptom resolution. The treatments included within this pathway therefore include:

- usual care
- education/advice
- activity restriction
- non-opioids
- opioids.

The second pathway would involve a stepped 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 treatments here include:

- manipulation
- traction
- passive PT
- active PT
- alternative treatments
- biological agents

followed by more invasive treatment (epidural followed by disc surgery if there was no symptom resolution).

The third pathway would involve immediate referral for surgery to alleviate symptoms.

There does not appear to be any data to determine the proportion of patients managed through each pathway and therefore the treatment pathways represent the decision choices available

for GPs and their patients on presentation. Each of the pathways and the treatment variations available within them were compared with 'inactive control', which, according to the findings from the MTC, had a non-zero probability of symptom resolution, but was assumed to cost £0 in the baseline model.

The decision tree model comprised the three treatment pathways: initial treatments, initial treatments followed by intermediate treatments and invasive treatments, and initial treatments followed by disc surgery. The treatment options available within each of the pathways are shown in *Table 167*.

The focus was on the binary outcomes used in the global effect measure from the MTC, representing successful or unsuccessful symptom resolution and with results expressed as incremental cost per patient with symptoms successfully resolved. Analysis also included utility gain associated with symptom resolution, with results expressed as incremental cost per utility gain (over a 12-month period). The heterogeneity of duration effect and not evidence of relapse and recurrence, made it difficult to extend the analysis beyond this time period, with the assumption made that the utility gained following successful treatment would continue for this period.

Dealing with uncertainty

A series of one-way sensitivity analyses were used to address uncertainty in the model. The baseline estimates were based around the best-case scenarios identified for cost and then adjusted to reflect what was regarded as worst-case scenarios. Similarly, the probabilities of success were those determined from the WinBUGS output from the MTC in the baseline model and then adjusted to assess the impact on baseline findings. The utility values for symptoms and symptom remission were also adjusted to determine impact on baseline findings.

TABLE 167 Treatments available within pathways

Pathways	Treatments
Initial treatments	Inactive control
	Usual care
	Education/advice
	Activity restriction
	Alternative/non-traditional
	Non-opioids
	Opioids
	Biological agents
	Intraoperative interventions
	Spinal cord stimulation
Intermediate treatments	Manipulation
	Traction
	Passive PT
	Active PT
Surgery	Epidural/nerve block
	Disc surgery

Data sources

The probabilities of success for each treatment were derived from the WinBUGS output from the MTC. The WinBUGS output provides a summary output of the posterior distributions of the relevant parameters. The probability of success is the median value of the posterior distribution of the global effect measure.

The probabilities of success are shown in *Table 168*.

The costs associated with managing patients with sciatica were based on clinical opinion and derived from published cost sources (and based on 2008–9 prices), as shown in *Table 169*.

Drug treatments were costed according to *British National Formulary* (BNF)[292] list prices at the time and calculated based on the dosage and durations in line with documented indications for use. Where required, it was assumed that dosage was based on an adult male of 65 kg. It was also assumed that paracetamol and ibuprofen were OTC medication, NSAIDs and opioids would be prescribed as slow-release tablets. Where multiple products were available, the least expense option was assumed.

It was assumed that each prescription required a GP consultation and that analgesics would be prescribed in accordance with the WHO analgesic ladder; therefore, a stepped approach would be taken to analgesia prescription and consultations would be separate. For non-opioid analgesia, two GP consultations were assumed with three consultations for opioid analgesia. Unit costs of GP consultations were taken from Curtis.[291] The base-case analysis assumed that analgesics were prescribed separately. NSAIDs and opioids were costed based on single treatment for base-case analysis and multiple analgesics in the sensitivity analysis.

Intermediate care interventions reflected treatments provided in secondary care outpatient settings and included non-traditional and alternative therapies. Unit costs were taken from published *NHS reference costs 2008–2009*.[293] It was assumed that an initial consultant

TABLE 168 Probabilities of success

Pathways	Treatments	Probability of success	Probability of failure
Inactive control		0.3828	0.6172
Initial treatments	Usual care	0.3393	0.6607
	Education/advice	0.5025	0.4975
	Activity restriction	0.4411	0.5589
	Non-opioids	0.6129	0.3871
	Opioids	0.4985	0.5015
Intermediate treatments	Alternative/non-traditional treatments	0.8523	0.1477
	Biological agents	0.9074	0.0926
	Manipulation	0.7518	0.2482
	Traction	0.4277	0.5723
	Passive PT	0.4147	0.5853
	Active PT	0.4043	0.5957
Invasive therapies	Epidural/nerve block	0.6577	0.3423
	Disc surgery	0.6330	0.3670
	Intraoperative interventions	0.7454	0.2546
	Spinal cord stimulation	0.6643	0.3357

TABLE 169 Derivation of costs

Description	Unit cost (£)	Cost (£)	Source of data
Primary care			
GP consultation for all patients (within 6 weeks)	35	Average two consultations (varies between one and three) £70	Curtis, 2009[291]
GP consultation for patients referred to intermediate care/surgery (± 6 weeks)	35	Referral usually triggered after three consultation £105	Curtis, 2009[291]
GP contact following discharge from intermediate care/surgery	35	Typically one follow-up to GP for post-operative analgesia/sick note	Curtis, 2009[291]
Other primary HP contact (surgery patients only)	10	Typically one intervention to remove suture by practice nurse	Curtis, 2009[291]

Drugs	Description	Dose	Cost (£)	Continuing therapy	Source of data
Prescriptions					
Paracetamol and/or ibuprofen	Likely to be OTC and patient self-management for all patients, but GP would start as initial/continuing therapy in first 6 weeks	Paracetamol: dosage 4 g per 24 hours at 6 week prescription = approximately 336 tablets	£3.57 (based on 16 tablets = £0.17)	1 week cost £0.60	BNF No. 59[292]
		Ibuprofen: dosage 1600 mg per 24 hours at 6 week prescription = approximately 168 tables (if 400 mg tablets)	£3.74 (based on 84 400 mg tablets = £1.87)	1 week cost £0.62	
Mild opioids (codeine phosphate)	Prescribed if initial analgesia is not working	240 mg per 24 hours at 6 weeks = 168 tablets (if 60 mg tablets)	6-week prescription = £11.88 (28 60 mg tablets = £1.98)	£1.98	BNF No. 59[292]
		If added in at second visit – 4 weeks prescription	4 weeks = £7.92		
Other NSAIDs (naproxen)	Prescribed if initial analgesia is not working and/or with mild opioid	1250 mg per 24 hours at 6 weeks = 210 tablets	6 weeks = £10.65 (based on 250 mg 28 tablets)	£1.78	BNF No. 59[292]
		4 weeks = 140 tablets	4 weeks = £7.10		
Strong opioids (morphine) – considered only after no success with mild opioids/combinations with NSAIDs	Often in combination with co-analgesic amitriptyline or gabapentin		£9.61 (MST 30 mg day) for 2 weeks	£4.81	BNF No. 59[292]
			£1.04 (25 mg per day) for 2 weeks	£0.52	
			£7.88 for 2 weeks (based on titrating dose from 900 mg towards maximum dose)	£5.52 (based on maximum dose of 3.6 g as maintenance)	
Diazepam	For muscle spasm	6 mg per 24 hours but p.r.n.		£1.96	BNF No. 59[292]

assessment would be undertaken with one follow-up, with routine pathology and haematology blood tests and magnetic resonance imaging (MRI) (one area post contrast) performed for diagnosis. Passive and physical active therapies, manipulation and traction were assumed to be a physiotherapist-administered interventions. Biological therapies are unlicensed for use in patients with sciatica in the NHS. Therefore, we assumed a similar dosage and duration in line with documented indications for other spinal conditions such as ankylosing spondylitis. For, the

TABLE 169 Derivation of costs *(continued)*

Intervention	Description	Cost (£)	Source of data
Intermediate care			
Initial consultation	First attendance consultant led (110N)	124 (94–147) – skill mix can vary	*NHS reference costs 2008–2009*[293]
	First physiotherapy contact (650A)	55 (53–53)	*NHS reference costs 2008–2009*[293]
MRI	RA027b– one area post contrast	195 (142–239)	*NHS reference costs 2008–2009*[293]
Pathology	Haematology	3 (2–4)	*NHS reference costs 2008–2009*[293]
	Biochemistry	1 (1–2)	
Follow-up	Consultant led (110N)	86 (64–99)	*NHS reference costs 2008–2009*[293]
	Follow-up physiotherapy	19 (19–19)	*NHS reference costs 2008–2009*[293]
Biological therapies	Unlicensed for use in patients with sciatica in the NHS. Therefore, assumed similar dosage and duration in line with documented indications for other spinal conditions such as ankylosing spondylitis		BNF No. 59;[292] *NHS reference costs 2008–2009*[293]
	For adalimumab, it was assumed to be a 12-week course with subcutaneous injection by a practice nurse	1647	
	For influximab (worst case), it was assumed to be an i.v. administration in an outpatient setting with prophylactic antihistamine	2219	
Epidural steroids	Outpatient Intermediate pain procedure (ABO5Z)	190 (125–205) – up to 3	*NHS reference costs 2008–2009*[293]
Procedure		**Cost (£)**	**Source of data**
Surgery			
Day-case extradural spinal minor (1) without CC (HCO6c)		980 (570–954)	*NHS reference costs 2008–2009*[293]
Inpatient extradural spinal minor (1) without CC (HCO6c), average stay 1.9 days		1657 (1956–2314)	*NHS reference costs 2008–2009*[293]
Inpatient extradural spinal minor (2) without CC (HCO6c), average stay 3.33 days		2858 (1699–3184)	*NHS reference costs 2008–2009*[293]
Follow-up consultant-led appointment		86 (64–99)	*NHS reference costs 2008–2009*[293]

BNF, *British National Formulary*; CC, complications and comorbidities; HP, health professional; i.v., intravenous; MST, modified release 12 hourly preparation (morphine salt); p.r.n., as needed.

base-case analysis, it was assumed that a 12-week course of adalimumab would be prescribed for subcutaneous injection by a practice nurse. The sensitivity analysis assumed an intravenous (i.v.) administration of infliximab in an outpatient setting with prophylactic antihistamine.

Intraoperative interventions are extra interventions during disc surgery (e.g. introduction of steroid around exposed nerve root, fat graft covering nerve root, exposed nerve root covered with a gel or membrane to reduce fibrosis, etc.) and are not routinely carried out in the UK NHS and have therefore been excluded. Spinal cord stimulation involves implantation of an electrode and is used only if disc surgery has failed and has therefore also been excluded from the model.

Epidural steroids were assumed to be a consultant outpatient intervention, with one treatment being used in the base-case and three treatments in the sensitivity analysis. Surgical unit costs

were taken from *NHS reference costs 2008–2009*.[293] It was assumed that an initial consultant assessment would be undertaken with one follow-up, with routine pathology and haematology blood tests and MRI (one area post contrast) performed for diagnosis. A follow-up consultant appointment was assumed with one GP follow-up and practice nurse intervention for removal of sutures. Surgery was costed on inpatient extradural spinal minor, (1) with an average length of stay of 1.9 days for base-case and inpatient extradural spinal minor and (2) with an average length of stay of 3.33 days for sensitivity analysis.

The resultant costs are shown in *Table 170*.

The utility values used in the model for symptoms and symptom resolution were derived from the review of studies. However, the lack of specific utility values for sciatica symptoms pre-intervention and following symptom resolution was problematic. The baseline values were derived from those in van den Hout *et al.*,[283] where the utility value at point of randomisation was 0.37 and the best value obtained was 0.83. The values were adjusted within the sensitivity analysis to compensate for the lack of consensus within the literature.

Cost-effectiveness results

The purpose of the cost-effectiveness assessment was to determine whether or not the additional costs required to increase likelihood of success, over and above usual care, can be regarded as representing value for money. The comparator chosen for this analysis was that of 'inactive control', which counterintuitively is more effective than usual care. Similarly, ultimate failures were assumed to have zero cost to NHS, although the extent to which this is reflected in practice is subject to some debate.

TABLE 170 Cost summary

Treatments	Base case (£)	Sensitivity analysis (£)
Initial treatments		
Inactive control	0.00	0.00
Usual care	73.74	80.68
Education/advice	81.00	81.00
Activity restriction	70.00	70.00
Alternative/non-traditional	70.00	70.00
Chemonucleolysis	Not included	Not included
Non-opioids	122.23	129.33
Opioids	130.26	152.71
Biological agents	1646.74	3467.24
Intraoperative interventions (not routine)	1462.74	2218.71
Spinal cord stimulation	1462.74	2218.71
Intermediate treatments		
Manipulation	349.00	578.00
Traction	349.00	578.00
Passive PT	349.00	578.00
Active PT	349.00	578.00
Surgery		
Epidural/nerve block	602.76	990.28
Disc surgery	1433.66	3794.71

A series of 100 + independent scenarios were considered in which each initial treatment was considered in relation to inactive control; combined with each intermediate treatment followed by epidural/nerve block and then disc surgery; or following an initial treatment, patients were immediately referred for disc surgery. The number of successful outcomes of each treatment regime was combined with the utility of success (0.83) and failure (0.37) to give a total utility measure for each treatment regime. It was assumed that there was no reduction in utility for previous unsuccessful interventions, so a successful outcome was deemed to have utility 0.83 in baseline, regardless of how many interventions were required to achieve success.

The model demonstrated that none of the treatment regimes resulted in 100% success. In terms of initial treatments to alleviate symptoms and wait for symptom resolution, the most successful regime in the first treatment pathway was non-opioids, with a probability of success of 0.613, with treatment being unsuccessful in 39 of every 100 patients treated. When the second treatment pathway was considered, the most successful strategy was non-opioids, followed by biological agents, followed by epidural/nerve block and disc surgery, with a probability of success of 0.996, that is treatment was unsuccessful in three out of every 1000 patients treated.

A conventional approach to examining the cost-effectiveness of the treatment regimes was employed. Firstly, it was determined whether or not any of the regimes was dominated by others with both lower costs and greater probability of success and, secondly, whether or not any of the treatments were subject to extended dominance, with a more expensive treatment regime strategy having a lower ICE than the less expensive regime. This process generated the 'efficiency frontier' of increasingly more costly and more effective regimes for the management of patients with sciatica.

Table 171 highlights the mean cost, probability of success and 12-month utility gain for all possible treatment strategies.

The majority of treatment strategies were excluded on the grounds of strict dominance (the next regime was both more effective and less costly) or extended dominance (a regime has an ICER that is higher than the next more effective regime). The regimes that represent the efficiency frontier are those based on non-opioids and are highlighted in *Table 172*.

In terms of net benefit, four of the five strategies would be regarded as cost-effective if the ceiling ratio for an additional unit of utility gain over a 12-month period was < £5100, and if the ceiling ratio for each additional success was < £2500.

Sensitivity analysis

The use of the highest cost estimates results in a similar overall picture and, although the cost per QALY estimates are higher, the stepped approaches based on non-opioids remain the most cost-effective strategies, as shown in *Table 173*.

When the highest cost scenarios are employed, four of the five strategies are cost-effective if the ceiling ratio for an additional success is < £6000 and < £13,100 for an additional unit of utility gain.

In order for the third pathway – immediate referral for surgery – to feature on the efficiency frontier, the costs associated with the treatment regimen following initial treatment with non-opioids, would have to fall by 49% or the likelihood of success would have to increase by 10 percentage points to 0.95.

TABLE 171 Mean cost, probability of success and utility gain (1000 patients)

Treatments	Mean cost (£)	No. of successes	Utility gain
Inactive control	0	383	176
Usual care	73,740	383	156
Usual care and active PT	304,324	606	279
Usual care and passive PT	304,324	613	282
Usual care and traction	304,324	622	286
Usual care and manipulation	304,324	836	385
Usual care and alternative/non-traditional treatments	304,324	902	415
Usual care and biological agents	1,161,741	939	432
Usual care and active PT and epidural	541,558	865	398
Usual care and passive PT and epidural	537,416	868	399
Usual care and traction and epidural	532,239	871	400
Usual care and manipulation and epidural	403,168	944	434
Usual care and alternative/non-traditional treatments and epidural	363,145	967	445
Usual care and biological agents and epidural	1,198,618	979	450
Usual care and active PT and epidural and disc surgery	738,621	951	437
Usual care and passive PT and epidural and disc surgery	731,039	951	438
Usual care and traction and epidural and surgery	721,562	952	438
Usual care and manipulation and epidural and surgery	485,275	979	451
Usual care and alternative/non-traditional treatments and epidural and surgery	412,005	988	454
Usual care and biological agents and epidural and surgery	1,229,251	992	456
Usual care and disc surgery	1,040,172	758	348
Activity restriction	70,000	441	203
Activity restriction and active PT	265,056	667	307
Activity restriction and passive PT	265,056	673	310
Activity restriction and traction	265,056	680	313
Activity restriction and manipulation	265,056	861	396
Activity restriction and alternative/non-traditional treatments	265,056	917	422
Activity restriction and biological agents	990,363	948	436
Activity restriction and active PT and epidural	465,737	886	408
Activity restriction and passive PT and epidural	462,233	888	408
Activity restriction and traction and epidural	457,854	891	410
Activity restriction and manipulation and epidural	348,670	953	438
Activity restriction and alternative/non-traditional treatments and epidural	314,814	972	447
Activity restriction and biological agents and epidural	1,021,558	982	452
Activity restriction and active PT and epidural and disc surgery	632,437	958	441
Activity restriction and passive PT and epidural and disc surgery	626,023	959	441
Activity restriction and traction and epidural and surgery	618,006	960	442
Activity restriction and manipulation and epidural and surgery	418,126	983	452
Activity restriction and alternative/non-traditional treatments and epidural and surgery	356,146	990	455
Activity restriction and biological agents and epidural and surgery	1,047,471	993	457
Activity restriction and disc surgery	887,525	795	366
Opioids	130,260	499	229
Opioids and active PT	305,284	701	323
Opioids and passive PT	305,284	706	325
Opioids and traction	305,284	713	328
Opioids and manipulation	305,284	876	403
Opioids and alternative/non-traditional treatments	305,284	926	426
Opioids and biological agents	956,100	954	439

TABLE 171 Mean cost, probability of success and utility gain (1000 patients) *(continued)*

Treatments	Mean cost (£)	No. of successes	Utility gain
Opioids and active PT and epidural	485,354	898	413
Opioids and passive PT and epidural	482,210	900	414
Opioids and traction and epidural	478,281	902	415
Opioids and manipulation and epidural	380,310	957	440
Opioids and alternative/non-traditional treatments and epidural	349,931	975	448
Opioids and biological agents and epidural	984,092	984	453
Opioids and active PT and epidural and disc surgery	634,934	962	443
Opioids and passive PT and epidural and disc surgery	629,179	963	443
Opioids and traction and epidural and surgery	621,985	964	443
Opioids and manipulation and epidural and surgery	442,633	984	453
Opioids and alternative/non-traditional treatments and epidural and surgery	387,018	991	456
Opioids and biological agents and epidural and surgery	1,007,343	994	457
Opioids and disc surgery	863,824	816	375
Education and advice	81,000	503	231
Education and advice and active PT	254,628	704	324
Education and advice and passive PT	254,628	709	326
Education and advice and traction	254,628	715	329
Education and advice and manipulation	254,628	877	403
Education and advice and alternative/non-traditional treatments	254,628	927	426
Education and advice and biological agents	900,253	954	439
Education and advice and active PT and epidural	433,262	899	413
Education and advice and passive PT and epidural	430,143	900	414
Education and advice and traction and epidural	426,245	903	415
Education and advice and manipulation and epidural	329,056	958	441
Education and advice and alternative/non-traditional treatments and epidural	298,919	975	448
Education and advice and biological agents and epidural	928,021	984	453
Education and advice and active PT and epidural and disc surgery	581,649	963	443
Education and advice and passive PT and epidural and disc surgery	575,939	963	443
Education and advice and traction and epidural and surgery	568,803	964	444
Education and advice and manipulation and epidural and surgery	390,882	984	453
Education and advice and alternative/non-traditional treatments and epidural and surgery	335,710	991	456
Education and advice and biological agents and epidural and surgery	951,088	994	457
Education and advice and disc surgery	808,713	817	376
Non-opioids	122,230	613	282
Non-opioids and active PT	257,328	769	354
Non-opioids and passive PT	257,328	773	356
Non-opioids and traction	257,328	778	358
Non-opioids and manipulation	257,328	904	416
Non-opioids and alternative/non-traditional treatments	257,328	943	434
Non-opioids and biological agents	759,683	964	444
Non-opioids and active PT and epidural	396,322	921	424
Non-opioids and passive PT and epidural	393,895	922	424
Non-opioids and traction and epidural	390,862	924	425
Non-opioids and manipulation and epidural	315,240	967	445
Non-opioids and alternative/non-traditional treatments and epidural	291,791	980	451
Non-opioids and biological agents and epidural	781,289	988	454
Non-opioids and active PT and epidural and disc surgery	594,629	915	421

continued

TABLE 171 Mean cost, probability of success and utility gain (1000 patients) *(continued)*

Treatments	Mean cost (£)	No. of successes	Utility gain
Non-opioids and passive PT and epidural and disc surgery	588,740	917	422
Non-opioids and traction and epidural and surgery	581,379	919	423
Non-opioids and manipulation and epidural and surgery	397,865	965	444
Non-opioids and alternative/non-traditional treatments and epidural and surgery	340,960	979	450
Non-opioids and biological agents and epidural and surgery	812,116	987	454
Non-opioids and disc surgery	688,457	858	395

TABLE 172 Cost-effectiveness acceptability efficiency frontier

Treatment	Cost (£)	Probability of success	Utility gain	Incremental cost (£)	Incremental success	ICER	Incremental utility gain	ICER
Inactive control	0	383	176					
Non-opioids and alternative/non-traditional treatments	257,328	943	434	257,328	560	459	258	999
Non-opioids, alternative/non-traditional treatments and epidural	291,791	980	451	34,463	38	916	17	1992
Non-opioids, alternative/non-traditional treatments, epidural and disc surgery	320,418	993	457	28,627	12	2311	6	5023
Non-opioids, biological therapies, epidural and disc surgery	799,237	995	458	478,819	3	178,700	1.23	388,478

TABLE 173 Switching treatments using highest cost scenarios

Treatment	Cost (£)	Utility gain	Success	Incremental cost (£)	Incremental success	ICER	Incremental utility	ICER
Inactive control	0	176	383					
Non-opioids	129,330	282	613	129,330	230	562	106	1222
Non-opioids and alternative/non-traditional treatments	353,074	434	943	223,744	330	678	152	1474
Non-opioids and alternative/non-traditional treatments and epidural	409,693	451	980	56,619	38	1506	17	3273
Non-opioids and alternative/non-traditional treatments and epidural and surgery	483,959	457	993	74,266	12	5995	6	13,032
Non-opioids and biological agents and epidural and surgery	1,553,556	458	995	1,069,598	3	399,184	1	867,791

Adjusting utility values and probability of success had limited effect on baseline findings, and would need to be increased outside the bounds of probability to affect the basic premise that stepped approaches are more cost-effective than direct referral for surgery following initial treatments (as the differential in effectiveness for disc surgery is not sufficient to offset the differential in cost from conducting the procedure).

Discussion

The economic model has demonstrated that stepped approaches based on initial treatment with non-opioids represent the most cost-effective regimens for the treatment of sciatica. The treatment regimes that constituted the efficiency frontier 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). Further, the extent of potential net benefit from these treatment strategies would have relatively minor impact on NHS budgets and, when a broader societal perspective is employed, the extent of such net benefits is likely to be considerably more.

The extent to which changes in parameter estimates affect baseline findings is small, with improbable reductions in cost and improvements in success rates required to suggest that direct referral to disc surgery represents a cost-effective approach to managing patients with sciatica.

However, there are a number of limitations associated with the analysis. Firstly, the nature of the evidence has meant that the time perspective is limited to an assumed 12-month duration, with no evidence available to inform the inclusion of relapse and recurrence within the model. The perspective of the NHS does not enable issues relating to work and productivity and the preferences of patients for symptom resolution and treatment duration. Further work is needed to establish patient preferences relating to time taken to achieve success and the implications of failure after a series of treatments.

Secondly, the assumption regarding ultimate failure having a zero cost to the NHS is contentious, but again lack of data and consensus has meant that it has not been possible to provide a counterview. It is highly likely that patients will resort to alternative therapies, but outside the conventional health-care system.

Thirdly, it is acknowledged that the nature of the specified model is simplistic and fails to account fully for structural and parameter uncertainty and distributions. Further work is required to consider the implications of different modelling approaches in determining the relative cost-effectiveness of treatment regimens relating to managing patients with sciatica. However, the extent to which the findings from this study are likely to change would require a dramatic change in the evidence base surrounding the range of treatments available for use within patients. The choice of the global effect as the indicator of success can also be viewed as a limitation, although it again would probably not have changed the nature of the findings significantly.

Conclusion

The stepped approaches to managing sciatica based on an initial treatment with non-opioids, represent the most cost-effective regimens relative to direct referral to disc surgery, with positive net benefits emerging if the acceptable ceiling ratio for an additional unit of success was < £2500 with base-case costs and < £6000 if higher costs were applied to the model. The strategy of referring patients who fail initial treatments directly to disc surgery is unlikely to be cost-effective, with highly improbable reductions in cost and/or rates of success being required

to elevate these regimens to the efficiency frontier. However, these findings remain tentative, and more research is required to develop the evidence base to inform more structurally appropriate economic models and to determine patient preferences regarding treatment durations and extent of invasive treatments that would be acceptable.

Chapter 10

Discussion

Summary of clinical effectiveness review

Description of studies

The number of studies evaluating each treatment category ranged from two (manipulation and education/advice) to 62 (disc surgery), with median sample sizes ranging from 55 (opioids) to 217 (education/advice). The proportion of studies that were RCTs also varied between treatment categories, with the lowest being for disc surgery (51%), anti-inflammatory biological agents (50%) and chemonucleolysis (47%).

In practice, the term sciatica is used by some clinicians for any leg pain referred from the back, whereas others prefer to restrict its use to pain originating from lumbar nerve root irritation, usually associated with disc herniation/prolapse. Most studies included patients with nerve root pain; although some included patients with referred pain, only one study of exercise therapy specifically included such patients. The presence of disc herniation was confirmed by imaging in a greater proportion of studies evaluating invasive treatments such as disc surgery (86%), epidural injections (62%) and chemonucleolysis (86%) than in studies evaluating less invasive interventions such as non-opioids (41%), traction (30%), alternative therapies (0%), exercise therapy (50%), activity restriction (20%) and education/advice (50%). The severity of herniation also varied slightly for disc surgery studies, with the proportion of studies that specifically included some patients with sequestered or extruded disc being higher (16%) than for other intervention categories. However, 17% of exercise therapy studies also included patients with sequestered or extruded discs, but the proportion of exercise therapy studies and other intervention categories will have been influenced by the small number of included studies (chemonucleolysis was 3% and all others 0%). The proportion of studies that limited inclusion to patients with acute sciatica (with the duration of symptoms being < 3 months) was much lower for invasive interventions such as surgery (6%), epidurals (7%) and chemonucleolysis (0%) than for less invasive interventions such as education (100%), activity restriction (80%), traction (50%) and exercise therapy (50%); surprisingly, this information was not reported for many studies. Five treatment categories included a small number of studies that restricted inclusion to patients experiencing their first episode (disc surgery 10%, epidural injections 3%, chemonucleolysis 8%, non-opioids 5% and biological agents 25%). The proportion of studies that included patients who had received previous treatment was higher for studies of invasive treatments such as disc surgery (65%), epidural injections (45%) and chemonucleolysis (83%) than for studies of less invasive interventions such as manipulation (0%), exercise therapy (0%) and traction (30%). However, the portion was also fairly high for opioids (67%) and activity restriction (40%) and low for biological agents (25%).

Summary of the findings comparing different interventions

An overall summary of the results for pair-wise analyses is presented in *Table 174* and for the MTC analyses in *Table 175*. The following discussion is based upon whether or not there is a statistically significant difference between the intervention groups in the direct comparison of all study types and the MTC for randomised and Q-RCTs. For the MTC analyses, only one follow-up interval (closest to 6 months) was considered. The treatment categories are compared in a set order and, once a comparison has been made, it is not discussed again, e.g. disc surgery

TABLE 174 Summary of the overall findings of the standard pair-wise analyses

Comparison	Short-term follow-up			Medium-term follow-up			Long-term follow-up			Adverse effects
	Global effect	Pain intensity	CSOMs	Global effect	Pain intensity	CSOMs	Global effect	Pain intensity	CSOMs	
Disc surgery vs usual care		+	+		+	<>	+	<>	<>	–
Disc surgery vs epidural					+			<>		<>
Disc surgery vs non-opioids				<>	<>					<>
Disc surgery vs disc surgery and non-opioids		–		<>						
Disc surgery plus exercise therapy vs exercise therapy	<>	+	<>	<>	<>	<>	<>	<>	<>	<>
Disc surgery vs disc surgery and acupuncture		–								
Disc surgery vs intraoperative interventions	<>	<>	<>		<>	<>	<>	–	<>	<>
Disc surgery vs chemonucleolysis	<>	<>	<>	<>	<>	<>	+ (marginal)	<>	<>	<>
Disc surgery vs disc surgery and chemonucleolysis							<>	<>		<>
Epidural vs inactive control	<>	+	+	<>	<>	<>	<>	<>	<>	<>
Epidural vs usual care	+	<>	+	<>	<>	<>				–
Epidural vs non-opioids		+	+	<>		<>				<>
Epidural vs epidural and non-opioids		<>	<>		<>	–		–	–	<>
Epidural vs chemonucleolysis	<>			<>			–			–
Epidural vs passive PT				+	<>	<>	+	<>	+	–
Epidural vs activity restriction				+						<>
Epidural vs acupuncture			<>		<>					
Epidural vs biological agents			<>		<>					<>
Physiotherapy vs physiotherapy and epidural	–									
Chemonucleolysis vs inactive control	<>	<>		+	<>		<>			<>
Chemonucleolysis vs manipulation		<>	<>			<>		<>		<>
Non-opioids vs inactive control	+	+	<>	<>	+	<>				–
Non-opioids vs opioids	<>	+								<>
Non-opioids vs acupuncture		+					<>			
Non-opioids vs biological agents		–	–							
Traction vs inactive control	<>	<>	<>	<>	<>					<>
Traction vs usual care	<>									<>
Traction vs exercise therapy	<>									

Comparison	Short-term follow-up			Medium-term follow-up			Long-term follow-up			
	Global effect	Pain intensity	CSOMs	Global effect	Pain intensity	CSOMs	Global effect	Pain intensity	CSOMs	Adverse effects
Traction vs passive PT	<>	<>	<>		<>	<>				<>
Exercise therapy vs exercise therapy and traction	<>	<>	<>		<>	<>				
Passive PT vs passive PT and traction		<>								
Activity restriction vs activity restriction and traction	<>	–	<>							+
Manipulation vs inactive control	<>			+						
Alternative interventions vs inactive control		+								
Exercise therapy vs activity restriction	<>									
Exercise therapy vs usual care	<>		–	<>	<>	<>	+	<>	<>	
Exercise therapy vs inactive control		+								
Activity restriction vs manipulation and exercise therapy	<>		–	<>	<>	<>				
Passive PT vs inactive control	+	+								
Biological agents vs inactive control		+	+		<>	+			<>	<>
Activity restriction vs education/advice	<>	<>	–	<>	<>	<>				<>
Opioids vs inactive control				<>	<>	<>				–
Opioids vs opioids and non-opioids				<>	<>	<>				

<>, no statistically significant difference between the intervention groups; +, statistically significant findings in favour of the intervention group; –, statistically significant findings in favour of the control group.
The CIs of the OR for the meta-analysis comparing disc surgery to chemonucleolysis touched, but did not cross the line of no effect (OR 1.44, 95% CI 1.00 to 2.09) and was therefore considered marginally statistically significant.

TABLE 175 Summary of the overall findings of the MTC analyses

Comparison (intervention vs control)[a]	Global effect all studies (OR)	Pain intensity all studies (WMD)	CSOMs all studies (SMD)	Global effect RCTs/Q-RCTs (OR)	Pain intensity RCTs/Q-RCTs (WMD)	CSOMs RCTs/Q-RCTs (SMD)
Disc surgery vs inactive control	2.78	–9.78	0.10	2.94	–8.87	0.29
Disc surgery vs usual care	3.37	–6.64	–0.06	2.57	–4.43	–0.06
Chemonucleolysis vs disc surgery	0.72	–1.44	0.27	0.81	–3.37	0.34
Non-opioids vs disc surgery	0.92	5.71	–0.00	0.88	3.05	–0.20
Intraoperative interventions vs disc surgery	1.70	–5.11	–0.14	1.7	–5.07	–0.15
Traction vs disc surgery	0.44	8.52	–0.47	0.46	7.57	–0.58
Manipulation vs disc surgery	1.76	–1.94		1.67	–3.95	
Alternative/non-traditional vs disc surgery	3.35	–16.36		3.16	–15.95	
Active PT vs disc surgery	0.40	6.64	0.08	0.50	5.55	0.09
Passive PT vs disc surgery	0.41	9.34	–0.58	0.41	8.71	–0.62
Biological agents vs disc surgery	5.68	–12.09	–0.78	5.48	–2.32	–0.71
Activity restriction vs disc surgery	0.46	27.68	–0.96	0.83	26.41	–1.10
Opioids vs disc surgery	0.58	19.12		0.55	16.33	
Education/advice vs disc surgery	0.59	26.84	–0.78	1.07	25.51	–0.96
Intraoperative interventions vs inactive control	4.73	–14.88	–0.04	4.99	–13.94	0.13
Intraoperative interventions vs usual care	5.72	–11.75	–0.21	4.36	–9.51	–0.21
Intraoperative interventions vs epidural	1.52	–2.01	0.14	1.59	–1.27	0.10
Intraoperative interventions vs chemonucleolysis	2.36	–3.66	–0.42	2.10	–1.65	–0.49
Intraoperative interventions vs non-opioids	1.85	–10.81	–0.13	1.93	–8.16	0.05
Traction vs intraoperative interventions	0.26	13.62	–0.31	0.27	12.71	–0.44
Manipulation vs intraoperative interventions	1.03	3.19		0.98	1.12	
Alternative/non-traditional vs intraoperative interventions	1.98	–11.27		1.85	–10.90	
Active PT vs intraoperative interventions	0.23	11.75	0.22	0.29	10.61	0.24
Passive PT vs intraoperative interventions	0.24	14.42	–0.43	0.24	13.75	–0.47
Biological agents vs intraoperative interventions	3.38	–6.99	–0.64	3.24	2.74	–0.57
Activity restriction vs intraoperative interventions	0.27	32.82	–0.81	0.49	31.41	–0.95
Opioids vs intraoperative interventions	0.34	24.23		0.32	21.36	
Education/advice vs intraoperative interventions	0.34	31.95	–0.62	0.63	30.61	–0.81
Epidural vs inactive control	3.10	–12.85	–0.16	3.14	–12.66	0.03
Epidural vs usual care	3.75	–9.71	–0.34	2.74	–8.19	–0.32
Epidural vs disc surgery	1.11	–3.10	–0.28	1.07	–3.78	–0.26
Chemonucleolysis vs epidural	0.65	1.65	0.55	0.76	–0.40	0.60
Non-opioids vs epidural	0.82	8.78	0.24	0.82	6.80	0.06
Traction vs epidural	0.39	11.68	–0.21	0.43	11.36	–0.33
Manipulation vs epidural	1.57	1.11		1.56	–0.17	
Alternative/non-traditional vs epidural	2.99	–13.28		2.95	–12.20	
Active PT vs epidural	0.35	9.84	0.33	0.47	9.29	0.36
Passive PT vs epidural	0.37	12.48	–0.31	0.38	1240	–0.36

TABLE 175 Summary of the overall findings of the MTC analyses *(continued)*

Comparison (intervention vs control)[a]	Global effect all studies (OR)	Pain intensity all studies (WMD)	CSOMs all studies (SMD)	Global effect RCTs/Q-RCTs (OR)	Pain intensity RCTs/Q-RCTs (WMD)	CSOMs RCTs/Q-RCTs (SMD)
Biological agents vs epidural	5.10	–8.93	–0.51	5.11	1.41	–0.48
Activity restriction vs epidural	0.41	30.90	–0.70	0.77	30.08	–0.84
Opioids vs epidural	0.52	22.21		0.52	20.08	
Education/advice vs epidural	0.53	29.97	–0.50	0.99	29.19	–0.70
Chemonucleolysis vs inactive control	2.00	–11.24	0.37	2.38	–12.28	0.63
Chemonucleolysis vs usual care	2.42	–8.02	0.21	2.07	–7.86	0.28
Non-opioids vs chemonucleolysis	1.27	7.15	–0.29	1.09	6.46	–0.54
Traction vs chemonucleolysis	0.60	10.03	–0.74	0.57	11.06	–0.92
Manipulation vs chemonucleolysis	2.45	–0.48		2.05	–0.62	
Alternative/non-traditional vs chemonucleolysis	4.64	–14.89		3.89	–12.57	
Active PT vs chemonucleolysis	0.55	8.17	–0.20	0.62	8.94	–0.25
Passive PT vs chemonucleolysis	0.57	10.76	–0.85	0.50	12.09	–0.98
Biological agents vs chemonucleolysis	7.90	–10.68	–1.05	6.76	1.17	–1.05
Activity restriction vs chemonucleolysis	0.64	29.21	–1.24	1.03	29.69	–1.45
Opioids vs chemonucleolysis	0.80	20.55		0.68	19.73	
Education/advice vs chemonucleolysis	0.81	28.35	–1.06	1.32	28.78	–1.30
Non-opioids vs inactive control	2.55	–4.07	0.08	2.59	–5.84	0.09
Non-opioids vs usual care	3.09	0.92	–0.08	2.26	–1.36	–0.26
Traction vs non-opioids	0.47	–2.87	–0.46	0.52	4.58	–0.39
Manipulation vs non-opioids	1.91	–7.56		1.89	–6.98	
Alternative/non-traditional vs non-opioids	3.65	–22.05		3.59	–18.97	
Active PT vs non-opioids	0.43	–0.96	0.08	0.57	2.45	0.29
Passive PT vs non-opioids	0.45	3.66	–0.56	0.46	5.61	–0.42
Biological agents vs non-opioids	6.19	–17.79	–0.76	6.20	–5.35	–0.53
Activity restriction vs non-opioids	0.50	22.05	–0.93	0.93	23.29	–0.89
Opioids vs non-opioids	0.63	13.41		0.62	13.27	
Education/advice vs non-opioids	0.64	21.13	–0.76	1.20	22.42	–0.74
Traction vs inactive control	1.20	–1.21	–0.37	1.36	–1.32	–0.29
Traction vs usual care	1.46	1.90	–0.53	1.19	3.29	–0.65
Manipulation vs traction	4.06	–10.48		3.62	–11.54	
Alternative/non-traditional vs traction	7.73	–24.96		6.84	–23.70	
Active PT vs traction	0.90	–1.85	0.54	1.07	–2.14	0.69
Passive PT vs traction	0.94	0.75	–0.10	0.87	1.03	–0.03
Biological agents vs traction	13.2	–20.58	–0.31	11.77	–9.85	–0.15
Activity restriction vs traction	1.05	19.08	–0.46	1.78	18.75	–0.52
Opioids vs traction	1.33	10.51		1.18	8.77	
Education/advice vs traction	1.35	18.20	–0.30	2.30	17.96	–0.37
Manipulation vs inactive control	4.88	–11.72		4.90	–12.79	
Manipulation vs usual care	5.91	–8.58		4.31	–8.49	
Alternative/non-traditional vs manipulation	1.91	–14.41		1.92	–11.97	
Active PT vs manipulation	0.22	8.57		0.30	9.55	
Passive PT vs manipulation	0.23	11.19		0.24	12.56	
Biological agents vs manipulation	3.36	–10.19		3.32	1.69	
Activity restriction vs manipulation	0.26	29.50		0.50	30.31	

continued

TABLE 175 Summary of the overall findings of the MTC analyses *(continued)*

Comparison (intervention vs control)[a]	Global effect all studies (OR)	Pain intensity all studies (WMD)	CSOMs all studies (SMD)	Global effect RCTs/Q-RCTs (OR)	Pain intensity RCTs/Q-RCTs (WMD)	CSOMs RCTs/Q-RCTs (SMD)
Opioids vs manipulation	0.33	20.95		0.33	20.29	
Education/advice vs manipulation	0.33	28.75		0.64	29.32	
Alternative/non-traditional vs inactive control	9.32	–26.08		9.25	–24.89	
Alternative/non-traditional vs usual care	11.27	–23.00		8.15	–20.33	
Active PT vs alternative/non-traditional	0.12	23.14		0.16	21.63	
Passive PT vs alternative/non-traditional	0.13	25.67		0.13	24.73	
Biological agents vs alternative/non-traditional	1.75	4.24		1.76	13.73	
Activity restriction vs alternative/non-traditional	0.14	44.08		0.26	42.63	
Opioids vs alternative/non-traditional	0.17	35.48		0.17	32.34	
Education/advice vs alternative/non-traditional	0.17	43.22		0.33	41.57	
Active PT vs inactive control	1.10	–3.04	0.17	1.46	–3.39	0.39
Active PT vs usual care	1.33	0.08	0.02	1.28	1.01	0.03
Passive PT vs active PT	1.04	2.59	–0.66	0.81	3.26	–0.72
Biological agents vs active PT	14.6	–18.76	–0.83	11.04	–7.82	–0.83
Activity restriction vs active PT	1.16	21.10	–1.02	1.65	20.99	–1.21
Opioids vs active PT	1.46	12.51		1.10	10.79	
Education/advice vs active PT	1.48	20.21	–0.85	2.14	20.11	–1.06
Passive PT vs inactive control	1.14	–0.40	–0.47	1.19	–0.23	–0.32
Passive PT vs usual care	1.38	–2.72	–0.64	1.04	4.29	–0.69
Biological agents vs passive PT	14.0	–21.31	–0.20	13.54	–10.83	–0.12
Activity restriction vs passive PT	1.12	18.47	–0.37	2.04	17.77	–0.47
Opioids vs passive PT	1.41	9.82		1.35	7.69	
Education/advice vs passive PT	1.43	17.60	–0.19	2.62	16.82	–0.32
Biological agents vs inactive control	15.77	–21.80	–0.68	16.04	–11.18	–0.44
Biological agents vs usual care	19.26	–18.67	–0.85	14.11	–6.66	–0.79
Activity restriction vs biological agents	0.08	39.74	–0.18	0.15	28.68	–0.36
Opioids vs biological agents	0.10	31.20		0.10	18.63	
Education/advice vs biological agents	0.10	38.94	–0.01	0.19	27.7 0	–0.22
Activity restriction vs inactive control	1.28	18.00	–0.84	2.43	17.44	–0.80
Activity restriction vs usual care	1.54	21.18	–1.03	2.14	21.96	–1.18
Opioids vs activity restriction	1.26	–8.58		0.67	–10.05	
Education/advice vs activity restriction	1.28	–0.88	0.17	1.29	–0.86	0.15
Opioids vs inactive control	1.60	9.34		1.62	7.41	
Opioids vs usual care	1.95	12.60		1.41	11.92	
Education/advice vs opioids	1.02	7.72		1.94	9.18	
Education/advice vs inactive control	1.63	17.04	–0.66	3.12	16.62	–0.65
Education/advice vs usual care	1.98	20.22	–0.83	2.73	21.04	–1.02

a OR > 1 favours the intervention; WMD < 0 favours intervention; SMD < 0 favours intervention.
Relative treatment effects that were statistically significant are shaded.

versus epidural injections medication is discussed only in the first paragraph and the comparison of epidural injections versus disc surgery is not repeated later. The term 'significantly' is used here in its statistical sense, not as a indication of effect size.

Disc surgery was found to be significantly better than usual care for reducing pain at short- and medium-term follow-up and improving back-specific function at short-term follow-up (according to one good-quality RCT). It was also found to be significantly better than conventional care in terms of overall improvement at long-term follow-up, but this finding is based on the meta-analysis of four studies, only one of which was a good-quality RCT that found no statistical difference between the groups. Two further studies that could not be included in the meta-analysis also reported on this outcome; one was a good-quality RCT that also found no significant difference between the intervention groups. Overall, disc surgery was associated with significantly more adverse effects than usual care. One poor-quality RCT reported that disc surgery was significantly better than epidural injection for reducing pain at medium-term follow-up. Intraoperative interventions (mainly involving application of corticosteroids to the affected nerve root) were better than conventional disc surgery in reducing pain at long-term follow-up (three medium-quality RCTs and one poor-quality RCT), but there was no difference for other outcome measures at any follow-up interval. Disc surgery was marginally but significantly better than chemonucleolysis in effecting global improvement at long-term follow-up, based on a meta-analysis of 18 RCTs, but, again, there was no difference for other outcome measures. One moderate-quality RCT found disc surgery plus exercise therapy to be marginally but significantly better than disc surgery alone for improving pain at short-term follow-up. According to one poor-quality RCT, disc surgery used in combination with non-opioids was also found to be significantly better than disc surgery alone for reducing pain at short-term follow-up. In the MTC analyses of disc surgery, there was a significant improvement in global effect in favour of disc surgery when compared with inactive control or usual care. There was a significantly worse result for pain intensity following disc surgery compared with disc surgery combined with intraoperative interventions. In the MTC analyses of intraoperative intervention, there was a significant improvement in global effect compared with inactive control or usual care.

Epidural injection was found to be significantly better than inactive control for reducing pain (four good- and three medium-quality RCTs) and improving back-related function (four good- and one poor-quality RCT) at short-term follow-up, but was also associated with a greater number of adverse effects. Epidural injection was superior to usual care in terms of global effect and condition-specific function at short-term follow-up, but these findings were based on one non-RCT and one moderate-quality RCT, respectively. Epidural injection was associated with more adverse effects than usual care. Epidural injection was better than non-opioids for reducing pain (two medium- and one poor-quality RCT) and improving back-related function (one medium-quality RCT) at short-term follow-up. In one medium-quality RCT, the addition of non-opioids to epidural injection resulted in significantly better outcomes for condition-specific function at medium- and long-term follow-up and greater pain reduction at long-term follow-up than epidural injection alone. In one medium-quality RCT, epidural injection was superior to passive PT for overall improvement at medium- and long-term follow-up, but not for reducing pain at long-term follow-up. One non-RCT found epidural injection to be significantly better than activity restriction in terms of overall improvement. One non-RCT found chemonucleolysis to be better than epidural injection for global effect at long-term follow-up. Epidural used in combination with physiotherapy was better than physiotherapy alone for overall improvement at short-term follow-up, according to one non-RCT. There was no significant difference between epidural injection and acupuncture or biological agents. In the MTC analyses of epidural injections, there was a significant improvement in pain intensity when compared with inactive

control or opioid medication. There was also a significant improvement in global effect when compared with inactive control or usual care.

Chemonucleolysis was superior to inactive control for overall improvement at medium-term follow-up (one medium-quality RCT, one poor-quality RCT and one Q-RCT), but not for any other outcomes at short- or medium-term intervals. There was no significant difference between chemonucleolysis and manipulation (one medium-quality RCT). In the MTC analyses of chemonucleolysis, there was a significant improvement in global effect compared with inactive control or usual care.

Non-opioid medication were better than inactive control for reducing pain at short-term follow-up (three medium-quality RCTs, one poor-quality RCT and one Q-RCT) and medium-term follow-up (one medium-quality RCT, one poor-quality RCT and one Q-RCT), but there were no difference between the interventions for other short- and medium-term outcome measures. Non-opioids, which included tricyclic antidepressants for treating neurogenic pain, were significantly superior to opioids for reducing pain at short-term follow-up, but there was no significant difference between the intervention groups for overall improvement; according to two poor-quality RCTs. Non-opioids were significantly better than acupuncture for reducing pain at short-term follow-up (one poor-quality RCT). Although a small, poor-quality HCS found biological agents to be better than non-opioids for reducing pain and improving condition-specific function at short-term follow-up, non-opioids resulted in significantly greater adverse effects than inactive control. In the MTC analyses of non-opioids, there was a significant improvement in the global effect when compared with the inactive control or usual care.

Traction was compared with the following treatment categories (mainly by one or two medium-quality RCTs) for which there were no significant findings: inactive control, usual care, exercise therapy, passive PT. According to two medium- and one poor-quality RCT, there was also no significant difference between traction used in combination with exercise therapy and exercise therapy used alone for most short-to-medium term outcomes. One medium-quality RCT found traction plus activity restriction to be significantly better than activity restriction alone for reducing pain, but there was no difference between the groups in terms of overall improvement and CSOMs at short-term follow-up. Activity restriction plus traction was associated with more adverse effects than traction alone. The MTC analyses found no significant findings.

Spinal manipulation was superior to inactive control for overall improvement at medium-term follow-up, but not short-term follow-up, according to one good-quality RCT. The MTC analysis of spinal manipulation, found no significant findings.

One moderate-quality RCT found alternative therapy (acupuncture) to be better than inactive control for the reduction of pain intensity at short-term follow-up. No other outcomes were evaluated. In the MTC analysis of alternative therapy, there was a significant improvement in pain intensity compared with inactive control, usual care, activity restriction, opioids, medication, or education/advice.

According to one medium-term crossover RCT, active PT/exercise therapy was better than inactive control for reducing pain at short-term follow-up. Exercise therapy was marginally significantly worse than usual care for condition-specific function at short-term follow-up, but significantly better in terms of overall improvement at long-term follow-up, according to one-good quality RCT. There was no significant difference for other outcomes. Exercise therapy was compared with activity restriction for the global effect at short-term follow-up by one poor-quality RCT, for which there was no significant difference between the interventions. According to a moderate-quality RCT, physiotherapy including exercise and passive PT was significantly

better than activity restriction for improving function at short-term follow-up. The MTC analysis of active PT/exercise therapy found no significant findings.

Passive PT was significantly better than inactive control in terms of overall improvement and pain reduction at short-term follow-up, according to one poor-quality crossover RCT. One non-RCT found passive PT in combination with epidural to be significantly better than passive PT alone in terms of overall improvement at short-term follow-up. In the MTC analysis of passive PT, there a significantly worse result in pain intensity compared with biological agents.

According to one non-RCT, anti-inflammatory biological agents were significantly better than inactive control for reducing pain at short-term follow-up and improving condition-specific function at short- and medium-term follow-up. However, there was no significant difference in terms of pain intensity at medium-term follow-up (one medium-quality RCT and one non-RCT) or condition-specific function at long-term follow-up (one medium-quality RCT). In the MTC analysis of biological agents, there was a significant improvement in pain intensity compared with inactive control, activity restriction, or opioids.

Activity restriction was less effective than advice to stay active in terms of CSOMs at short-term follow-up, but there was no difference between the intervention groups for other outcome measures at short- and medium-term follow-up, according to two moderate-quality RCTs. In the MTC analysis of activity restriction trials, there was a significantly worse result in pain intensity from activity restriction compared with usual care.

There was no significant difference between opioids medication and inactive control (one medium-quality RCT) or a combination of opioids and non-opioids (one medium-quality crossover RCT) in terms of global pain or CSOMs at medium-term follow-up. However, opioids were associated with more adverse effects than inactive control. In the MTC analysis of opioids, there was a significantly worse result in terms of pain intensity from opioids compared with inactive control or usual care.

Summary of cost-effectiveness review

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 favourable benefit, such as with disc surgery, robust findings could not be reliably drawn. While an evidence base is emerging, there remains a lack of well-designed economic evaluations. Of particular note are the lack of published decision models and the relevance of these studies to the UK NHS setting.

Summary of economic evaluation

Description of economic evaluation

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 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/QALY ratios. Similarly, costs were combined with likelihood of success to generate ICERs.

A number of sensitivity analyses were conducted on the baseline findings.

Results of economic evaluation

The initial treatment of non-opioids followed by biological agents and epidural then disc surgery for those who have failed is the most effective strategy and has an incremental cost per QALY of £4500 compared with the option of not providing surgery. The strategy of referring patients who fail initial treatments directly to disc surgery is dominated by the stepped treatment pathway, with referral for surgery being the most expensive strategy and generally less effective than the stepped approaches. The stepped approaches remain the more cost-effective options even when the use of biological agents or alternative therapies is not included, as the differential in effectiveness for disc surgery is not sufficient to offset the differential in cost from conducting the procedure. For referral directly to disc surgery to be the cost-effective strategy the success rate for disc surgery would need to be 40% higher or the costs of surgery 30% lower.

All of the treatment strategies are within the cost per QALY threshold considered to represent value for money of £20,000–30,000 relative to inactive control. However, a number would be excluded on the grounds of being dominated by a more effective and less costly strategy. The issue of which strategy is the most cost-effective is therefore far from conclusive, and more research is required to determine patient preferences regarding treatment durations and extent of invasive treatments that would be acceptable.

Comparison with previous systematic reviews

Previous systematic reviews of sciatica have examined individual treatments or have considered non-surgical or surgical management strategies separately. Where multiple interventions have been included, they have been analysed either using a narrative synthesis or with pair-wise meta-analyses using direct comparisons of individual treatments. Indirect comparisons have not been attempted and this is the first review to use a MTC method. Previous reviews of non-surgical treatments have found either no evidence of effectiveness[16,17] or conflicting evidence,[294,295] or have reached different conclusions concerning the effectiveness of ESIs.[17,23,24,294] The Cochrane systematic review of surgical management has also made direct comparisons using pair-wise meta-analyses, particularly in comparison with chemonucleolysis,[26] but because of study heterogeneity was unable to combine the results of four RCTs comparing discectomy with non-surgical treatment and concluded that the results suggested only a temporary benefit of disc surgery at 1-year follow-up. This review, however, justified the effectiveness of discectomy

by using an indirect comparison of chemonucleolysis with placebo and chemonucleolysis with disc surgery. Chemonucleolysis was more effective than placebo and discectomy more effective than chemonucleolysis; therefore, disc surgery was superior to placebo. In our review, the same RCTs comparing chymopapain with placebo and chymopapain with surgery, were identified. Five additional RCTs, one non-RCT, 13 CCSs and one HCS comparing chymopapain with disc surgery were identified. In the MTC analysis it was possible to make a more robust comparison of disc surgery compared with placebo. The OR in terms of global effect was 2.8 (95% credible interval 1.4 to 5.6) in favour of disc surgery. The WMD in pain intensity was –9.8 (95% credible interval –26.5 to 6.8) in favour of disc surgery. The SMD in CSOMs was 0.1 (95% credible interval –1.4 to 1.5) in favour of disc surgery. Thus, disc surgery was significantly better than placebo in terms of the global effect but not pain intensity and CSOMs.

Assumptions, limitations and uncertainties

One of the strengths of this review is the extensive literature searches that were undertaken to identify published, unpublished and grey literature. Where possible, non-English language reports were translated; however, we were unable to translate a number of studies published in Chinese, which may have affected the overall findings relating to alternative therapy, particularly acupuncture. Forty-two ongoing (or not yet reported) studies were identified, the findings of which may influence our conclusions: 26 compared different treatment categories including surgery versus usual care ($n = 1$), surgery versus mixed treatments ($n = 1$), epidural versus inactive control ($n = 7$), epidural versus usual care ($n = 1$), epidural versus other ($n = 1$), opioids versus inactive control ($n = 2$), alternative versus mixed treatments ($n = 1$), active PT versus mixed treatments ($n = 1$), biological agents versus inactive control ($n = 4$) and others versus inactive control ($n = 1$).

Our review represents an attempt to answer the question 'Which treatment should I use for sciatica?' In order for the findings of the review to be relevant to the full spectrum of patients who suffer from sciatica, we tried to be as inclusive as possible. Observational studies and non-RCTs were included, as they are likely to have better external validity than RCTs[296,297] and thus provide more generalisable findings. For example, participants keen to have surgery may have been less likely to accept randomisation to either surgery or usual care. Furthermore, some interventions may not have been evaluated by RCTs. The inclusion of observational studies and non-RCTs means that these interventions would not be excluded owing to lack of RCTs or, alternatively, lead to an increase in the precision of the overall findings for interventions evaluated by only a limited number of RCTs.

However, the RCT is widely regarded as the design of choice when assessing the effectiveness of health-care interventions[298] and we acknowledge the controversy over the inclusion of non-randomised evidence. The observed effect of an intervention may not necessarily be due to the therapeutic intervention itself, it could be due to confounding factors such as the natural course of sciatica (including variability of the disease status or the influence of different prognostic factors), extraneous factors (such as lifestyle, the use of other medication and placebo effect) and information errors (such as incorrect assessment or reporting of the outcome measure). A well-conducted RCT would provide an unbiased estimate of effect by ensuring the comparator groups are the same for these factors and only differ in terms of the intervention given. Observational studies, on the other hand, are likely to be affected by selection bias and confounding and may therefore yield estimates of association that deviate from the true underlying relationship beyond the play of chance.[299] However, not all RCTs are well conducted, and they are generally smaller than observational studies. It is therefore unclear whether or not a poorly conducted

RCT provides a better estimate of the treatment effect than a large, well-conducted observational study. When summarising the findings of the pair-wise analyses in our review, priority was given to RCTs, and the quality of the studies noted.

Poor reporting and variation in the way data were analysed in the included studies meant that imputation or substitution of missing data was necessary in order for the meta-analyses to be as inclusive as possible (increasing precision of the findings). Omitting studies with missing SDs may induce bias in the summary effect estimate,[300] and Furukawa *et al.*[33] have shown that it is safe to borrow SDs from other studies. Where SDs were missing and could not be estimated from the published data, we imputed them using a weighted mean SD.[33,300] This is based on the assumption that the variance is similar between studies and that the data are not skewed.[28] Ideally, the impact of this assumption would be assessed using sensitivity analysis. However, this was not possible in the time frame available and will be done at a later date. This will include comparing the pooled mean differences of studies that have reported SDs against the pooled estimate of the same studies based on imputed SDs to see if they converge.[33] Further sensitivity analyses are also needed to assess the impact of substituting mean values with medians.

Our review explored the use of MTC synthesis methodology[274] to simultaneously compare all treatment modalities for sciatica, by providing estimates for all possible pair-wise comparisons, based on both the direct and indirect evidence. One of the main assumptions underpinning these methods is that included studies represent a coherent body of data whose relative treatment effects are effectively identical or at least exchangeable throughout.[301] Comparing two treatments indirectly, but in very different populations, is likely to produce misleading results if the treatments interact with population characteristics.[302] Our review included a diverse set of studies with a number of potential sources of heterogeneity, including the diagnostic criteria used, type and extent of herniation, severity of sciatica, duration of symptoms, previous treatment, mode of administration and dosages of treatments, study design, study quality, outcome measures and duration of follow-up. These characteristics especially varied between invasive and non-invasive treatments. The MTC methods can be used to show the degree of inconsistency in the evidence base.[301] Although we have used informal methods for comparing estimated effects from the (direct pair-wise) meta-analyses and the MTC analysis, more formal methods to assess coherence and consistency of the evidenced network using deviance information criteria[302] and related statistics are yet to be made.

Sciatica is a condition where, in clinical practice, a sequential stepped-care approach using different treatment modalities is considered useful, usually starting with non-invasive treatments and progressing to more invasive treatments if symptoms persist. However, primary studies tended to examine individual treatments in isolation and the clinical effectiveness of treatment strategies in our review were also compared on an equal basis, irrespective of their position in the care pathway. Owing to the novel and speculative use of MTC methods and the breadth of our review, covering such a broad condition with a large number of possible treatments, we did not incorporate a stepped-care approach in the MTC analyses. The optimum sequence of treatment modalities and what sequence is best for which patients are therefore not known. However, we plan to undertake further analyses to develop these methods, in order to derive comparative estimates of the effectiveness of the different interventions, conditional on the administration of previous interventions. Multiple treatments may also be administered sequentially in the hope of producing additive effects using combined therapy; therefore, the additive and interaction effects of multiple interventions also need to be explored.

When a stepped-care approach is used, the characteristics of the patient will vary in different parts of the clinical pathway. This means that the prognosis or baseline risk of the study population is likely to differ (inconsistently) for different interventions. For example, disc surgery

is usually offered to patients who have failed conservative treatment, which means that patients receiving surgery will differ in terms of the type, severity and duration of symptoms compared with those receiving conservative treatment. This trend was reflected in the included studies, with the method and criteria used for diagnosing sciatica (and therefore the patient population) differing according to the invasiveness of the treatment, which was likely to have affected the findings of the MTC analysis. This inconsistency is also present when making informal comparisons between treatment categories in the pair-wise meta-analyses. We plan to further explore this effect as part of the proposed analysis of sequential treatments.

Different countries appear to have a different preference for various treatment modalities, as well as the use of co-interventions. When simultaneously comparing treatment modalities for sciatica, it is important to note that the use of inactive control, usual care and co-interventions is likely to vary across treatment categories and between studies. There is also likely to be a placebo effect occurring with inactive control, which appears to vary according to the type of intervention being used, e.g. sham traction or placebo acupuncture. This is likely to account for why inactive control was shown to be more effective than usual care for global effect (but not for pain intensity) in the MTC analyses, although these findings were not statistically significant.

Implications for further research

The MTC analyses (for all studies and RCTs/Q-RCTs) showed alternative therapy and biological agents to be promising interventions for reducing pain intensity. However, only one non-RCT[270] and one moderate-quality RCT[271] compared biological agents with inactive control, and one moderate-quality RCT[261] compared acupuncture with inactive control; two studies[261,270] reported statistically significant findings in favour of the intervention. One small HCS found biological agents to be more effective than non-opioids and one poor-quality RCT found non-opioids to be more effective than acupuncture. Further research is needed on the use of alternative therapy and biological agents compared with interventions that are currently being used in practice, such as non-opioids and epidural injections. Four ongoing RCTs have been identified comparing the biological agent anti-TNF-α with placebo.

Interestingly, the MTC analyses showed opioids to be significantly less effective than inactive control for reducing pain intensity. In the pair-wise analysis, two small, poor-quality RCTs[229,230] found non-opioids to be significantly more effective than opioids at reducing pain at short-term follow-up, and one medium-quality crossover RCT[214] found no statistically significant difference between opioids and inactive control for global pain and CSOMs at medium-term follow-up. Further research is needed to provide more evidence for the use of opioids and drugs used to treat neurogenic nerve pain, such as tricyclic antidepressants and gabapentin, for the treatment of sciatica. Two ongoing RCTs have been identified, one comparing opioids and the tricyclic antidepressant nortriptyline with placebo and the other comparing anticonvulsant pregabalin (Lyrica®, Pfizer) with placebo (see *Appendix 4*).

There were more studies evaluating invasive interventions, such as surgery, epidural and chemonucleolysis than there were studies evaluating non-invasive interventions, such as education/advice, alterative therapies, manipulation and opioids. More research is needed for non-invasive treatments such as manipulation and exercise therapy. Further research is also needed to compare invasive treatments such as epidural and surgery, which was only evaluated by one poor-quality RCT.

Further research is needed to evaluate exactly which intervention within each treatment category is most effective and whether or not this differs for any subgroup of patients. We have

identified a number of studies that compared treatments within the same treatment category (e.g. microdicectomy vs open discectomy), the findings of which are not presented here, but would help answer these questions.

Further research is needed to determine patient preferences regarding treatment durations and extent of invasive treatments that would be acceptable.

Further work to consider implications of ultimate treatment failure and loss of utility is also needed.

Mixed treatment comparison methods include indirect comparisons which are made without breaking within-study comparison and, hence, fully respect the randomised structure of the evidence.[303] Further research is needed to explore the potential effect of including observational and non-RCTs in MTC analyses. More sophisticated methods, such as the confidence profile method[297] or using Bayesian statistics,[296] could also be explored as a means of incorporating information relating to the differences in study design or internal and external validity in the meta-analyses.

Chapter 11

Conclusions

The review findings provide support for the effectiveness of currently used invasive treatments for treating sciatica, such as disc surgery and epidural corticosteroid injections; however, these were also associated with more adverse effects than usual care. They also provide support for the effectiveness of non-opioid medication for reducing pain in sciatica. Chemonucleolysis was also effective for reducing pain, but is no longer used in the UK NHS. With the exception of non-opioids, there were only a few studies evaluating each of the non-invasive treatment categories. The findings of these studies do not provide support for the effectiveness of opioid analgesia, which is widely used in this patient group. The mixed treatment analyses and limited pair-wise analyses suggest that less frequently used treatments such as acupuncture and experimental treatments such as anti-inflammatory biological agents may be effective. There was also a limited evidence base showing that spinal manipulation and exercise therapy may be effective. The findings do not support the use of activity restriction or traction.

The MTC method enabled both the simultaneous comparison of all treatment categories and the comparison of treatments that had not been directly compared in RCTs or observational studies. However, encouraging results for the interventions (e.g. biological agents) from a small number of poor-quality studies need to be treated with caution. Sciatica is generally treated using a stepped-care approach, starting with non-invasive treatments, such as non-opioid medication, and progressing, if necessary, to more invasive treatments, such as epidural injections or surgery. This means that the population of patients treated with non-invasive treatments in the MTC analyses is likely to differ from that treated with invasive treatments, which may have affected the MTC findings. However, the findings of the pair-wise and MTC analyses were broadly similar.

In terms of cost-effectiveness, the argument for stepped approaches based on an initial treatment with non-opioids, relative to direct referral for surgery, was apparent and, although there are a number of limitations associated with the economic model, this finding was shown to be relatively robust.

Further RCTs with concurrent economic evaluation are needed to evaluate the use of biological agents and acupuncture compared with interventions that are currently being used in practice, such as non-opioids and epidural injections. Four RCTs comparing biological agents with placebo that are in progress, have been identified from searches of trial registries (see *Appendix 4*). Further research is also needed comparing the use of opioids with drugs used to treat neurogenic nerve pain or other treatments currently used in practice. One RCT of oral morphine compared with nortriptyline or placebo was identified from the trial registries (see *Appendix 4*). Further work is also needed to develop alternative economic modelling approaches to assess the relative cost-effectiveness of treatment regimes in these proposed trials.

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Contribution of authors

Ruth Lewis (Lecturer) was co-principal investigator and lead reviewer responsible for writing the protocol and clinical effectiveness section of the review, involved in the study selection, data extraction and validity assessment, conducted the conventional pair-wise and MTC analyses and jointly co-ordinated the final report.

Nefyn Williams (Clinical Senior Lecturer and GP) was co-principal investigator with overall responsibility for the project, was involved in the study selection, data extraction and validity assessment and contributed to the analyses as well as the protocol and report writing.

Hosam Matar (Research Associate) was involved in the study selection, data extraction and validity assessment.

Nafees Din (Research Associate) carried out the literature searches and was involved in the study selection, data extraction and validity assessment.

Deb Fitzsimmons (Senior Lecturer) was responsible for conducting and writing the review of economic evaluations, conducting the service provider survey, was involved in the economic model and contributed to the protocol writing.

Ceri Phillips (Professor of Health Economics) was responsible for the development of the economic model and writing the cost-effectiveness section and contributed to the protocol writing.

Mari Jones (Postdoctoral Research Fellow) was involved in the development of the economic model.

Alex Sutton (Professor of Medical Statistics) was involved in and oversaw all aspects of the clinical effectiveness analyses, provided input at all stages and contributed to the protocol and report writing.

Kim Burton (Director of the Spinal Research Unit, University of Huddersfield) provided clinical input at various stages of the review, contributed to the analyses of adverse effects and the discussion and commented on the draft report.

Sadia Nafees (Research Assistant) was involved in the study selection and contributed to the report writing.

Maggie Hendry (Research Fellow) provided input at various stages of the review and commented on the draft report.

Ian Rickard (Patient Representative) provided input at various stages of the review and commented on the draft report.

Rob Chakraverty (Sports Physician) provided clinical input at various stages of the review and commented on the draft report.

Clare Wilkinson (Professor of General Practice and GP) provided input at various stages of the review and commented on the draft report.

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NETSCC, Health Technology Assessment
Alpha House
University of Southampton Science Park
Southampton SO16 7NS, UK
Email: hta@hta.ac.uk
www.hta.ac.uk

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