National Guideline Centre

Low back pain and sciatica in over 16s: assessment and management

Invasive treatments

NICE guideline NG59
Methods, evidence and recommendations
November 2016

Guideline updates

December 2020: in the recommendation on stopping opioid analgesics we added links to other NICE guidelines and resources that support discussion with patients about opioid prescribing and safe withdrawal management.

September 2020: NICE's original guidance on low back pain and sciatica in over 16s was published in 2016. It was partially updated in September 2020.

See the NICE website for the guideline recommendations and the evidence review for the 2020 update.

This document preserves evidence reviews and committee discussions for areas of the guideline that were not updated in 2020.

Final, 2016

Commissioned by the National Institute for Health and Care Excellence

Royal College of Physicians

Low back pain and sciatica in over 16s: assessment and management

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and, where appropriate, their guardian or carer.

ISBN
978-1-4731-2188-1

Contents

Acknowledgements, GDG membership, algorithm and methods

Further details on acknowledgements, GDG membership, algorithm and methods used to develop this guideline can be found in part 1 of the guideline, 'Low back pain and sciatica: assessment and non-invasive treatments'.

Full list of recommendations

The term 'low back pain' is used to include any non-specific low back pain which is not due to cancer, fracture, infection or an inflammatory disease process.

The current recommendations can be found at
https://www.nice.org.uk/guidance/ng59/chapter/Recommendations

22 Spinal injections

22.1 Introduction

There are many different types of spinal injections performed for low back pain. There are a variety of different techniques, and many are used in conjunction with other therapies, for example, fitness, stretching and exercise programmes. Many injections can be used. Usually the injected agents aim to sooth inflamed tissue or calm excessive nerve activity, but some (sclerosants) aim to induce inflammation and stimulate healthy new tissue growth. Whilst prolotherapy and trigger point injections are not spinal injections as such, these were considered as they can also be used for low back pain. This chapter excludes epidural injections and facet joint radiofrequency denervation, which are considered elsewhere.

Facet joint injections target the small joints linking the spinal vertebrae, known as the facet joints. Each vertebra has 2 connections below, one each side, and 2 above. Injections of local anaesthetic or steroid into selected joints are used to try to temporarily reduce or stop back pain. It is usually used in conjunction with an exercise programme. It is unlikely that the substances injected would remain for long.

Medial branch blocks are injections of local anaesthetic on to the medial branch nerves that supply the facet joints. It is usually done to define those who would respond to radiofrequency denervation of the positive tested levels.

Intradiscal therapy is aimed at treating internal disc disruption (IDD), which some therapists believe can be a cause of low back pain. Both steroids and non-steroidal anti-inflammatory drugs have been injected into the disc in an attempt to suppress inflammation and reduce pain.

Prolotherapy (also known as proliferation therapy or regenerative injection therapy) involves injecting tissue with an irritant solution. This may be a joint, ligament or tendon insertion, or injected into connective tissue or muscle.

Trigger Point Injections use various mixtures of local anaesthetics and a steroid, or botulinum toxin. A trigger point is argued to be a painful or irritable knot in a muscle. Injections are usually carried out in an outpatient setting, and repeated at intervals.

The GDG agreed that the main area of uncertainty that this review would address was the effectiveness of various agents, rather than the route or mode of administration.

22.2 Review question: What is the clinical and cost effectiveness of spinal injections in the management of non-specific low back pain?

For full details see review protocol in Appendix C.

Table 1: PICO characteristics of review question

Population	People aged 16 years or above with non-specific low back pain. • Populations with low back pain only and low back pain with or without sciatica will be pooled for analysis.
Interventions	**Agents (alone and in combination):**

	• Steroid • Local anaesthetic • Sclerosants (prolotherapy, phenol, hypertonic glucose, dextrose, glycerol) • Botulinum toxin • Hyaluronans **Strata:** • Image guided facet joint injections • Other image guided injections • Prolotherapy/sclerosants • Other non-image guided injections (for example, trigger point injections)
Comparison(s)	Interventional agents to be compared versus each other (across class comparisons) and versus other treatments below: • Sham (needle alone)/placebo/saline • Usual care • Other treatment (non-invasive and invasive treatments being considered by the guideline)

Outcomes	**Critical**
	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).
	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).
	• Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BPI, BDI, STAI)
	Important
	• Responder criteria (>30% improvement in pain or function)
	• Adverse events:
	  ○ morbidity
	  ○ mortality
	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Study design	RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found (for strata rather than agent), non-randomised studies will be included.

22.3 Clinical evidence

Thirty one studies were included in the review (several studies were published in multiple papers).[1-31]

The search was extended to cohort studies for all comparisons due to insufficient evidence and 2 studies were identified that met the inclusion criteria.[32,33]

A combined search for the epidurals injections for sciatica review and the spinal injections review identified four Cochrane reviews [34-37]. One of them[36] was not included as it included studies in people with neuropathic pain syndromes and not low back pain. The other reviews[34,35,37] were not included as the stratification of people with low back pain, low back pain with or without sciatica and sciatica was unclear. The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol. The included studies have been summarised in **Table 2**, **Table 3**, **Table 4** and **Table 5** below. Evidence from these studies is summarised in the GRADE clinical evidence

profile/clinical evidence summary below (**Table 7** to **Table 16**). See also the study selection flow chart in Appendix E, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

22.3.1 Heterogeneity

For the comparison of steroid versus saline within the "other image guided injection" strata, there was substantial heterogeneity between the studies when they were meta-analysed for pain and function at both time points reported. Pre-specified subgroup analyses were performed on these outcomes (splitting the studies by different agents that were injected). The subgroup analysis explained the heterogeneity for pain and function, in both the short and long term. However, it could not be applied as people the injection agents were the same in both Cao 2011-1 and Cao 2011-1 populations. [13] These studies remained pooled together in the subgroup analyses as a result.

Table 2: Summary of studies included in the review: strata of image-guided facet joint injections

Study	Intervention and comparison	Population	Outcomes	Comments
Monotherapy				
Carette 1991[1]	Steroid (20 mg, 1 ml methylprednisolone mixed with 1 ml saline) Saline (2 ml)	n=97 Single injection with 6 months follow-up Canada	Pain (VAS) Function-Mean Sickness Impact Profile (MSIP)-less known scale (study downgraded)	Fluoroscopic guided. Injections in the lower 2 lumbar facet joints (L4-L5 and L5-SI). Initial testing of facet joint etiology, using prior image guided injections of local anaesthetic; if this reduced pain then a facet joint etiology was confirmed. These participants were then eligible for study if the pain returned within 2 weeks at a severity of at least 50% of their original pain. Letter sent to referring physician and explained to patients that concurrent treatment needed to be limited. At each visit, patients were given supply of acetaminophen and information on intake and other treatment was recorded.
Fuchs 2005[2]	Steroid (10 mg triamcinolone acetonide in 1 ml crystalline suspension)	n=60 Multiple injections at weekly intervals for 3 weeks	Pain (VAS) Function (ODI/RMDQ/ LBOS)	CT guided Intra-articular Injections given in the facet joints at the three levels in the

Study	Intervention and comparison	Population	Outcomes	Comments
	Hyaluronan (10 mg sodium hyaluronate in a 1 ml buffer)	with 6 months follow-up Germany		lower lumbar spine(L5-S1, L5-L4 AND L4-L3). No concurrent treatment details reported.
Jackson 1992[3]	Anaesthetic (1% Lidocaine, 1 ml) Saline (1 ml)	n=25 Single injection with 1 year follow-up USA	Function (Mean Motion Pain Assessment (MPA)Score)-differences in MPA scores termed as "pain relief", however scores reported for ten specific movements which rendered data un-usable	Fluoroscopic guided (facet joint arthrograms). Unilateral intra-articular injection of the L4-L5 and L5-SI facet joints corresponding to the side and site of pain. No concurrent treatment reported.
Combination therapy				
Lilius 1989[5] Lumbar Facet Joint Syndrome trial	Steroid + anaesthetic: into joints (6 ml/30 mg bupivacaine mixed with 2 ml/80 mg methylprednisolone – injection into the 2 facet joints) Steroid + anaesthetic: pericapsularly around joints (6 ml/30 mg bupivacaine mixed with 2 ml/80 mg methylprednisolone – injection to the 2 facet joints) Saline: into joints (8 ml into the 2 facet joints)	n=109 Single injection (in each of the 2 facet joints) with 3 month follow-up Finland	Pain (subjective pain scale, 0-100)results reported graphically so data un-usable)	Fluoroscopy guided. Pericapsular injections in the facet joints at L3/L4 and L4/L5 in 15 patients and L4/L5 and L5/SI in 94 patients. No concurrent treatment.
Mayer 2004[12,38]	Combined biomechanical exercise/injection-Steroid + anaesthetic) + (1ml 0.5% bupivacaine and 1ml of a depot corticosteroid preparation mixed with 1 ml 2% lidocaine) Biomechanical exercise only controls	n=70 Single injection with 24 months follow-up USA	Pain (VAS) Function (Million Visual Analog Scale (MVAS)) Responder criteria (pain relief >50%) Responder criteria (improvement in disability>50%)	Fluoroscopic guided. Intra-articular injections into 1 to 3 levels bilaterally. Prior to treatment facet blocks were given to confirm a facet joint etiology. Other invasive and non-invasive treatments: both groups received home exercise programme of stretches, taught at the pre-treatment assessment

Study	Intervention and comparison	Population	Outcomes	Comments
				session and subsequently supervised by a physiotherapist at each successive visit. In between follow-up measures patients were also supervised twice a week and advised on exercises as part of the stretching programme. In the final week there were daily sessions. No concurrent treatment reported.
Kawu 2011[32]	Steroid plus anaesthetic: into facet joints (0.5ml (20 mg) of Methylprednisolone acetate and 0.5ml of 0.25% Bupivacaine Biomechanical Exercise (McKenzie regimen)	n=18 unclear how many injections with a 6 month follow-up Nigeria	Pain (VAS) Function (ODI)	X-Ray guided. Facet joint infiltrated and levels to be injected were selected by tenderness elicited over the joint which correlated to MRI findings. No concurrent treatment reported.

Table 3: Summary of studies included in the review: strata of other image guided injections

Study	Intervention and comparison	Population	Outcomes	Comments
Monotherapy				
Cao 2011-1[13]	Steroid (betamethasone, 3 ml) Saline (3 ml)	n=60 Single injection with 6 months follow-up China	Pain (VAS) Function (ODI)	CT guided Intradiscal injections n=60 with type 1 Modic changes to endplates. 60 patients randomised to 3 subgroups, each with 20 patients each. One subgroup consisting of 20 patients not included in review as had non-protocol treatment (herbal remedy). No concurrent treatment reported.
Cao 2011-2[13]	Steroid (betamethasone, 3ml) Saline (3ml)	n=60 Single injection with 6 months follow-up China	Pain (VAS) Function (ODI)	CT guided. Intradiscal injections n=60 with type 2 Modic changes to endplates. 60 patients randomised to 3 subgroups, each with 20

Study	Intervention and comparison	Population	Outcomes	Comments
				patients each. One subgroup consisting of 20 patients not included in review as had non-protocol treatment (herbal remedy). No concurrent treatment reported.
Khot 2004[14]	Steroid (Methylprednisolone acetate 40 mg in 1 ml) Saline (1ml)	n=120 Single injection with 1 year follow-up UK	Function (ODI)	Fluoroscopic guided. Intradiscal injections. No concurrent treatment reported.
Simmons 1992[39]	Steroid(Methylprednisolone(Depo-Medrol) Anaesthetic(1.5ml) (Bupivacaine 0.5%)	n=25 Unclear how many injections with a follow-up of 10-14 days US	Pain (VAS– graph results reported so data was unusable) Function(ODI– graph results reported so data was unusable)	Fluoroscopic guided. Intradiscal injections. No concurrent treatment reported.
Yu 2012[31]	Discography +Steroid (5 mg of dexamethasone) Discography +Saline	n=45 Single injection with 24 months follow-up China	Pain (VAS 0-10) Function (ODI)	CT-guided. Interdiscal injections. All patients had discography prior to the injection treatment. No concurrent treatment reported.
Combination therapy				
Kader 2012[4]	Steroid + anaesthetic (methylprednisolone 80mg and bupivacaine 1-2 ml of 0.5%) Other mixed modality exercise (Back education and standard physiotherapy - pain talk, ergonomics advise, anatomy teaching and goal setting. Warm up on bike, pain relief via heat/ice, US, IFC or PSWD, McKenzie, Maitland or Mulligan exercise/manual	n=63 Single injection with 10 weeks follow-up UK	Pain (McGill) Function (ODI) QoL (EQ-5D)	Image-intensifier guided. Perifacet injections at L4/5 and L4/SI levels bilaterally. Type and frequency of analgesic intake was recorded and reported. Authors report that daily analgesic had been cut down/stopped at the end of the intervention in the majority of patients who had physiotherapy compared to perifacet injections.

Study	Intervention and comparison	Population	Outcomes	Comments
	therapy. Some retraining of transversus/multifidus without a gym ball and daily home exercise programme -20 minutes swimming or walking)			
Manchikanti 2007[6,40] (Manchikanti 2008[7,40], Manchikanti 2010[8,40])	Steroid + anaesthetic (betamethasone at 0.15 mg/ml mixed with bupivacaine) Anaesthetic (bupivacaine 0.25%)	n=30 Single injection with 12 months follow-up USA	Pain (NRS 0-10) Function (ODI) Responder criteria (pain relief >50%)	Fluoroscopy guided nerve blocks. Injected in the indicated medial branches at L1-L4 levels and L5 dorsal ramus Diagnostic blocks using 1% lidocaine. Patients with lidocaine-positive results were further studied using 0.25% bupivacaine on a separate occasion, usually 3 to 4 weeks after the first injection. Concurrent treatment: opioid and non-opioid analgesics, adjuvant analgesics as prescribed prior to treatment. If significant improvements and there was no medical necessity for these drugs to be continued, medications were stopped or doses decreased. If required, doses were also increased. Patients also continued previously directed exercise programs.
Manchikanti 2008C[9,40] (Manchikanti 2011[10,40], Manchikanti 2012[11,40])	Steroid + anaesthetic (betamethasone 6 mg, or non-particulate betamethasone 6 mg, or methylprednisolone 40 mg mixed with lidocaine 0.5% 10 ml)	n=120 Single injection with 24 months follow-up USA	Pain (NRS 0-10) Function (ODI)	Fluoroscopy guided. Caudal epidural injections. All participants received facet joint nerve blocks with lidocaine (0.5 ml 1%); blockade of facet joint nerve was conducted with 0.25% bupivacaine. Repeat caudal epidural injections were performed when increased levels of

Study	Intervention and comparison	Population	Outcomes	Comments
	Anaesthetic (lidocaine 0.5% 10 ml)			pain were reported with deteriorating relief below 50%. Non-responsive participants treated with conservative management were followed without further epidural injections with medical management. Nearly all participants were undergoing conservative management before joining the study i.e. analgesic (opioid/non-opioid) or exercise, drug dosages were decreased/stopped if no longer needed and increased if needed. Exercise and job attendance was continued.
Manchikanti 2010C[15,40] (Manchikanti 2012[16,40], Manchikanti 2013[17,40])	Steroid + anaesthetic (6mg non particulate betamethasone mixed with 5ml lidocaine) Anaesthetic (6ml lidocaine hydrochloride 0.5%)	n=120 Single injection with 24 months follow-up USA	Pain (NRS 0-10) Function (ODI) Adverse events (mortality)	Fluoroscopy guided. Interlaminar space injection. Preceded by diagnostic facet nerve block tests to exclude facet joint etiology. Concurrent treatment: continuation of previously directed structured exercise programs, employment, and medical therapy.
Carrasco 2003[33]	Botox (12.5 units in 1 ml volume at each of the 8 sites for a total of 100 units per patient) Steroid (2mg/ml-1.5 ml to each of the 4-6 sites) +anaesthetic (bupivacaine 0.5%)	n=51 multiple injections with unclear follow-up USA	Pain (VAS)- study reported change in pain scores from pre-treatment values narratively	EMG guided. Trigger-point injections. Patients were selected from a list of patients that had all received Botox treatment in the 3 month preceding data collection in this retrospective cohort study. No concurrent treatment reported.

Table 4: Summary of studies included in the review: strata of prolotherapy/sclerosants

Study	Intervention and comparison	Population	Outcomes	Comments
Monotherapy				
Kotilainen 1997[18]	Sclerosant (1 ml of 50% glycerol) Anaesthetic (2 ml of 0.5% Bupivacaine)	n=15 Single injection with 1 month follow-up Finland	Pain (VAS)	Fluoroscopy guided. Intradiscal injection into 1 disc interspace. No concurrent treatment.
Combination therapy:				
Dechow 1999[19]	Sclerosant + anaesthetic (solution of 5 ml of dextrose 25%, glycerine 25% and phenol 2.4% made up to 100 ml with sterile water combined with 5 ml of 1% Lignocaine) Anaesthetic (normal saline solution combined with 5 ml of 1% lignocaine)	n=74 3 injections once/week with 6 months follow-up UK	Pain (McGill) Function (ODI)	Non-image guided. All injections were made from a single insertion into the following sites: tip of the spinous process of L4 and L5, and associated supraspinous and interspinous ligaments, apophyseal joint capsules at L4-5 and L5-SI; attachment of the iliolumbar ligaments at the transverse processes of the L5;attachment of the iliolumbar and dorsolumbar fascia to the iliac crest; and attachments of the long and short fibres of the posterior sacroiliac ligaments and the sacral and iliac attachments of the interosseous sacroiliac ligaments. Outcomes reported as general and not meta-analysed.
Klein 1993[21,41]	Sclerosant + anaesthetic (30mls total: dextrose,25%; glycerine, 25% and phenol 2.4% made up to 100% with pyrogen-free water. 15 ml of this solution was combined with	n=79 Multiple injections (1 every week for 6 weeks) with 6 months follow-up USA	Pain (VAS 0-8) Function (RMDQ)	Fluoroscopy guided Injection was directed at the following structures: apophyseal joint capsules and laminae at L4-5 and L5-S1, iliolumbar ligaments and dorsolumbar fascia, posterior sacroiliac and

Study	Intervention and comparison	Population	Outcomes	Comments
	15 ml of 0.5% lidocaine) Anaesthetic (30 ml total: 15 ml of 0.5% lidocaine and 15 ml saline)			interosseous sacroiliac ligaments, L4-5 supraspinous and interspinous ligaments, and the interspinous ligaments and decussating tendons of the erector spinae L5-SI. Concurrent treatment: 6 patients were taking narcotics (codeine or Percodan) at entry into the study and 57% were using pain medications or muscle relaxants.
Ongley 1987[22]	Sclerosant + anaesthetic (Dextrose 25%, Glycerine 25%, phenol 2.5% and pyrogen-free water to 100%. Solution was diluted with an equal volume of 0.5% plain Lignocaine to make comparable to the placebo injection) and single forceful manipulation on first day of treatment Saline (0.9%) and less forceful manipulation (compared to intervention group) on first day of treatment.	n=82 Multiple injections with 6 months follow-up USA	Pain (VAS 0-7.5) Function (RMDQ)	Non-image guided Injection was directed at the following structures: apophyseal joint capsules and laminae at L4-5 and L5-S1, iliolumbar ligaments and dorsolumbar fascia, posterior sacroiliac and interosseous sacroiliac ligaments, L4-5 supraspinous and interspinous ligaments, and the interspinous ligaments and decussating tendons of the erector spinae L5-SI. Concurrent treatment: patients were advised to stop all treatments apart from paracetamol and avoid any other treatments during course of study.

Table 5: Summary of studies included in the review: strata of other non-image guided injections

Study	Intervention and comparison	Population	Outcomes	Comments
Monotherapy				

Study	Intervention and comparison	Population	Outcomes	Comments
Foster 2001[25]	Botox (100U/ml in saline – 40units given at each site) Saline	n=31 Injection at each of the 5 lumbar sites at 8 weeks follow-up USA	Responder criteria (≥50% improvement in pain)	Non-image guided Injections were given at 5 lumbar (L1 to L5) or if pain involved the upper sacral region, lumbosacral (L2 to S1) sites; each site received 40 units (total 200 units). All patients were injected only once unilaterally on the side of the pain or pain predominance. Concomitant treatment: variety of analgesic and antispasmodic medications, including baclofen, NSAIDs, antidepressants, and muscle relaxants. No numbers reported.
Combination therapy				
Bourne 1984[23]	Steroid+ Anaesthetic - methylprednisolone 40mg/ml 0.25 ml water for injection 0.75 ml + 2% lignocaine hydrochloride solution 1.0 ml) Steroid + Anaesthetic - triamcinolone 10 mg/ml 1 ml + 2% lignocaine hydrochloride injection Anaesthetic (1% Lignocaine hydrochloride, 2ml)	n=57 Multiple injections at various average period of treatments(range :3.6-5.6) and a 2 week follow-up UK	Responder criteria (but definition does not meet protocol inclusion criteria)	Non-image guided No concurrent treatment reported. No baseline values reported.
Colhado 2013[26]	Steroid + anaesthetic (methylprednisolone acetate 80mg + 5ml levobupivacaine + 3 ml Saline)	n=60 2 epidural blocks per group with a 24 hours follow-up Brazil	Pain (VAS and NRS 0-100)	Non-image guided. Epidural injections. All patients underwent 2 epidural blocks separated by an interval of 15 days

Study	Intervention and comparison	Population	Outcomes	Comments
	Steroid (80 mg methylprednisolone mixed with 8 ml saline)			but were randomised according to agent given. Hence the study is shown to have four arms to reflect each group at the first and second epidural block. No concurrent treatment reported.
Sonne 1985[29]	Steroid + Anaesthetic (1 ml of Methylprednisolone mixed with 5 ml of 1% Lignocaine) Saline (5 ml of isotonic saline)	n=30 Max of three injections given at 1 week intervals 2 weeks follow-up Denmark	Pain (VAS – graph results reported so data was unusable) Responder criteria (definition not given so data was unusable)	Non-image guided Injected at the site of iliolumbar ligament. No concurrent treatment reported.
Serrao 1992[30]	Steroid + Sclerosant (80 mg of methylprednisolone suspended in 10 ml normal saline + 3 ml 5% dextrose) Anaesthetic + Sclerosant (10 ml of normal saline and 2 mg midazolam dissolved in 3 ml 5% dextrose)	n=28 Single injection with 2 months follow-up UK	Pain (VAS– graph results reported so data was unusable) Pain (McGill-– graph results reported so data was unusable) Psychological distress (HADS- narrative description that neither treatment improved the depression scores at 2 months when compared with pre-treatment values)	Steroid + sclerosant: steroid injected into lumbar epidural space and sclerosant injected into the lumbar intrathecal space. Anaesthetic + Sclerosant: saline injected into the lumbar epidural space; steroid + sclerosant mixture injected into the lumbar intrathecal space. Concurrent treatment: patients were instructed not to change their self-medication attitudes but to adjust to their doses according to their normal custom.

22.3.2 Data unsuitable for meta-analysis

Table 6: Other image guided injections: Botox versus saline

Study	Outcome	Intervention results	Risk of bias
Carrasco 2003[33]	Pain (Scale not specified), at >4 months - 1 year	Significant decrease in pain (no scale specified) with a mean reduction of 0.83 points from pre-treatment baseline. Conversely no significant difference in pain scores with anaesthetic/steroid injection (mean decrease of 0.50 points from baseline).	Very high
	Pain (Margolis Pain Scale), at >4 months - 1 year	There was no significant difference in either treatment group with the Margolis pain scale though Botox injections were slightly more effective than standard anaesthetic/steroids in reducing pain scale scores from the pre-treatment baseline (mean decrease of 0.58 ± 0.46 points with Botox compared with 0.48±0.74 points with steroids).	Very high
	Adverse events	Both therapies were safe and well tolerated although mild flu like symptoms lasting 3-4 days were noted.	Very high

22.3.3 Clinical evidence summary tables

22.3.3.1 Image-guided facet joint injections

Table 7: Evidence Summary table: Steroid versus saline

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Saline	Risk difference with Image-guided FJI: Steroid (95% CI)
Pain Severity (VAS, 0-10) ≤ 4 months	96 (1 study)	LOW[a] due to risk of bias		The mean pain severity(VAS,0-10) ≤ 4 months in the control groups was 4.7	The mean pain severity(VAS,0-10) ≤ 4 months in the intervention groups was 0.2 lower (1.14 lower to 0.74 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Saline	Risk difference with Image-guided FJI: Steroid (95% CI)
Pain Severity (VAS,0-10) >4 months	95 (1 study) >4 months	VERY LOW [a,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-10) >4 months in the control groups was 5.0	The mean pain severity(VAS,0-10) >4 months in the intervention groups was 1 lower (1.94 to 0.06 lower)
Function (MSIP, 0-100) ≤ 4 months	96 (1 study) ≤4 months	LOW[1] due to risk of bias		The mean function(msip) ≤ 4 months in the control groups was 9.8	The mean function(msip) ≤ 4 months in the intervention groups was 0.5 lower (2.72 lower to 1.72 higher)
Function (MSIP, 0-100) >4 months	95 (1 study) >4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean function(msip) >4 months in the control groups was 10.8	The mean function(msip) >4 months in the intervention groups was 3 lower (6.16 lower to 0.16 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 8: Evidence Summary table: Steroid versus hyaluronans

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Hyaluronans	Risk difference with Image-guided FJI: Steroid (95% CI)
Pain Severity (VAS, 0-10) ≤ 4 months	59 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS, 0-10) ≤ 4 months in the control groups was 3.01	The mean pain severity(VAS, 0-10) ≤ 4 months in the intervention groups was 1.07 higher (0.18 lower to 2.32 higher)
Pain Severity (VAS, 0-10) >4 months	59 (1 study) >4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS, 0-10) >4 months in the control groups was 3.34	The mean pain severity(VAS, 0-10) >4 months in the intervention groups was 0.46 higher (0.73 lower to 1.65 higher)

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Hyaluronans	Risk difference with Image-guided FJI: Steroid (95% CI)
Function (ODI, 0-100) ≤4 month	59 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean function (ODI) ≤ 4 month in the control groups was 6.15	The mean function (ODI) ≤ 4 month) in the intervention groups was 0.95 higher (1.41 lower to 3.31 higher)
Function (ODI, 0-100) >4 months	59 (1 study) >4 months - 1 year	LOW[a] due to risk of bias		The mean function (ODI)>4 months in the control groups was 6.50	The mean function (ODI)>4 months in the intervention groups was 0.20 lower (2.37 lower to 1.97 higher)
Function (RMDQ, 0-24) ≤ 4months	59 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean function (RMDQ) ≤ 4 months in the control groups was 7.2	The mean function (RMDQ) ≤ 4 months in the intervention groups was 1.20 higher (1.48 lower to 3.88 higher)
Function (RMDQ, 0-24) >4 months	59 (1 study)	LOW[a] due to risk of bias		The mean function(RMDQ) >4 months in the control groups was 8.32	The mean function (RMDQ) >4 months in the intervention groups was 1.22 lower (3.83 lower to 1.39 higher)
Function (LBOS, 0-75) ≤4 months	59 (1 study) ≤4 months	VERY LOW[a.b] due to risk of bias, imprecision		The mean function(LBOS) ≤4 months in the control groups was 31.3	The mean function(LBOS) ≤4 months in the intervention groups was 0.4 higher (30.53 lower to 31.33 higher)
Function (LBOS, 0-10) >4 months	59 (1 study)	VERY LOW[a.b] due to risk of bias, imprecision		The mean function(LBOS) >4 months in the control groups was 30.9	The mean function(LBOS) >4 month in the intervention groups was 1.9 lower (32.39 lower to 28.59 higher)

a Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
b Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 9: Evidence Summary table: Steroid plus biomechanical exercise versus biomechanical exercise

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Biomechanical Exercise	Risk difference with Image-guided FJI: steroid+ biomechanical exercise (95% CI)
Pain severity (VAS,0-10) ≤ 4 months	70 (1 study) 6 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-10) ≤ 4 months in the control groups was 5.9	The mean pain severity(VAS,0-10) ≤ 4 months in the intervention groups was 0.5 lower (1.38 lower to 0.38 higher)
Function (MVAS,0-150) ≤ 4 months	70 (1 study) 6 weeks	VERY LOW[a.b] due to risk of bias, imprecision		The mean function(mvas,0-150) ≤ 4 months in the control groups was 92.2	The mean function(mvas,0-150) ≤ 4 months in the intervention groups was 6.6 lower (17.58 lower to 4.38 higher)
Positive Responders (Pain VAS>50%) ≤4 months	70 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.06 (0.67 to 1.67)	Moderate	
				500 per 1000	30 more per 1000 (from 165 fewer to 335 more)
Positive Responders (Disability MVAS>50%) ≤4 months	70 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.07 (0.78 to 1.45)	Moderate	
				677 per 1000	47 more per 1000 (from 149 fewer to 305 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID

Table 10: Evidence Summary table: Steroid plus anaesthetic versus biomechanical exercise (cohort)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Biomechanical Exercise	Risk difference with Image guided FJI: cohort: Steroid plus anaesthetic (95% CI)
Pain Severity (VAS,0-10) ≤4 months	18 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-10) ≤4 months in the control groups was 5.5	The mean pain severity(VAS,0-10) ≤4 months in the intervention groups was 1.2 lower (2.55 lower to 0.15 higher)
Pain Severity (VAS,0-10) >4 months	18 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-10) >4 months - 1 year in the control groups was 5.0	The mean pain severity(VAS,0-10) >4 months in the intervention groups was 1 lower (2.45 lower to 0.45 higher)
Function(ODI, 0-100) ≤4 months	18 (1 study) ≤4 months	VERY LOW[a] due to risk of bias		The mean function(ODI,0-100) ≤4 months in the control groups was 46.2	The mean function(ODI,0-100) ≤4 months in the intervention groups was 5.6 lower (11.63 lower to 0.43 higher)
Function(ODI, 0-100) >4 months	18 (1 study) >4 months - 1 year	VERY LOW[a] due to risk of bias		The mean function(ODI,0-100) >4 months in the control groups was 46.2	The mean function(ODI,0-100) >4 months in the intervention groups was 6.1 lower (14.47 lower to 2.27 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID

22.3.3.2 Other image-guided injections

Table 11: Evidence Summary table: Steroid versus saline

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Saline	Risk difference with Other Image-guided Injections: Steroid (95% CI)

Pain Severity (VAS,0-10) ≤4 months	125 (3 studies)	LOW[á] due to risk of bias		The mean pain severity(VAS,0-10) ≤4 months in the control groups was 6.81	The mean pain severity(VAS,0-10) ≤4 months in the intervention groups was 4.19 lower (4.55 to 3.82 lower)
Pain Severity (VAS,0-10) ≤4 months - Injection agent: Betamethasone	80 (2 studies)	VERY LOW[a,c] due to risk of bias, inconsistency		The mean pain severity(VAS,0-10) ≤4 months - injection agent: betamethasone in the control groups was 6.9	The mean pain severity(VAS,0-10) ≤4 months - injection agent: betamethasone in the intervention groups was 5.2 lower (5.66 to 4.74 lower)
Pain Severity (VAS,0-10) ≤4 months - Injection agent: Dexamethasone	45 (1 study)	LOW[a] due to risk of bias		The mean pain severity(VAS,0-10) ≤4 months - injection agent: dexamethasone in the control groups was 6.72	The mean pain severity(VAS,0-10) ≤4 months - injection agent: dexamethasone in the intervention groups was 2.44 lower (3.04 to 1.84 lower)
Pain Severity (VAS,0-10) >4 months	125 (3 studies)	LOW[a] due to risk of bias		The mean pain severity(VAS,0-10) >4 months in the control groups was 6.81	The mean pain severity(VAS,0-10) >4 months in the intervention groups was 3.38 lower (3.76 to 3.01 lower)
Pain Severity (VAS,0-10) >4 months - Injection agent: Betamethasone	80 (2 studies)	VERY LOW[a, c] due to risk of bias, inconsistency		The mean pain severity(VAS,0-10) >4 months - injection agent: betamethasone in the control groups was 6.95	The mean pain severity(VAS,0-10) >4 months - injection agent: betamethasone in the intervention groups was 4.76 lower (5.2 to 4.31 lower)
Pain Severity (VAS,0-10) >4 months - Injection agent: Dexamethasone	45 (1 study)	LOW[a] due to risk of bias		The mean pain severity(VAS,0-10) >4 months - injection agent: dexamethasone in the control groups was 6.67	The mean pain severity(VAS,0-10) >4 months - injection agent: dexamethasone in the intervention groups was 0.28 lower (0.95 lower to 0.39 higher)

Function (ODI, 0-100) ≤4 months	125 (3 studies)	LOW[a] due to risk of bias		The mean function(ODI), 0-100 ≤4 months in the control groups was 42.18	The mean function(ODI), 0-100 ≤4 months in the intervention groups was 21.4 lower (24.09 to 18.71 lower)
Function (ODI, 0-100) ≤4 months - Injection agent: Betamethasone	80 (2 studies)	VERY LOW[a,c] due to risk of bias, inconsistency		The mean function(ODI), 0-100 ≤4 months - injection agent: betamethasone in the control groups was 37.65	The mean function(ODI), 0-100 ≤4 months - injection agent: betamethasone in the intervention groups was 27.95 lower (31.72 to 24.19 lower)
Function(ODI, 0-100) ≤4 months - Injection agent: Dexamethasone	45 (1 study)	LOW[a] due to risk of bias		The mean function(ODI), 0-100 ≤4 months - injection agent: dexamethasone in the control groups was 46.7	The mean function(ODI), 0-100 ≤4 months - injection agent: dexamethasone in the intervention groups was 14.6 lower (18.44 to 10.76 lower)
Function(ODI, 0-100) >4 months	223 (4 studies)	VERY LOW[a.b] due to risk of bias, imprecision		The mean function(ODI,0-100) >4 months in the control groups was 46.63	The mean function(ODI,0-100) >4 months in the intervention groups was 12.02 lower (14.79 to 9.24 lower)
Function(ODI, 0-100) >4 months - Injection agent: Betamethasone	80 (2 studies)	VERY LOW[a,b] due to risk of bias, inconsistency		The mean function(ODI,0-100) >4 months - injection agent: betamethasone in the control groups was 39.1	The mean function(ODI,0-100) >4 months - injection agent: betamethasone in the intervention groups was 24.06 lower (28.13 to 20 lower)
Function(ODI, 0-100) >4 months - Injection agent: Methyprednisolone acetate	98 (1 study)	LOW[a] due to risk of bias		The mean function(ODI,0-100) >4 months - injection agent: methyprednisolone acetate in the control groups was 49.8	The mean function(ODI,0-100) >4 months - injection agent: methyprednisolone acetate in the intervention groups was 1.1 lower (7.11 lower to 4.91 higher)

Function(ODI, 0-100) >4 months - Injection agent: Dexamethasone	45 (1 study)	LOW[a] due to risk of bias		The mean function(ODI,0-100) >4 months - injection agent: dexamethasone in the control groups was 51.0	The mean function(ODI,0-100) >4 months - injection agent: dexamethasone in the intervention groups was 1.8 lower (6.7 lower to 3.1 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 or 2 increments because of Heterogeneity, I^2=50%, p=0.04, unexplained by subgroup analysis

[c] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID

Table 12: Evidence Summary table: Steroid plus anaesthetic versus anaesthetic

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with	Risk difference with Other image-guided injections: Steroid+ Anaesthetic (95% CI)
Pain Severity(NRS,0-10)≤ 4 months	270 (3 studies) <4 months	MODERATE[a] due to risk of bias		The mean pain severity(NRS,0-10)≤ 4 months in the control groups was 3.7	The mean pain severity(NRS,0-10)≤ 4 months in the intervention groups was 0.19 lower (0.49 lower to 0.1 higher)
Pain Severity(NRS,0-10) >4 months	248 (3 studies) >4 months	LOW[a,c] due to risk of bias		The mean pain severity(NRS,0-10) >4 months in the control groups was 3.8	The mean pain severity(NRS,0-10) >4 months in the intervention groups was 0.24 lower (0.59 lower to 0.12 higher)
Function(ODI,0-100) ≤ 4 months	270 (3 studies) <4 months	MODERATE[a] due to risk of bias		The mean function(odi,0-100) ≤ 4 months in the control groups was 14.9	The mean function(odi,0-100) ≤ 4 months in the intervention groups was 0.41 lower (1.67 lower to 0.85 higher)
Function (ODI,0-100) >4 months	248 (3 studies) >4 months	MODERATE[a] due to risk of bias		The mean function (odi,0-100) >4 months in the control groups was 14.9	The mean function (odi,0-100) >4 months in the intervention groups was 0.00 higher (1.4 lower to 1.4 higher)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with	Risk difference with Other image-guided injections: Steroid+ Anaesthetic (95% CI)
Pain improvement(>50%) ≤ 4 months	150 (2 studies) <4 months	MODERATE[a] due to risk of bias	RR 0.95 (0.84 to 1.09)	850 per 1000	43 fewer per 1000 (from 136 fewer to 77 more)
Pain improvement(>50%) >4 months	150 (2 studies) >4 months	LOW[a,b] due to risk of bias, inconsistency	RR 0.97 (0.81 to 1.16)	Moderate	
				758 per 1000	23 fewer per 1000 (from 144 fewer to 121 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis.

C Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID

Table 13: Evidence Summary table: Steroid plus anaesthetic versus mixed modality exercise

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with mixed modality exercise	Risk difference with Image-guided FJI: Steroid + anaesthetic (95% CI)
Quality of life (EQ5D, 0-1)	36 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		The mean QoL(EQ5D) in the control groups was 0.32	The mean QoL(EQ5D) in the intervention groups was 0.02 lower (0.55 lower to 0.51 higher)
Pain Severity (McGill, 0-78) ≤4 months	36 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean pain severity(McGill) ≤ 4 months in the control groups was 23	The mean pain severity(McGill) ≤ 4 months in the intervention groups was 7.6 lower (16.22 lower to 1.02 higher)

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with mixed modality exercise	Risk difference with Image-guided FJI: Steroid + anaesthetic (95% CI)
Function (ODI, 0-100) ≤4 month	36 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean function(ODI) ≤ 4 month in the control groups was 23.9	The mean function(ODI) ≤ 4 month in the intervention groups was 3.5 higher (5.23 lower to 12.23 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID

22.3.3.3 Prolotherapy injections

Table 14: Evidence Summary table: Sclerosant versus anaesthetic

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Anaesthetic	Risk difference with Prolotherapy Injections: Sclerosant (95% CI)
Pain Severity (VAS,0-10)≤ 4 months	11 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-10)≤ 4 months in the control groups was 5.0	The mean pain severity(VAS,0-10)≤ 4 months in the intervention groups was 0.10 lower (8.06 lower to 7.86 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID

Table 15: Evidence Summary table: Sclerosant plus anaesthetic versus saline

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Saline	Risk difference with Prolotherapy Injections: Sclerosant + anaesthetic (95% CI)
Pain Severity (VAS,0-7.5) ≤4 months	81 (1 study) ≤4 months	LOW[a,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-7.5)≤ 4 months in the control groups was 2.93	The mean pain severity(VAS,0-7.5)≤ 4 months in the intervention groups was 1.16 lower (1.81 to 0.51 lower)
Pain Severity (VAS,0-7.5)>4 months	81 (1 study) >4 months	LOW[a.,b] due to risk of bias, imprecision		The mean pain severity(VAS,0-7.5)>4 months in the control groups was 3.08	The mean pain severity(VAS,0-7.5)>4 months in the intervention groups was 1.58 lower (2.26 to 0.9 lower)
Function (RMDQ,0-33)≤ 4 months	81 (1 study) ≤4 months	MODERATE[b] due to imprecision		The mean function(RMDQ)≤ 4 months in the control groups was 8.49	The mean function(RMDQ)≤ 4 months in the intervention groups was 3.79 lower (6.28 to 1.3 lower)
Function (RMDQ, 0-33)>4 months	81 (1 study) >4 months	MODERATE[b] due to imprecision		The mean function (RMDQ)>4 months in the control groups was 8.29	The mean function (RMDQ)>4 months in the intervention groups was 4.86 lower (7.44 to 2.28 lower)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 16: Evidence Summary table: Sclerosant plus anaesthetic versus anaesthetic

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Anaesthetic	Risk difference with Prolotherapy Injections: Sclerosant + anaesthetic (95% CI)
Pain Severity (VAS,0-8) >4 months	79 (1 study) >4 months	MODERATE[a] due to imprecision		The mean pain severity(VAS,0-8)>4 months in the control groups was 2.85	The mean pain severity(VAS,0-8)>4 months in the intervention groups was

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Anaesthetic	Risk difference with Prolotherapy Injections: Sclerosant + anaesthetic (95% CI)
					0.56 lower (1.34 lower to 0.22 higher)
Function (RMDQ, 0-24) >4 months	79 (1 study) >4 months	MODERATE[a] due to imprecision		The mean function(RMDQ)>4 months in the control groups was 4.38	The mean function(RMDQ)>4 months in the intervention groups was 0.34 lower (2.05 lower to 1.37 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

22.3.3.4 Other non-image guided injections

Table 17: Evidence Summary table: Botox versus saline

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Saline	Risk difference with Other Non-Image guided Injections: Botox (95% CI)
Responder criteria (VAS>50%) ≤4 months	30 (1 study) ≤4 months	MODERATE[a] due to imprecision	RR 4.50 (1.16 to 17.44)	Moderate	
				133 per 1000	465 more per 1000 (from 21 more to 1000 more)

[a] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 18: Evidence Summary table: Steroid+ anaesthetic versus steroid

Outcomes	No of Participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Steroid	Risk difference with Other Non-Image guided Injections: Steroid + anaesthetic (95% CI)

Pain Severity (First Block NRS,0-10) ≤4 month	60 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(first block NRS,0-10) ≤4 month in the control groups was 2.6	The mean pain severity(first block NRS,0-10) ≤4 month in the intervention groups was 0.44 higher (0.72 lower to 1.6 higher)
Pain Severity (Second Block NRS,0-10) ≤4 month	60 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(second block NRS,0-10) ≤4 month in the control groups was 2.057	The mean pain severity(second block NRS,0-10) ≤4 month in the intervention groups was 0.44 higher (0.77 lower to 1.66 higher)
Pain Severity (First Block VAS,0-10) ≤4 month	60 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(first block VAS,0-10) ≤4 month in the control groups was 2.79	The mean pain severity(first block VAS,0-10) ≤4 month in the intervention groups was 0.57 higher (0.61 lower to 1.75 higher)
Pain Severity (Second Block VAS,0-10) ≤4 month	60 (1 study) ≤4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(second block VAS,0-10) ≤4 month in the control groups was 2.13	The mean pain severity(second block VAS,0-10) ≤4 month in the intervention groups was 0.25 higher (0.94 lower to 1.44 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

22.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix F.

Unit costs

The unit cost for image-guided injections would be based either on intermediate or major pain procedures: £521 (HRG code: AB05Z) and £714 (HRG code: AB04Z), respectively (NHS reference costs 2013-2014).[42]

22.5 Evidence statements

22.5.1 Clinical

22.5.1.1 Image guided facet joint injections

In people with low back pain there was clinical benefit for steroid injections compared with saline demonstrated in evidence from 1 study for both pain and function greater than 4 months (very low quality, n=95), but no clinically important difference at equal to or less than 4 months.

Clinical benefit for steroid compared to hyaluronans was seen in pain in the short term (very low quality; 1 study; n=59) with no clinically important difference between treatments in any other outcome reported at either short or long term.

There was no clinically important difference seen when a steroid injection was given in combination with biomechanical exercise compared to biomechanical exercise. Clinical benefit was seen however in pain at short and long term, but not in function, when injections of steroid and anaesthetic plus biomechanical exercise were compared to biomechanical exercise in a nonrandomised study (very low quality; n=18).

22.5.1.2 Other image-guided injections

Evidence from 3 studies showed a clinical benefit in terms of improving pain and function in the group receiving a steroid injection (bethametasone or dexamethasone) versus saline in the short term (low quality, range of n = 45-80). Evidence from 2 studies also showed clinical benefit of steroid injections (betamethasone) for pain and function in the long term (very low quality; n=80), but this was not observed when dexamethasone (low quality; n=45), or methylprednisolone acetate in the case of function (low quality; n=98), was used as injectate.

Evidence from 3 studies showed that there was no clinically important difference between treatments for all outcomes reported when steroid plus anaesthetic was injected compared to anaesthetic injection alone irrespective of route of administration being caudal epidural, medial branch blocks or interlaminar injections(moderate quality, n=270). Evidence from 1 study comparing

steroid plus anaesthetic versus mixed modality exercise reported no benefit of injection for quality of life, pain or function in the short term (low quality; n=36).

22.5.1.3 Prolotherapy injections

There was no clinically important difference between treatments for outcomes reported when a sclerosant was injected compared to anaesthetic (1 study; very low quality; n=11) or an injection of sclerosant in combination with an anaesthetic was compared to anaesthetic (1 study; moderate quality; n=79). However, evidence from a single study demonstrated a clinical benefit favouring the injection of sclerosant plus anaesthetic compared to saline for pain and function in both the short and long term (low to moderate quality; n=81).

22.5.1.4 Other non-image-guided injections

Evidence from 1 study for the comparison of botulinum toxin versus saline showed clinical benefit of botulinum toxin for responder criteria in pain (moderate quality; n=30). Evidence from 1 study for the comparison of steroid in combination with anaesthetic versus steroid alone demonstrated no clinically important difference between the treatments for pain (first or second block) at either short or long term (very low quality; n=60).

22.5.2 Economic

- No relevant economic evaluations were identified.

22.6 Recommendations and link to evidence

Recommendations	The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations
Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Responder criteria (>30% improvement in pain or function), adverse events, and healthcare utilisation were also considered as important. Evidence was reported for all of outcomes except for psychological distress and healthcare utilisation. For image guided facet joint injections, evidence was only available for pain, function and responder criteria. There was no evidence for any of the other outcomes. For other image guided injections, evidence was only available for pain, function, quality of life (EQ-5D) and for responder criteria. Evidence for prolotherapy injections was only available for pain and function and for other non-image guided injections, evidence was found for pain and responder criteria only. The majority of outcomes described in other non-image guided stratum were in a format that rendered the data un-suitable for meta-analysis.
Trade-off between clinical benefits and harms	**Image guided facet joint injections** **Steroid versus saline** A clinical benefit in pain (VAS) was observed in the long term (greater than 4 months - 1 year) although no clinically important difference was seen short term (less than 4

months). A similar effect was also seen for function (MSIP), however, it was noted that the baseline values were very low and therefore it was unlikely that much improvement could be demonstrated from this baseline. The GDG noted that the lack of short term effect with some evidence of a long term effect raised some doubt on the long term effect being solely due to the injection. The authors of the study stated that there was no pharmacological/biological reason for the observed effect and were uncertain about the validity of the results. The GDG noted that image guided facet joint injections of steroid are widely used but there is a paucity of evidence to support their ongoing use. It was noted that there was no evidence of clinical harm from the studies reviewed.

Steroid versus hyaluronans

Very low quality evidence demonstrated that steroids were more effective at improving pain (assessed by VAS) than hyalurons in the short term although no clinically important difference between treatments was seen long term. It was noted that use of hyalurons may cause inflammation and therefore an increase in pain, although both groups did improve from their baseline pain levels. Three different measures of function were reported (ODI, RMDQ and Low Back Pain Outcome Score (LBOS)); all of which showed no clinically important difference between treatments.

Steroid plus biomechanical exercise versus biomechanical exercise

No clinically important difference in pain, function or responder criteria was observed at the short term follow ups. As there was uncertainty around the effects reported from this single trial, the GDG considered that no clear conclusion could be made about the benefits of steroid injections compared to biomechanical exercise from this very low quality evidence.

Steroid plus anaesthetic versus biomechanical exercise

Very low quality non randomised evidence for this comparison came from a very small trial and demonstrated a clinical benefit in pain (VAS) in both the short and long term although no clinically important difference was observed for function (assessed by ODI) at any time point.

Other image guided injections

Steroid versus saline

An overall clinical benefit in pain (assessed by VAS) and function (assessed by ODI) favouring the use of steroid injected intra-discally was seen in the short term and long term. Subgroup analysis by injection agent to address heterogeneity revealed no clinically important difference in pain in the long term from low quality evidence at high risk of bias taken from 1 small trial. The results for function in the long term were more heterogeneous; subgroup analysis by injection agent showed benefit favouring steroid was only maintained in the long term in results taken from 1 trial. This very low quality evidence at high risk of bias reported inconsistent results separately for 2 distinct populations with or without modic changes. There was concern raised by the GDG that the inpatient population set in a hospital in China was not reflective of current UK practise and did not have confidence in the effects reported as a result.

The potential risk of harm for intra-discal injections was also highlighted including risk of infection and risk of prolapse (although this risk is not captured by RCTs). Given the applicability issue and risk of potential harm, the GDG concluded that the evidence in this area was inadequate to base a recommendation on.

Steroid in combination with anesthetic versus anesthetic

Moderate quality evidence from 3 studies showed no clinically important difference in pain (assessed by VAS), function (assessed by ODI) and responder criteria for pain improvement exceeding 50% in either the short or long term irrespective of the route of administration of the injection.

Steroid in combination with anesthetic versus combined treatment

One study included assessed the effects of steroid plus anaesthetic versus a combination package of self-management (back education and home exercise), biomechanical exercise (McKenzie and stability), manual therapy (manipulation/mobilisation, Maitland and Mulligan), electrotherapy (ultrasound) and heat/ice. There was no clinical benefit seen in terms of any of the outcomes reported in this study. The GDG noted that the study was a very small trial and that the baseline scores for all outcomes were different between groups and both groups were in the 'normal' range at baseline, and therefore it would be unlikely to observe a meaningful change over the course of the trial. It was however also highlighted that the comparator arm consisted of a 10 week intensive rehabilitation programme -is a very active intervention. The GDG discussed that the lack of a difference observed between arms could be indicative of positive evidence for both injections of steroid and anaesthetic as well as the combination of education and physiotherapy. However, the limitations of the single small study precluded firm conclusions being drawn.

Prolotherapy Injections

Sclerosant versus anaesthetic

The only evidence identified for this comparison was from a very small trial that reported only 1 outcome relevant to the review protocol (pain assessed by VAS). This showed no difference between treatments in the short term with considerable uncertainty in the direction of the effect.

Sclerosant plus anaesthetic versus saline

Evidence from 1 study indicated that injection of sclerosant and anaesthetic was more effective than saline in improving pain (assessed by VAS) and function (assessed by RMDQ) in both the short and long term. The GDG expressed caution with the interpretation of these results as people in the intervention group received a forceful manipulation, concurrent to the injection on the first day of treatment, whereas those in the saline group received non-forceful manipulation. The GDG were unable to be certain that the clinical benefit in pain and function was directly attributable to the spinal injections.

Sclerosant plus anaesthetic versus anaesthetic

No clinically important difference was seen between treatments in terms of pain (assessed by VAS) and function (assessed by RMDQ) in the long term. No data was presented for short term results.

Other non-image guided injections

Botulinum toxin versus saline

A clinical benefit in responder criteria for pain improvement exceeding 50% was seen in favour of botulinum toxin in the short-term. However, as this was from a single small trial (15 patients in each arm) and was not in a critical outcome measure, the GDG felt that this was insufficient evidence to make a recommendation.

Steroid plus anaesthetic versus steroid

Evidence from 1 study demonstrated no short-term clinically important difference between treatments in terms of pain (NRS) between injections of steroid and anaesthetic or steroid alone. The evidence was from a study which stratified

	participants according to how many diagnostic blocks they had received, however the outcome was the same for each strata. The GDG expressed concern with the interpretation of the study as the description provided suggested the population may be people with sciatica although the study specifically stated it was for treatment of low back pain. In addition, the study only looked at the immediate short term effect of the diagnostic blocks up till a maximum of 24 hours which the GDG did not feel was very useful information. It was noted that in the studies included in this review, no data were available on adverse events. The GDG noted that they are aware of studies/clinical reports (that did not meet inclusion criteria for this review) reporting serious adverse effects of spinal injections although these were relatively rare. **Summary** Overall the GDG agreed that there was no consistent good quality evidence to recommend the use of spinal injections for the management of low back pain. There was minimal evidence of benefit from injections, and reason to believe that there was a risk of harm, even if rare. The GDG consequently agreed that it was appropriate to recommend against the use of spinal injections for people with low back pain.
Trade-off between net clinical effects and costs	No economic evaluations were identified from the published literature. Use of injections for low back pain will be associated with costs relating to the drugs, consumables and equipment (e.g. imaging) used and the personnel time required to deliver the therapy. Intervention costs will also depend on the number of injections given. If effective, upfront intervention costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient. However, given the GDG's conclusions that there was a lack of evidence of clinical benefit for injections (for any of the agents or modalities reviewed), intervention costs were not considered justified.
Quality of evidence	**Image guided facet joint injections** Low to very low quality evidence for this stratum came from 4 studies of which 2 reported data graphically and the third was a small trial comparing steroid and hyaluronan. The weight of evidence rested on 1 main RCT, in which Mean Sickness Impact Profile (MSIP) was used to assess improvement in function. However, the GDG were unclear as to what magnitude of change could be considered meaningful and therefore were unable to place much significance on this outcome. **Other image guided injections** The evidence for this stratum was rated as low or very low quality, mainly due to risk of bias (and sometimes due to additional imprecision). The majority of evidence for the comparison steroid versus saline came from a reasonably sized trial which reported outcomes separately for 2 very distinct populations with or without modic changes. The results reported were often inconsistent and there was concern that the study population wouldn't be entirely representative of the guideline population, however the GDG agreed that the same response would be expected in either case. There was concern that the results reported in this study had not been reproducible in other similar studies and whilst they may be clinically important, there was considerable doubt regarding their validity. The applicability of this study to a UK setting was also questioned as this study population were all in-patients. The GDG did not consider the study Manchikanti 2007 to be suitable for inclusion in the image guided facet joint strata despite the study classifying the injections as facet joint injections. This was because the agents were administered to the medial branches at L1-L4 levels and L5 dorsal ramus which the GDG did not feel qualified as

	a facet joint injection. The study was therefore included in the 'other image guided injections' strata. The small study population received numerous injections during the study period which further compromised the quality of the outcomes reported; the GDG did not feel they could make accurate judgement of clinical importance for these reasons. **Prolotherapy injections** The majority of evidence in this stratum was of low quality as there was serious imprecision attached to all the effects reported. One trial reported the inclusion of forceful manipulation in the treatment arm which the GDG considered to be a risk of bias affecting interpretation of the evidence. They did not feel they could make accurate judgement of clinical importance from this evidence as the manipulation could have compromised the clinical benefit shown for the combination treatment for both the outcomes pain and function in the short and long term periods. **Other non-image guided injections** Overall low quality evidence for this stratum reported came from 2 studies. One of these trials had a very small sample size which made judging clinical importance for the outcome responder criteria pain (VAS) exceeding 50% improvement difficult for the GDG. There was also considerable polarity of opinion in the GDG regarding the second trial. One concern was that the study might include sciatica patients as some included patients had nerve compression and also reported 2 diagnostic blocks for each group with short follow up of 6, 12 and 24 hours. The GDG felt that this trial was largely irrelevant and did not have much confidence in the outcomes reported.
Other considerations	The GDG noted that many sclerosants were not licensed as injection agents for the treatment of low back pain in the UK but were licensed for other indications, however they did not agree that there was evidence to recommend these injections for low back pain. The GDG were aware of existing NICE interventional procedure guidance for Therapeutic endoscopic division of epidural adhesions (IPG333) recommending special arrangements for clinical governance, consent, audit and research.[43] This procedure was therefore excluded from this review and if its use is considered for people with low back pain, existing guidance should be followed.

23 Radiofrequency denervation for facet joint pain

23.1 Introduction

Some people who are given a diagnosis of low back pain may have pain arising from 1 or more spinal structures where nociceptive/pain innervation has been established, for example, muscles, joints, ligaments and discs. There are no reliable clinical or radiological features to discriminate between these potential sources of low back pain. The evidence to support the idea of back pain arising from discrete structures comes from studies using precisely targeted local anaesthetic blockade.[44]

The lumbar facet joints are pairs of joints that stabilize and guide motion in the spine. These joints are well innervated by the medial branches of the dorsal rami. The prevalence of facet joint pain in heterogeneous populations using local anaesthetic nerve blockade (medial branch block), where 75–100% pain relief is used as a criterion standard, is thought to be 25–40%.[40,45]

In current clinical practice, people with low back pain may be offered local anaesthetic facet joint nerve blockade to determine the presence or absence of a facet joint pain component. Those who experience significant but short term relief may then be offered a neurodestructive procedure called 'radiofrequency denervation' in an attempt to achieve longer term pain relief.

Radiofrequency denervation has evolved as a treatment for spinal pain over the last 40 years and is a minimally invasive and percutaneous procedure performed under local anaesthesia or light intravenous sedation. Radiofrequency energy is delivered along an insulated needle in contact with the target nerves. This focussed electrical energy heats and denatures the nerve. This process may allow axons to regenerate with time requiring the repetition of the radiofrequency procedure.

Radiofrequency denervation is not an appropriate treatment of people who have sciatica without back pain.

23.2 Review question: What is the clinical and cost effectiveness of radiofrequency denervation for facet joint pain in the management of non-specific low back pain?

For full details see review protocol in Appendix C.

Table 19: PICO characteristics of review question

Population	People aged 16 years or above with non-specific low back pain. • Populations with low back pain only and low back pain with/without sciatica will be pooled for analysis. NOTE: low back pain with sciatica is excluded
Interventions	• Radiofrequency denervation of facet joint medial branch NOTE: pulsed radiofrequency is excluded
Comparisons	• Placebo/sham • Usual care/waiting list • Other treatment within guideline scope
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).

	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index) • Psychological distress (HADS, GHQ, BPI, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: ○ morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)
Study design	RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found, non-randomised studies will be included.

23.3 Clinical evidence

Eight RCTs were included in the review; these are summarised in **Table 20** below. [46-53] Evidence from these studies is summarised in the GRADE clinical evidence profile/clinical evidence summary below. All the studies compared radiofrequency denervation with a placebo/sham procedure, except for 1 which used medial nerve block as the comparison intervention.[53] All studies (except Civelek et al. 2012) randomised patients who had responded favourably to either an initial diagnostic nerve block,[47,49-51] or an intra-articular (IA) joint injection.[48,52] See also the study selection flow chart in Appendix E, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

Two Cochrane reviews were identified but could not be included. One review included studies in people with neck as well as back pain.[54] The other review included people with low back pain other than facet joint pain.[55] The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol. One study was included but could not be analysed as no relevant outcomes were reported.[46]

Table 20: Summary of studies included in the review

Study	Intervention	Comparison	Population	Outcomes	Comments
Civelek 2012[53]	Radiofrequency denervation 80ºC lesion for 120 seconds	Medial branch nerve block Medial branch block with methylprednisolone and bupivacaine	Low back pain without sciatica n=100 Immediate + 1, 6 and 12 months follow-up Turkey	Quality of life (EQ-5D) Pain severity (VNS)	No diagnostic nerve block given prior to randomisation Anaesthetic: lidocaine 1% in injection group only. None given to RF group. Responders (1 week after the procedure) were then placed in a spine rehabilitation programme for 4-6 weeks to maximise the functional gains. Partial or non-

Study	Intervention	Comparison	Population	Outcomes	Comments
					responders were offered surgery or physical therapy. Does not specify if this was done for 1 or both arms of the study.
Gallagher 1994[47]	Radiofrequency denervation 80°C lesion for 90 seconds	Placebo/sham	Low back pain with/without sciatica n=30 Immediate + 1 month and 6 months follow-up UK	Pain severity (VAS and McGill)	True diagnostic nerve block given; responders were randomised Anaesthetic: lignocaine 2% (0.5 ml).
Leclaire 2001[48]	Radiofrequency denervation 80°C lesion for 90 seconds 2 neurotomies performed for each nerve (1 at proximal portion, and 1 at distal of the articular facet nerve).	Placebo/sham	Low back pain with/without sciatica n=70 Immediate + 12 weeks follow-up Canada	Pain severity (VAS) Function (RMDQ and ODI)	Not true diagnostic nerve block given (IA joint injection); responders were randomised Anaesthetic: lidocaine 1% (2 ml).
Nath 2008[49]	Radiofrequency denervation 85°C lesion for 60 seconds Multiple lesions made (6 lesions in total, lateral and medial to the first 2 lesions).	Placebo/sham	Low back pain with/without sciatica n=70 Immediate + 6 months follow-up Sweden	Pain severity (VAS) Healthcare utilisation (analgesic consumption)	True diagnostic nerve block given; responders were randomised Had 2 diagnostic blocks: 1. Screening block (patients with at least 80% relief went to have second block); 2. Second block (patients with at least 80% relief and able to participate in the trial were randomised. Anaesthetic bupivacaine 0.5% (2 ml).

Study	Intervention	Comparison	Population	Outcomes	Comments
Tekin 2007[51]	Radiofrequency denervation (conventional) 80°C lesion for 90 seconds Lesions made at the levels concerned	Placebo/sham	Low back pain without sciatica n=60 (N=40 in the 2 relevant arms to this review) Immediate + post-operation + 6 months and 1 year follow-up Turkey	Pain severity (VAS) Function (ODI) Healthcare utilisation (analgesic use) Adverse events (complications)	True diagnostic nerve block given; responders were randomised Anaesthetic prilocaine 2% (0.5 ml) or 0.5% bupivacaine (0.5 ml) given to sham group. NOTE: the trial has 3 arms. The pulsed RF arm does not meet our review inclusion criteria and so results from this arm have not been included.
Van Kleef 1999[50]	Radiofrequency denervation 80°C lesion for 60 seconds Lesion made on 1 or both sides	Placebo/sham	Low back pain with/without sciatica n=31 Immediate + 8 weeks follow-up Netherlands	Pain severity (VAS) Function (ODI) Healthcare utilisation (analgesic use) Responder criteria (≥50% pain reduction)	True diagnostic nerve block given; responders were randomised Anaesthetic lignocaine 1% (1 ml).
Van Wijk 2005[52]	Radiofrequency denervation 80°C lesion for 60 seconds Lesion made on 1 or both sides	Placebo/sham	Low back pain with/without sciatica n=81 Immediate + 3 months and 1 year follow-up Netherlands	Pain severity (VAS) Quality of life (SF-36) Healthcare utilisation (analgesic use) Responder criteria (back pain reduction >50%) Adverse events	Not true diagnostic nerve block given (IA joint injection); responders were randomised Anaesthetic mepivacaine 2% (0.5 ml)

23.3.1 Radiofrequency denervation versus placebo/sham – data unsuitable for meta-analysis

Table 21: Radiofrequency denervation versus placebo/sham for lower back pain

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Van wijk 2005[52]	Back pain (VAS 0-10), change from baseline at ≤4 months	MD: -2.1	40	MD: -1.6	41	Very high
Van wijk 2005[52]	HC utilisation: mean analgesic intake over past 2 weeks (change from baseline) at ≤4 months	MD: -0.1	40	MD: -0.2	41	Very high
Tekin 2007[51]	HC utilisation: analgesic use, % patients at >4 months	40%	20	95%	20	Very high

23.3.2 Clinical evidence summary

Table 22: Radiofrequency denervation compared with placebo/sham for low back pain

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo/sham	Risk difference with RF denervation (95% CI)
Pain (VAS) 0-10 ≤ 4 months	96 (4 studies)	MODERATE[a] due to risk of bias		*	The mean pain (VAS) 0-10 - <4 months in the intervention groups was 1.46 lower (2.06 to 0.86 lower)
Pain (VAS) 0-10 - >4 months	160 (3 studies)	LOW[a] due to risk of bias		*	The mean pain (VAS) 0-10 - >4 months in the intervention groups was 1.57 lower (2.2 to 0.95 lower)
Pain (McGill) ≤ 4 months	30 (1 study)	LOW[a,b] due to risk of		*	The mean pain (McGill) - <4 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo/sham	Risk difference with RF denervation (95% CI)
		bias, imprecision			7 lower (14.11 lower to 0.11 higher)
Pain (McGill) >4 months	30 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean pain (McGill) - >4 months in the intervention groups was 5 lower (20.43 lower to 10.43 higher)
Function ODI 0-100 (change and final values) ≤ 4 months	66 (3 studies)	LOW[a,b] due to risk of bias, imprecision		*	The mean function ODI 0-100 (change and final values) - <4 months in the intervention groups was 4.38 lower (7.31 to 1.45 lower)
Function ODI 0-100 (change and final values) >4 months	40 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean function ODI 0-100 (change and final values) - >4 months in the intervention groups was 5.6 lower (9.59 to 1.61 lower)
Function RMDQ 0-100 (change and final values≤ 4 months	70 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean function RMDQ 0-100 (change and final values) - <4 months in the intervention groups was 2.6 higher (6.21 lower to 11.41 higher)
Quality of life (SF-36) - General health ≤ 4 months	81 (1 study)	MODERATE[a] due to risk of bias		The mean quality of life (sf-36) - general health - <4 months in the control groups was -1.3	The mean quality of life (sf-36) - general health - <4 months in the intervention groups was 3.1 higher (3.72 lower to 9.92 higher)
Quality of life (SF-36) - Mental health ≤ 4 months Scale from: 0 to 100.	81 (1 study)	LOW[a,b] due to risk of		The mean quality of life (sf-36) - mental health - <4 months in the control groups	The mean quality of life (sf-36) - mental health - <4 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo/sham	Risk difference with RF denervation (95% CI)
		bias, imprecision		was 0.7	2 higher (9.07 lower to 13.07 higher)
Quality of life (SF-36) - Pain ≤ 4 months Scale from: 0 to 100.	81 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) - pain - <4 months in the control groups was 11.6	The mean quality of life (sf-36) - pain - <4 months in the intervention groups was 0.2 higher (9.29 lower to 9.69 higher)
Quality of life (SF-36) - Physical functioning ≤ 4 months Scale from: 0 to 100.	81 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) - physical functioning - <4 months in the control groups was 7.8	The mean quality of life (sf-36) - physical functioning - <4 months in the intervention groups was 3.1 lower (11.09 lower to 4.89 higher)
Quality of life (SF-36) - Social functioning ≤ 4 months Scale from: 0 to 100.	81 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) - social functioning - <4 months in the control groups was 2.6	The mean quality of life (sf-36) - social functioning - <4 months in the intervention groups was 2.7 higher (11.7 lower to 17.1 higher)
Quality of life (SF-36) - Vitality ≤ 4 months Scale from: 0 to 100.	81 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) - vitality - <4 months in the control groups was -2.4	The mean quality of life (sf-36) - vitality - <4 months in the intervention groups was 7.7 higher (0.64 to 14.76 higher)
AEs: treatment related pain (moderate or severe) - no. of patients ≤ 4 months	78 (1 study)	LOW[a,b] due to risk of bias, imprecision	RR 1.64 (1 to 2.69)	Moderate	
				359 per 1000	230 more per 1000 (from 0 more to 607 more)
AEs: change of sensibility (irritating or evident dysaesthesia or allodynia) - no. of patients ≤ 4 months	79 (1 study)	VERY LOW[a,b] due to risk of	RR 5.13 (0.25 to 103.45)	Moderate	
				†	†

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo/sham	Risk difference with RF denervation (95% CI)
		bias, imprecision			
AEs: loss of motor function (irritating or evident motor loss) - no. of patients ≤ 4 months	79 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.36 (0.02 to 8.55)	Moderate	
				24 per 1000	15 fewer per 1000 (from 24 fewer to 181 more)
HC utilisation: analgesic use (no. of tablets/4 days) ≤ 4 months	31 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean hc utilisation: analgesic use (no. of tablets/4 days) - <4 months in the intervention groups was 3.24 lower (6.6 lower to 0.12 higher)
HC utilisation: analgesic use (global perception of improvement, 0-6) - >4 months	40 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean hc utilisation: analgesic use (global perception of improvement, 0-6) - >4 months in the intervention groups was 0.8 lower (1.56 to 0.04 lower)
Responder criteria (percentage of patients with >50% pain reduction - global perceived effect) ≤ 4 months	31 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	OR 9.53 (1.05 to 86.28)	Moderate	
				†	†
Responder criteria (number of patients with >50% back pain or pain reduction - global perceived effect) ≤ 4 months	111 (2 studies)	MODERATE[b] due to imprecision	RR 1.74 (1.15 to 2.63)	Moderate	
				390 per 1000	289 more per 1000 (from 58 more to 636 more)
Responder criteria (number of patients with >50% back pain or pain reduction - global perceived effect) ≤ 4 months	31 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 3.73 (0.92 to 15.21)	Moderate	
				390 per 1000	341 more per 1000 (from 10 fewer to 1000 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo/sham	Risk difference with RF denervation (95% CI)
Responder criteria (number of patients with >50% back pain reduction - VAS) ≤ 4 months	81 (1 study)	LOW[b] due to imprecision	RR 0.95 (0.51 to 1.76)	Moderate	
				341 per 1000	17 fewer per 1000 (from 167 fewer to 260 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

* Control rate not reported in study only mean difference given

†Not estimable. No events in control group.

Table 23: Radiofrequency denervation compared with medial branch block for low back pain

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with medial branch block	Risk difference with RF denervation (95% CI)
Pain (VNS) 0-10 - <4 months	100 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean pain (VNS) 0-10 - <4 months in the intervention groups was 1.2 lower (1.79 to 0.61 lower)
Pain (VNS) 0-10 - >4 months	100 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		*	The mean pain (VNS) 0-10 - >4 months in the intervention groups was 2.3 lower (3.42 to 1.18 lower)
Quality of life (EQ-5D) 5-15 scale - <4 months	100 (1 study)	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision		*	The mean quality of life (eq-5d) 5-15 scale - <4 months in the intervention groups was 0.4 lower (0.97 lower to 0.17 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with medial branch block	Risk difference with RF denervation (95% CI)
Quality of life (EQ-5D) 5-15 scale - >4 months	100 (1 study)	VERY LOW[a,b,c] due to risk of bias, indirectness, imprecision		*	The mean quality of life (eq-5d) 5-15 scale - >4 months in the intervention groups was 1.3 lower (2.87 lower to 0.27 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

[c] Downgraded by 1 or 2 increments because of Heterogeneity, I^2=50%, p=0.04, unexplained by subgroup analysis.

* Control rate not reported in study only mean difference given

23.4 Economic evidence

Published literature

One economic evaluation was identified that included radiofrequency denervation as comparator and has been included in this review. [52] This is summarised in the economic evidence profile below (Table 24) and the economic evidence table in Appendix I.

See also the economic article selection flow chart in Appendix F

Table 24: Economic evidence profile: radiofrequency denervation – placebo/sham comparison only

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Van Wijk 2005[52] (Netherlands)	Partially applicable [(a)]	Potentially serious limitations [(b)]	• With-RCT analysis (same paper) • Cost-consequence analysis (various health outcomes) • Population: Low back pain population (with/without sciatica) (> 6 months with focal tenderness over the facet joints) • Two comparators in full analysis: 1. Sham lesion 2. Radiofrequency lesion Follow-up: 3 months [(c)]	2-1: £186 [(d)]	See clinical review van Wijk 2005 (SF-36, VAS-back, global perceived effect on back pain, analgesic intake).	n/a	No relevant analyses available.

(a) Dutch resource use data (1996-1999) and unit costs (year not reported, assumed to be 2003) may not reflect current NHS context. QALYs were not used as the health outcome measure (SF-36 reported, however QALYs were not calculated).

(b) A longer time horizon may be preferable if effects may persist beyond 3 months. Within-trial analysis and so does not reflect full body of available evidence for this comparison; van Wijk 2005 is 1 of 7 studies included in the clinical review for radiofrequency denervation versus placebo sham. No sensitivity analyses undertaken. Source of unit costs unclear.

(c) 1 year data was supposed to be reported by the study, however at this time-point most patients were unblinded and there was loss-to follow-up.

(d) Cost components incorporated: Intervention costs (including staff time, materials, overheads, administration, accommodation and day care facilities), additional medical consumption over 3 month follow-up (medical, paramedical, and pharmaceutical treatment). Intervention costs were the same for both interventions. Study reported the cost of sham lesion to be equal to radiofrequency denervation. Including the cost of a sham was deemed inappropriate and was excluded here

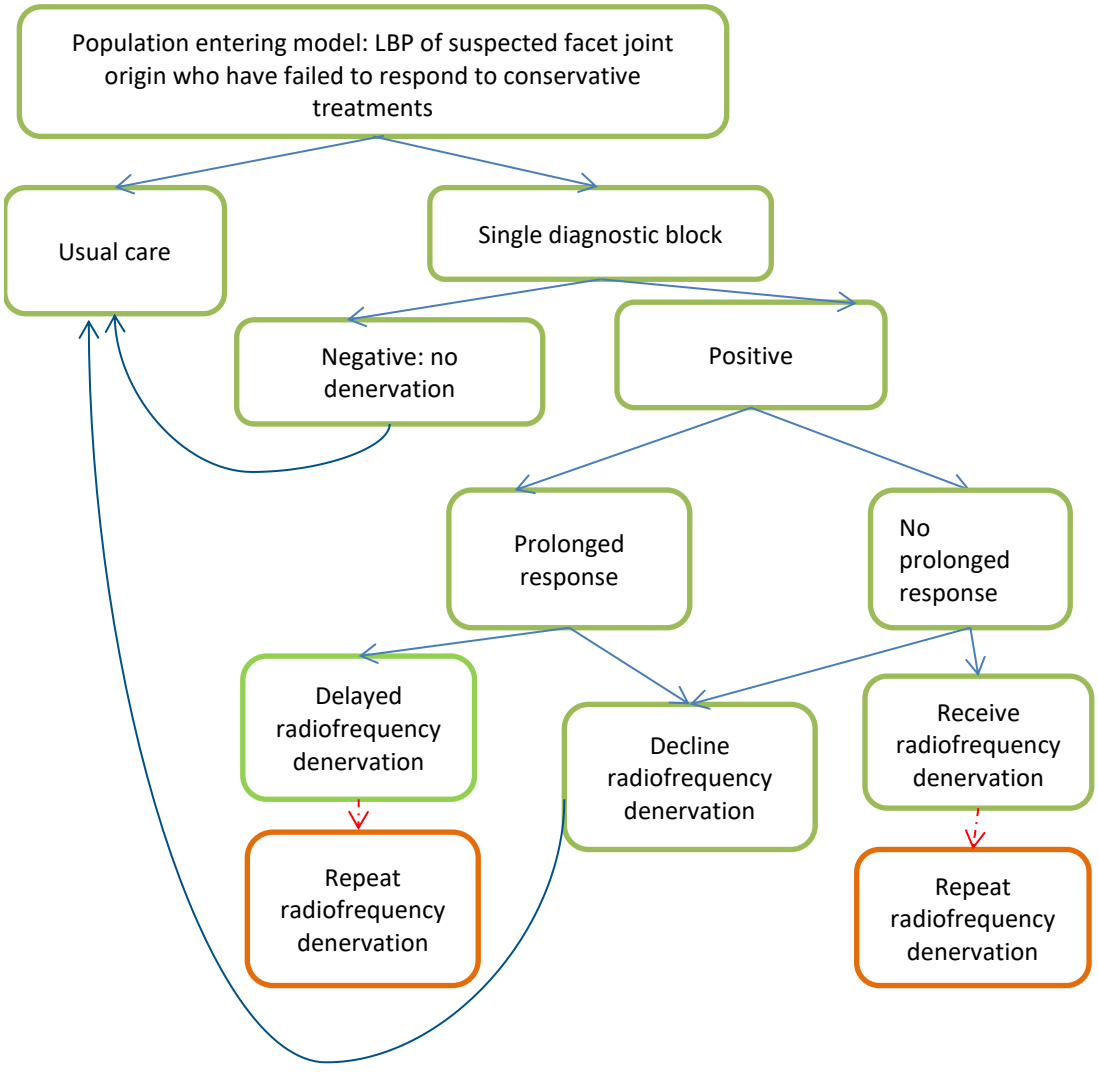
New cost-effectiveness analysis

An original economic analysis was prioritised and conducted for this question. A summary is reported below, while the full description is reported in Appendix N.

Model overview/Methods

The model compares radiofrequency denervation to usual care, defined as active management in primary care. The overall structure of the model is shown in the figure below:

Figure 1: Pathway in the model



The model begins at the point of referral for people with low back pain, suspected to be originating from facet joint pain, where non-invasive management has been unsuccessful. In the radiofrequency

denervation arm the person is given an initial diagnostic block to see if they are likely to respond to radiofrequency denervation. Those who have a negative response to this injection do not receive radiofrequency denervation, and directly receive usual care. A positive response can be temporary or prolonged. Those who do not have a prolonged positive response receive radiofrequency denervation immediately unless they decline the treatment, in which case they receive usual care. If the diagnostic block has a prolonged effect there is a delay in radiofrequency denervation treatment, or again the patient could decline radiofrequency denervation and after this delayed period move to usual care. Sensitivity analysis included repeat radiofrequency denervation procedures.

A time horizon of 28 months was implemented to reflect the duration of the treatment effect for both the diagnostic block and 1 radiofrequency denervation procedure. This is extended to 52 months in the sensitivity analysis to include the possibility of a second radiofrequency denervation procedure. A UK NHS/PSS perspective was taken.

A Markov model with a 1 month cycle was developed to account for natural mortality and additional radiofrequency denervation procedures and was evaluated by cohort simulation. Both costs and outcomes were discounted at 3.5% (and 1.5% for the sensitivity analysis), consistent with the NICE reference case.

The clinical review data for this question provided a cohort population to be analysed that were 35% male, with a mean pain score greater than 4. The entry age into the model was 52 years old.

Key data and assumptions

Probability data:

The probability of a positive response to the diagnostic block was based on a study included in the clinical review.[49] Due to a lack of data, all other probability data in the model were based on GDG opinion. Threshold sensitivity analysis was undertaken to account for this.

Table 25 - Base case probability inputs

Input	Point estimate	Source
Probability of a positive diagnostic block	69%	Nath 2008[49]
Probability of declining radiofrequency denervation after a positive block	10%	GDG opinion
Probability of a prolonged response to diagnostic block	15%	GDG opinion
Proportion of patients repeating radiofrequency denervation after the effect of the first radiofrequency denervation wears off	10%	GDG opinion

Effectiveness data:

Change in pain score measured on the VAS was the intermediate outcome obtained from the systematic review of clinical evidence conducted for the guideline. In this review radiofrequency denervation was compared to sham and the change in pain score was estimated for both at follow up. However in the economic model radiofrequency denervation was compared to usual care, therefore the placebo effect which could be influencing the outcome in the sham arm of the RCTs should be removed from the effectiveness of the usual care arm. To do this, the pain score in the usual care intervention was assumed to be the same as the weighted pain score at baseline in the radiofrequency denervation arm of the RCTs included in the meta-analysis, as patients in the usual

care arm do not receive any intervention, while the pain score after patients receive radiofrequency denervation was the same as that observed at follow-up in the radiofrequency denervation arm of the same RCTs (weighted average).

Using the baseline pain score in the usual care intervention would overestimate the effectiveness of radiofrequency denervation as in reality some patients would also have some spontaneous improvement in pain score over time. For this reason, the base case assumption was varied in a sensitivity analysis where the effectiveness from the sham arm of the RCTs at follow up was used to estimate the effectiveness of usual care and the incremental change with the radiofrequency denervation arm was used to estimate the intervention effectiveness.

There is also the possibility of false positive results from the diagnostic block. However this is taken into account in the mean reduction of pain score in the radiofrequency denervation arm, which would be greater if false positives were minimised.

The model also included an assumption that there is no improvement from the baseline pain score observed in the radiofrequency denervation arm of the included RCTs to account for the fact that the economic model radiofrequency denervation is compared to usual care while in the clinical review the comparator was sham.

Lastly, there was no evidence on the duration of the effectiveness of radiofrequency denervation and was therefore decided by GDG opinion.

Utilities:

No direct data was available to estimate quality of life. Therefore, HRQoL values were determined by using a mapping study by Mueller et al. (2013)[56] to translate the pain scores from the data available from the clinical review conducted for this guideline question into EQ-5D scores using a US tariff. For further detail see Appendix N.

An assumption was made that the pain score and subsequent utility value associated with a prolonged response to diagnostic block is equal to the score/utility of radiofrequency denervation.

Table 26 - Effectiveness data used in the base case model

	Usual care	Prolonged diagnostic block	Radiofrequency denervation
Pain score	5.7	3.6	3.6
Associated EQ-5D	0.5992	0.6846	0.6846
Duration of pain relief (months)	NA	4	24

Cost data:

All costs included in the model were 2013/14 NHS reference costs, as shown in the table below. An assumption was made that patients receiving usual care will not incur additional costs compared to patients who received radiofrequency denervation or prolonged response diagnostic block. This is a very conservative assumption and was therefore varied in sensitivity analysis.

Table 27 - Base case cost inputs

Input	Cost	Source
Initial outpatient appointment	£168	Based on a Consultant-led outpatient appointment, First Non-Admitted Face to Face Attendance, Service: Pain management (NHS reference costs 2013/2014)
Diagnostic block	£521	Based on HRG code: AB05Z Intermediate Pain Procedures (NHS reference costs 2013/2014)
Follow-up appointment (telephone/face-to-face)	£121	Based on non-Consultant-led outpatient appointment, Follow-up Non-Admitted Non-Face to Face Attendance, Service: Pain management / Consultant-led outpatient appointment, Follow-up Non-Admitted Face to Face Attendance, Service: Pain management (NHS reference costs 2013/2014)
Radiofrequency denervation	£640	Based on HRG code: AB08Z - Pain Radiofrequency Treatments (NHS reference costs 2013/2014)

Sensitivity analysis:

Both probabilistic and deterministic sensitivity analysis were undertaken to account for model uncertainty. For more information on the distribution used for each parameter in the probabilistic sensitivity analysis see Appendix N.

[Deterministic] sensitivity analysis undertaken:

- A repeat denervation after the first wears off
- Pain score using sham data from meta-analysis
- Pain score excluding Leclaire 2001
- A positive diagnostic block assumed to be less effective than radiofrequency denervation
- Using the cost of referral to an interface clinic (around 80% of consultant)
- Threshold analysis on the probability of positive diagnostic block
- Two-way sensitivity analysis where the duration of effects for both radiofrequency denervation and block were decreased to 0 and 4 months respectively.
- Threshold analysis for the proportion of people declining radiofrequency denervation
- Threshold analysis for the proportion of people repeating radiofrequency denervation within SA1
- After the effect of the first radiofrequency denervation wears off patients receive another and the duration of effect of radiofrequency denervation is varied in a threshold analysis.
- Costs and effects discounted at 1.5%.

Results

The model was run 10,000 times using different parameter values chosen from the distribution assigned to each of the parameters to account for the uncertainty in the model. The table below shows that in this base-case analysis radiofrequency denervation is cost effective.

Table 28 - Base case results (probabilistic analysis)

Strategy	Mean cost per patient (£)	Incremental costs (£)	Mean QALYs per patient	Incremental QALYs	ICER (£ per QALY gained)	Probability that strategy is most cost-effective [£20k per QALY]
Usual care	0		2.1402	0	0	30%
radiofrequency denervation	1282	1282	2.2549	0.1147	11,178	70%

Radiofrequency denervation remains cost-effective at a threshold of £20,000 per QALY in all sensitivity analyses, except if the duration of radiofrequency denervation is less than 16 months, if the probability of declining radiofrequency denervation is greater than 50% and if the probability of a positive diagnostic block is less than 40%.

Limitations and interpretation

The model was built around some important assumptions such as the duration of pain relief after a prolonged response to diagnostic block and radiofrequency denervation.

There were also some deviations from the NICE reference case, such as the use of mapping functions to estimate EQ5D values from an intermediate outcome and the use of the USA EQ5D tariffs. The uncertainty around the EQ5D scores could not be captured in the probabilistic model as the software did not allow us to link probabilistic value of the pain score to a distribution around the relevant utility value.

Another important limitation of the model is the quality of the clinical evidence around the effectiveness of radiofrequency denervation; these studies were low to moderate quality and their limitations are explained in section 23.3. As there was no data on radiofrequency denervation versus usual care and there was the assumption that people in the usual care arm would maintain the initial pain score, in reality there could be an improvement over time. This was however addressed in a sensitivity analysis where data from the placebo arm were used instead.

The GDG considered the various limitations of the model together with the main results and concluded that although radiofrequency denervation is a cost effective intervention in the base case analysis and in various sensitivity analyses, there is not enough confidence to make a firm recommendation for this intervention. In addition, as the low back pain population is wide, there are concerns on the potential cost impact of a firm recommendation if many people were eligible for the intervention.

Unit costs

The breakdown of the cost for radiofrequency denervation in a person who responds positively to a diagnostic block and then receives radiofrequency denervation is detailed below and in **Table 29**.

For radiofrequency denervation, the process from referral would usually be:

1. Initial outpatient appointment, usually with a pain medicine consultant.
2. Diagnostic block - based on HRG code: AB05Z Intermediate Pain Procedures.
3. Radiofrequency denervation dependent on diagnostic block – based on HRG code: AB08Z Pain Radiofrequency Treatments.

4. Follow up appointment, usually a telephone consultations with a nurse specialist.

Table 29: Radiofrequency denervation: unit costs

Component	Unit cost	Source/notes
Cost if diagnostic block is positive and radiofrequency denervation undertaken		
Initial outpatient appointment	£168	Based on a Consultant-led outpatient appointment, First Non-Admitted Face to Face Attendance, Service: Pain management (NHS reference costs 2013/2014)[57,58]
Diagnostic block	£521	Based on HRG code: AB05Z Intermediate Pain Procedures (NHS reference costs 2013/2014)[57,58]
Radiofrequency denervation	£640	Based on HRG code: AB08Z Pain Radiofrequency Treatments (NHS reference costs 2013/2014)[57,58]
Follow-up appointment	£121	Based on non-Consultant-led outpatient appointment, Follow-up Non-Admitted Non-Face to Face Attendance, Service: Pain management (NHS reference costs 2013/2014)[57,58]
Total cost per patient	**£1,450**	

23.5 Evidence statements

23.5.1 Clinical

23.5.1.1 Radiofrequency denervation compared with placebo/sham for low back pain

Evidence from 4 studies demonstrated clinical benefit in pain for radiofrequency denervation compared to placebo/sham at both the short and long term follow-ups of less than and greater than 4 months (low to moderate quality, n=160). In contrast there was no difference in function between treatments at any time point. Conflicting evidence from 1 study for quality of life at less than 4 months follow up showed clinical benefit for radiofrequency denervation compared to placebo/sham for the SF-36 domains of general health and vitality. Radiofrequency denervation was inferior to sham for the domains of mental health, pain and social function. There was no difference between treatments for the domain physical function (low quality, n=81). Evidence from a single study reporting adverse events at less than 4 months follow up demonstrated an increase in adverse effects for radiofrequency denervation in terms of the number of patients with moderate or severe treatment related pain(low quality, n=79). There was no difference in other adverse events (change of sensibility and loss of motor function) at short term follow up when radiofrequency denervation was compared to placebo/sham in the same study (very low quality). Additionally when compared with placebo/sham, benefit for radiofrequency denervation in responders to pain reduction measured by global perceived effect was demonstrated by 2 studies at both the less than and greater than 4 months follow up time points although this was not seen for pain reduction measured by VAS at less than 4 months reported by a single study (low quality, n=111).

23.5.1.2 Radiofrequency denervation versus medial branch block

Evidence from a single study demonstrated clinical benefit in terms of pain for radiofrequency denervation compared to medial branch blocks at both the short and long term follow-ups of less than and greater than 4 months (very low quality, n=100).

23.5.2 Economic

One cost-consequence analysis found that radiofrequency denervation was more costly and more effective (£186 more per patient, SF-36 general health and vitality and global perception of reduction in back pain and pain responder criteria) compared to sham for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.

One original economic model found that radiofrequency denervation was cost effective compared to usual care for treating low back pain suggestive of facet joint origin that has not resolved despite non-invasive management (ICER £11,178). This analysis was assessed as partially applicable with potentially serious limitations.

23.6 Recommendations and link to evidence

Recommendations	**The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations**
Research recommendations	**The current research recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations-for-research**
Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Responder criteria (>30% for pain and function), adverse events, and healthcare utilisation were also considered as important. Evidence was reported for all of the critical outcomes except for psychological distress, and there was evidence for all of the outcomes that were considered important for this review.
Trade-off between clinical benefits and harms	**Radiofrequency denervation versus placebo/sham** Pain relief (VAS) was seen in studies in both the short term (up to 4 months) and long term (greater than 4 months). However, there was no clinical benefit seen in terms of function (for both ODI and RMDQ). The GDG noted that the baseline ODI scores reported in the study informing this outcome were different between groups and both groups were in the 'minimal disability' range post intervention. The RMDQ scale reported by 1 study was not reported in a standard way and had been converted to a 0-100 scale by the authors, with higher scores indicating benefit, rather than the standard 0-24 scale where higher scores indicate decline in function. Therefore the GDG were not able to place much confidence in these outcomes. For quality of life (SF-36), evidence from a single study showed clinical benefit for the domains of general health and vitality. However, in terms of physical function, the benefit was in favour of the placebo group. It was noted however that there were large baseline differences for physical function between the intervention and sham groups, with the intervention groups being 10 points worse at baseline, and that this data showing benefit to the placebo group was not considered reliable. The GDG therefore agreed that the benefits seen in quality of life outweighed the harm. The GDG also noted that 1 study selectively reported domains of SF-36; for role physical and role emotional scales, the results were reported in terms of 'number of

patients who went up or down by 1 or more classes' rather than mean differences, which is not standard reporting of SF-36 data and therefore were not able to be included in this systematic review.

The GDG noted there was limited data on adverse events from the included evidence, and they considered it alongside their expert opinion and knowledge to inform decision making. Only 1 study reported adverse event data, and reported no adverse events (in terms of complications) in either the placebo or the radiofrequency arms. However the GDG noted that there was clinically significant harm for the radiofrequency group in terms of treatment-related pain (graded as moderate/severe) at the short term. It was noted that there was some treatment-related harm in the sham group as well, so both groups experienced pain that was considered to be related to the procedure. Data were only reported for less than 4 months but the GDG noted that one would not expect any treatment-related pain to occur beyond 4 months. The study reported 2 adverse events (5%) which were change of sensibility (dysaesthesia or allodynia) in the radiofrequency denervation group. The GDG noted that these particular adverse events were important outcomes to the patient, although the event rate in the study was very small, it was higher than expected (based on the GDG's clinical experience). However the size of the study itself was very small (n=79) and only reported this outcome at less than 4 months. The group therefore agreed that although the effect size for these adverse events was considered clinically important, because of the concerns noted, they did not have confidence in extrapolating this data to clinical practice. The GDG also considered that although allodynia may occur, it is likely to only affect a small number of patients. They concluded that as the risk is low and the 5% seen in the evidence is higher than would be expected, the benefits observed in terms of pain and quality of life outweighed this risk of harm. The study additionally reported 'loss of motor function' as an adverse event. The event rate was extremely small (zero events versus 1 event in the radiofrequency group and placebo/sham group respectively). This was considered as clinically important, but again due to the study having a small sample size, short duration of follow up, and low event rate, this risk of harm was also not considered to outweigh the benefits. The GDG considered that although there was limited data from the included studies on adverse events, there are no case reports that the GDG are aware of reporting serious complications (such as paralysis or death) from radiofrequency denervation.

Several studies looked at analgesic use following the procedure at less than four months. There was no detail provided regarding number of treatments per day or what the baseline medication intake was. The GDG considered that there was no clinically important difference between groups, but this could not be accurately interpreted from the data reported. Patient perception of their global improvement of analgesic use rated on a 0-6 scale, at greater than 4 months was reported by 1 study. This was noted as a small effect on a scale that was difficult to interpret or determine whether there was benefit or not and did not consider it informative for decision making.

The GDG considered the evidence for responder criteria (≥50% reduction in pain) which was reported by several studies. There was clinical benefit at both short and long term follow up for global perception of reduction in back pain and pain; however there was no difference in the short-term in reported peak pain on VAS (median of 4 measurements). It was noted that this was from the same study, but as the study only reported 'peak pain' the global perception of pain reduction may be more informative.

The GDG noted that 2 of the studies included in the review did not include a true diagnostic medial branch block and this may have resulted in an unselected patient

	population. The majority of studies used 1 diagnostic medial branch block. The GDG were mindful that had all studies included a true medial branch block, the effect size may have been larger. **Radiofrequency denervation versus medial branch block** One study compared radiofrequency denervation with medial branch block (with a local anaesthetic and steroid). The GDG noted that the study only looked at 2 outcomes relevant to this review; pain and quality of life assessed by EQ-5D. There were no data reported for adverse events. Pain assessed on a VNS was lower in the group receiving radiofrequency denervation at both short and long-term follow-ups, and this reduction was considered clinically important. The quality of life data (EQ-5D) showed no clinical difference between interventions but the GDG noted that the EQ-5D data was incompletely reported, and had not been analysed in the typical format that is appropriate for EQ-5D (i.e. summarised as a scale of 0-1; it was not weighted or in a linear scale). They were therefore unable to interpret the EQ-5D data and so it was not considered to be useful for decision-making.
Trade-off between net clinical effects and costs	One cost-consequence analysis was identified that compared radiofrequency denervation with sham. This study reported higher cost with radiofrequency denervation (£186 when cost of sham is excluded as not real world treatment option). This within-trial analysis was 1 of seven studies included in the clinical review for radiofrequency denervation. It was the only study reporting adverse events and health related quality of life. However, unlike the other studies, it does not report function or pain outcomes (with the exception of responder criteria) and therefore it is difficult to determine whether or not this study reflects the wider body of evidence. A detailed summary of the clinical outcomes are summarised in the 'Trade-off between clinical benefits and harms' section above. This study was judged by the GDG to show benefit for radiofrequency denervation with regards to health related quality of life and the global perception of reduction in back pain and pain responder criteria. The reported change of sensibility (adverse event) for radiofrequency denervation was considered by the GDG, and they felt it did not outweigh the benefits. As QALYs weren't calculated it is not possible to judge if it is cost effective. It was noted that in this study participants did not receive a diagnostic block but rather an intra-articular injection and therefore the selection of eligible patients for radiofrequency denervation may not reflect current practice. Furthermore, the GDG highlighted that the intervention cost outlined in the study (£197) is lower than current practice. Finally, the GDG noted that this procedure would require a follow-up appointment either in person or by telephone. This was not detailed in the study. The unit cost of radiofrequency denervation was estimated to be £1,450 per person who had a positive response to a diagnostic block and went on to receive radiofrequency denervation (NHS reference costs 2013-2014[58]). This cost includes an initial consultant-led outpatient appointment with the pain management service, a diagnostic block (HRG code AB05Z: intermediate pain procedure), radiofrequency denervation (HRG code AB08Z: pain radiofrequency treatments) and a non-consultant-led non-face to face outpatient appointment. Given that radiofrequency denervation reduces pain it is plausible that downstream healthcare utilisation (such as other interventions) might also be reduced however there was very little evidence regarding this.

	An original economic model was built for this guideline; this was based on pain score reported in the clinical review conducted for this guideline and also on some expert opinion for duration of treatment effects. The population in the model reflects the population included in the RCTs, who were people with a pain score of 5 or more. The model showed that radiofrequency denervation is cost effective in the base case compared to usual care. The pain score at baseline was used for the usual care arm instead of the pain score in the placebo arm of the trials to reflect what would happen in real life. This was varied in a sensitivity analysis which showed that radiofrequency denervation was still cost effective if pain score for usual care was obtained from the placebo arm. The results were sensitive to the duration of the intervention; in the base case it was assumed that the pain relief from radiofrequency denervation would last for 24 months; when this was less than 16 months radiofrequency denervation was not cost effective anymore as the ICER would go above the £20,000 per QALY threshold. No imaging before the procedure was considered in the model as the GDG experts advised this would not be required and therefore would be an inefficient use of NHS resources. The GDG considered the various limitations of the model together with the main results and concluded that although radiofrequency denervation is a cost effective intervention in the base case analysis and in various sensitivity analyses, there was not enough confidence to make a strong ('offer') recommendation for this intervention. In addition, as the low back pain population is potentially very large, the GDG expressed concern about the potential cost impact of a strong recommendation. The committee agreed the recommendation should include the criteria that should be met before radiofrequency denervation should be considered. It was noted there were several criteria limiting the likelihood of radiofrequency denervation being carried out and therefore, even in the context of the guideline as a whole, they did not expect this recommendation to generate a significant resource impact.
Quality of evidence	In this review, most of the studies reported evidence for radiofrequency denervation versus placebo/sham and 1 study compared radiofrequency denervation to medial branch block. Seven RCTs relevant to the review protocol were identified. The GDG deemed this sufficient evidence to base a recommendation on and therefore the search was not extended to cohort studies. The GDG noted that the favourable (clinically important) evidence of radiofrequency for improvement of pain, quality of life and responder criteria (in terms of pain) was mostly moderate and low quality. Although a number of the trials were small, the data for pain came from 4 trials. The GDG did not place much confidence in the study comparing radiofrequency denervation with medial branch block. This was because although the study met the inclusion criteria of the review, the methods used did not follow current clinical practice (diagnostic medial branch block was not performed on any of the participants prior to randomisation), but rather, all participants were randomised to radiofrequency denervation or a medial branch block (which would not pre-select those who were most likely to respond to treatment). Additionally, people in both groups were given additional therapy in the form of a rehabilitation programme if they showed a post-intervention response. The GDG highlighted limitations that could be drawn from the study by LeClaire et al. It was noted that a letter to the editors was published by the authors acknowledging some of the methodological limitations. [59] In particular the criteria used to select patients, as the study was carried out prior to medial branch blocks

	being commonly used for diagnostic purposes. This resulted in the study enrolling 94% of back pain patients from a pain clinic. The GDG estimate and are aware of research showing that the proportion of back pain patients whose pain is related to the facet joint is approximately 40-60% in clinical practice, and therefore this study likely includes a large proportion of patients who would not have facet joint pain and would not be expected to benefit from this treatment. For function (ODI), the GDG noted that post intervention value for the radiofrequency denervation group was very low (and was 10 points lower for physical function than the control group). This meant that the modest improvement seen may be as a consequence of the 'ceiling effect'. The quality of the evidence was therefore downgraded to reflect this. Some quality of life characteristics were only reported as numbers up and numbers down, which further reduced the quality of the data. The same study additionally reported baseline differences between the groups for a few of the quality of life domains, and the evidence for this outcome was therefore downgraded as a result. The GDG recognised that many of the studies of radiofrequency denervation are compared with placebo/sham rather than usual care or waiting list control, which was the most common comparison with other non-invasive interventions reviewed in the guideline. It was also noted that the study reporting analgesic use ended blinding at 3 months and did not provide a definition of whether the analgesic use measured was prescribed or not. The GDG noted that in the study comparing radiofrequency denervation with a medial branch block, responders 1 week after treatment (in both arms) were entered into a rehabilitation programme which may affect subjective outcomes, but as this was for both arms, this was not considered to be a limitation to the study. The economic evaluation was assessed as partially applicable with potentially serious limitations.
Other considerations	The GDG highlighted that all of the evidence came from populations with chronic pain (ranging from 2 to 3 years duration or longer) who had failed to respond to conservative treatment. The mean pain scores in the studies reviewed was >5 and the GDG considered that this would reflect the population for which RF might be appropriate. It was agreed that the recommendation should emphasize that this treatment should be considered only for that population (people with chronic pain with a score of 5 or more on a visual analogue scale, or equivalent) and not for all people with low back pain. The GDG noted that current clinical practice is to administer a single initial diagnostic medial branch block to identify the population who might respond to radiofrequency denervation, and that the majority of the studies included in this review conformed to this practice. The GDG also agreed that patients who experienced prolonged pain relief from medial branch blocks (i.e. an analgesic effect outlasting the expected duration of local anaesthesia) should be offered radiofrequency denervation rather than repeated medial branch blocks when seeking further treatment. The GDG agreed that this recommendation would equally apply for pregnant women and this should be considered on a case by case basis. The GDG were concerned about the potential for re-referrals as some nerve regrowth may be expected after the procedure. The GDG were aware of a study finding that of 55 patients, 17 had repeat procedures. It was noted that the

subgroup involved would have been patients that had not responded well to any other intervention.

The health economic model suggests that radiofrequency denervation is cost effective over usual care provided the duration of pain relief exceeds 16 months. However, the GDG did not review the evidence for repeat radiofrequency denervation. The GDG were aware of the recent development of a National Spinal Radiofrequency Registry and would encourage clinicians performing this intervention to submit patient outcome information to this database. The GDG agreed that clinicians should be cautious about recommending repeat denervation procedures until longer term effectiveness data becomes available. They agreed that a research recommendation was required to inform long terms outcomes from radiofrequency ablation, beyond the timeframe of evidence in this review.' In terms of cost and implementability, the GDG noted that it would be helpful for clinicians to be able to identify patients who may be suitable for this intervention. Although no reliable clinical features or physical signs identify 'facet joint pain' accurately, a recent UK based consensus group have published clinical features suggestive of a facet joint pain component.[60] The GDG agreed that the features identified by the consensus group might be helpful in identifying those patients who may benefit from a radiofrequency denervation.

- The features include: Increased pain unilaterally or bilaterally on lumbar para-spinal palpation
- Increased back pain on 1 or more of the following:
  - extension (more than flexion)
  - rotation
  - extension/side flexion
  - extension/rotation

AND

- No radicular symptoms

AND

- No sacroiliac joint pain elicited using a provocation test.

Radiofrequency denervation is a technically demanding procedure and should only be performed by appropriately trained clinicians.

Research recommendation

The lumbar facet joints are pairs of joints that stabilize and guide motion in the spine. These joints and periarticular structures are well innervated by the medial branches of the dorsal rami. The prevalence of pain thought to be arising from the facet joints and periarticular structures in heterogeneous populations using local anaesthetic nerve blockade (medial branch block), where 75–100% pain relief is used as a criterion standard, is thought to be 25–40%. (Manchikanti, 2000[45]).

The current guidance recommends that for people with low back pain who have failed to respond to conservative management, local anaesthetic medial branch nerve blockade to determine the presence or absence of a pain arising from the facet joints and periarticular structures may be offered. Those who experience significant but short term relief may then be offered a neurodestructive procedure called 'radiofrequency denervation' in an attempt to achieve longer term pain relief.

Radiofrequency denervation has evolved as a treatment for spinal pain over the last 40 years and is a minimally invasive and percutaneous procedure performed under local anaesthesia or light intravenous sedation. Radiofrequency energy is delivered along an insulated needle in contact with the target nerves. This focussed electrical

	energy heats and denatures the nerve. This process may allow axons to regenerate with time requiring the repetition of the radiofrequency procedure. The duration of pain relief following radiofrequency denervation is uncertain. Data from randomised controlled trials suggests relief is maintained for at least 6-12 months but no study has reported longer term outcomes. Pain relief for more than 2 years would not be an unreasonable clinical expectation. The de novo economic model undertaken for this guideline for radiofrequency denervation suggested that the treatment is likely to be cost effective provided the duration of effect exceeds 16 months. If radiofrequency denervation is repeated, we do not know whether the outcomes and duration of these outcomes are similar to the initial treatment. If repeated radiofrequency denervation is to be offered, we need to be more certain that this intervention is both effective and cost effective.

24 Epidural injections for sciatica

24.1 Introduction

The epidural space lies within the spinal canal, outside the dura mater, and contains the spinal nerve roots, fat, connective tissue and blood vessels. An epidural injection is an injection of a therapeutic substance into this canal. Administration may involve a caudal injection at the base of the spine, in the midline between the vertebral laminae (interlaminar epidural) or laterally, through the intervertebral foramen (transforaminal epidural, nerve root injection, dorsal root ganglion injection).

The most commonly used epidural injectate for the management of sciatica is corticosteroid, with or without local anaesthetic. The immunosuppressant and anti-inflammatory effects of corticosteroids provide a theoretical basis and rationale for epidural injection. However, some studies suggest that local anaesthetic epidural injection alone may also be therapeutic. Recent studies have also examined the role of anti-TNF (Tumour Necrosis Factor) agents into the epidural space on the premise of a TNF-α mediated inflammatory mechanism.

Although performed widely since the 1950s, the administration of steroids into the epidural space remains unlicensed. HES data from 2010–2011 estimates that nearly 79,000 epidural and nerve root injections were performed in England.[61]

Currently there are areas of uncertainty beyond the effectiveness of epidural injections to be considered, including the ideal route of administration, the use of imaging to improve accuracy, the timing of injection and the safety profile.

24.2 Review question: What is the clinical and cost effectiveness of epidural injections in the management of people with sciatica?

For full details see review protocol in Appendix C.

Table 30: PICO characteristics of review question

Population	People aged 16 or above with sciatica and:
	• Primarily (≥70%) disc prolapse (likely to be confirmed by imaging), other spinal pathologies may or may not also be present.
	• Primarily (≥70%) not disc prolapse (confirmed by imaging).
	• Mixed population / unclear spinal pathology (no clinical diagnosis);
	  ○ Trial participants required to have pathology confirmed by imaging but could have either disc prolapse or other spinal pathology for inclusion.
	  ○ Pathology not confirmed (may or may not have had imaging).

Interventions	• Steroid (including steroid and saline) • Local anaesthetic • Anti-tumour necrosis factor (TNF) • Combination: local anaesthetic and steroid
Comparisons	• Sham (needle alone) / placebo / saline • Usual care • Each other (including head to head comparisons between strata)

	• Other treatment (non-invasive and invasive treatments being considered by the guideline for sciatica)

Outcomes	**Critical**
	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).
	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).
	• Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BDI, STAI)
	Important
	• Responder criteria (>30% improvement in pain or function)
	• Adverse events:
	  ○ morbidity
	  ○ mortality
	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit, surgery)

Study design	RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found, non-randomised studies will be included.

24.3 Clinical evidence

24.3.1 Clinical evidence summary: Image guided epidurals

Twenty RCTs were included in the image-guided epidurals part of the review, of which 3 were reported in 7 studies, giving a total of 24 studies; these are summarised in **Table 31** below.[62-85] Karppinen 2001 was also reported in Karppinen 2001A, Manchikanti 2008 was also reported in Manchikanti 2012B and 2012I and Riew 2000 was also reported in Riew 2006. Evidence from these studies is summarised in the GRADE clinical evidence profile/clinical evidence summary below. See also the study selection flow chart in Appendix E, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

There was no RCT data that could be incorporated in this review for the comparison of steroid versus placebo/sham. The search was therefore widened to look for cohort study data for this comparison; however no relevant cohort studies were identified. A combined search for the epidurals injections for sciatica review and the spinal injections review identified four Cochrane reviews [34-37]. One of them[36] was not included as it included studies in people with neuropathic pain syndromes and not low back pain. The others reviews[34,35,37] were not included as the stratification of people with low back pain, low back pain with or without sciatica and sciatica was unclear, however any relevant studies included in the reviews were included and re-extracted in this review where appropriate. The studies included in these Cochrane reviews were individually assessed and included if they matched the protocol.

24.3.1.1 Heterogeneity

For the comparison of steroid and anaesthetic versus anaesthetic (>70% prolapse), there was substantial heterogeneity between the studies when they were meta-analysed for pain, responder criteria for pain (>50% reduction in pain) at both short and long term follow-ups, and for responder criteria for function at less than 4 months. Pre-specified subgroup analyses, by route of administration were performed on these outcomes which mostly explained the heterogeneity for

pain at longer term follow-up and responder criteria for pain at both time points. Heterogeneity remained for pain and responder criteria for function at less than 4 months however. A random effects meta-analysis was therefore applied to these 2 outcomes, and the evidence was downgraded for inconsistency in GRADE.

For the comparison of steroid and anaesthetic versus anaesthetic (mixed population / unclear spinal pathologies), there was substantial heterogeneity between the studies when they were meta-analysed for pain at and function (ODI) at less than 4 months. Pre-specified subgroup analyses were performed on these outcomes however it did not explain the heterogeneity for pain, and could not be applied to because all of the studies used the same route of administration. A random effects meta-analysis was therefore applied to these 2 outcomes, and the evidence was downgraded for inconsistency in GRADE.

Table 31: Summary of studies included in the review: image- guided

Study	Intervention	Comparison	Population	Outcomes	Comments
Steroid versus placebo/sham/usual care					
Kraemer 1997[74]	Steroid (triamcinolone – 10mg)	Saline	Intractable sciatica (hospitalised patients) All had disc protrusion N=49 Immediate (single injection); unclear follow-up Germany	Major adverse events	Data was not included in this review because the outcomes reported were graphically presented only.
Koc 2009[73]	Steroid(10 mL of solution containing 60 mg of triamcinolone acetonide (1.5 mL), 15 mg of 0.5% bupivacaine hydrochloride (3 mL), and 5.5 mL of physiologic saline (0.9% NaCl)	Usual care (home-based therapeutic exercise program consisting of stretching exercises for the hip flexors, hamstrings and lumbar paraspinal muscles, and strengthening exercises for abdominal and gluteal muscles to be	Spinal stenosis N=34 Immediate (single injection); 6 month follow up Turkey	Pain (VAS; data reported as medians) Function (physical mobility, data reported as medians)	Image guidance method: fluoroscopic Concomitant treatment: Patients used a home-based therapeutic exercise program consisting of stretching exercises for the hip flexors, hamstrings and lumbar paraspinal muscles, and strengthening exercises for abdominal and gluteal muscles to be performed twice daily for a

Study	Intervention	Comparison	Population	Outcomes	Comments
		performed twice daily for a period of 6 months, and oral diclofenac sodium 75 mg twice a day for 2 weeks.			period of 6 months, and oral diclofenac sodium 75 mg twice a day for 2 weeks.
Anaesthetic versus placebo/sham					
Ghahreman 2010[68]	Anaesthetic 0.75ml of 0.5% bupivacaine Transforaminal injection NOTE: This study also had 2 additional arms which did not meet our protocol, and so the data were not extracted for these (IM steroid and IM saline). The additional steroid + anaesthetic arm data has been extracted elsewhere in this review.	Saline	Lumbar radicular pain Hernia N=150 in all 5 arms Immediate (up to 3 injections) + 1 year follow-up Australia	Pain Responder criteria (>50% reduction in pain) Healthcare use: surgery	Image guidance method: fluoroscopic Concomitant treatment: rescue therapy (analgesics, surgery or open-label steroids)
Steroid + anaesthetic versus placebo/sham					
Autio 2004[62]	Steroid + anaesthetic (methylprednisolone 40mg/ml +bupivacaine 5mg/ml) Periradicular infiltration	Saline	Unilateral sciatica Hernia N=160 Immediate (single injection) + 2 year follow-up Europe	No relevant outcomes reported, so this study was included, but no data extracted.	Image guidance method: fluoroscopic Concomitant treatment: none reported
Ghahreman 2010[68]	Steroid + anaesthetic (1.75 ml of triamcinolone 40mg/L + 0.75ml of 0.5% bupivacaine).	Saline	Lumbar radicular pain Hernia N=150 in all 5 arms	Pain Responder criteria (>50% reduction in pain) Healthcare use: surgery	Image guidance method: fluoroscopic Concomitant treatment: rescue

Study	Intervention	Comparison	Population	Outcomes	Comments
	Transforaminal injection NOTE: This study also had 2 additional arms which did not meet our protocol, and so the data were not extracted for these (IM steroid and IM saline). The additional anaesthetic arm data has been extracted elsewhere in this review.		Immediate (up to 3 injections) + 1 year follow-up Australia		therapy (analgesics, surgery or open-label steroids)
Karppinen 2001 / 2001A [71,72]	Steroid + anaesthetic (methylprednisolone 40mg/mL + 5mg/mL bupivacaine). Periradicular (transforaminal) infiltration	Saline	Lumbrosacral radicular pain Mostly hernia N=160 Immediate (single injection) + 3 and 6 months and 1 year follow-up Finland	Pain Function: ODI NOTE: pain data reported as the mean difference in the study was found to be incorrect and so the data has been calculated as a change from baseline. No SDs were given for the baseline values and therefore these scores cannot be meta-analysed and so have been reported narratively in this review.	Image guidance method: fluoroscopic Concomitant treatment: both groups received back school instructions; if pain was persistent patients received pain medication and traditional physiotherapy.
Anti-TNF versus placebo					
Cohen 2009[64]	3 arms of different doses: 2mls of etanercept mixed in sterile water – doses of 2mg, 4mg, and 6mg Transforaminal epidural	Saline, 2mls.	Unilateral radiating pain dermatomally from the back to below the knee Hernia N=24	Pain (NRS) Function: ODI Healthcare use (% reduction in medication) Adverse events	Image guidance method: fluoroscopic Concomitant treatment: both groups could receive rescue medication

Study	Intervention	Comparison	Population	Outcomes	Comments
			Immediate (1 or 2 injections depending how many levels affected) + 3 and 6 months follow-up USA		(NSAID or tramadol) if they had debilitating pain.
Freeman 2013[66]	3 arms of different doses: Etanercept 0.5mg, 2.5mg, and 12.5mg Transforaminal epidural	Placebo (details not reported)	Lumbrosacral radicular pain Hernia N=160 2 injections,(2 weeks apart)+ 26 weeks follow-up Europe	Pain Function: ODI Adverse events	Image guidance method: contrast flow/ fluoroscopic Concomitant treatment: none mentioned
Steroid versus anaesthetic					
Ghahreman 2010[68]	Steroid (1.75 ml of triamcinolone 40mg/L) Transforaminal injection NOTE: This study also had 2 additional arms which did not meet our protocol, and so the data were not extracted for these (IM steroid and IM saline). The additional placebo epidural arm has been compared to each of the interventions in another part of this review	Anaesthetic (0.75ml of 0.5% bupivacaine)	Lumbar radicular pain Hernia N=150 in all 5 arms Immediate (up to 3 injections) + 1 year follow-up Australia	Pain Responder criteria (>50% reduction in pain) Healthcare use: surgery	Image guidance method: fluoroscopic Concomitant treatment: rescue therapy (analgesics, surgery or open-label steroids)
Anti-TNF + anaesthetic versus anaesthetic					
Cohen 2012[65]	Anti-TNF + anaesthetic (4mg etanercept + 0.5% bupivacaine)	Anaesthetic(0.5% bupivacaine) + saline	Lumbosacral radiculopathy Hernia or annular tear (% not given) N=84	Pain (NRS) Function: ODI Responder criteria (>50% improvement in pain)	Image guidance method: fluoroscopic Concomitant treatment: both

Study	Intervention	Comparison	Population	Outcomes	Comments
	NOTE: The additional steroid + anaesthetic epidural arm has been compared to each of the interventions in another part of this review.		Immediate (1 or 2 injections); 1, 3 and 6 months follow-up. USA	Adverse events	groups could receive rescue medication (opioid increase, or NSAID or tramadol) if they had debilitating pain.
Steroid + anaesthetic versus anaesthetic					
Cohen 2012[65]	Steroid + anaesthetic (60 mg methylprednisolone + 0.5% bupivacaine) Transforaminal injection NOTE: The additional anti-TNF + anaesthetic epidural arm have been compared to each of the interventions in another part of this review.	Anaesthetic(0.5% bupivacaine) + saline	Lumbosacral radiculopathy Hernia or annular tear (% not given) N=84 Immediate (1 or 2 injections); 1, 3 and 6 months follow-up. USA	Pain (NRS) Function: ODI Responder criteria (>50% improvement in pain) Adverse events	Image guidance method: fluoroscopic Concomitant treatment: both groups could receive rescue medication (opioid increase, or NSAID or tramadol) if they had debilitating pain.
Friedly 2014[67]	Steroid + anaesthetic (1-3ml /60-120mg triamcinolone or 6-12mg betamethasone or 8-10mg dexamethasone or 60-120mg methylprednisolone + 1-3ml /0.25% - 1% lidocaine) Lumbar transforaminal epidural	Anaesthetic (1-3ml /0.25% - 1% lidocaine)	Central lumbar spinal stenosis N=400 Immediate (single injection) + 6 weeks follow-up USA	Quality of life (EQ-5D) Pain Function: RMDQ Responder criteria (>30% improvement in pain and in RMDQ) Serious AEs	Image guidance method: fluoroscopic Concomitant treatment: none reported
Ghahreman 2010[68]	Steroid + anaesthetic (1.75 ml of triamcinolone 40mg/L + 0.75ml of 0.5% bupivacaine). Transforaminal injection	Anaesthetic (0.75ml of 0.5% bupivacaine)	Lumbar radicular pain Hernia N=150 in all 5 arms Immediate (up to 3	Pain Responder criteria (>50% reduction in pain) Healthcare use: surgery	Image guidance method: fluoroscopic Concomitant treatment: rescue

Study	Intervention	Comparison	Population	Outcomes	Comments
	NOTE: This study also had 2 additional arms which did not meet our protocol, and so the data were not extracted for these (IM steroid and IM saline). The additional placebo arm data has been extracted elsewhere in this review.		injections) + 1 year follow-up Australia		therapy (analgesics, surgery or open-label steroids)
Ghai 2015[69]	Steroid + anaesthetic (80 mg, 2 mL of methylprednisolone /6 mL of 0.5% lidocaine) parasagittal interlaminar (PIL) approach	Anaesthetic (8ml of 0.5% lidocaine)	Sciatica on MRI Hernia N=69 Immediate (1 or >1 injection) + 1 year follow-up India	Pain (NRS) Function (ODQ) Responder criteria (>50% pain relief) Adverse events (complications) Healthcare use (additional injections)	Image guidance method: fluoroscopic (C-arm) Concomitant treatment: conservative management including analgesics and/or exercise program. Job attendance continued. Patients were encouraged to engage in physical activities. No additional occupation/physical therapy or any other interventions were offered beyond the protocol.
Hagihara 2009[70]	Steroid + anaesthetic (betamethasone 1ml /4mg +lidocaine 2ml) Unclear rout of administration of the epidural	Anaesthetic (3ml lidocaine)	Sciatica on MRI Underlying pathology not stated N=69 Immediate (1 or >1 injection) + 1	Pain (VAS and PPI) Surgery	Image guidance method: fluoroscopic Concomitant treatment: none reported

Study	Intervention	Comparison	Population	Outcomes	Comments
			week follow-up Japan		
Manchikanti 2008/2012B/2012I [75,76,78]	Steroid + anaesthetic (1ml nonparticulate betamethasone, 6mg + 9ml lidocaine 0.5%) Caudal epidural	Anaesthetic (lidocaine 0.5%)	Spinal stenosis with radicular pain N=100 Immediate (at least 1 injection) + 2 year follow-up USA	Pain Function: ODI Responder criteria (>50% improvement in pain and ODI) Healthcare use: opioid dose Major AEs	Image guidance method: fluoroscopic Concomitant treatment: both groups continued with previous exercise programs, drug therapy, and work.
Manchikanti 2012H[77]	Steroid + anaesthetic (6mg betamethasone or 40mg methylprednisolone +lidocaine 0.5%) Caudal epidural	Anaesthetic (lidocaine 0.5%)	Lumbar disc herniation and radiculitis Hernia N=88 Immediate (single injection) + 2 year follow-up USA	Pain Function: ODI Responder criteria (>50% improvement in pain) Healthcare use: morphine dose	Image guidance method: fluoroscopic 20 patients in the combination arm each received 1 of 3 steroids : betamethasone (brand name or non-particulate) or methylprednisolone Concomitant treatment: both groups continued with previous exercise programs, drug therapy, and work.
Manchikanti 2014B[79]	Steroid + anaesthetic (3mg or 0.5ml betamethasone + lidocaine 1%) Lumbar transforaminal epidural	Anaesthetic (lidocaine 1%, 1.5ml)	Lumbar disc herniation and unilateral radiculitis Hernia N=120 Immediate (single injection at each nerve root level) + 2 year follow-up	Pain Function: ODI Responder criteria (>50% improvement in pain and in ODI) Healthcare use: opioid dose	Image guidance method: fluoroscopic Concomitant treatment: both groups were given structured exercise programs. Employed people continued working. Drug

Study	Intervention	Comparison	Population	Outcomes	Comments
			USA		therapy was decreased or stopped if required; if increase in opioid therapy then the patient was withdrawn.
Manchikanti 2015C[80]	Steroid + anaesthetic (1ml or 6mg betamethasone + 0.5% lidocaine 5mls) Lumbar interlaminar epidural	Anaesthetic (lidocaine 0.5%, 6 mL)	Central spinal stenosis with radicular pain N=120 Immediate (single injection at each nerve root level) + 2 year follow-up USA	Pain Function: ODI	Image guidance method: fluoroscopic Concomitant treatment: both groups were given structured therapeutic exercise program along with medical therapy, and continued employment. Majority of patients were taking opioids, non-opioid analgesics and adjuvant analgesics. Repeat procedures were performed in patients with deterioration of pain relief and/or functional status below 50%.
Ng 2005[82]	Steroid + anaesthetic (methylprednisolone 40mg/ml +bupivacaine 0.25%) Periradicular infiltration (transforaminal)	Anaesthetic (bupivacaine 0.25%)	Unilateral leg pain (chronic radicular pain) Hernia and spinal stenosis (49% hernia) N=88 Immediate (single injection) + 12 weeks follow-up UK	Pain Function: ODI	Image guidance method: fluoroscopic Concomitant treatment: none reported

Study	Intervention	Comparison	Population	Outcomes	Comments
Riew 2000 and -Riew 2006[83,84]	Steroid + anaesthetic (betamethasone, 1ml of 6mg/ml +bupivacaine 1ml of 0.25%) Periradicular infiltration (transforaminal)	Anaesthetic (1 ml bupivacaine 0.25%)	Lumbar radicular pain Hernia and spinal stenosis (75% hernia) N=55 Immediate (1 or >1 injection) + mean 13 months, range 13-28 months follow-up USA	Surgery	Image guidance method: fluoroscopic Concomitant treatment: none reported
Tafazal 2009[85]	Steroid + anaesthetic (2ml methylprednisolone 40mg/ bupivacaine 0.25%)) Periradicular infiltration epidural (transforaminal)	Anaesthetic (2ml bupivacaine 0.25%)	Sciatica/nerve root compression on MRI Hernia and spinal stenosis (51% hernia) N=150 Immediate (1 injection) + 12 weeks and 1 year follow-up UK	Pain (VAS) Function: ODI Surgery	Image guidance method: fluoroscopic Concomitant treatment: not to alter their oral analgesic medication during the follow-up period and did not have any additional treatments such as physiotherapy.
Steroid + anaesthetic versus combination of non-invasive interventions					
Murakibhavi 2011[81]	Epidural injections 20mls normal saline, 2 ml of 2 % xylocaine, 2 ml triamcinolone acetate Repeated every 2-3 weeks for 3 months as required.	Combination of non-invasive interventions (defined as a combination of pharmacological + manual therapy + electrotherapy + biomechanical exercise: Tizanidine (6-12 mg/24 hours),	Low back pain + unilateral or bilateral sciatica >3 months not responding to rest +analgesics MRI evidence of disc herniation/degernation N=102 1 year follow-up India	Quality of life (Numerical pain intensity, NPI) Pain (VAS) Pain (NRS) Function (ODI) Psychological distress (Beck depression scale) Responder criteria (complete relief of pain)	Concomitant treatment not reported

Study	Intervention	Comparison	Population	Outcomes	Comments
		Diclofenac 50-100mg/24 hours, Amitriptyline 10-50mg ON, Bilateral skin traction, Physiotherapy, TENS, Short wave diathermy and Back extension exercises)			
Steroid + anaesthetic versus anti-TNF + anaesthetic					
Cohen 2012[65]	Steroid + anaesthetic (60 mg methylprednisolone + 0.5% bupivacaine) NOTE: The additional anaesthetic epidural arm has been compared to each of the interventions in another part of this review.	Anti-TNF + anaesthetic(4mg etanercept + 0.5% bupivacaine)	Lumbosacral radiculopathy Hernia or annular tear (% not given) N=84 Immediate (1 or 2 injections); 1, 3 and 6 months follow-up. USA	Pain (NRS) Function: ODI Responder criteria (>50% improvement in pain) AEs	Image guidance method: fluoroscopic Concomitant treatment: both groups could receive rescue medication (opioid increase, or NSAID or tramadol) if they had debilitating pain.
Steroid versus other treatments					
Bronfort 2004[86]	Steroid (details of dose and regimen not reported)	Self-management (self-care education) Manual therapy - mixed modality (manipulation/mobilisation + massage + heat/cold)	Unilateral or bilateral radiating pain of lumbar origin Underlying pathology not reported. N=32 Up to 3 injections,(over 12 weeks) + 52 weeks follow-up	Data was not included in this review because it was not reported for each group separately, only for all patients as a whole.	Image guidance method: fluoroscopic Concomitant treatment: both groups were allowed prescription strength rescue medication during the 12-week treatment period if they

Study	Intervention	Comparison	Population	Outcomes	Comments
			USA		experienced severe pain.

24.3.2 Clinical evidence summary: Non image guided epidurals

Fifteen RCTs were included in the review; these are summarised in **Table 32** below. [87-98] Evidence from these studies is summarised in the GRADE clinical evidence profile/clinical evidence summary below. All the studies compared non image guided epidurals of either steroid, anaesthetic agents, or a combination of both.

No studies comparing the use of anti TNF were identified.

See also the study selection flow chart in Appendix E, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

Table 32: Summary of studies included in the review: non image- guided

Study	Intervention	Comparison	Population	Outcomes	Comments
Steroid versus placebo/sham/usual care					
Carette 1997[1,87]	Epidural injections of 80mg methyl prednisolone mixed with 8 mls of normal saline Repeated at 3 and 6 weeks if required	Epidural injection of 1 ml of normal saline Repeated at 3 and 6 weeks if required	First or recurrent of unilateral or bilateral sciatica, with CT evidence of disc herniation Duration 1-12 months N= 158 Canada	Function (ODI) Pain (VAS) Pain (McGill score: present pain intensity) Pain (McGill score : pain rating index) AE- morbidity (minor complications)	Concomitant treatment: acetaminophen tablets (325mg)
Klenerman 1984[88]	20 mls Bupivacaine 0.25% (made up in normal saline)	20 mls Normal saline Needling into the intraspinous ligament but no injection	Unilateral sciatica +/- objective neurological signs. Less than 6 months duration. Never had hospital treatment No diagnostic imaging N=74 UK	N/A	Data was not included in this review because there were no relevant outcome data reported.
Spijkerhuiges 2014 and 2015[90,99]	Segmental epidural steroid injection of 80mg triamcinolone in	Usual care provided by the GP	Lumbosacral radicular syndrome	Function (RMDQ) Pain (NRS back pain)	Concomitant treatment was usual care provided by the GP

Study	Intervention	Comparison	Population	Outcomes	Comments
	10mls normal saline + usual care		Between2-4 weeks duration N=73 Netherlands No diagnostic imaging Netherlands	Pain (NRS leg pain) Pain (NRS pain during day) Pain (NRS pain during night) Pain (NRS total pain) Quality of Life (SF-36)	
Snoek 1977[100]	Lumbar extradural injection of 80mg methyl prednisolone acetate at level of the disc lesion	Lumbar extradural injection of 2 mls of normal saline at level of the disc lesion	Sciatic or femoral nerve pain +neurological deficit correlating with compression of 4/5th or lumbar, or 1st sacral nerve root, and myelographic findings No diagnostic imaging. N=51 Norway	Healthcare use: Discontinuance of analgesic consumption	Concomitant treatment included bed rest for first 7 days of hospitalisation standardised physiotherapy programme and in patient admission for 14 +/-4 days. Patients not improved referred for neurosurgical opinion.
Valat 2003 [89]	3 x epidural injections (2 day intervals) of 50mg prednisolone	3 x epidural injections (2 day intervals) of 2 mls normal saline	Inpatients referred for sciatica lasting between 15-180 days All patients with causes other than herniated disc were excluded. N=42 France	Function (RMDQ) Pain (VAS) AE- morbidity (minor complications)	Concomitant treatment: NSAIDs >20 days from first injection. Non opioid analgesics, bed rest, mild lumbar tractions and lumbar belts authorised.
Anaesthetic versus placebo/sham/usual care					
Coomes 1961[91]	Outpatient epidural into the sacral region: 50mls 0.5% Procaine. Advised to take any oral	Bed rest at home on a fracture board +/- inpatient admission for analgesia	Sciatica not controlled by simple analgesia, and only comfortable in bed rest	N/A	Data was not included in this review because there were no relevant outcome data reported.

Study	Intervention	Comparison	Population	Outcomes	Comments
	analgesia, no advice on bed rest given		UK		
Klenerman 1984[88]	20 mls Bupivacaine 0.25% (made up in normal saline)	20 mls Normal saline Needling into the intraspinous ligament but no injection	Unilateral sciatica +/- objective neurological signs. Less than 6 months duration. Never had hospital treatment No diagnostic imaging N=74 UK	Healthcare utilisation (number of patients that had back surgery at follow-up)	Concomitant treatment: after epidurals if the pain was still severe (not defined) then patients were offered physiotherapy
Steroid + anaesthetic versus placebo/sham					
Arden 2005[92]	3 x lumbar epidurals of 10mls of 0.25% bupivacaine and 80mg triamcinolone acetonide at weeks 0, 3 and 6.	3 x epidurals of 2 mls normal saline into the intraspinous ligament at weeks 0, 3 and 6.	Unilateral sciatica 1-18 months duration N=228 UK No diagnostic imaging UK	Function (ODI) Pain (VAS leg pain) Pain (VAS back pain) Responder criteria: improvement on leg pain, and back pain (Likert scale) Healthcare use: Analgesic use Surgery Further physiotherapy Pain management referrals Other injection techniques AE morbidity (minor)	Concomitant treatment: All patients received a standardised physiotherapy package before the study focusing mainly on education and exercise regimens. They had access to analgesics and anti-inflammatory medicines as required.
Cuckler 1985 [94]	Epidural injections into 3rd and 4th vertebral space, of 2 mls sterile water, 80mg of methyl prednisolone,	Epidural injections into 3rd and 4th vertebral space of 2 mls of saline, 5mls of 1% procaine	Radicular pain, either disc herniation, or spinal stenosis who had failed >2 weeks of conservative treatment. Results	Responder criteria: Improvement of symptoms	Concomitant treatment of mild analgesics only.

Study	Intervention	Comparison	Population	Outcomes	Comments
	and 5 mls of 1 % procaine		presented separately for disc herniation N=73 USA		
Steroid + Anaesthetic versus pharmacological therapy					
Dincer 2007[96]	Caudal injection: 40mg methyl prednisolone, 7mls 2% prilocaine HCL, 10ml NaCL	Pharmacological interventions- NSAIDS: diclofenac sodium 75mg, sustained release, oral, twice daily for 14 days	Sub-acute or chronic (1-12 months) low back pain + radicular pain with MRI imaging confirming lumbar disc herniation Turkey	Pain (VAS) Function (ODI) Healthcare use (use of paracetamol)	Concomitant treatment: lumbopelvic mobilisation and lumbar stabilisation exercises daily. After 15 days both groups allowed paracetamol only if needed.
Laiq 2009[93]	• Epidural injection of 80mg methyl prednisolone and 3 mls of 2% xylocaine diluted to 8mls with normal saline Ibuprofen 400mg if needed	Combined pharmacological therapy: Pharmacological interventions (NSAIDS, Opioids+ Muscle relaxant)+ Self-management • Ibuprofen 400mg TDS during 1st month • Tramadol SR 100mg OD during 1st 2 months • Tinizidine 2 mg BD for 1st 3 months • Famotadine 40mg throughout treatment Bed rest for 1st month	Lumbar radicular pain >2 weeks duration MRI evidence of disc herniation N=52 Pakistan	Pain (VAS) AE- morbidity (minor complications)	Concomitant treatment: analgesics when needed after 3 months
Steroid + Anaesthetic versus combination of non-invasive interventions					

Study	Intervention	Comparison	Population	Outcomes	Comments
Buchner 2000[95]	3 x Epidural injections of 100mg methylprednisolone in 10 mls 0.25% bupivacaine within 14 days of admission • + Combination of interventions (same as the interventions in the comparison arm)	• Combination of non-invasive interventions (defined as combination of self-management + pharmacological + mixed modality exercises + electrotherapy + manual therapy + postural therapy: Bed rest, administration of analgesic (worst pain treated with tramadol) and non-steroidal anti-inflammatory drugs for the initial pain period. After initial improvement the patients received a standard program of graded rehabilitation including hydrotherapy, electroanlagesia, postural exercise classes (back school) and	Inpatients with radicular pain MRI evidence of disc herniation N= 36 Germany	Pain (VAS)	Concomitant treatment, usual care / combination of interventions (defined as bed rest, administration of analgesics (NSAIDS and tramadol for worst pain). After initial improvement both groups had standard program of graded rehabilitation including hydrotherapy, electroanalgesia, postural exercise classes (back school) and later spinal mobilising physiotherapy)

Study	Intervention	Comparison	Population	Outcomes	Comments
		later spinal mobilising physiotherapy (soft tissue and joint mobilisation, muscle stabilisation program, strengthening by dynamic and static exercises)			
Steroid + anaesthetic versus. anaesthetic					
Beliveau 1971[101]	Epidural of 40mls of procaine 0.5% in normal saline, with 2 mls of methylprednisolone	Epidural of 42 mls of procaine 0.5% in normal saline	Moderate to severe unilateral sciatica +/- neurological signs N=48 UK	No relevant outcomes reported.	Data was not included in this review because there were no relevant outcome data reported.
Breivik 1976[102]	Epidurals of 20mls bupivacaine 0.25% with 80mg depot methyl prednisolone	Epidurals of 20mls bupivacaine 0.25% followed by 100mls saline	Chronic low back pain + sciatica unresponsive to conservative treatment >several months duration N=35 Norway	N/A	11 patients had already undergone surgery for prolapsed intervertebral discs Data was not included in this review because there were no relevant outcome data reported. Concomitant treatment of medical and physical therapy
Datta 2011[103,104]	Caudal epidural of 10-15mls of 0.125% bupivacaine and 80mg methyl prednisolone	Caudal epidural of 10-15mls of 0.125% bupivacaine	Recurrent episodes of sciatica >4 weeks and less than 1 year	Pain (VAS) Healthcare use Use of NSAIDS Use of physiotherapy	Concomitant treatment of NSAIDS

Study	Intervention	Comparison	Population	Outcomes	Comments
	Caudal epidural of 10-15mls of 0.125% bupivacaine and 80mg triamcinolone Caudal epidural of 10-15mls of 0.125% bupivacaine and 15mg dexamethasone		CT evidence of herniated disc corresponding to symptoms N=207 India		
El Zahaar 1991	Epidural injection of 2mls of 4% carbocaine and 5mls of hydrocortisone (concentration not given) made up to 30mls	Epidural injection of 2mls of 4% carbocaine made up to 30mls	Patients with both disc herniation and spinal stenosis + clinical diagnosis of sciatica were included but presented separately CT/Myelographic confirmation of diagnosis N=63 Egypt	Responder outcome (pre-injection symptoms)- this has been grouped as responder criteria for radicular pain from inference in the study Healthcare use: spinal surgery	Concomitant treatment: Not listed
Rogers 1992[98]	Epidural injection of 14 mls of lignocaine 2%, 80mg methyl prednisolone and 2 mls normal saline	Epidural injection of 14mls of lignocaine 2%, with normal saline 6mls	Diagnosis of sciatica + positive straight leg test No diagnostic imaging N= 30 UK	Healthcare use (analgesic use) Healthcare use (surgery)	6 patients had already had epidural steroid injections for episodes of sciatica Concomitant treatment not reported
Steroid versus anaesthetic					
Klenerman 1984[88]	80 mg of Depro-medrone in normal saline made up to 20 ml	20 mls Bupivacaine 0.25% (made up in normal saline)	Unilateral sciatica +/- objective neurological signs. Less than 6 months duration.	Healthcare use (surgery)	Concomitant treatment: after epidurals if the pain was still severe (not defined) then patients were offered physiotherapy

Study	Intervention	Comparison	Population	Outcomes	Comments
			Never had hospital treatment No diagnostic imaging N=74 UK		

24.3.3 Data unsuitable for meta-analysis

Table 33: Image-guided steroid + anaesthetic versus usual care lumbar spinal stenosis

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Koc 2009[73]	Pain (VAS, 0-10), change from baseline at ≤4 months (3 months)	Image-guided steroids + anaesthesia Median= 2.05; Usual care median = 2.77 Results reported as percentages (medians). Patients analysed: image-guided steroids + anaesthetics =10; usual care =9.				VERY HIGH
	Pain (VAS, 0-10), change from baseline at >4 months (6 months)	Image-guided steroids + anaesthesia Median= 2.30; Usual care median = 2.01 Results reported as percentages (medians) and are change scores. Patients analysed: image-guided steroids + anaesthetics -=10; usual care=9.				VERY HIGH
Koc 2009[73]	Function (RMDQ,0-24), change from baseline at ≤4 months (3 months)	Image-guided steroids + anaesthetics Median= 31.2; usual care Median=31.0 Results reported as percentages (medians) and are change scores. Patients analysed: image-guided steroids + anaesthetics -=10; usual care = 9.				VERY HIGH
	Function (RMDQ,0-24), change from baseline at >4 months (6 months)	Image-guided steroids + anaesthetics Median= 31.2; usual care Median=31.0 Results reported as percentages (medians) and are change scores. Patients analysed: image-guided steroids + anaesthetics -=10; usual care = 9.				VERY HIGH

Table 34: Image-guided steroid + anaesthetic versus placebo/sham for sciatica primarily caused by (≥70%) disc prolapse

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
KARPPINEN 2001[71]	Pain (NRS 0-10), change from baseline at >4 months	Mean difference: 0.12 (favouring sham/placebo)*				VERY HIGH
	Pain (NRS 0-10), change from baseline at >4 months	Mean difference: 0.39 (favouring sham/placebo)*				VERY HIGH

*Data calculated from that provided in the study. Study did not report SD at baseline and therefore only the MD without SD could be calculated. The MDs reported in the paper itself at follow-up were found to be incorrect.

Table 35: Image-guided steroid + anaesthetic versus anaesthetic for sciatica primarily caused by (≥70%) disc prolapse

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
GHAI 2015[69]	Pain (NRS 0-10) at ≤4 months	Statistically significant difference between groups (favours steroid + anaesthetic); p=0.002				VERY HIGH
	Leg Pain (NRS 0-10) at >4 months	Statistically significant difference between groups (favours steroid + anaesthetic); p=0.001				VERY HIGH
	Function (ODQ 0-100) at ≤4 months	Statistically significant difference between groups (favours steroid + anaesthetic); p=0.02				VERY HIGH
	Function (ODQ 0-100) at >4 months	Statistically significant difference between groups (favours steroid + anaesthetic); p=0.007				VERY HIGH

Note: Results of the table to be reviewed during consultation as data has been mislabelled in the study (confirmed by authors) and effect should favour anaesthetic treatment. Erratum to be published soon and data can be changed to reflect this before publication.

Table 36: Image-guided anti-TNF versus placebo/sham for sciatica primarily caused by (≥70%) disc prolapse

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
COHEN 2009[64]	Leg Pain (NRS 0-10) at ≤4 months	Final score: 0.78 (SD 1.16)	6	3.0 No SD or 95% CI given; data from 1 patient only	1	VERY HIGH
	Leg Pain (NRS 0-10) at >4 months	Final score: 0.96 (SD 1.4)	6	4.0 No SD or 95% CI given; data from 1 patient only	1	VERY HIGH
FREEMAN 2013[66]	Function (ODI 0-100) at ≤4 months	The anti-TNF 0.5 mg group showed a statistically significant reduction in mean and % change in ODI from baseline to week 4. At 3 months, consistently maintained a ≥10 point change from baseline and a ≥30% reduction above the placebo group.				VERY HIGH

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
COHEN 2009[64]	Function (ODI 0-100) at ≤4 months	Final score: 14.3 (SD 12.4)	6	22.0 No SD or 95% CI given; data from 1 patient only	1	VERY HIGH
	Function (ODI 0-100) at >4 months	Final score: 15.0 (SD 9.7)	6	42.0 No SD or 95% CI given; data from 1 patient only	1	VERY HIGH
FREEMAN 2013[66]	Surgery at >4 months	5/49 patients (across all groups) underwent surgery. Percentage of patients undergoing surgery was similar in all the groups (exact numbers not reported).				VERY HIGH
COHEN 2009[64]	HC use: reduction in medication (mean % change) at ≤4 months	72% (range 10-100)	17	17% (range 0-50)	5	VERY HIGH
	HC use: reduction in medication (mean % change) at >4 months	72% (range 10-100)	17	17% (range 0-50)	5	VERY HIGH

Table 37: Non image guided: Steroid + anaesthetic versus combinations of non-invasive interventions for Sciatica caused by (≥70%) disc prolapse

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Buchner 2000[95]	Pain >4 months (VAS) At 6 months	Final score: 3.29 (range 0-8.5)	17	Final score: 3.92 (range 0-10) No SD or 95% CI given;	19	VERY HIGH

24.3.4 Clinical evidence summary: Image-guided epidurals

Table 38: Image guided: Anaesthetic versus sham/placebo for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Anaesthetic versus sham/placebo (95% CI)
Leg pain (0-10, final value) ≤4 months	64 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean leg pain (0-10, final value) ≤4 months in the control groups was 5.5	The mean leg pain (0-10, final value) ≤4 months in the intervention groups was 1.2 higher (0.15 lower to 2.55 higher)
Responder criteria: >50% reduction in pain ≤4 months	64 (1 study)	LOW[b] due to imprecision	RR 0.39 (0.09 to 1.74)	Moderate	
				189 per 1000	115 fewer per 1000 (from 172 fewer to 140 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

Table 39: Image guided: Anti-TNF (mean of 3 doses) versus sham/placebo for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Anti-TNF (mean of 3 doses) versus sham/placebo (95% CI)
Mean daily worst leg pain (0-10, change score) ≤4 months	37 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		The mean daily worst leg pain (0-10, change score) ≤4 months in the control groups was 5.42	The mean daily worst leg pain (0-10, change score) ≤4 months in the intervention groups was 1.32 lower (3.3 lower to 0.66 higher)
Adverse events ≤4 months	24 (1 study)	LOW[a,b] due to risk of bias	Not estimable	*	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Anti-TNF (mean of 3 doses) versus sham/placebo (95% CI)
Adverse events >4 months	24 (1 study)	LOW[a,b] due to risk of bias	Not estimable	*	

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

* Zero events in both arms

Table 40: Image guided: Steroid + and anaesthetic versus Sham/placebo for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus Sham/placebo (95% CI)
Intensity of leg pain - Intensity of leg pain ≤4 months	65 (1 study)	MODERATE[b] due to imprecision		*	The mean intensity of leg pain - intensity of leg pain ≤4 months in the intervention groups was 1.40 lower (2.79 to 0.01 lower)
Function - ODI ≤4 months	160 (1 study)	LOW[a,b] due to risk of bias, imprecision		*	The mean function - ODI ≤4 months in the intervention groups was 1.3 lower (8.6 lower to 6 higher)
Function - ODI >4 months	160 (1 study)	MODERATE[a] due to risk of bias		*	The mean function - ODI >4 months – 1 year in the intervention groups was 0.4 lower (7 lower to 6.2 higher)
Responder criteria: >50% reduction in pain ≤4 months	65 (1 study)	HIGH	RR 2.83	Moderate	
				189 per 1000	346 more per 1000 (from 64 to 945 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus Sham/placebo (95% CI)
			(1.34 to 6.0)		

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

*No control rate reported in study, only mean difference

Table 41: Image guided: Steroid and anaesthetic versus anaesthetic for sciatica primarily caused by >70% disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid+ anaesthetic versus anaesthetic (>70% prolapse) (95% CI)
Pain (0-10, change/final scores) ≤4 months transforaminal epidural	233 (3 studies) ≤4 months	MODERATE[a] due to risk of bias		The mean pain (0-10, change/final scores) ≤4 months transforaminal epidural in the control groups was 3.78	The mean pain (0-10, change/final scores) <4 months transforaminal epidural in the intervention groups was 0.52 lower (1.04 lower to 0 higher)
Pain (0-10, change/final scores) ≤4 months caudal epidural	353 (1 study) ≤4 months	LOW[a,b] due to risk of bias, imprecision		The mean pain (0-10, change/final scores) ≤4 months caudal epidural in the control groups was 4.1	The mean pain (0-10, change/final scores) <4 months caudal epidural in the intervention groups was 0.70 lower (1.33 to 0.07 lower)
Pain (0-10, change/final scores) >4 months - transforaminal approach	120 (1 study)	HIGH		The mean pain (0-10, change/final scores) >4 months - transforaminal approach in	The mean pain (0-10, change/final scores) >4 months - transforaminal approach in the intervention groups was 0.2 higher (0.37 lower to 0.77 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid+ anaesthetic versus anaesthetic (>70% prolapse) (95% CI)
				the control groups was 4.0	
Pain (0-10, change/final scores) >4 months - caudal epidural	120 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean pain (0-10, change/final scores) >4 months - caudal epidural in the control groups was 4.2	The mean pain (0-10, change/final scores) >4 months - caudal epidural in the intervention groups was 0.6 lower (1.24 lower to 0.04 higher)
Function ODI (0-100, change/final score) ≤4 months	240 (3 studies)	LOW[a,b] due to risk of bias, imprecision		The mean ODI score (0-100, change/final score) <4 months in the control groups was 16.5	The mean ODI score (0-100, change/final score) ≤4 months in the intervention groups was 2.46 lower (4.16 to 0.75 lower)
Function (ODI) (0-100, final score) >4 months	240 (2 studies)	MODERATE[a] due to risk of bias		The mean ODI score (0-100, final score) >4 months in the control groups was 15.25	The mean ODI score (0-100, final score) >4 months in the intervention groups was 1.4 lower (3.16 lower to 0.36 higher)
Responder criteria: >50% reduction in pain ≤4 months - transforaminal approach	233 (3 studies)	VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision	RR 1.29 (1.06 to 1.57)	Moderate	
				767 per 1000	222 more per 1000 (from 46 more to 437 more)
Responder criteria: >50% reduction in pain ≤4 months - caudal epidural	120 (1 study)	LOW[a,b] due to risk of bias, imprecision	RR 1.04 (0.86 to 1.26)	Moderate	
				767 per 1000	31 more per 1000 (from 107 fewer to 199 more)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid+ anaesthetic versus anaesthetic (>70% prolapse) (95% CI)
Responder criteria: >50% reduction in pain ≤4 months - interlaminar (parasagittal approach)	69 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.71 (1.19 to 2.46)	650 per 1000	462 more per 1000 (from 124 more to 949 more)
Responder criteria: >50% reduction in pain >4 months - transforaminal approach	178 (2 studies)	MODERATE[b] due to imprecision	RR 0.84 (0.64 to 1.10)	Moderate	
				650 per 1000	92 fewer per 1000 (from 208 fewer to 58 more)
Responder criteria: >50% reduction in pain >4 months - caudal epidural	120 (1 study)	LOW[a,b] due to risk of bias, imprecision	RR 1.08 (0.83 to 1.40)	Moderate	
				650 per 1000	52 more per 1000 (from 111 fewer to 260 more)
Responder criteria: >50% reduction in pain >4 months - interlaminal (parasagittal) approach	69 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.51 (1.11 to 2.04)	Moderate	
				650 per 1000	331 more per 1000 (from 72 more to 676 more)
Responder criteria: >50% reduction in ODI ≤4 months - transforaminal approach	120 (1 study)	LOW[a,b] due to risk of bias, imprecision	RR 0.91 (0.73 to 1.14)	Moderate	
				750 per 1000	67 fewer per 1000 (from 202 fewer to 105 more)
Responder criteria: >50% reduction in ODI ≤4 months - caudal epidural	120 (1 study)	MODERATE[b] due to imprecision	RR 1.19 (0.93 to 1.53)	Moderate	
				617 per 1000	117 more per 1000 (from 43 fewer to 327 more)
Responder criteria: >50% reduction in ODI >4 months	240 (2 studies)	MODERATE[a] due to risk of bias	RR 1.03 (0.86 to 1.23)	Moderate	
				658 per 1000	20 more per 1000 (from 92 fewer to 151 more)
HC use: Surgery >4 months				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid+ anaesthetic versus anaesthetic (>70% prolapse) (95% CI)
	55 (1 study)	LOW[a,b] due to risk of bias, imprecision	RR 0.43 (0.23 to 0.82)	667 per 1000	380 fewer per 1000 (from 120 fewer to 514 fewer)
HC use: opioid intake, mg dose in last 12 months ≤4 months	240 (2 studies)	MODERATE[a] due to risk of bias		The mean hc use: opioid intake, mg dose in last 12 months <4 months in the control groups was 40.7	The mean hc use: opioid intake, mg dose in last 12 months ≤4 months in the intervention groups was 4.73 lower (13.53 lower to 4.08 higher)
HC use: opioid intake, mg dose in last 12 months >4 months	240 (2 studies)	MODERATE[a] due to risk of bias		The mean hc use: opioid intake, mg dose in last 12 months >4 months in the control groups was 37.85	The mean hc use: opioid intake, mg dose in last 12 months >4 months in the intervention groups was 3.98 lower (12.8 lower to 4.84 higher)
HC use: number of patients having additional injections>4 months	69 (1 study) >4 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.84 (0.58 to 1.22)	Moderate	
				667 per 1000	107 fewer per 1000 (from 280 fewer to 147 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

[c] Downgraded by 1 increment for inconsistency if I^2 between 50% and <75%. Downgraded by 2 increments if I^2 >75%.

Table 42: Image guided: Steroid + anaesthetic versus anaesthetic for sciatica primarily caused by non-disc lesion

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Anaesthetic	Risk difference with Steroid+ anaesthetic (95% CI)

Quality of life (EQ-5D) ≤4 months	386 (1 study)	LOW[a] due to risk of bias		The mean quality of life (eq-5d) <4 months in the control groups was 0.68	The mean quality of life (eq-5d) ≤4 months in the intervention groups was 0.02 higher (0.02 lower to 0.06 higher)
Pain (0-10, change/final scores) ≤4 months	606 (3 studies)	LOW[a] due to risk of bias		The mean pain (0-10, change/final scores) <4 months in the control groups was 3.7	The mean pain (0-10, change/final scores) ≤4 months in the intervention groups was 0.06 lower (0.40 lower to 0.28 higher)
Pain (0-10, change/final scores) >4 months	220 (2 studies)	MODERATE[a] due to risk of bias		The mean pain (0-10, change/final scores) >4 months in the control groups was 4.0	The mean pain (0-10, change/final scores) >4 months in the intervention groups was 0.08 lower (0.57 lower to 0.41 higher)
RMDQ score (0-24, change score) ≤4 months	386 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		The mean RMDQ score (0-24, change score) <4 months in the control groups was -3.1	The mean RMDQ score (0-24, change score) ≤4 months in the intervention groups was 1.1 lower (2.21 lower to 0.01 higher)
ODI score (0-100, change/final score) ≤4 months	100 (1 study)	MODERATE[a] due to risk of bias		The mean ODI score (0-100, change/final score) <4 months in the control groups was 25	The mean ODI score (0-100, change/final score) ≤4 months in the intervention groups was 0.18 lower (2.12 lower to 1.76 higher)
ODI score (0-100, final score) >4 months	100 (1 study)	MODERATE[a] due to risk of bias		The mean ODI score (0-100, final score) >4 months in the control groups was 25	The mean ODI score (0-100, final score) >4 months in the intervention groups was 1.34 lower (8.59 lower to 0.91 higher)
Responder criteria: >30% reduction in pain ≤4 months	386 (1 study)	LOW[a] due to risk of bias	RR 1.01 (0.83 to 1.24)	Moderate	
				492 per 1000	5 more per 1000 (from 84 fewer to 118 more)
Responder criteria: >50% reduction in pain ≤4 months	100 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.94 (0.7 to 1.26)	Moderate	
				660 per 1000	40 fewer per 1000 (from 198 fewer to 172 more)
				Moderate	

Responder criteria: >50% reduction in pain >4 months	100 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.05 (0.67 to 1.65)	420 per 1000	21 more per 1000 (from 139 fewer to 273 more)
Responder criteria: >30% reduction in RMDQ ≤4 months	386 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.85 (0.64 to 1.12)	Moderate	
				373 per 1000	56 fewer per 1000 (from 134 fewer to 45 more)
Responder criteria: >50% reduction in ODI ≤4 months	100 (1 study)	LOW[a,b] due to risk of bias, imprecision	RR 0.86 (0.6 to 1.24)	Moderate	
				580 per 1000	81 fewer per 1000 (from 232 fewer to 139 more)
Responder criteria: >50% reduction in ODI >4 months	100 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.1 (0.7 to 1.71)	Moderate	
				420 per 1000	42 more per 1000 (from 126 fewer to 298 more)
HC use: opioid intake, mg dose in last 12 months ≤4 months	100 (1 study)	MODERATE[a] due to risk of bias		The mean hc use: opioid intake, mg dose in last 12 months <4 months in the control groups was 33.3	The mean hc use: opioid intake, mg dose in last 12 months ≤4 months in the intervention groups was 0.2 lower (12.69 lower to 12.29 higher)
HC use: opioid intake, mg dose in last 12 months >4 months	100 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean hc use: opioid intake, mg dose in last 12 months >4 months in the control groups was 35.7	The mean hc use: opioid intake, mg dose in last 12 months >4 months in the intervention groups was 3.2 lower (18.6 lower to 12.2 higher)
SAEs ≤4 months	500 (2 studies)	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.8 (0.22 to 2.94)	Moderate	
				13 per 1000	3 fewer per 1000 (from 10 fewer to 25 more)
SAEs >4 months	100 (1 study)	MODERATE[a] due to risk of bias	Not estimable	*	

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

*Zero events in both arms

Table 43: Image guided: Steroid + anaesthetic versus anaesthetic for sciatica primarily caused by mixed population/ unclear spinal pathologies

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Anaesthetic	Risk difference with Steroid+ anaesthetic (95% CI)
Pain (0-10, change/final scores) ≤4 months	332 (4 studies)	VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision		The mean pain <4 months-transforaminal epidural in the control groups was -0.03	The mean pain (0-10, change/final scores) ≤4 months in the intervention groups was 0.06 lower (0.30 lower to 0.19 higher)
Pain, PPI (0-5, change score) ≤4 months	69 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain <4 months-approach not specified in the control groups was 4.17	The mean pain, ppi (0-5, change score) ≤4 months in the intervention groups was 0.04 higher (0.35 lower to 0.43 higher)
ODI score (0-100, change/final score) ≤4 months	263 (3 studies)	VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision		The mean function score ≤4 months in the control group was 12.3	The mean ODQ score (0-100, change/final score) ≤4 months in the intervention groups was 0.01 lower (2.83 lower to 2.85 higher)
HC use: Surgery ≤4 months	127 (2 studies)	VERY LOW[a,b] due to risk	RR 0.79 (0.36 to 1.74)	Moderate	
				183 per 1000	38 fewer per 1000 (from 117 fewer to 135 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Anaesthetic	Risk difference with Steroid+ anaesthetic (95% CI)
		of bias, imprecision			
HC use: Surgery >4 months	129 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.65 (0.3 to 1.4)	Moderate	
				215 per 1000	75 fewer per 1000 (from 150 fewer to 86 more)
HC use: medication reduction (>20% opioid use or cessation non-opioids) ≤4 months	58 (1 study)	MODERATE[b] due to imprecision	RR 1.3 (0.8 to 2.11)	Moderate	
				467 per 1000	140 more per 1000 (from 93 fewer to 518 more)
HC use: medication reduction (>20% opioid use or cessation non-opioids) >4 months	24 (1 study)	MODERATE[b] due to imprecision	RR 1.22 (0.85 to 1.77)	Moderate	
				750 per 1000	165 more per 1000 (from 112 fewer to 577 more)
Adverse events: complications >4 months	129 (1 study)	LOW[a] due to risk of bias	Not estimable	*	
Adverse events: complications ≤4 months	124 (1 study)	LOW[a] due to risk of bias	Not estimable	*	

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

[c] Downgraded by 1 increment for inconsistency if I^2 between 50% and <75%. Downgraded by 2 increments if I^2 >75%.

* Zero events in both arms

Table 44: Image guided: steroid and anaesthetic epidural versus combinations of non-invasive interventions for Sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus combination of non-invasive interventions (95% CI)
Quality of life(HRQoL -Numerical pain intensity, NPI)>4 months	100 (1 study) >4 months	MODERATE[a] due to risk of bias		The mean hrqol in the control groups was 5.58	The mean hrqol in the intervention groups was 2.24 lower (2.76 to 1.72 lower)
Pain (VAS,0-10) >4 months	100 (1 study) > 4 months	MODERATE[a] due to risk of bias		The mean pain in the control groups was 6.08	The mean pain in the intervention groups was 3.39 lower (3.65 to 3.13 lower)
ODI score (0-100) >4 months	100 (1 study) > 4 months	MODERATE[a] due to risk of bias		The mean function in the control groups was 24.87	The mean function in the intervention groups was 12.59 lower (13.42 to 11.76 lower)
Psychological distress BDI >4 months	100 (1 study) >4 months	MODERATE[a] due to risk of bias		The mean psychological distress in the control groups was 13.26	The mean psychological distress in the intervention groups was 4.67 lower (5.44 to 3.9 lower)
Responder criteria (complete relief of pain) >4 months	102 (1 study) >4 months	HIGH	RR 3.45 (2.07 to 5.73)	Study population	
				240 per 1000	588 more per 1000 (from 257 more to 1000 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 45: Image guided: Anti-TNF + anaesthetic versus anaesthetic for sciatica primarily caused by >70% disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Anti-TNF + anaesthetic versus anaesthetic (95% CI)
Pain (0-10, change/final scores) ≤4 months	56 (1 study)	LOW[a] due to imprecision		The mean pain (0-10, change/final scores) <4 months in the control groups was 3.78	The mean pain (0-10, change/final scores) ≤4 months in the intervention groups was 0.22 lower (1.76 lower to 1.32 higher)
ODI score (0-100, final score) ≤4 months	56 (1 study)	MODERATE[a] due to imprecision		The mean ODI score (0-100, final score) <4 months in the control groups was 30	The mean ODI score (0-100, final score) ≤4 months in the intervention groups was 10.26 higher (0.69 to 19.83 higher)
HC use: Surgery ≤4 months	56 (1 study)	LOW[a] due to imprecision	RR 1.38 (0.48 to 4.01)	Moderate	
				167 per 1000	63 more per 1000 (from 87 fewer to 503 more)
Responder criteria: >50% reduction in pain ≤4 months	56 (1 study)	LOW[a] due to imprecision	RR 0.98 (0.53 to 1.79)	Moderate	
				433 per 1000	9 fewer per 1000 (from 204 fewer to 342 more)
Responder criteria: >50% reduction in pain >4 months	56 (1 study)	LOW[a] due to imprecision	RR 0.96 (0.5 to 1.85)	Moderate	
				400 per 1000	16 fewer per 1000 (from 200 fewer to 340 more)
HC use: medication reduction (>20% opioid use or cessation non-opioids) ≤4 months	56 (1 study)	LOW[a] due to imprecision	RR 0.74 (0.39 to 1.42)	Moderate	
				467 per 1000	121 fewer per 1000 (from 285 fewer to 196 more)
HC use: medication reduction (>20% opioid use or cessation non-opioids) >4 months	23 (1 study)	LOW[a] due to imprecision	RR 0.85 (0.49 to 1.48)	Moderate	
				750 per 1000	112 fewer per 1000 (from 382 fewer to 360 more)

[a] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 46: Image guided: Steroid + anaesthetic versus Anti-TNF + anaesthetic for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus Anti-TNF + anaesthetic (95% CI)
Pain (0-10) ≤4 months	54 (1 study)	MODERATE[a] due to imprecision		The mean pain (0-10) <4 months in the control groups was 3.56	The mean pain (0-10) ≤4 months in the intervention groups was 1.02 lower (2.63 lower to 0.59 higher)
ODI score (0-100, final score) ≤4 months	54 (1 study)	MODERATE[a] due to imprecision		The mean ODI score (0-100, final score) <4 months in the control groups was 40.26	The mean ODI score (0-100, final score) ≤4 months in the intervention groups was 16.16 lower (26.15 to 6.17 lower)
Responder criteria: >50% reduction in pain ≤4 months	54 (1 study)	LOW[a] due to imprecision	RR 1.18 (0.66 to 2.11)	Moderate	
				423 per 1000	76 more per 1000 (from 144 fewer to 470 more)
Responder criteria: >50% reduction in pain >4 months	54 (1 study)	LOW[a] due to imprecision	RR 0.74 (0.35 to 1.59)	Moderate	
				385 per 1000	100 fewer per 1000 (from 250 fewer to 227 more)
HC use: Surgery ≤4 months	54 (1 study)	LOW[a] due to imprecision	RR 0.93 (0.34 to 2.52)	Moderate	
				231 per 1000	16 fewer per 1000 (from 152 fewer to 351 more)
HC use: medication reduction (>20% opioid use or cessation non-opioids) ≤4 months	54 (1 study)	MODERATE[a] due to imprecision	RR 1.75 (0.96 to 3.22)	Moderate	
				346 per 1000	259 more per 1000 (from 14 fewer to 768 more)
HC use: medication reduction (>20% opioid use or cessation non-opioids) >4 months – 1 year	23 (1 study)	MODERATE[a] due to imprecision	RR 1.44 (0.89 to 2.32)	Moderate	
				636 per 1000	280 more per 1000 (from 70 fewer to 840 more)

[a] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

24.3.5 Clinical evidence summary: non-image-guided epidurals

Table 47: Non image guided: steroid epidural versus placebo for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus placebo/sham (95% CI)
Pain (VAS) VAS	174 (2 studies) 3-4 months	MODERATE[a] due to risk of bias		The mean pain (VAS) in the control groups was 3.58	The mean pain (VAS) in the intervention groups was 0.19 lower (1.09 lower to 0.71 higher)
Pain McGill: present pain intensity McGill scale	156 (1 study) 3 months	HIGH		The mean pain McGill: present pain intensity in the control groups was 1.9	The mean pain McGill: present pain intensity in the intervention groups was 0 higher (0.49 lower to 0.49 higher)
Pain (McGill score: pain rating index) McGill score	156 (1 study) 3 months	HIGH		The mean pain (McGill score: pain rating index) in the control groups was 1.9	The mean pain (McGill score: pain rating index) in the intervention groups was 0 higher (5.93 lower to 5.93 higher)
Function ODI/RMDQ	221 (2 studies) 3-12 months	LOW[a,b] due to risk of bias, imprecision		The mean function in the control groups was 36.25	The mean function in the intervention groups was 0.1 standard deviations lower (0.37 lower to 0.16 higher)
Adverse events-morbidity no of minor adverse events	232 (2 studies) 3-12 months	LOW[a,b] due to risk of bias, imprecision	RR 1.36 (0.81 to 2.3)	132 per 1000	48 more per 1000 (from 25 fewer to 172 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 48: Non image guided: steroid epidural versus placebo for sciatica in a population with unclear spinal pathology

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
Healthcare use – discontinuation of analgesics	51 (1 study) 8-20 months	VERY LOW[a,b] due to risk of bias, imprecision	2.44 (0.9 to 6.67)	167 per 1000	240 more per 1000 (from 17 fewer to 945 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 49: Non image guided: steroid epidural versus usual care with sciatica in a population with unclear spinal pathology

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
Quality of life (SF-36) 0-100 ≤4 months - Mental composite	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - mental composite in the control groups was 61.2	The mean quality of life (sf-36) 0-100 ≤4 months - mental composite in the intervention groups was 3.8 higher (2.65 lower to 10.25 higher)
Quality of life (SF-36) 0-100 ≤4 months - Physical composite	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - physical composite in the control groups was 59.4	The mean quality of life (sf-36) 0-100 ≤4 months - physical composite in the intervention groups was 9.5 higher (2.32 to 16.68 higher)
Quality of life (SF-36) 0-100 ≤4 months - Physical functioning	50 (1 study)	LOW[a,b] due to risk of		The mean quality of life (sf-36) 0-100 ≤4 months - physical functioning in	The mean quality of life (sf-36) 0-100 ≤4 months - physical functioning in the

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
		bias, imprecision		the control groups was 79	intervention groups was 8.7 higher (1.03 to 16.37 higher)
Quality of life (SF-36) 0-100 ≤4 months - Physical role limitations	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - physical role limitations in the control groups was 45.7	The mean quality of life (sf-36) 0-100 ≤4 months - physical role limitations in the intervention groups was 14 higher (5.68 lower to 33.68 higher)
Quality of life (SF-36) 0-100 ≤4 months - Social functioning	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - social functioning in the control groups was 44.5	The mean quality of life (sf-36) 0-100 ≤4 months - social functioning in the intervention groups was 4.4 higher (3.32 lower to 12.12 higher)
Quality of life (SF-36) 0-100 ≤4 months - Emotional role limitations	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - emotional role limitations in the control groups was 74	The mean quality of life (sf-36) 0-100 ≤4 months - emotional role limitations in the intervention groups was 13.5 higher (2.69 lower to 29.69 higher)
Quality of life (SF-36) 0-100 ≤4 months - Emotional well-being	50 (1 study)	MODERATE[a] due to risk of bias		The mean quality of life (sf-36) 0-100 ≤4 months - emotional well-being in the control groups was 71	The mean quality of life (sf-36) 0-100 ≤4 months - emotional well-being in the intervention groups was 1.2 lower (9.33 lower to 6.93 higher)
Quality of life (SF-36) 0-100 ≤4 months - Energy/fatigue	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - energy/fatigue in the control groups was 56.7	The mean quality of life (sf-36) 0-100 ≤4 months - energy/fatigue in the intervention groups was 2.4 lower (11.24 lower to 6.44 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
Quality of life (SF-36) 0-100 ≤4 months - Pain	50 (1 study)	MODERATE[a] due to risk of bias		The mean quality of life (sf-36) 0-100 ≤4 months - pain in the control groups was 48.4	The mean quality of life (sf-36) 0-100 ≤4 months - pain in the intervention groups was 3.1 higher (2.14 lower to 8.34 higher)
Quality of life (SF-36) 0-100 ≤4 months - General health perceptions	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - general health perceptions in the control groups was 66.7	The mean quality of life (sf-36) 0-100 ≤4 months - general health perceptions in the intervention groups was 6.8 higher (0.72 lower to 14.32 higher)
Quality of life (SF-36) 0-100 ≤4 months - Change in perceived help	50 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 ≤4 months - change in perceived help in the control groups was 55.3	The mean quality of life (sf-36) 0-100 ≤4 months - change in perceived help in the intervention groups was 2.6 higher (10.99 lower to 16.19 higher)
Quality of life (SF-36) 0-100 >4 months - Mental composite	50 (1 study)	MODERATE[a] due to risk of bias		The mean quality of life (sf-36) 0-100 >4 months - mental composite in the control groups was 65.2	The mean quality of life (sf-36) 0-100 >4 months - mental composite in the intervention groups was 1.8 higher (4.92 lower to 8.52 higher)
Quality of life (SF-36) 0-100 >4 months - Physical composite	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - physical composite in the control groups was 67.6	The mean quality of life (sf-36) 0-100 >4 months - physical composite in the intervention groups was 11.9 higher (4.64 to 19.16 higher)
Quality of life (SF-36) 0-100 >4 months - Physical functioning	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - physical functioning in the control groups was 87	The mean quality of life (sf-36) 0-100 >4 months - physical functioning in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
					7.5 higher (0.36 lower to 15.36 higher)
Quality of life (SF-36) 0-100 >4 months - Physical role limitations	50 (1 study)	LOW[a] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months – 1 year - physical role limitations in the control groups was 63.2	The mean quality of life (sf-36) 0-100 >4 months - physical role limitations in the intervention groups was 29.1 higher (8.55 to 49.65 higher)
Quality of life (SF-36) 0-100 >4 months - Social functioning	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - social functioning in the control groups was 47.1	The mean quality of life (sf-36) 0-100 >4 months - social functioning in the intervention groups was 4.6 higher (3.26 lower to 12.46 higher)
Quality of life (SF-36) 0-100 >4 months - Emotional role limitations	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - emotional role limitations in the control groups was 85.2	The mean quality of life (sf-36) 0-100 >4 months - emotional role limitations in the intervention groups was 9.1 higher (7.57 lower to 25.77 higher)
Quality of life (SF-36) 0-100 >4 months - Emotional well-being	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - emotional well-being in the control groups was 72.2	The mean quality of life (sf-36) 0-100 >4 months - emotional well-being in the intervention groups was 4.8 lower (13.13 lower to 3.53 higher)
Quality of life (SF-36) 0-100 >4 months - Energy/fatigue	50 (1 study)	MODERATE[a] due to risk of bias		The mean quality of life (sf-36) 0-100 >4 months - energy/fatigue in the control groups was 57	The mean quality of life (sf-36) 0-100 >4 months - energy/fatigue in the intervention groups was 1.4 lower (10.2 lower to 7.4 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
Quality of life (SF-36) 0-100 >4 months - Pain	50 (1 study)	MODERATE[a] due to risk of bias		The mean quality of life (sf-36) 0-100 >4 months - pain in the control groups was 51.2	The mean quality of life (sf-36) 0-100 >4 months - pain in the intervention groups was 1.5 lower (6.81 lower to 3.81 higher)
Quality of life (SF-36) 0-100 >4 months - General health perceptions	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - general health perceptions in the control groups was 73.5	The mean quality of life (sf-36) 0-100 >4 months - general health perceptions in the intervention groups was 4.7 higher (3.16 lower to 12.56 higher)
Quality of life (SF-36) 0-100 >4 months - Change in perceived help	50 (1 study)	LOW[a,b] due to risk of bias, imprecision		The mean quality of life (sf-36) 0-100 >4 months - change in perceived help in the control groups was 73.3	The mean quality of life (sf-36) 0-100 >4 months - change in perceived help in the intervention groups was 14.5 higher (0.53 to 28.47 higher)
Pain score ≤4 months - NRS leg pain	63 (1 study) 13 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score ≤4 months - NRS leg pain in the control groups was 2.7	The mean pain score ≤4 months - NRS leg pain in the intervention groups was 1.1 lower (2.42 lower to 0.22 higher)
Pain score ≤4 months - NRS back pain	63 (1 study) 13 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score ≤4 months - NRS back pain in the control groups was 3	The mean pain score ≤4 months - NRS back pain in the intervention groups was 0.9 lower (2.27 lower to 0.47 higher)
Pain score ≤4 months - NRS total pain	63 (1 study) 13 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score ≤4 months - NRS total pain in the control groups was 3.2	The mean pain score ≤4 months - NRS total pain in the intervention groups was 0.7 lower (2.02 lower to 0.62 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
Pain score ≤4 months - NRS pain during night	63 (1 study) 13 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score ≤4 months - NRS pain during night in the control groups was 2.6	The mean pain score ≤4 months - NRS pain during night in the intervention groups was 0.9 lower (2.27 lower to 0.47 higher)
Pain score ≤4 months - NRS pain during day	63 (1 study) 13 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score ≤4 months - NRS pain during day in the control groups was 3.1	The mean pain score ≤4 months - NRS pain during day in the intervention groups was 0.7 lower (2.09 lower to 0.69 higher)
Pain score >4 months - NRS leg pain	63 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score >4 months - NRS leg pain in the control groups was 1.4	The mean pain score >4 months - NRS leg pain in the intervention groups was 0.4 lower (1.44 lower to 0.64 higher)
Pain score >4months - NRS back pain VAS	63 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score >4months - NRS back pain in the control groups was 2	The mean pain score >4months - NRS back pain in the intervention groups was 0.7 lower (1.92 lower to 0.52 higher)
Pain score >4 months - NRS pain during day	63 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score >4 months - NRS pain during day in the control groups was 2.2	The mean pain score >4 months - NRS pain during day in the intervention groups was 1 lower (2.27 lower to 0.27 higher)
Pain score >4 months - NRS pain during night	63 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score >4 months - NRS pain during night in the control groups was 1.8	The mean pain score >4 months - NRS pain during night in the intervention groups was 1 lower (2.19 lower to 0.19 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid versus usual care (95% CI)
Pain score >4 months - NRS total pain	63 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain score >4 months - NRS total pain in the control groups was 2.1	The mean pain score >4 months - NRS total pain in the intervention groups was 0.8 lower (2.07 lower to 0.47 higher)
Function ≤ 4 months ODI	63 (1 study) 13 weeks	LOW[a,b] due to risk of bias, imprecision		The mean function score - disability ≤ 4 months in the control groups was 7.6	The mean function score - ≤ 4 months in the intervention groups was 2.3 lower (5.32 lower to 0.72 higher)
Function >4 months ODI	63 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean function score >4 months in the control groups was 4.1	The mean function score - >4 months in the intervention groups was 1.8 lower (4.35 lower to 0.75 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 50: Non image guided: steroid and anaesthetic epidural versus placebo for sciatica in a population with unclear spinal pathology

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus placebo (95% CI)
Pain≤ 4 months - VAS leg pain VAS	228 (1 study) 52 weeks	MODERATE[a] due to risk of bias		The mean pain> 4 months - VAS leg pain in the control groups was 2	The mean pain> 4 months - VAS leg pain in the intervention groups was 0.3 lower (1.21 lower to 0.61 higher)
Pain≤ 4 months - VAS back pain VAS	228 (1 study) 52 weeks	MODERATE[a] due to risk of bias		The mean pain> 4 months - VAS back pain in the control groups was 0.9	The mean pain> 4 months - VAS back pain in the intervention groups was 0.1 lower (0.93 lower to 0.73 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus placebo (95% CI)
Pain >4 months - VAS leg pain VAS	228 (1 study) 12 weeks	MODERATE[a] due to risk of bias		The mean pain ≤4 months - VAS leg pain in the control groups was 1.8	The mean pain ≤4 months - VAS leg pain in the intervention groups was 0.5 lower (1.36 lower to 0.36 higher)
Pain >4 months - VAS back pain VAS	228 (1 study) 12 weeks	MODERATE[a] due to risk of bias		The mean pain ≤4 months - VAS back pain in the control groups was 0.7	The mean pain ≤4 months - VAS back pain in the intervention groups was 0.3 lower (1.08 lower to 0.48 higher)
Function (ODI)≤4 months ODI	228 (1 study) 12 weeks	MODERATE[a,b] due to risk of bias		The mean function score - (ODI)≤4 months in the control groups was -12	The mean function score - (ODI)≤4 months in the intervention groups was 0 higher (5.22 lower to 5.22 higher)
Function - (ODI) >4 months ODI	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision		The mean function score - (ODI) >4 months in the control groups was -14	The mean function score - (ODI) >4 months in the intervention groups was 2 lower (8.12 lower to 4.12 higher)
Psychological distress ≤ 4months - HAD anxiety HAD	228 (1 study) 12 weeks	LOW[a,b] due to risk of bias, imprecision		The mean psychological distress ≤ 4months - had anxiety in the control groups was -3	The mean psychological distress ≤ 4months - had anxiety in the intervention groups was 1 higher (0.04 lower to 2.04 higher)
Psychological distress ≤ 4months - HAD depression HAD	228 (1 study) 12 weeks	MODERATE[a] due to risk of bias		The mean psychological distress ≤ 4months - had depression in the control groups was -2	The mean psychological distress ≤ 4months - had depression in the intervention groups was 0 higher (1.04 lower to 1.04 higher)
Psychological distress >4 months - HAD depression HAD	214 (1 study) 52 weeks	MODERATE[a] due to risk of bias		The mean psychological distress >4 months - had depression in the control groups was -3	The mean psychological distress >4 months - had depression in the intervention groups was 0 higher (1.21 lower to 1.21 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus placebo (95% CI)
Psychological distress >4 months - HAD anxiety HAD	203 (1 study) 52 weeks	MODERATE[a] due to risk of bias		The mean psychological distress >4 months - had anxiety in the control groups was -2	The mean psychological distress >4 months - had anxiety in the intervention groups was 0 higher (1.38 lower to 1.38 higher)
Responder criteria - Improvement on leg pain 75% improvement on leg pain likert	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision	RR 1.18 (0.92 to 1.53)	472 per 1000	86 more per 1000 (from 43 fewer to 208 more)
Responder criteria - Improvement on back pain 75% improvement on back pain likert	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision	RR 1.11 (0.84 to 1.47)	435 per 1000	47 more per 1000 (from 78 fewer to 177 more)
Healthcare utilisation (further physiotherapy) No. undertaking further physiotherapy >4 months	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision	RR 1.23 (0.88 to 1.81)	250 per 1000	59 more per 1000 (from 50 fewer to 194 more)
Healthcare utilisation (referral to pain management services) No. referred to pain management >4 months	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision	Peto odds ratio 0.12 (0.01 to 1.94)	19 per 1000	17 fewer per 1000 (from 19 fewer to 17 more)
Healthcare utilisation (further epidurals) No. referred for further epidurals >4 months	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision	RR 1.32 (0.68 to 2.53)	120 per 1000	37 more per 1000 (from 40 fewer to 166 more)
Healthcare utilisation (analgesics) - ≤4 months Mean analgesic use/week	228 (1 study) 12 weeks	MODERATE[a] due to risk of bias		The mean healthcare utilisation (analgesics) - ≤4 months in the	The mean healthcare utilisation (analgesics) - ≤4 months in the

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus placebo (95% CI)
				control groups was 16	intervention groups was 7 lower (16.26 lower to 2.26 higher)
Healthcare utilisation (analgesics) - >4 months – 1 year Mean analgesic use/week	228 (1 study) 52 weeks	MODERATE[a] due to risk of bias		The mean healthcare utilisation (analgesics) - >4 months – 1 year in the control groups was 16	The mean healthcare utilisation (analgesics) - >4 months – 1 year in the intervention groups was 2 lower (12.35 lower to 8.35 higher)
Healthcare utilisation (surgery) 75% improvement on back pain likert	228 (1 study) 52 weeks	MODERATE[a] due to risk of bias	RR 1.08 (0.57 to 2.04)	139 per 1000	11 more per 1000 (from 62 fewer to 131 more)
Adverse events- morbidity minor adverse events	228 (1 study) 52 weeks	LOW[a,b] due to risk of bias, imprecision	RR 0.9 (0.41 to 1.99)	102 per 1000	10 fewer per 1000 (from 60 fewer to 101 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 51: Steroid +anaesthetic epidural versus combination of non-invasive interventions for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus pharmacological treatment (NSAIDS) (95% CI)
Pain ≤4 months VAS	139 (1 study) 2 weeks	MODERATE[a] due to risk of bias		The mean pain ≤4 months in the control groups was 4.39	The mean pain ≤4 months in the intervention groups was 0.97 lower (11.95 lower to 10.01 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 52: Non image guided: steroid and anaesthetic epidural versus pharmacological treatment (NSAIDS) for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus pharmacological treatment (NSAIDS) (95% CI)
Pain ≤4 months VAS	64 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision		The mean pain ≤4 months in the control groups was 4.1	The mean pain ≤4 months in the intervention groups was 0.8 lower (1.49 to 0.11 lower)
Function ≤4 months ODI	64 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision		The mean function ≤4 months in the control groups was 20.3	The mean function ≤4 months in the intervention groups was 4.1 lower (8.9 lower to 0.7 higher)
Healthcare utilisation (analgesics) No. using paracetamol	64 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision	RR 0.55 (0.20 to 1.50)	267 per 1000	121 fewer per 1000 (from 218 fewer to 108 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 53: Non image guided: steroid and anaesthetic epidural versus pharmacological treatment (combination) for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus pharmacological treatment (combination) (95% CI)
Pain - ≤ 4 months VAS	50 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain - ≤ 4 months in the control groups was 5	The mean pain - ≤ 4 months in the intervention groups was 0.5 lower (1.23 lower to 0.23 higher)
Pain -> 4 months VAS	50 (1 study) 6 months	LOW[a,b] due to risk of bias, imprecision		The mean pain -> 4 months in the control groups was 6.5	The mean pain -> 4 months in the intervention groups was 0.5 lower (1.26 lower to 0.26 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus pharmacological treatment (combination) (95% CI)
Adverse events - morbidity	50 (1 study) 6 months	LOW[a,b] due to risk of bias, imprecision	RR 1.25 (0.38 to 4.12)	160 per 1000	40 more per 1000 (from 99 fewer to 499 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 54: Non image guided: steroid and anaesthetic epidural versus anaesthetic epidural for sciatica primarily caused by (≥70%) disc prolapse

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus anaesthetic (95% CI)
Pain ≤ 4 months - Methyl prednisolone versus bupivacaine VAS	105 (1 study) 3 months	MODERATE[a,b] due to risk of bias		The mean pain ≤ 4 months - methyl prednisolone versus bupivacaine in the control groups was 6.18	The mean pain ≤ 4 months - methyl prednisolone versus bupivacaine in the intervention groups was 1.28 lower (1.69 to 0.87 lower)
Pain ≤4 months - Triamcinolone + Bupivicaine versus anaesthetic VAS	107 (1 study) 3 months	MODERATE[a] due to risk of bias		The mean pain ≤4 months - triamcinolone + bupivicaine versus anaesthetic in the control groups was 6.8	The mean pain ≤4 months - triamcinolone + bupivicaine versus anaesthetic in the intervention groups was 1.38 lower (1.71 to 1.05 lower)
Pain≤4 months - Dexamethasone + Bupivicaine versus anaesthetic VAS	105 (1 study) 3 months	MODERATE[a] due to risk of bias		The mean pain≤4 months - dexamethasone + bupivicaine versus anaesthetic in the control groups was 6.8	The mean pain≤4 months - dexamethasone + bupivicaine versus anaesthetic in the intervention groups was 0.98 lower (1.47 to 0.49 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus anaesthetic (95% CI)
Responder criteria (>75% improvement in pain subjectively) ≤4 months:	33 (1 study) 1 days	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.03 (0.67 to 1.58)	714 per 1000	21 more per 1000 (from 236 fewer to 414 more)
Responder criteria(>75% improvement in pain subjectively) >4 months:	33 (1 study) 20.8 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.9 (0.52 to 1.56)	643 per 1000	64 fewer per 1000 (from 309 fewer to 360 more)
Healthcare utilisation- surgery: N= had surgery at follow up	33 (1 study) 20.8 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.23 (0.35 to 4.02)	214 per 1000	49 more per 1000 (from 139 fewer to 647 more)
Healthcare utilisation- physiotherapy - Methyl Prednisolone + Bupivicaine versus anaesthetic No. referred for further physiotherapy	81 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision	RR 0.51 (0.26 to 0.99)	452 per 1000	223 fewer per 1000 (from 13 fewer to 348 fewer)
Healthcare utilisation- physiotherapy - Tiamcinoline + Bupivicaine versus anaesthetic No. referred for further physiotherapy	84 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision	RR 0.37 (0.17 to 0.78)	452 per 1000	287 fewer per 1000 (from 96 fewer to 383 fewer)
Healthcare utilisation- physiotherapy - Dexamethasone + Bupivicaine versus anaesthetic No. referred for further physiotherapy	82 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision	RR 0.66 (0.37 to 1.18)	452 per 1000	152 fewer per 1000 (from 304 fewer to 64 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 55: Non image guided: Steroid and anaesthetic epidural versus anaesthetic for sciatica primarily caused by (≥70%) spinal stenosis

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus anaesthetic (95% CI)
Responder criteria (>75% improvement in pain subjectively) ≤4 months: spinal stenosis	30 (1 study) 1 days	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.11 (0.55 to 2.24)	500 per 1000	55 more per 1000 (from 225 fewer to 620 more)
Responder criteria (>75% improvement in pain subjectively) >4 months – 1 year: spinal stenosis	30 (1 study) 20.8 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.17 (0.43 to 3.13)	333 per 1000	57 more per 1000 (from 190 fewer to 710 more)
Healthcare utilisation- surgery: spinal stenosis N= had surgery at follow up	30 (1 study) 20.8 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.76 (0.38 to 1.54)	583 per 1000	140 fewer per 1000 (from 362 fewer to 315 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs

Table 56: Non image guided: steroid and anaesthetic epidural versus anaesthetic epidural for sciatica in a population with unclear spinal pathology

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus anaesthetic (95% CI)
Healthcare utilisation - analgesics - Reduced drug intake No. reduced analgesia at follow-up	29 (1 study) 1 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.24 (0.58 to 2.68)	429 per 1000	359 fewer per 1000 (from 168 fewer to 672 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Steroid + anaesthetic versus anaesthetic (95% CI)
Healthcare utilisation - surgery No. referred for surgery Follow-up: mean 1 months	30 (1 study)	VERY LOW[a,b] due to risk of bias, imprecision	RR 1 (0.31 to 3.28)	267 per 1000	267 more per 1000 (from 83 fewer to 876 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 57: Non image guided: steroid epidural versus anaesthetic epidural for sciatica in a population with unclear spinal pathology

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Anaesthetic versus steroid (95% CI)
Healthcare utilisation (surgery) no. referred for surgery	35 (1 study) 1 months	VERY LOW[a,b] due to risk of bias, imprecision	peto odds ratio 0.11 (0.01 to 1.77)	0 per 1000	*

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.
*Not estimable as zero events in 1 treatment arm

24.4 Economic evidence

Published literature

Two economic evaluations were identified that included epidural injections for sciatica as a comparator and have been included in this review.[97,105] These are summarised in the economic evidence profiles below (**Table 58**, **Table 59**) and the economic evidence table in Appendix I.

Five economic evaluations were selectively excluded due to a combination of applicability and methodological limitations.[99,106-109] These studies are listed in Appendix M, with reasons for exclusion given.

See also the economic article selection flow chart in Appendix F.

Table 58: Economic evidence profile: Steroid plus local anaesthetic (non-image guided) versus placebo

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Price 2005[97] (UK)	Partially applicable (a)	Potentially serious limitations (b)	• With-RCT analysis (associated clinical paper Arden 2005) • Cost-utility analysis (QALYs) • Population: Adults with low back pain and sciatica (unclear spinal pathology). • Two comparators in full analysis: (c) 1.Placebo (injection of 2ml of normal saline into the interspinous ligament) 2. Steroid plus local anaesthetic epidural, non-image guided (lumbar epidural injection of 80mg triamcinolone acetonide and 10ml of 0.125% bupivacaine) • Follow-up: 1 year	2−1: £265 (d)	2−1: 0.0059350 QALYs (e)	2 vs 1: £44,701 per QALY gained	No bootstrapping undertaken. A sensitivity analysis was conducted where the costs were adjusted assuming only 1 epidural injection was administered and the impact on QALYs is assumed to be unchanged. ICER = £25,746. Additional sensitivity analyses were undertaken, where the maximum healthcare professional resource use reported in the trial were used to estimate intervention costs and where the patient is assumed to require an overnight stay. In both cases this increased the total cost of intervention 2 and therefore the ICER.

(a) UK resource use data (1999-2002) and unit costs (2002/3) may not reflect current NHS context. Non-NICE reference case utility measure used to estimate QALYs (SF-6D), unclear if UK population valuations were used.

(b) Within-trial analysis and so does not reflect full body of available evidence for this comparison; Arden 2005 is 1 of 3 studies included in the clinical review for steroid epidurals + local anaesthetic versus placebo (non-image guided). Limited sensitivity analyses undertaken.

(c) All participants received a standard physiotherapy package prior (education and exercise) and analgesia as required. Injections were repeated at 3 and 6 weeks in relation to response. The indication for repeat injection was less than a 75% improvement in Oswestry Disability Questionnaire from the baseline visit.

(d) 2002-2003 UK pounds. Cost components incorporated: For those receiving intervention 2 only: assessment and review by clinician, medical and nursing time incurred during procedure, nursing time on recovery post-procedure, drug and equipment use associated with procedure and pathology and radiology use.

(e) QALYs were calculated using patient-level SF-36 data, converted to SF-6D utility, collected at baseline, 3, 6, 12, 26 and 52 weeks. At 12 weeks the average scores converged for intervention 1 and 2. The area under the curve approach was used to calculate incremental QALYs

Table 59: Economic evidence profile: Steroid (non-image guided) epidural versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Spijker-Huiges 2014[105] (Netherlands)	Partially applicable (a)	Potentially serious limitations (b)	• With-RCT analysis (associated clinical paper Spijker-Huiges 2014A) • Cost-effectiveness analysis (health outcome: 1point improvement in NRS back pain score) • Population: Adults with sciatica (unclear spinal pathology). • Two comparators in full analysis: 1. Usual care provided by GP (pain treatment with analgesics, advice to maintain normal activities and referral if necessary) 2. Steroid epidural, non-image guided (segmental epidural injection of 80mg of triamcinolone in normal saline) • Follow-up: 1 year	2−1: £58 (c)	2−1: 0.97 mean change in NRS back pain score (d)	£60 per 1 point improvement in NRS back pain	Bootstrapping undertaken but only from a societal perspective which is not presented here. No other sensitivity analyses were conducted.

(a) Dutch resource use data (2005-2007) and unit costs (date unclear) may not reflect current NHS context. QALYs were not used as the health outcome measure.

(b) Within-trial analysis and so does not reflect full body of available evidence for this comparison; Spijker-Huiges 2014A is 1 of many studies included in the clinical review for steroid epidurals versus usual care (non-image guided). No sensitivity analyses undertaken.

(c) Year unclear, assumed to be 2007 Euros converted using 2007 purchasing power parities[110].Cost components incorporated: Intervention cost (for intervention 2 only), GP care, hospital care, additional examinations, medication, physiotherapy, alternative therapies and home help visits.

(d) Mean change in NRS back pain score calculated from point estimate for the ICER reported in the study

The study by Spijker-Huiges 2015[99] was not combined with the previous one as the costs were reported only from a societal perspective and the QALYs calculated did not match with the results of the previous study and the individual SF36 scores reported for each intervention, ie while the individual SF36 scores show an improvement in the group receiving epidural, the QALY estimates were in favour of the control group.

24.5 Evidence statements

24.5.1 Clinical

24.5.1.1 Image guided epidurals versus sham/placebo (primarily caused by >70% disc prolapse)

In people with sciatica there was clinical benefit of an anti-TNF epidural compared with placebo for leg pain demonstrated in evidence from 1 study at up to 4 months (very low quality, n=37). When the epidural was a steroid combined with an anaesthetic, there was clinical benefit favouring the intervention arm for leg pain and number of responders with greater than or equal to 50% reduction in pain, but no difference for function (n=65, moderate quality).When anaesthetic only was administered, no difference between anaesthetic or sham was observed for pain or number of responders. No evidence was available for the other critical outcomes or for steroid mono-therapy.

24.5.1.2 Image guided epidurals versus active control

In people with sciatica primarily caused by >70% prolapse, non-disc lesion, or unclear spinal pathologies, there was no clinical benefit of a steroid plus anaesthetic epidural compared with anaesthetic alone for pain and function at either short or longer term follow up (only data for up to 4 months was available for the unclear spinal pathologies evidence). The evidence ranged from very low to high quality, and from 1 to 4 studies, n=69 to 606. When anti-TNF was combined with anaesthetic (in sciatica primarily caused by >70% prolapse), there was no benefit compared to anaesthetic alone observed for pain or function at ≤4 months (1 study, low and moderate quality, n=56). No evidence was available for the other critical outcomes or for other interventions.

In people with sciatica primarily caused by >70% prolapse, there was clinical benefit of a steroid combined with anaesthetic epidural compared with combinations of non-invasive interventions or compared with anti-TNF with anaesthetic for leg pain or function at less than or equal to 4 months (1 study, moderate quality, n=100 and n=54 for the different comparisons respectively). There was also clinical benefit for quality of life for the comparison with non-invasive combinations. No evidence was available for the other critical outcomes or interventions.

24.5.1.3 Non image guided epidurals versus sham/placebo

In people with sciatica primarily caused by >70% prolapse, there was no clinical benefit of a steroid compared with placebo for function at greater than 4 months follow-up (low quality, 2 studies, n=221), and pain at up to 4 months (moderate quality, 2 studies, n=174). There was no evidence for this comparison for any of the critical outcomes in the population with an unclear pathology. When steroid was combined with anaesthetic (in sciatica with an unclear pathology) there was no clinical benefit for pain or function demonstrated by 1 study at both short and long term follow-ups (moderate and low quality, n=228).

24.5.1.4 Non image guided epidurals versus active control

In people with sciatica with an unclear pathology, there was a clinical benefit of steroid compared to usual care for leg pain and function demonstrated in evidence from 1 study at up to 4 months but not at greater than 4 months and most of the quality of life domains at both short and long term follow up (low quality, n=63).

In people with sciatica primarily caused by >70% prolapse, there was no clinical benefit of steroid combined with anaesthetic compared with pharmacological treatment (NSAIDs) for pain and function demonstrated in evidence from 1 study at up to 4 months (low quality, n=64), or for pain when compared with a combination of pharmacological interventions at both short and long term follow up (1 study, low and very low quality, n=50).

In people with sciatica primarily caused by >70% prolapse, there was clinical benefit of steroid combined with anaesthetic compared with anaesthetic demonstrated in evidence from 1 study for pain at up to 4 months when using a combination of methylprednisolone or triamcinolone in combination with bupivacaine (moderate quality, n=105). However there was no benefit when dexamethasone and bupivacaine were used (moderate quality, n=105). There was no evidence for any of the critical outcomes for this comparison in the sciatica caused by spinal stenosis or unclear pathology populations.

24.5.2 Economic

- One cost-utility analysis found that non-image guided epidural injections of steroid plus anaesthetic was not cost effective compared to placebo for adults with low back pain and sciatica (ICER: £44,701 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-effectiveness analysis found that non-image guided steroid epidural was more costly and more effective than placebo for adults with sciatica (ICER: £60 per 1 point improvement in NRS back pain score). This analysis was assessed as partially applicable with potentially serious limitations.

24.6 Recommendations and link to evidence

Recommendations	**The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations**
Research recommendations	**The current research recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations-for-research**
Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Adverse events (mortality and morbidity), and healthcare utilisation were also considered as important. For image-guided epidurals, evidence was reported for all of the critical outcomes, but there were limited data for quality of life. For non-image-guided epidurals there was no evidence for quality of life.
Trade-off between clinical benefits and harms	The GDG agreed that there was sufficient RCT evidence for all comparisons except for image-guided epidurals versus placebo/sham. However, there was no relevant cohort data found to address this.

The GDG agreed that the evidence for the effectiveness of epidurals was conflicting. They noted that sciatic symptoms usually improve over the course of a few months in the majority of people without treatment. The placebo-controlled trials did show some evidence of an effect for epidurals, particularly for the combination of steroid plus anaesthetic. The evidence suggested the important component was the steroid, but there was no evidence of benefit of steroid alone or anaesthetic alone when compared to placebo/sham for any critical outcome. As a responder analysis suggested a 35% increase in the probability that people obtain substantial pain relief following epidural injections (steroid plus anaesthetic) compared to placebo, it was agreed that epidural injection of local anaesthetic and steroid should be considered as a treatment option. Most of the RCT evidence in the review came from people with acute and moderately severe sciatica, and the GDG considered that this would be the population most likely to benefit from epidural injection.

The group discussed the evidence for anti-TNF. There was no evidence found for non-image guided anti-TNF, but there was evidence for image-guided anti-TNF epidurals. Despite the evidence showing a positive effect of image-guided anti-TNF epidurals on pain and function, the GDG noted that the evidence was limited as it came from three studies which could not be pooled together because different comparisons were used. The group discussed the risks associated with the different routes of administration of an epidural. The opinion of the group was that serious complications are very rare. The most common adverse event was a temporary increase in pain which the GDG considered could be outweighed by the potential benefits.

The group discussed that there is some guidance in the UK suggesting epidurals should be given under image-guidance based on safety grounds, although there was limited evidence for a difference in effectiveness of image guided compared to non-image guided epidural injections from this review. It was therefore agreed that a recommendation for future research should be drafted to ascertain the evidence base for safety and effectiveness for image guided and non- image guided epidural injections.

Summary

Overall, the GDG considered that epidural injection, whether administered under image guidance or without, is a relatively safe and routinely used procedure, and had some evidence demonstrated by placebo-controlled trials for effectiveness in pain relief for epidurals of local anaesthetic and steroid. There was insufficient/ lack of evidence for effectiveness to support epidural injections using anti-TNF.

The studies were conducted in small populations who had at least moderately severe sciatica and did not have further treatment options available to them (other than surgery). The evidence reviewed by the GDG suggests that epidural injection of local anaesthetic and steroid may reduce the number of people who would require surgical intervention. This evidence was reinforced by evidence from 2 trials that were included in the spinal decompression review (See Chapter 28) that compared decompression to epidurals showing that 50% of people who had an epidural did not go on to have surgery. The group therefore agreed that in acute, severe sciatica where patients would otherwise be offered surgery, an epidural injection of local anaesthetic and steroid should be considered.

The group discussed the evidence that had been conducted in sciatica patients with central spinal canal stenosis. The populations studied comprised people with neurogenic claudication primarily. There was insufficient evidence that epidural injections of local anaesthetic and steroid were effective in this group of people and it was noted that current opinion also reflects this. The group therefore agreed to

	make a recommendation against using epidurals in people with claudicant leg symptoms caused by central spinal canal stenosis. The GDG discussed that the purpose of this review had been to determine efficacy of different injectates, rather than comparing image guided to non-image guided injections. However, the stratification of the review by those delivered under image guided to those that weren't did not demonstrate a clear indication of improved efficacy of image guided epidurals over non-image guided. They therefore agreed that a research recommendation was warranted in this area.
Trade-off between net clinical effects and costs	Two economic evaluations were included comparing non-image guided epidural with either usual care or placebo in a population of adults with sciatica.[97, 105] In particular the study by Price *et al.* (2005)[97] was a cost-utility analysis comparing the intervention with placebo which concluded that epidural increased costs and improved health (increased QALYs), with an incremental cost-effectiveness ratio of £44,701 per QALY gained. In sensitivity analysis where the costs were adjusted assuming only 1 epidural injection was administered and the impact on QALYs was assumed to be unchanged, the ICER went down to £25,746. The group noted that as the recommendation for epidurals was for the acute sciatica population (most likely to be defined as having symptoms for <3 months), then multiple injections would not usually be performed within this short period of time. The GDG discussed the likely higher effectiveness observed with placebo as opposed to no treatment and concluded that if epidural was compared to no treatment or usual care it would probably be associated with a higher QALY gain, and therefore it would be more cost effective. In the same study no cost was attached to the placebo arm while in reality patients could incur the cost of other treatments such as medications and the cost of their side effects. The GDG noted that the studies from which the cost effectiveness data was derived did not have a diagnosis of sciatica confirmed by imaging. The GDG felt that clinical diagnosis alone may overestimate the numbers of patients with true sciatica and lower their confidence in the results. There was evidence suggesting that epidural injection may reduce the number of people with severe sciatica requiring surgical intervention; this would generate some cost savings. For these reasons, the GDG decided not to make a strong recommendation on epidural injections but they concluded that they may be cost effective for some patients and therefore it should be considered.
Quality of evidence	The quality of the evidence for both image guided and non-image guided epidurals was mostly low or moderate (due to risk of bias usually caused by selection or performance bias, small sample sizes and imprecision) across all of the outcomes and comparisons in the review. There was evidence to show an effect of anti-TNF (image-guided), however this was only from single studies, which mostly had small sample sizes. Some of the studies had incomplete reporting of outcome data (for example, no standard deviations were reported for some outcomes and 1 study only had data for 1 participant in the comparison arm). This also meant that the evidence was rated as being at high risk of bias and so overall the group did not have confidence in the findings. The GDG had more confidence in the evidence for epidurals in sciatica patients with spinal stenosis (steroid was given as an adjunct) because the main study contributing to the meta-analysis was conducted in 400 participants. The group were less confident in the results of the other contributing study, since it was smaller and although it was also conducted in spinal stenosis patients, it differed considerably to the other studies in the review. The population consisted of chronic sciatica patients with over 100 months of pain, and patients could be given as many epidural

	injections as they needed (the average given was 4). The GDG felt that this did not reflect clinical practice.
Other considerations	The group discussed the effectiveness of giving multiple / subsequent epidural injections. The group noted that as the recommendation for epidurals was for the acute sciatica population (most likely to be defined as having symptoms for <3 months), then multiple injections would not usually be performed within this short period of time. The GDG agreed that this recommendation would equally apply for pregnant women and should be considered alongside BNF guidance. The GDG were aware of existing NICE interventional procedure guidance for Therapeutic endoscopic division of epidural adhesions (IPG333) recommending special arrangements for clinical governance, consent, audit and research.[43] This procedure was therefore excluded from this review and if it's use is considered for people with sciatica, existing guidance should be followed. **Research recommendation** **Why this is important:** Epidural injection of therapeutic substances that include corticosteroids is commonly offered to people with sciatica. Epidural injection might improve symptoms, reduce disability and speed up return to normal activities. Several different procedures have been developed for epidural delivery of corticosteroids. Some practitioners inject substances through the caudal opening to the spinal canal in the sacrum (caudal epidural), whereas others direct the injection through the foraminal space at the presumed level of nerve root irritation (transforaminal epidural). There is a rationale that transforaminal epidurals might be most effective, by ensuring delivery of corticosteroids directly to the region in which the nerve root might be compromised. However, transforaminal epidural injection requires imaging, usually within a specialist setting, potentially limiting treatment access and increasing costs. Caudal epidural injection might be undertaken without imaging, or with ultrasound guidance in a non-specialist setting, but, it has been argued, the drug might not reach the affected nerve root and therefore this approach might not be as effective as would be transforaminal injection. Empirical evidence that 1 approach is clearly superior to the other is currently lacking. Access to the two procedures varies between healthcare providers, and people who do not respond to caudal corticosteroid injection might subsequently receive image guided epidural injection. People with sciatica might therefore currently experience unnecessary symptoms at unnecessary cost to the NHS than would be the case if the most cost effective modes of delivering epidural corticosteroid injections were used.

25 Surgery and prognostic factors

25.1 Introduction

Surgery for low back pain and sciatica is most commonly carried out when more conservative treatments have failed. As with most major invasive procedures, surgery to manage back pain and sciatica carries with it an inherent risk of serious harm.

For surgery in people with low back pain, a number of prognostic factors are thought to be linked to better or worse response to surgery. These include a history of previous spinal fusion surgery, smoking status, BMI and psychological distress. The likelihood of successful surgery may be important therefore to help inform the clinical decision to refer a person for surgery. In people with suspected sciatica however, the prognostic factors for response to surgery are thought to be distinct and may be more affected by the presence of radicular symptoms and presence of pathology on imaging.

This review intends to ascertain the evidence for whether these prognostic factors are indicative of response to surgical intervention in people with low back pain or sciatica.

25.2 Review question: Does history of previous fusion surgery, smoking status, BMI or psychological distress predict response to surgery in people with non-specific low back pain?

For full details see review protocol in Appendix C.

Table 60: Characteristics of review question (low back pain)

Population	People aged 16 or above with non-specific low back pain (with/without sciatica) or low back pain without sciatica who have failed to respond to appropriate conservative therapy.
Prognostic variable/s under consideration	• History of previous fusion surgery • Smoking • BMI >30 • Psychological distress
Confounding factors	Duration of symptoms

Outcomes	**Critical**
	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).
	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).
	• Function (for example the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BPI, BDI, STAI)
	• Adverse events
	  ○ Mortality
	  ○ Morbidity
	  ○ Re-operation rate
	Important

	• Surgery conversion rate
Study design	• Prospective and retrospective cohorts (with multivariate analysis adjusted for key confounders (if none are identified those with multivariate analysis adjusted for other confounders will be included) • Randomised trials (if appropriate) with multivariate analysis adjusted for key confounders (if none are identified those with multivariate analysis adjusted for other confounders will be included) • Systematic reviews of the above

25.3 Review question: Does image concordant pathology or presence of radicular symptoms predict response to surgery in people with suspected sciatica?

Table 61: Characteristics of review question (Sciatica)

Population	People aged 16 or above with sciatica who have failed to respond to appropriate conservative therapy.
Prognostic variable/s under consideration	• Image concordant pathology (diagnosis supported by imaging - i.e. MRI or CT. To see if compression is present or not) • Radicular symptoms (pain that extends to leg vs. pain in back/buttock only)
Confounding factors	• Duration of symptoms

Outcomes	**Critical**
	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).
	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).
	• Function (for example the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BPI, BDI, STAI)
	• Adverse events
	  ○ Mortality
	  ○ Morbidity
	  ○ Re-operation rate
	Important
	• Surgery conversion rate

Study design	• Prospective and retrospective cohorts (with multivariate analysis adjusted for key confounders (if none are identified those with multivariate analysis adjusted for other confounders will be included) • Randomised trials (if appropriate) with multivariate analysis adjusted for key confounders (if none are identified those with multivariate analysis adjusted for other confounders will be included) • Systematic reviews of the above

25.4 Clinical evidence

A.1.1 Low back pain

Four studies were included in the review.[111-116] Evidence from these are summarised in the clinical evidence profile below (table 63) See also the study selection flow chart in Appendix E, forest plots in Appendix K, Grade tables in Appendix J, study evidence tables in Appendix H and exclusion list in Appendix L.

We searched for studies with multivariable analysis for all the prognostic factors included in the review protocol. Although the four included studies carried out multivariable analyses, they all adjusted for different confounding variables (defined in table 63).

Table 62: Summary of studies included in the review

Study	Population	Prognostic variable(s)	Confounders	Outcomes	Limitations
Ostelo 2005[112] (Prospective study conducted within the framework of RCT)	Single cohort of people with low back pain with/without sciatica recruited from multicentre in the Netherlands N=105 Type of surgery= no details provided	BMI, Psychological distress-negative affectivity (Negative Emotionality sub-scale of the Multi-dimensional Personality Questionnaire)NEM >1-≤4 vs NEM ≤1 (reference)and NEM >4 vs NEM ≤1(reference) (High is worse outcome) Radicular symptoms (pain that extends to leg vs. pain in back/buttock only)-Preoperative-LP (VAS >43)	Duration of complaints before surgery, age, gender, BMI, whether or not pain medication was taken at baseline because the residual complaints, number of days in hospital following the surgery, severity of pain in back and leg (both on VAS), pain catastrophising (Pain Catastrophising Scale, PCS), fear of movement (Tampa scale for Kinesiophobia, TSK)	Recovered Function (RMDQ≤4) Recovered Back Pain (VAS ≤10 mm), Recovered Leg Pain (VAS ≤10 mm) Follow-up= 12 months	High risk of bias. Cross- sectional study design. Key confounder defined in the protocol adjusted for in the multivariate analysis. Variables showing a promising relationship in the univariate analysis were included in the multivariate analysis.
Pearson 2012[113] (combined prospective RCT and observati	Single cohort with spinal stenosis (with/without sciatica) recruited from multicentre in the United States	BMI, Smoking status	Duration of symptoms, age, gender, centre, baseline ODI score income, treatment preference, compensation status, baseline	Treatment Effect = change in Function ODI (surgery)-change in Function ODI (non-operative)	Very high risk of bias. Combination of RCT and cross-sectional study design; high rate of protocol non-adherence and the consistency

Study	Population	Prognostic variable(s)	Confounders	Outcomes	Limitations
onal cohort)	N=634 Type of surgery= standard open decompressive laminectomy compared to the non-operative treatment of usual care.		Stenosis Bothersomeness Index, joint problems, stomach problems and bowel problems	Follow-up= 4 years	of findings in RCT and key confounder defined in the protocol adjusted for in the multivariate analysis.
Silverplats 2010[115] (Prospecti ve cohort)	Single cohort, consecutive patients with low back pain with/without sciatica recruited in Sweden N=171 Type of surgery=midlin e approach to dissect the paravertebral muscles down to the laminae and the interlaminar was resected. Partial laminotomy performed when required	Radicular Symptoms (VAS Leg Pain), Smoking, Psychological distress (Zung Depression Scale, ZDS)	Duration of pain, age gender, level of disc hernia, use of analgesics, time on sick leave, baseline leg and back pain, ZDS and ODI	Pain (VAS) Follow-up=2 years	Very high risk of bias. Cross-sectional study design. Key confounder defined in the protocol adjusted for in the multivariate analysis. All predictors that showed a potential influence in the initial bivariate analyses were included. Results were only reported narratively with no statistics (apart from p-values given)
Trief 2000[116] (Prospecti ve cohort) study in patients	Single cohort of patients with low back pain recruited in the USA N=159	Psychological Distress (Dallas Pain Questionnaire)	Duration of pain, age gender	Function (Dallas Pain Questionnair e)	Very high risk of bias. The study reported other data/outcomes which did not meet the criteria set in the protocol. The

Study	Population	Prognostic variable(s)	Confounders	Outcomes	Limitations
with low back pain	Type of surgery=Lumbar spine surgery. Majority (67.7% underwent fusion)				statistic reported for the data that met the inclusion criteria is not interpretable and does not answer the question posed in this review.

A.1.2 Sciatica

Two studies were included in the review.[117,111] Evidence from these are summarised in the clinical evidence profile below (table 63) See also the study selection flow chart in Appendix E, forest plots in Appendix K, Grade tables in Appendix J, study evidence tables in Appendix H and exclusion list in Appendix L.

We searched for studies with multivariable analysis for all the prognostic factors included in the review protocol. Although the 2 included studies carried out multivariable analyses, they all adjusted for different confounding variables (defined in table 63). There was no evidence found for image concordant pathology as a prognostic factor in people with sciatica.

Table 63: Summary of studies included in the review

Study	Population	Prognostic variable(s)	Confounders	Outcomes	Limitations
Cook 2015 [117](Retrospective cohort study)	Single cohort recruited from multicentre spine outcomes registry in the USA N=1108 Type of surgery=discectomy	Radicular symptoms (pain that extends to leg vs. pain in back/buttock only)-Preoperative-LP VAS, Leg pain greater than back pain	Age, BMI, gender, previous back surgery history, baseline ODI, baseline back pain VAS, baseline SF-12 PCS and MCS scores, presence/absence of complications, levels of surgery and diagnosis.	Function (ODI>10) Follow-up=23.5 months (range 12-49 months)	Very high risk of bias. Key confounder defined in the protocol not adjusted for in the multivariate analysis. Results found significant with p values 0.10 in the univariate analysis were included in four distinct MVA models

Study	Population	Prognostic variable(s)	Confounders	Outcomes	Limitations
Lee 2010 [111](Retrospective cohort study)	Single cohort recruited in South Korea N=40 Type of surgery=discectomy	Radicular symptoms (pain that extends to leg vs. pain in back/buttock only)-Preoperative-LP VAS	Duration of pain, age, gender, BMI, smoking, surgical levels and whether the surgery was a revision operation or the primary operation.	Percentage change in pain (VAS) Percentage change in function (ODI) Follow-up= 1 year	Very high risk of bias. Cross-sectional study design. Key confounder defined in the protocol adjusted for in the multivariate analysis. Results found significant in the univariate analysis were included in the MVA although there was poor reporting of the rationale for inclusion of the prognostic factors.

25.4.1 Low back pain

Table 64: Clinical evidence summary: Smoking (surgery: open decompressive laminectomy)

Risk factors/outcomes/population	Number of studies	Mean difference and SE in single study	Imprecision	GRADE
Smoking versus non-smoking for predicting the treatment effect(TE=change in ODI(surgery) – Change in ODI(non-operative) at 4 years on patients with spinal stenosis (low back pain and/or Sciatica population)	1	Adjusted Mean Difference[Standard Error]: 10.1 (3.055)[a, b]	No serious imprecision	LOW

[a] Methods multivariable analysis, including key covariates used in analysis to assess if smoking versus non-smoking is an independent risk factor. Key covariates included: Duration of symptoms, Age, Gender, Centre, Baseline ODI score income, treatment preference, compensation status, baseline Stenosis Bothersomeness Index, joint problems, stomach problems and bowel problems
[b] ANCOVA results

Table 65: Clinical evidence summary: BMI >30 (surgery not defined)

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
BMI>30 versus BMI< 25 for predicting the effect on recovered Function (RDQ≤4) at 3 months (patients with back or leg pain)	1	Adjusted OR : 0.79 [0.21, 2.94]	Serious[b]	VERY LOW

[a] 95% CI around the median crosses null line.
Note: Methods multivariable analysis, including key covariates used in analysis to assess if BMI>30 versus BMI< 25 is an independent risk factor. Duration of complaints before surgery, age, gender, BMI, whether or not pain medication was taken at baseline because the residual complaints, number of days in hospital following the surgery, severity of pain in back and leg (both on VAS), pain catastrophising (Pain Catastrophising Scale, PCS), fear of movement (Tampa scale for Kinesiophobia, TSK)

Table 66: Clinical evidence summary: Psychological Distress (surgery not defined)

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
Psychological Distress (Negative Affectivity (NEM>1-≤4 versus NEM ≤1) on Back Pain (VAS≤10mm) at 3 months (patients with back or leg pain) NEM scale:1-5, high is poor outcome	1	Adjusted OR : 0.55 [0.19, 1.61]	No serious imprecision	LOW
Psychological Distress (Negative Affectivity (NEM>4 versus NEM ≤1) on Back Pain (VAS≤10mm) at 3 months (patients with back or leg pain) NEM scale:1-5, high is poor outcome	1	Adjusted OR : 0.21 [0.06, 0.78]	Serious[b]	VERY LOW

[a] *95% CI around the median crosses null line.*

Note: Methods multivariable analysis, including key covariates used in analysis to assess Negative Affectivity (NEM>1-≤4/NEM >4 versus NEM ≤1 is an independent risk factor. Duration of complaints before surgery, age, gender, BMI, whether or not pain medication was taken at baseline because the residual complaints, number of days in hospital following the surgery, severity of pain in back and leg (both on VAS), pain catastrophising (Pain Catastrophising Scale, PCS), fear of movement (Tampa scale for Kinesiophobia, TSK)

25.4.2 Sciatica

Table 67: Clinical evidence summary: Radicular symptoms (continuous outcome) (surgery: open decompressive laminectomy)

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
Pre-op predominant Leg Pain (Bothersomeness Scale,0-6 point Likert-type scale) versus pre-op predominant Back Pain (Bothersomeness Scale,0-6 point Likert-type scale predicting the treatment effect (TE=change in ODI(surgery) – Change in ODI(non-operative)) at 4 years on patients with	1	Adjusted Mean Difference(Standard Error): -4.2 (1.088)	No serious imprecision	VERY LOW

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
spinal stenosis (low back pain and/or Sciatica population.				

Note: Methods multivariable analysis, including key covariates used in analysis to assess if Pre-op radicular pain to leg is an independent risk factor. Key covariates included: Duration of symptoms, Age, Gender, Centre, Baseline ODI score income, treatment preference, compensation status, baseline Stenosis Bothersomeness Index, joint problems, stomach problems and bowel problems.

Table 68: Clinical evidence summary: Radicular symptoms (surgery not defined)

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
Pre-operative leg pain (VAS >43) versus Leg Pain (VAS ≤43)on leg pain VAS≤10 mm) at 3 months (patients with back or leg pain)	1	Adjusted OR : 0.24 [0.10, 0.58]	No serious imprecision	VERY LOW
Pre-operative leg pain (VAS >43) versus leg pain (VAS ≤43) on leg pain (VAS≤10 mm) at 12 months (patients with back or leg pain)	1	Adjusted OR : 0.38 [0.16, 0.75]	No serious imprecision	VERY LOW

Note: Methods multivariable analysis, including key covariates used in analysis to assess if Pre-operative Leg Pain (VAS >43) versus Leg Pain (VAS ≤43 is an independent risk factor. Duration of complaints before surgery, age, gender, BMI, whether or not pain medication was taken at baseline because the residual complaints, number of days in hospital following the surgery, severity of pain in back and leg (both on VAS), pain catastrophising (Pain Catastrophising Scale, PCS), fear of movement (Tampa scale for Kinesiophobia, TSK)

Table 69: Clinical evidence summary: Radicular symptoms (categorical outcome) (surgery: dissection of the paravertebral muscles down to the laminae and resection of the interlaminar)

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
Effects of Pre-op leg pain (VAS) on Function (ODI>10) at 1 year (patients with Sciatica	1	Adjusted OR : 0.523 [0.135, 2.028]	Serious[b]	VERY LOW

[a] 95% CI around the median crosses null line.

Note: Methods multivariable analysis, including key covariates used in analysis to assess if pre-op Leg Pain (VAS) is an independent risk factor. Key covariates included: Duration of pain, age, gender, BMI, smoking, surgical levels and whether the surgery was a revision operation or the primary operation.

Table 70: Clinical evidence summary: Radicular symptoms (surgery: discectomy)

Risk factors/outcomes/population	Number of studies	OR Effect and CI in single study	Imprecision	GRADE
Leg pain greater than back pain on 50% improvement in pain in 1 year	1	Adjusted OR : 1.02 [0.70, 1.48]	No serious imprecision	LOW
Leg pain greater than back pain on 30% improvement in function assessed by ODI in 1 year	1	Adjusted OR : 1.71 [1.18, 2.47]	No serious imprecision	LOW
Leg pain greater than back pain on 50% improvement in function assessed by ODI in 1 year	1	Adjusted OR : 1.93 [1.35, 2.77]	No serious imprecision	LOW

Methods multivariable analysis, including key covariates used in analysis to assess if leg pain greater than back pain is an independent risk factor. Key covariates included: Age, BMI, gender, previous back surgery, history, baseline ODI, baseline back pain VAS, baseline SF-12 PCS and MCS scores, presence/absence of complications, levels of surgery and diagnosis

25.5 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix F.

25.6 Evidence statements

25.6.1 Clinical

25.6.1.1 Low back pain

Smoking

Low quality evidence from a single cohort study with a multivariable analysis, showed smoking status was a prognostic factor after adjusting for duration of symptoms in predicting improvement in function after surgery, favouring not smoking, in people with low back pain (n=634).

BMI >30

Very low quality evidence from a single cohort study with multivariable analysis gave some indication that a BMI greater than 30 may be a prognostic factor in predicting poorer response to surgery in terms of improving function in people with low back pain (n=105) after adjusting for duration of complaints before surgery. This was highly imprecise with an adjusted odds ratio of 0.79 [0.21, 2.94].

Psychological Distress

Low-very low quality evidence from a single cohort study with multivariable analysis, suggested that psychological distress was a prognostic factor in predicting response to surgery in terms of improving back pain after adjusting for duration of complaints before surgery, with lower levels of distress predicting better outcome, in people with low back pain or sciatica (n=105).

History of previous fusion surgery

No relevant evidence was identified.

25.6.1.2 Sciatica

Radicular symptoms

Very low quality evidence from a single cohort study with multivariable analysis suggested presence of radicular symptoms was a prognostic factor for predicting the response to surgery

at less than or equal to 4 months after adjusting for duration of symptoms (n=105). Low- very low quality evidence from 4 cohort studies with multivariable analyse is, suggested presence of radicular symptoms was a prognostic factor in predicting response to surgery at greater than 4 months in people with sciatica (n=1782) after adjusting for duration of symptoms, duration of complaints before surgery and duration of pain. This evidence indicated that greater radicular symptoms / higher leg pain scores indicated better response to surgery.

Image-concordant pathology

No relevant evidence was identified

25.6.2 Economic

No relevant economic evaluations were identified.

25.7 Recommendations and link to evidence

Recommendations	The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations
Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity; function, psychological distress and adverse events (mortality, morbidity and re-operation rate) were the outcomes that were critical for decision making. Surgery conversion rate was also considered as important. Evidence was reported for all prognostic factors that were pre-specified in the protocol except for history of fusion surgery for people with low back pain and image concordant pathology in the sciatica population. **Low back pain** Evidence for the prognostic factors smoking, BMI >30 and psychological distress was available for the outcomes of pain and function only. There was no evidence for any of the other outcomes. **Sciatica** Evidence for the prognostic factor radicular symptoms (pain that extends to leg versus pain in back/buttock only) was available for the outcome of pain and function only, and no evidence was found for any of the other outcomes.
Trade- off between clinical benefits and harms	Overall, there was a paucity of evidence to effectively explore the effect of prognostic factors on the outcomes of people with low back pain or sciatica following surgery. It was acknowledged by the GDG that in the low quality, evidence identified in this review, there was a trend towards worse outcomes in the groups of people who had prognostic factors identified-for example; smoking and high BMI. **Low back pain** There was evidence that non-smokers had a greater improvement in function following surgery compared to smokers. Other evidence reported negative effects on pain and function outcomes following surgery in people with a higher BMI or with psychological distress. The strength of this evidence was weak however and the GDG agreed that this carried significant uncertainty. There was scant evidence supporting better surgical outcome in people who did not have a prognostic factor identified (for example, there were no trials investigating the surgical outcomes of patients post smoking cessation). **Sciatica** The evidence suggested better outcomes for patients for patients with predominant leg pain following surgery for sciatica. The GDG noted that the evidence for leg pain prior to surgery was in a population undergoing surgery for sciatica and therefore would be expected to have a more favourable outcome from surgery. The GDG considered that the influence of predominant leg pain on the treatment effect seen at 4 years could be as a result of the long follow up time adopted in this study given that sciatica has a generally favourable prognosis over the long term. **Summary** The type of surgery carried out was different in each study and not defined in the case of 2 trials. Therefore, differences in surgical outcome could possibly be due to the surgical technique adopted rather than the prognostic factor, despite the adjustments for confounders in the multivariate analyses. Unfortunately, it was not possible to statistically explore this difference due to lack of data.

	The GDG agreed that there was insufficient evidence to suggest that smoking and obesity reliably impacted the prognosis for patients undergoing surgical treatment. It was however acknowledged that weight loss and smoking cessation have public health benefits and therefore should be encouraged. (See the NICE guideline for obesity and smoking cessation for more information). It was noted that these prognostic factors may increase the risk of surgery, but do not appear to affect the outcome, and the benefits of surgery in some may outweigh the risks. It was agreed that the prognostic factors identified should not preclude a surgical opinion where the benefits of surgery might outweigh the potential risks.
Trade-off between net clinical effects and costs	No economic evaluations were identified from the published literature. The GDG considered whether making a recommendation to not base decision for referral for a surgical opinion on these prognostic factors may lead to additional referrals for surgery if CCGs are currently refusing referrals for surgery on the basis of these factors, which in turn could result in an increase in the number of people having surgery. The GDG noted however that this recommendation was unlikely to impact sciatica surgery referrals as people are not currently being denied referral for surgical opinion on the basis of their BMI, smoking status or psychological distress, however the recommendation has been made specific to sciatica because the evidence reviewed elsewhere in this guideline has led to surgery only being recommended for sciatica rather than low back pain.
Quality of evidence	The evidence was from 5 prospective cohort and 1 retrospective cohort studies and ranged from low to very low quality mainly due to high risk of bias due to selection and attrition bias. For the prognostic factors of BMI, psychological distress and radicular symptoms, data came from a single, relatively small (N=105) trial, and the evidence was graded as very low quality with serious imprecision. Evidence was only available at short follow up time of 3 months for the majority of outcomes. The GDG noted that it may have been beneficial if the categories of obesity had been stratified further in the study rather than just the 2 cut-offs that were considered (i.e. <25 and >30) as this might reveal further differences in prognosis. A referent of BMI <25 was used in the study and data for the BMI=25-30 group reported separately compared to this referent (in addition the BMI>30 group of interest). The evidence for the prognostic factors of smoking and radicular symptoms was of overall very low quality due to selection bias demonstrated by unclear confounding of all the key confounders that could influence outcomes in the MVA and an >10% group differential attrition bias related to outcomes with no appropriate imputation in the studies.
Other considerations	The GDG discussed the ethical issues around shared decision making regarding spinal surgery and using information based on limited prognostic factors to decide treatment for patients. They agreed that using the limited evidence to deny treatment to certain people would be unethical. The GDG noted that the recommendation was based upon the prognostic factors identified in the protocol and there may be other factors, for example, age and the presence of co-morbidities.

26 Disc replacement

26.1 Introduction

Disc replacement, or spine arthroplasty, is an operation carried out to treat spinal pain. The indications and rationale are similar to those of spinal fusion. The procedure involves replacing intervertebral units with artificial discs that can act as a functional prosthetic replacement. The pain relief stems from removal of the painful disc. Single discs can be replaced, or alternatively, several levels can be replaced during the same surgery. Some clinicians consider that the advantage of disc arthroplasty over spinal fusion is that it preserves movement, which may have some benefits. Other clinicians have the view that the movement confers no significant clinical advantage.

The specific selection procedures mean that only a small number of people are suitable for surgery, and the surgical approach inevitably carries with it risks of serious harm. Since it was first introduced, the frequency of use of this procedure appears to have fallen.

26.2 Review question: What is the clinical and cost-effectiveness of disc replacement surgery in people with non-specific low back pain?

For full details see review protocol in Appendix C

Table 71: PICO characteristics of review question

Population	People aged 16 or above with non-specific low back pain. • Populations with low back pain only and low back pain with/without sciatica will be pooled for analysis
Intervention	Disc replacement surgery
Comparisons	• Usual care • Other treatment (interventions listed in our guideline review protocols)

Outcomes	**Critical**
	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).
	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).
	• Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BPI, BDI, STAI)
	Important
	• Responder criteria (> 30% improvement in pain or function)
	• Adverse events:
	  ○ morbidity
	  ○ mortality
	• Revision rate
	• Failure rate
	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)
	Outcomes to be recorded at:
	• Short term (≤ 4 months) (8 weeks to 4 months)

	• Long-term: ○ >4 months - 1 year (4 months to 1 year) for all outcomes ○ 0-2 years for critical outcomes ○ 0-10 years for failure rates and revision rates.
Study design	RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found, non-randomised studies will be included.

26.3 Clinical evidence

A search was undertaken for randomised trials comparing the clinical and cost effectiveness of performing disc replacement surgery in people with low back pain. Five randomised controlled trials were included in the review; 2 of the studies were published as multiple papers: Berg 2009A,[118-122] Gornet 2011,[123] Hellum 2011,[124-128] Li 2013,[129,130] Sasso 2008.[131,132]

All studies included people with low back pain with or without sciatica, and compared disc replacement to other treatment. Four studies compared disc replacement to spinal fusion,[118,123,130,132] while 1 compared disc replacement to a 3-element MBR programme.[124]

The search was extended to cohort studies due to insufficient evidence and 2 further studies were included .[133-135]

Berg2009A,[118-122] Gornet2011[123] and Lee2015 [133,136] are also included in the Spinal fusion chapter (See Chapter 27).

One Cochrane review[137,138] was identified but was not included as the stratification of the people with low back pain, low back pain with/without sciatica and sciatica was unclear. The studies included in the Cochrane review were individually assessed and included if they matched the protocol.

The included studies are summarised in **Table 72** below. Evidence from these studies is summarised in the clinical evidence summary below (**Table 74**, **Table 74** and **Table 75**). See also the study selection flow chart in Appendix E, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

26.3.1 Summary of included studies

Table 72: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Berg 2009A[118-122]	Total disc replacement (Charite, ProDisc, Maverick) Spinal fusion (posterolateral fusion or posterior lumbar interbody fusion)	Low back pain with or without sciatica N=152 5 years follow up Sweden	Health-related quality of life (EQ-5D) Pain severity (Back pain VAS, leg pain VAS) Function (ODI) Reoperations (number of patients; device-	All smokers were encouraged to give up smoking before treatment Postoperatively, patients in both groups increased their activities as quickly as they could tolerate and were instructed to be as mobile as possible without restriction

Study	Intervention and comparison	Population	Outcomes	Comments
			related, number of events)	(though sport and heavy lifting were to be avoided for 6 weeks and 3 months, respectively). Walking, together with a small programme to activate back and trunk muscles, were recommended Postoperatively, all patients were referred to outpatient physiotherapy Postoperatively, a soft lumbar orthosis was used for 6 weeks in the total disc replacement group, as recommended by some suppliers Part of the evidence was reported in a format that could not be analysed in this report, and has been presented in Table 73
Gornet 2011[123]	Total disc replacement (Maverick) Spinal fusion (stand-alone anterior lumbar interbody fusion)	Low back pain with or without sciatica N=577 2 years follow up United States of America	Health-related quality of life (SF-36) Pain severity (Back pain NRS, leg pain NRS) Function (ODI) Reoperations (number of patients) Adverse events (number of patients: any reported; possibly device-related)	No details given of any concomitant treatment or post-operative instructions/advice One patient was randomised to the investigational group but received control treatment and was analysed in the control group Adverse events were reported at the unclear 'operative' time point and were therefore extracted as ≤ 4 months outcome Adverse events were reported for the intervention group only; this format that could not be analysed in this report and has been presented in Table 73

Study	Intervention and comparison	Population	Outcomes	Comments
Hellum 2011[124-128]	Total disc replacement (ProDisc II) 3-elements MBR (multidisciplinary biopsychosocial rehabilitation programme: cognitive, physical and education components)	Low back pain without sciatica N=173 2 years follow up Norway	Health-related quality of life (EQ-5D, SF-36) Pain (VAS) Function (ODI) Adverse events (morbidity)	Intervention group: no major postoperative restrictions; patients were not referred for post-operative physiotherapy, but at 6 weeks follow up they could be referred if required. Control group: no details given of any concomitant treatment or post-operative instructions/advice
Lee 2015 [133,136]	Total disc replacement (ProDisc-L) Spinal fusion (TLIF)	Low back pain without sciatica N=74 5 years follow up Singapore	No relevant outcomes reported (time-point of revision surgery was unclear therefore this outcome was not extracted)	No details given of any concomitant treatment or post-operative instructions/advice
Li 2013[129,130]	Total disc replacement (Aesculap Activ-L) Spinal fusion (arthrodesis spinal fusion of facet joints with autograft bones)	Low back pain with or without sciatica N=68 3 years follow up China	No relevant outcomes reported (responder outcome was not defined as pain or function but only as generic symptomatic improvement mainly including low back pain, therefore it was not extracted)	Review condition defined as 'Lower lumbar pain during activities with or without radicular leg pain' Early rehabilitation was implemented in both groups.
Nabhan 2007[134]	Disc replacement (Aesculap AG) Spinal fusion (Xia II Spinal System with TLIF-PEEK Cage)	Low back pain N=24 1 year follow up Germany	No relevant outcomes reported	Intervention group: if foraminal stenosis was identifies on preoperative MRI, this was removed. In case where posterior longitudinal ligament was ossified, this was released Control group: no details given of any concomitant treatment or post-operative instructions/advice

Study	Intervention and comparison	Population	Outcomes	Comments
Sasso 2008[131,132]	Total disc replacement (FlexiCore) Spinal fusion (circumferential fusion with posterior pedicle screw instrumentation; 1 patient received anterior fusion with LT cages)	Low back pain with or without sciatica N=76 2 years follow up United States of America	Pain severity (VAS) Function (ODI)	No details given of any concomitant treatment or post-operative instructions/advice Evidence was reported in a format that could not be analysed in this report, and has been presented in Table 73

Table 73: Disc replacement versus spinal fusion: data unsuitable for meta-analysis

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Sasso 2008[132]	Pain severity (NRS, 0-10) ≤ 4 months	Mean: 3.9	39	Mean: 3.3	19	Very high
	Pain severity (NRS, 0-10) >4 months (1 year)	Mean: 1.8	35	Mean: 2.6	17	Very high
	Pain severity (NRS, 0-10) > 4 months (2 years)	Mean: 1.6	11	Mean: 2.0	8	Very high
	Function (ODI, 0-100) ≤ 4 months	Mean: 30	39	Mean: 32	19	Very high
	Function (ODI, 0-100) >4 months (1 year)	Mean: 24	35	Mean: 32	18	Very high
	Function (ODI, 0-100) > 4 months (2 years)	Mean: 6	11	Mean: 12	7	Very high
Hellum 2011[124-128]	Adverse events (morbidity) > 4 months (2 years): total number of complications in the disc replacement group at 2 years follow-up: 26/77 (34%). Complications included: 1 intimal lesion in left common iliac artery; 1 arterial thrombosis of dorsalis pedis artery; 4 blood loss > 1500 ml; 1 retrograde ejaculation; 1 abdominal hernia; 1 superficial hematoma; 1 ileus; 2 temporary warm left foot; 1 temporary nausea at 1 year follow-up; 2 sensory loss; 2 radicular pain. '1 patient had a serious complication: at 3 month follow-up, the polyethylene inlay was found to be dislodged. During revision surgery, injury to the left common iliac artery led to compartment syndrome resulting in a lower leg amputation'.					Very high

Table 74: Clinical evidence summary: Disc replacement versus spinal fusion in low back pain (low back pain with/without sciatica)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Spinal fusion	Risk difference with Disc replacement (95% CI)
Quality of life (SF-36 - mental component summary score (MCS), 0-100) ≤ 4 months	559 (1 study) 3 months	LOW[a] due to risk of bias		The mean health related quality of life (sf-36) ≤ 4 months - mental component summary score (mcs) in the control groups was 48.5	The mean health related quality of life (sf-36) ≤ 4 months - mental component summary score (mcs) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Spinal fusion	Risk difference with Disc replacement (95% CI)
					2.8 higher (0.65 to 4.95 higher)
Quality of life (SF-36 - physical component summary score (PCS), 0-100) ≤ 4 months	559 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean health related quality of life (sf-36) ≤ 4 months - physical component summary score (pcs) in the control groups was 36.9	The mean health related quality of life (sf-36) ≤ 4 months - physical component summary score (pcs) in the intervention groups was 4.5 higher (2.75 to 6.25 higher)
Quality of life (SF-36 - mental component summary score (MCS), 0-100) >4 months (1 year)	556 (1 study) 1 years	LOW[a] due to risk of bias		The mean health related quality of life (sf-36) >4 months (1 year) - mental component summary score (mcs) in the control groups was 49.3	The mean health related quality of life (sf-36) >4 months (1 year) - mental component summary score (mcs) in the intervention groups was 2 higher (0.09 lower to 4.09 higher)
Quality of life (SF-36 - physical component summary score (PCS), 0-100) >4 months (1 year)	556 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean health related quality of life (sf-36) >4 months (1 year) - physical component summary score (pcs) in the control groups was 41.6	The mean health related quality of life (sf-36) >4 months (1 year) - physical component summary score (pcs) in the intervention groups was 3.1 higher (0.96 to 5.24 higher)
Quality of life (SF-36 - mental component summary score (MCS), 0-100) > 4 months (2 years) SF-36 mental component summary score. Scale from: 0 to 100.	524 (1 study) 2 years	LOW[a] due to risk of bias		The mean health related quality of life (sf-36) > 4 months (2 years) - mental component summary score (mcs) in the control groups was 50	The mean health related quality of life (sf-36) > 4 months (2 years) - mental component summary score (mcs) in the intervention groups was 1.4 higher (0.71 lower to 3.51 higher)
Quality of life (SF-36 - physical component summary score (PCS), 0-100) > 4 months (2 years)	524 (1 study) 2 years	VERY LOW[a,b] due to risk		The mean health related quality of life (sf-36) > 4 months (2 years) - physical component summary score (pcs) in the	The mean health related quality of life (sf-36) > 4 months (2 years) - physical component summary score (pcs) in the

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Spinal fusion	Risk difference with Disc replacement (95% CI)
		of bias, imprecision		control groups was 42.1	intervention groups was 3 higher (0.68 to 5.32 higher)
Quality of life (EQ-5D, 0-1) >4 months (1 year)	152 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean health related quality of life (eq-5d) > 4 months in the control groups was 0.63	The mean health related quality of life (eq-5d) > 4 months in the intervention groups was 0.08 higher (0.01 lower to 0.17 higher)
Quality of life (EQ-5D, 0-1) > 4 months (2 years)	152 (1 study) 2 years	LOW[a] due to risk of bias		The mean health related quality of life (eq-5d) > 4 months - 2 years in the control groups was 0.69	The mean health related quality of life (eq-5d) > 4 months - 2 years in the intervention groups was 0.02 lower (0.11 lower to 0.07 higher)
Function (ODI, 0-100) ≤ 4 months	559 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI) ≤ 4 months in the control groups was 32	The mean function (ODI) ≤ 4 months in the intervention groups was 8.6 lower (11.76 to 5.44 lower)
Function (ODI, 0-100) >4 months (1 year)	708 (2 studies) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI) >4 months (1 year) in the control groups was 25.1	The mean function (ODI) >4 months (1 year) in the intervention groups was 5.9 lower (8.87 to 2.92 lower)
Function (ODI, 0-100) > 4 months (2 years)	676 (2 studies) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI) > 4 months (2 years) in the control groups was 23.9	The mean function (ODI) > 4 months (2 years) in the intervention groups was 4.69 lower (7.86 to 1.52 lower)
Pain severity (Back pain NRS, 0-10) ≤ 4 months	559 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (back pain NRS) ≤ 4 months in the control groups was 2.7	The mean pain severity (back pain NRS) ≤ 4 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Spinal fusion	Risk difference with Disc replacement (95% CI)
					0.92 lower (1.35 to 0.49 lower)
Pain severity (Back pain VAS/NRS, 0-10) >4 months (1 year)	708 (2 studies) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (back pain VAS/NRS) >4 months (1 year) in the control groups was 2.9	The mean pain severity (back pain VAS/NRS) >4 months (1 year) in the intervention groups was 0.73 lower (1.15 to 0.31 lower)
Pain severity (Back pain VAS/NRS, 0-10) > 4 months (2 years)	676 (2 studies) 2 years	LOW[a] due to risk of bias		The mean pain severity (back pain VAS/NRS) > 4 months (2 years) in the control groups was 5.28	The mean pain severity (back pain VAS/NRS) > 4 months (2 years) in the intervention groups was 0.51 lower (0.96 to 0.06 lower)
Pain severity (Leg pain NRS, 0-10) ≤ 4 months	559 (1 study) 3 months	LOW[a] due to risk of bias		The mean pain severity (leg pain NRS) ≤ 4 months in the control groups was 1.74	The mean pain severity (leg pain NRS) ≤ 4 months in the intervention groups was 0.06 higher (0.37 lower to 0.49 higher)
Pain severity (Leg pain VAS/NRS, 0-10) >4 months (1 year)	708 (2 studies) 1 years	LOW[a] due to risk of bias		The mean pain severity (leg pain VAS/NRS) >4 months (1 year) in the control groups was 2.02	The mean pain severity (leg pain VAS/NRS) >4 months (1 year) in the intervention groups was 0.57 lower (0.97 to 0.18 lower)
Pain severity (Leg pain VAS/NRS, 0-10) > 4 months (2 years)	676 (2 studies) 2 years	LOW[a] due to risk of bias		The mean pain severity (leg pain VAS/NRS) > 4 months (2 years) in the control groups was 4.02	The mean pain severity (leg pain VAS/NRS) > 4 months (2 years) in the intervention groups was 0.38 lower (0.82 lower to 0.05 higher)
		VERY LOW[a,b]		Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Spinal fusion	Risk difference with Disc replacement (95% CI)
Adverse events (number of patients) ≤ 4 months (operative)	577 (1 study)	due to risk of bias, imprecision	RR 1.67 (0.98 to 2.86)	87 per 1000	58 more per 1000 (from 2 fewer to 162 more)
Adverse events (possibly device-related; number of patients) ≤ 4 months (operative)	577 (1 study)	VERY LOW[a,c] due to risk of bias, imprecision	RR 2.13 (0.10 to 44.15)	Moderate	
				0 per 1000	0 fewer per 1000
Reoperations (number of patients) > 4 months (2 years)	676 (2 studies) 2 years	VERY LOW[a,c] due to risk of bias, imprecision	RR 0.97 (0.59 to 1.57)	Moderate	
				100 per 1000	3 fewer per 1000 (from 41 fewer to 57 more)
Reoperations (number of patients) > 4 months (5 years)	152 (1 study) 5 years	VERY LOW[a,c] due to risk of bias, imprecision	RR 0.75 (0.24 to 2.35)	Moderate	
				83 per 1000	21 fewer per 1000 (from 63 fewer to 112 more)
Device-related reoperations (number of events) > 4 months (5 years)	152 (1 study) 5 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.41 (0.2 to 0.83)	Moderate	
				278 per 1000	164 fewer per 1000 (from 47 fewer to 222 fewer)

(a) Downgraded by 2 increments if the majority of the evidence was at very high risk of bias
(b) Downgraded by 1 increment if the confidence interval crossed 1 MID
(c) Downgraded by 2 increments if the confidence interval crossed both MIDs

Table 75: Clinical evidence summary: Disc replacement versus 3-elements MBR in low back pain (low back pain without sciatica)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with 3-elements MBR	Risk difference with Disc replacement (95% CI)
Quality of life (EQ-5D, 0-1) >4 months (1 year).	172 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean health-related quality of life (eq-5d) > 4 months in the control groups was 0.55	The mean health-related quality of life (eq-5d) > 4 months in the intervention groups was 0.13 higher (0.03 to 0.23 higher)
Quality of life (EQ-5D, 0-1) > 4 months (2 years)	172 (1 study) 2 years	LOW[a] due to risk of bias		The mean health-related quality of life (eq-5d) > 4 months - 2 years in the control groups was 0.63	The mean health-related quality of life (eq-5d) > 4 months - 2 years in the intervention groups was 0.06 higher (0.03 lower to 0.15 higher)
Quality of life (SF-36 - mental component summary score (MCS, 0-100) >4 months (1 year)	172 (1 study) 1 years	LOW[a] due to risk of bias		The mean health-related quality of life (sf-36) >4 months (1 year) - mental component summary score (mcs) in the control groups was 49.2	The mean health-related quality of life (sf-36) >4 months (1 year) - mental component summary score (mcs) in the intervention groups was 1 higher (2.77 lower to 4.77 higher)
Quality of life (SF-36 - physical component summary score (PCS), 0-100) >4 months (1 year)	172 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean health-related quality of life (sf-36) >4 months (1 year) - physical component summary score (pcs) in the control groups was 37.3	The mean health-related quality of life (sf-36) >4 months (1 year) - physical component summary score (pcs) in the intervention groups was 5.5 higher (2.03 to 8.97 higher)
Quality of life (SF-36, mental component summary score (MCS), 0-100) > 4 months (2 years)	172 (1 study) 2 years	LOW[a] due to risk of bias		The mean health-related quality of life (sf-36) > 4 months (2 years) - mental component summary score (mcs) in the control groups was 48.6	The mean health-related quality of life (sf-36) > 4 months (2 years) - mental component summary score (mcs) in the intervention groups was 2.1 higher (1.55 lower to 5.75 higher)

Quality of life (SF-36, physical component summary score, 0-100 > 4 months (2 years)	172 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean health-related quality of life (sf-36) > 4 months (2 years) - physical component summary score (pcs) in the control groups was 37.7	The mean health-related quality of life (sf-36) > 4 months (2 years) - physical component summary score (pcs) in the intervention groups was 5.6 higher (2.33 to 8.87 higher)
Pain severity (Back pain VAS, 0-10) >4 months (1 year)	172 (1 study) 1 year	LOW[a] due to risk of bias		The mean pain severity (VAS) >4 months (1 year) in the control groups was 5.32	The mean pain severity (VAS) >4 months (1 year) in the intervention groups was 1.76 lower (2.61 to 0.91 lower)
Pain severity (Back pain VAS, 0-10) > 4 months (2 years)	172 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS) > 4 months (2 years) in the control groups was 4.97	The mean pain severity (VAS) > 4 months (2 years) in the intervention groups was 1.43 lower (2.29 to 0.57 lower)
Function (ODI, 0-100) ≤ 4 months	172 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI) ≤ 4 months in the control groups was 30.6	The mean function (ODI) ≤ 4 months in the intervention groups was 9.1 lower (13.17 to 5.03 lower)
Function (ODI, 0-100) >4 months (1 year)	172 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI) > 4 months in the control groups was 29.2	The mean function (ODI) > 4 months in the intervention groups was 8.9 lower (13.88 to 3.92 lower)
Function (ODI, 0-100) > 4 months (2 years)	172 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI) > 4 months - 2 years in the control groups was 26.7	The mean function (ODI) > 4 months - 2 years in the intervention groups was 6.9 lower (11.57 to 2.23 lower)

(a) Downgraded by 2 increments if the majority of the evidence was at very high risk of bias
(b) Downgraded by 1 increment if the confidence interval crossed 1MID

26.4 Economic evidence

Published literature

Two economic evaluations were identified with the relevant comparison and have been included in this review.[121,128] These are summarised in the economic evidence profile below (**Table 76**) and the economic evidence tables in Appendix I.

One economic evaluation relating to this review question was identified but was excluded[119,139] as it was based on the same data reported in the included study by Fritzell et al (2011).[121,140] This is listed in Appendix M, with reasons for exclusion given.

See also the economic article selection flow chart in Appendix F.

Table 76: Economic evidence profile: Total disc replacement versus fusion

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Fritzell 2011[121,140] (Sweden)	Partially applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial (RCT, associated clinical paper Berg 2011) • Cost-utility analysis (QALYs) • Population: Adults with low back pain with/without sciatica. • Two comparators in full analysis: 1. Total disc replacement surgery 2.Fusion(either ALIF or PLIF according to surgeon preference) • Follow-up: 2 years	Saves £1,587 [(c)]	0.01 [(d)]	Intervention 1 dominates intervention 2 (lower costs and higher QALYs)	Bootstrapping of ICER conducted but only from a societal perspective not a health care provider perspective. Therefore this is not reported here. Two additional sensitivity analyses were conducted. - The costs were discounted at 3%; this did not impact the total cost difference between the 2 comparators. - Reoperation costs were excluded from total healthcare costs. The total costs (mean per patient) were: Intervention 1: £9,710 Intervention 2: £10,235 Incremental (2−1): £525 (95% CI: -£827 to £1,710; p=NR)

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) Swedish resource use data (2002-2005) and unit costs (2006) may not reflect current NHS context. No discounting applied in base case analysis, discounting of costs at 3% applied in sensitivity analysis, however this is not in line with NICE reference case.

(b) Within-trial analysis and so does not reflect full body of available evidence for this comparison; Berg 2009 is 1 of the studies included in the clinical review for disc replacement surgery. Bootstrapping of ICER not undertaken from a healthcare payer perspective. Potential conflict of interest, study funded by manufacturers of surgical devices.

(c) 2006 Swedish Krona converted using 2006 purchasing power parities[110]. Cost components include: Intervention cost (index procedure for surgery), post-surgery hospital cost (including re-operation costs), primary care costs (including private care) and back-related drug costs.

(d) EQ-5D collected pre-operatively, 1 year and 2 years follow-up. QALYs were calculated using the area under the curve approach adjusted for baseline utility.

Table 77: Economic evidence profile: Total disc replacement versus multidisciplinary rehabilitation

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects (QALYs)	Cost effectiveness	Uncertainty
Johnsen 2014[128,141] (Norway)	Partially applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial (RCT, associated clinical paper Hellum 2011) • Cost-utility analysis (QALYs) • Population: Adults with chronic low back pain for more than 1 year and degenerative changes in lumbosacral intervertebral discs • Two comparators in full analysis: 1. Total disc replacement surgery 2. 3-elements MBR (multidisciplinary biopsychosocial rehabilitation programme: cognitive, physical and education components) • Follow-up: 2 years	£3,245 [(c)]	0.34 [(d)]	£9544 per QALY gained	Bootstrapping analysis was conducted using a societal perspective and therefore the 95% CI around the ICER is not reported. Using the intention to treat analysis total disc replacement was more costly but also more effective, however the costs included the societal perspective therefore results are not reported. Where missing data were not inputted but dropped, the effectiveness of total disc replacement was lower, however the costs included the societal perspective therefore results are reported. When SF-6D instead of EQ5D was used, the incremental QALY gain was 0.11, and the ICER was £29,500.

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) Norwegian resource use data (2004-2007) and unit costs may not reflect current NHS context. No discounting conducted.

(b) Within-trial analysis and so does not reflect full body of available evidence for this comparison. Bootstrapping of ICER not undertaken.

(c) 2012 euros converted using 2012 purchasing power parities[110]. Cost components include: Intervention cost, hospital follow up (reoperations, admissions, visits), GP consultations, physical therapist consultations, visits to complementary practitioners, medications.

(d) EQ-5D collected at baseline, 6 weeks, and 3, 6, 12, 24 months follow-up. QALYs constructed through area under the curve method

The 2 included studies compared total disc replacement with another type of surgery[121,140] or with a non-invasive intervention[128,141] and they both concluded that total disc replacement is cost effective in the base case. However the real extent of uncertainty around this conclusion could not be assessed as the probabilistic sensitivity analyses were conducted using societal costs.

In addition, the comparator in Fritzell 2011[121,140 121,14045,4644,45] is not recommended in this guideline as it is not considered cost effective. Therefore in this study disc replacement has been compared to a cost-ineffective intervention, which could explain why it is cost effective.

26.5 Evidence statements

26.5.1 Clinical

26.5.1.1 Disc replacement versus spinal fusion (Low back pain with/without sciatica)

Evidence from 1 study comparing disc replacement to anterior lumbar interbody fusion suggested clinical benefit of disc replacement for quality of life (SF-36 mental component) both at short and long term, but this was not demonstrated for the SF-36 physical component summary score (low to very low quality; n=577). Clinical benefit of disc replacement compared to posterior lumbar interbody fusion for quality of life (EQ-5D) at 1 year was also observed ; however, this was not demonstrated at 2 years (1 study, low to very low quality; n=152). Evidence from the 2 studies also demonstrated no clinical difference between disc replacement and spinal fusion for pain (back and leg pain VAS) or function (ODI) at both short and long term (low to very low quality; n=577, n=152). Further evidence informing these outcomes, could not be analysed as the results were inadequately reported for analysis.

In terms of adverse events, evidence from a single study showed greater numbers of adverse events for disc replacement compared to spinal fusion below 4 months (low to very low quality; n=577).

There was no clinical difference between the 2 procedures for the reoperation outcome at 2 years (2 studies; low to very low quality; n=577, n=152) and at 5 years (1 study; low to very low quality; n=152), while there was evidence of clinical benefit favouring disc replacement for device-related reoperations at 5 years (1 RCT; low to very low quality; n=152).

26.5.1.2 Disc replacement versus 3-MBR (low back pain without sciatica)

Evidence from 1 study demonstrated a clinically important benefit of disc replacement when compared to 3-element MBR for quality of life (EQ-5D and SF-36 physical component) in the long-term but this was not demonstrated for the SF-36 mental component. A benefit of disc replacement was also shown for back pain severity in the long-term. There was no clinical difference for function in the short or longer term (low to very low quality; n=173).

26.5.2 Economic

- One cost-utility analysis found that total disc replacement was dominant (less costly and more effective) compared to spinal fusion in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations.
- One cost-utility analysis found that total disc replacement was cost-effective compared to 3-element MBR (ICER: £9,544 per QALY gained). This study was partially applicable with potentially serious limitations.

26.6 Recommendations and link to evidence

Recommendations	The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations

Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Responder criteria (for pain and function), adverse events, revision rate, failure rate and healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit) were also considered as important outcomes. In this review, there was no evidence for the psychological distress for any of the comparisons. There was also no evidence identified for responder criteria, failure rate or healthcare utilisation for disc replacement versus spinal fusion.
Trade-off between clinical benefits and harms	**Disc replacement versus spinal fusion for low back pain with/without sciatica** The GDG noted that evidence for the comparison was limited, with outcomes analysed from 2 RCTs only. Although the majority of outcomes demonstrated no clinical difference between disc replacement and spinal fusion, some clinical benefit for disc replacement was observed in terms of quality of life. The GDG were concerned that the benefits observed came mainly from a study comparing disc replacement to anterior lumbar interbody fusion (BAK cages technique). The GDG was aware that anterior procedures in the lumbar spine for back pain are not commonly performed in the UK setting, and that the BAK cages technique shows a low fusion rate and would not be considered appropriate for a stand-alone anterior fusion in clinical practice. The GDG had serious concerns about the high number of severe adverse events associated with disc replacement in comparison to spinal fusion. When compared to posterior lumbar interbody fusion, disc replacement demonstrated a clinical benefit in the number of device related reoperations. However, the GDG emphasised the complexity of revision disc replacement procedures in patients, resulting in surgeons applying a much higher threshold for carrying out reoperations. For 1 of the intervention trials, insufficient data were reported for pain and function to be meta-analysed and therefore conclusions could not be drawn with any degree of certainty although the GDG noted that the magnitude of the between group differences appeared small. **Disc replacement versus 3 element -MBR for low back pain without sciatica** The GDG observed that the comparison between disc replacement and 3-element MBR could be inappropriate, as people with low back pain would often take part in a MBR programme before undergoing surgery. The GDG noted that evidence for this comparison came from a single RCT. Although there was some benefit observed in the outcomes reported, the GDG expressed concerns over the serious adverse events related with disc replacement, in particular 1 lower leg amputation and four cases of considerable blood loss (greater than 1500 ml) out of 80 participants. It was noted that this is a high occurrence of adverse events in studies not powered to detect harm. GDG opinion was that this rate was reflective of the risk observed in practice. **Summary** The GDG noted that there were some signs of benefit from disc replacement compared to other interventions, but this evidence was very limited and not consistent across outcomes. Furthermore the GDG felt the risk of harms associated with disc replacement outweighed the potential benefits. The GDG were aware of the lack of long term follow-up data for disc replacement surgery. The GDG expressed their concerns about this, particularly as disc replacement is often performed in younger age-groups in consideration of its claimed motion preservation benefits. However, it was highlighted that there is currently limited evidence of disc replacement benefits regarding motion and adjacent level degeneration compared to other surgical procedures, and the reported risks of disc

	replacement would often prevail over the benefits. As a result, the GDG agreed that the limited evidence of effectiveness alongside the above concerns meant it was appropriate to recommend against the use of disc replacement in people with low back pain with/without sciatica.
Trade-off between net clinical effects and costs	Two cost–utility analyses were identified for disc replacement. The first analysis, Fritzell 2011, was a within-trial analysis (associated RCT: Berg 2009) which found that total disc replacement was dominant (less costly and more effective) compared to spinal fusion in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations. It was noted that all cost elements were higher for the spinal fusion group and that 1 of the key cost drivers was the higher rate of re-operations in the spinal fusion surgery group. The second analysis, Johnsen 2014, was a within-trial analysis (associated RCT: Hellum 2011) which found that total disc replacement was cost-effective compared to 3-element MBR (ICER: £9,544 per QALY gained). This study was partially applicable with potentially serious limitations. The unit cost for spinal fusion surgery was estimated to be £7,337 per patient. This cost is based on the weighted average for complications and co-morbidities of the following HRG codes: Extradural Spine Major 2 with CC Score 5+ (HC01A); Extradural Spine Major 2 with CC Score 2-4 (HC01B); Extradural Spine Major 2 with CC Score 0-1 (HC01C); Extradural Spine Major 1 with CC Score 5+ (HC02D); Extradural Spine Major 1 with CC Score 2-4 (HC02E); Extradural Spine Major 1 with CC Score 0-1 (HC02F). The cost of total disc replacement surgery was also discussed by the GDG. This surgical procedure is included in the same HRG codes as spinal fusion and therefore the 2 surgeries do not differ in unit cost. The GDG noted that the comparator in the first study may have affected the overall conclusions as spinal fusion was found not to be a cost effective interventions itself. Therefore, disc replacement could have been shown to be cost effective in the studies only because it was compared to a cost ineffective intervention. In the 2 economic studies a probabilistic sensitivity analysis was reported only using the societal perspective, which is excluded in our guideline, therefore no evidence on uncertainty around the mean ICER was available from them. One way sensitivity analysis was undertaken in the study comparing disc replacement with 3-element MBR, where SF6D was used as a quality of life measure instead of EQ5D.The ICER was around £29,000 and the intervention was not cost effective anymore. Overall, the GDG were concerned about the lack of evidence of effect and the safety of the procedure. Taking into account the overall body of clinical effectiveness evidence, the uncertainty around the cost effectiveness studies, and the concerns around safety, the GDG decided to recommend against this procedure.
Quality of evidence	The evidence included in the review ranged from a GRADE quality rating of low to very low. This was due to the high risk of bias within the studies included as a result of incomplete blinding, high drop-out rates and baseline differences between the groups for several characteristics including baseline values of outcomes considered as critical for decision making in this review (leg pain, low back pain scores and SF-36 mental health sub score). The GDG expressed particular concern over the high number of patients that dropped out of the disc replacement group during the trial comparing 3-element MBR versus disc replacement (30% versus 17%). As the trial featured ITT analysis with last value carried forward (assuming patients had no improvement after dropout), this raised a concern about data interpretation. The imprecise nature of the outcomes included in this review further contributed to decreasing the GRADE quality rating.

	As stated above, the GDG raised concerns about the comparators in the included studies as they were either procedures without proven efficacy, or in the case of MBR, would be expected to be offered earlier in the pathway as an option prior to surgery. The economic evidence was assessed as partially applicable with potentially serious limitations.
Other considerations	The GDG agreed there may be specific causes of low back pain for which disc replacement might be an appropriate treatment which are beyond the scope of this guideline. The GDG were aware of NICE Interventional procedures guidance for Prosthetic intervertebral disc replacement in the lumbar spine, IP306 which recommend normal arrangements for clinical governance, consent and audit for this procedure. However, evidence reviewed by this GDG suggests that there was very limited evidence available of effectiveness of these procedures and this did not outweigh the risks and therefore the GDG agreed that it is appropriate to recommend against the use of disc replacement techniques for this population.

27 Spinal fusion

27.1 Introduction

Spinal fusion is an operation performed to achieve solid bone union between spinal vertebrae to prevent movement. This involves using the patient's own bone or artificial bone substitutes. The procedure of spinal fusion is commonly carried out as a component part of many types of spinal operation, such as operations to correct deformity, remove tumours and treat spinal fractures. Sometimes a fusion is done as part of an operation to decompress the spinal neurological structures; this is known as a decompression.

In clinical practice, spinal fusion is sometimes used to treat severe and constant low back pain that has not resolved despite the use of other more conservative treatments. Screws, rods or other implants may be used as an internal splint to stabilise the spine while the fusion is occurring.

There are different surgical approaches to the spine: from the back, the front or the side. The outcomes from the different approaches are similar. However, the risks of harm vary according to the approach and specific methods used. The risk of harm should be considered in terms of the probability of benefit and the alternative treatments that are known to have a treatment effect.

27.2 Review question: What is the clinical and cost effectiveness of spinal fusion/arthrodesis in people with non-specific low back pain?

For full details see review protocol in Appendix C.

Table 78: PICO characteristics of review question

Population	People aged 16 or above with non-specific low back pain.
Intervention	Spinal fusion/arthrodesis
Comparisons	• Usual care; waiting list • No surgery • Different type of surgery (e.g. anterior approach fusion versus disc replacement) • Other treatment (interventions listed in our guideline review protocols)

Outcomes	**Critical**
	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D).
	• Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).
	• Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BPI, BDI, STAI)
	Important
	• Adverse events:
	  ○ post-operative complications (e.g. infection)
	  ○ increased risk of requiring surgery at adjacent segments
	  ○ Mortality.
	• Revision rate
	• Failure rate

	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)
Study design	RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found, non-randomised studies will be included.

27.3 Clinical evidence

Nine studies were included in the review (found in 18 papers).[118,120-123,142-154] As there was only 1 RCT for the comparison of spinal fusion versus usual care, the search was extended to cohort studies for this comparison as well as spinal fusion versus no surgery for which there were no randomised trials. One cohort study was identified that met the inclusion criteria for fusion versus usual care and was included in the review. One Cochrane review[137,138] was identified but was not included as the stratification of the people with low back pain, low back pain with/without sciatica and sciatica was unclear, however the study included were individually assessed and included in this review if they matched the review protocol.

One non-randomised study was identified comparing spinal fusion with spinal decompression; [155] data for which is reported in chapter 28. Evidence for spinal fusion versus disc replacement can also be found in Chapter 26.The included studies have been summarised in **Table 79** below. Evidence from these studies is summarised in the GRADE clinical evidence profile/clinical evidence summary below (action flow chart in Appendix B, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

27.3.1 Summary of included studies

Table 79: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Berg 2009[118,121,122,139]	Fusion (either PLF[d] or PLIF[ca] according to surgeon preference) Total Disc Replacement (TDR)	Low back pain with or without sciatica n=152 1 + 2 year follow-up (5 year follow up for complications and reoperations) Sweden	Pain (VAS) Function (ODI) Quality of Life (SF-36 and EQ-5D) Averse events-complications Reoperations	Single centre trial Pain was assessed for back and leg separately; only back pain was reported in this review No details reported of concurrent treatment
Brix 2003[142-147]	Posterolateral fusion with transpedicular screws 3 element MBR program: duration of supervised treatment period was 1 week at first, followed by 2 weeks at home and another supervised period of 2 weeks. Average duration of the rehabilitation	Low back pain without sciatica n=64 1 year follow-up (4 year follow up data reported for combined results of Brix 2003 and Brix 2006 trials) Norway	Pain (VAS) Function (ODI, General Function Score (GFS)) Reoperations(4 year)	Multi-centre trial Concurrent treatment: consumption of analgesics, anxiololytics, hypnotics, sedatives, antidepressants, anti-inflammatory agents and muscle relaxants were recorded 1 week before follow up and daily till 1 year follow up. Consumption of

Study	Intervention and comparison	Population	Outcomes	Comments
	program was about 25 hours per week. Patients stayed at a patient hotel and treatments were conducted in the outpatient clinic during the day. Three daily workouts were performed; aerobics or outdoor activities, water gymnastics, and individual exercises. Endurance and co-ordination exercises were also recommended. Additionally, individual consultations, group lessons and discussions were given. During the first week, a specialist in physical medicine gave a lecture to the patients to describe pain receptors in the discs, facet joints and muscles; the reflexive interplay between various structures and the ability to suppress and reinforce various peripheral stimuli. Fear avoidance techniques were used to reinforce that patients could not harm the discs by engaging in normal activities; patients were constantly challenged in their thoughts about participation in physical activities previously labelled as not recommended.			each drug was calculated and daily doses defined.

Study	Intervention and comparison	Population	Outcomes	Comments
Brix 2006[148]	Posterolateral fusion with transpedicular screws 3 element MBR program: same as Brix 2003	Low back pain without sciatica N=57 Patients with previous surgery for disc herniation 1 year follow-up Norway	Pain (VAS) Function (ODI, and General Function Score, GFS)	Multi-centre trial No details reported of concurrent treatment - implies same as Brix 2003
Fairbank 2005[149,151]	Fusion (technique based on surgeon preference) 3 element MBR program: Intensive rehabilitation programme modelled on a daily outpatient programme of education and exercise running 5 days per week for 3 weeks continuously. Most centres offered 75 hours of intervention (range 60-110 hours) with 1 day of follow-up sessions at 1.2,6 or 12 months after treatment. Program was led by physiotherapists and clinical psychologists as well as medical support. Daily exercise included stretching of the major muscle groups, spinal flexibility exercises, general muscle strengthening, spine stabilisation exercise, and cardiovascular endurance exercise using any mode of aerobic exercise. Hydrotherapy was also used in all but 1 centre. Lastly,	Low back pain without Sciatica N=349 2 year follow up UK	Function (ODI) Quality of Life (SF-36) Quality of Life (EQ-5D-data presented in graphical format and therefore has was not able to be used in this review) Healthcare Utilisation(hospitalisation, health professional visit, prescriptions)	Multi-centre trial The patient population included a proportion of patients with Spondylolisthesis (<15% in each treatment group) A high number of patients randomised to rehabilitation underwent surgical stabilisation of the spine-10 instead if rehabilitation, 38 in addition to rehabilitation contributing to a >40% cross-over rate of patients who had both treatments No details reported of concurrent treatment

Study	Intervention and comparison	Population	Outcomes	Comments
	principles of cognitive behaviour therapy was used to identify and overcome fears/unhelpful beliefs that many patients develop when in pain			
Fritzell 2001[140,152]	Fusion (either ALIF[a], PLF[d] or PLIF[c]) Usual Care: non-surgical treatment program. Main component was physical therapy which could be supplemented with other forms of treatment such as information and education, treatment aimed at pain relief (TENS, acupuncture, injections), cognitive and functional training and coping strategies	Low back pain with or without sciatica N=294 2 year follow up Sweden	Pain (VAS) Function (ODI, GFS, and Million Visual Analogue Scale, MVAS) Adverse events-Complications Reoperations	Multi-centre trial Less than 4 months data was reported graphically (shows benefit for fusion). However, this data was therefore not extractable. No details reported of concurrent treatment
Gornet 2011[123]	Fusion Lumbar Disc Arthroplasty	Low back pain with or without sciatica N=577 3 month, 1 year and 2 year follow-up USA	Pain (VAS) Function (ODI) Quality of Life (SF-36) Adverse events-Mortality Adverse events-Complications	RCT Groups were comparable for baseline values for ODI, VAS and SF36. The proportion of men and medication use was significantly higher in the Disc Arthroplasty group No concurrent details reported
Lee 2013[136,150]	Fusion only Decompression (laminectomy with flavectomy without fusion)	Low back pain with or without sciatica N=50 6 month and 2 year follow up USA	Pain (VAS)-reported as change with no corresponding statistics for meta-analysis Function (ODI)-reported as change with no corresponding	Retrospective cohort review Groups were matched for age, gender, race, surgery date, surgery level and the status of spinal stenosis at the surgery segment

Study	Intervention and comparison	Population	Outcomes	Comments
			statistics for meta-analysis	No concurrent details reported
Ohtori 2011[153]	Fusion (ALF[b] or PLF[b]) Mixed modality exercise treatment: aerobic+ biomechanical. Daily walking (30 minutes x2 per day) and muscle stretching (body and leg)(15 minutes x 2 per day). Instruction for daily walking was made by 1 physician and was performed independently by the patient at home. Muscle stretching was performed at 1 hospital by a physiotherapist. These treatments were performed over 2 years and a physician checked monthly that both treatments were performed precisely as instructed. If the patients did not perform the walking and stretching as instructed, the patients were excluded from study	Low back pain only N=41 1 and 2 year follow-up Japan	Pain (VAS, and Japanese Orthopaedic Association Score, JOAS) Function (ODI)	Multi-centre trial All patients underwent discography and discoblock for a degenerated disc at single level for strict diagnosis of discogenic low back pain Concurrent treatment: only non-steroidal anti-inflammatory drugs were used in both groups. Opioids were not permitted
Smith 2014[154,156]	Fusion (instrumented lumbar fusion) Usual care: non-operative treatment modalities including physical therapy, epidural injections, and medications	Low back pain N=96 58-63 month average follow-up USA	Quality of life (SF-12) Pain (NRS) Function (ODI)	Retrospective review All patients had a positive, concordant lumbar discogram No details reported of concurrent treatment

(a) ALIF-Anterior Lumbar Interbody Fusion
(b) ALF- Anterior Lumbar Fusion
(c) PLIF- Posterior Lumbar Interbody Fusion
(d) PLF-Posterior Lumbar Fusion

27.3.2 Data unsuitable for meta-analysis

Table 80: Fusion versus decompression for spinal stenosis

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Lee 2013[136],[150]	Back pain (VAS) at 6 months follow up	The decrease in back pain score after treatment was greater in the Fusion group compared to the Decompression group. Back pain VAS score improved from 7.4 to 2.7 over the first 6 months in the Fusion Group (change= 4.7) and improved from 5.6 to 2.1 (change=3.5) in the Decompression Group				Very high
	Back pain (VAS) at 24 months follow up	The decrease in back pain score after treatment was greater in the Fusion group compared to the Decompression group. Back pain VAS score improved from 7.4 to 2.8 over 24 months in the Fusion Group (change =4.6) and from 5.6 to 3.4 (change=2.2) in the Decompression Group				Very high
	Leg pain (VAS) at 6 months follow up	The decrease in leg pain score after treatment was greater in the Fusion group compared to the Decompression group. Leg pain VAS score improved from 7.9 to 2.0 over the first 6 months in the Fusion Group (change= 5.9) and improved from 6.6 to 1.7 (change=4.9) in the Decompression Group				Very high
	Leg pain (VAS) at 24 months follow up	The decrease in leg pain score after treatment was greater in the Fusion group compared to the Decompression group. Leg pain VAS score improved from 7.9 to 2.0 over the first 6 months in the Fusion Group (change= 5.9) and improved from 6.6 to 2.4 (change=4.2) in the Decompression Group				Very high
	Function (ODI) at 6 months follow up	The decrease in ODI score after treatment was greater in the Decompression group compared to the Fusion group. ODI score improved from 20.0 to 6.5 over the first 6 months in the Fusion Group (change= 13.5) and improved from 25.4 to 11.0 (change=14.4) in the Decompression Group				Very high
	Function (ODI) at 24 months follow up	The decrease in ODI score after treatment was greater in the Decompression group compared to the Fusion group. ODI score improved from 20.0 to 11 over the first 6 months in the Fusion Group (change= 9) and improved from 25.4 to 15.1 (change=10.4) in the Decompression Group				Very high

Table 81: Clinical evidence profile: Fusion versus Usual Care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Spinal Fusion (95% CI)
Pain Severity (VAS,0-10) >4 months	264 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS,0-10) >4 months in the control groups was 5.83	The mean pain severity (VAS,0-10) >4 months in the intervention groups was 1.51 lower (2.09 to 0.93 lower)
Function (ODI,0-100) >4 months	264 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI,0-100) >4 months in the control groups was 45.6	The mean function (ODI,0-100) >4 months in the intervention groups was 9.9 lower (14.59 to 5.21 lower)
Function (General Function Score, GFS,0-100) >4 months	264 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (general function score,gfs,0-100) >4 months in the control groups was 45.5	The mean function (general function score,gfs,0-100) >4 months in the intervention groups was 11.4 lower (17.29 to 5.51 lower)
Function (Million Visual Analogue Score,MVAS,0-100) >4 months	264 (1 study) 2 years	LOW[a] due to risk of bias		The mean function (million visual analogue score,mvas,0-100) >4 months in the control groups was 60.4	The mean function (million visual analogue score,mvas,0-100) >4 months in the intervention groups was 14.8 lower (20.11 to 9.49 lower)
Adverse events-Complications (2 years)	283 (1 study)	LOW [a] due to risk of bias	OR 5 (2.45 to 10.19)	Study population	
				0 per 1000	*
Reoperations (2 years)	283 (1)	LOW[a] due to risk of bias	OR 4.12 (1.3 to 13.1)	Study population	
				0 per 1000	*

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1MID or by 2 increments if the confidence interval crossed both MID's.

*Peto odds ratio reported as there is zero events in 1 treatment arm

Table 82: Clinical evidence profile: Fusion versus Usual Care (cohort)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Spinal Fusion versus Usual Care (95% CI)
Pain Severity (NRS,0-10) >4 months - 1 year	96 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (NRS,0-10) >4 months - 1 year in the control groups was 4.4	The mean pain severity (NRS,0-10) >4 months - 1 year in the intervention groups was 0.8 lower (1.94 lower to 0.34 higher)
Function (ODI,0-100)>4 months - 1 year	96 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI,0-100)>4 months - 1 year in the control groups was 34.2	The mean function (ODI,0-100)>4 months - 1 year in the intervention groups was 1.1 higher (7.87 lower to 10.07 higher)
Quality of life, SF-36 (PCS, 0-100) >4 month	96 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36 (pcs, 0-100) >4 month in the control groups was 43.8	The mean quality of life, sf-36 (pcs, 0-100) >4 month in the intervention groups was 1.9 higher (1.12 lower to 4.92 higher)
Quality of life, SF-36(MCS, 0-100) >4 month	96 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36(mcs, 0-100) >4 month in the control groups was 48.7	The mean quality of life, sf-36(mcs, 0-100) >4 month in the intervention groups was 2.6 lower (6.96 lower to 1.76 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MID's.

Table 83: Clinical evidence summary: Fusion versus Other treatment

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other Treatment	Risk difference with Spinal Fusion (95% CI)
Pain Severity (VAS,0-10) >4 months - 1 year (3 element MBR)	118 (2 studies) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS,0-10) >4 months - 1 year (3 element MBR) in the control groups was 4.91	The mean pain severity (VAS,0-10) >4 months - 1 year (3 element MBR) in the intervention groups was 0.4 lower (1.29 lower to 0.48 higher)
Pain Severity (VAS,0-10) >4 months - 1 year (Mixed Modality: Aerobic+ biomechanical exercise)	41 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS,0-10) >4 months - 1 year (mixed modality: aerobic+ biomechanical exercise) in the control groups was 5.6	The mean pain severity (VAS,0-10) >4 months - 1 year (mixed modality: aerobic+ biomechanical exercise) in the intervention groups was 2.83 lower (5.68 lower to 0.02 higher)
Pain Severity (VAS,0-10) >4 months - 2 year(Mixed Modality: Aerobic+ biomechanical exercise)	41 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS,0-10) >4 months - 2 year(mixed modality: aerobic+ biomechanical exercise) in the control groups was 4.7	The mean pain severity (VAS,0-10) >4 months - 2 year(mixed modality: aerobic+ biomechanical exercise) in the intervention groups was 3.06 lower (6.08 to 0.04 lower)
Function (ODI,0-100) >4 months - 3 element MBR (1 year)	118 (2 studies) 1 years	LOW[a] due to risk of bias		The mean function (ODI,0-100) >4 months - 3 element MBR (1 year) in the control groups was 19.4	The mean function (ODI,0-100) >4 months - 3 element MBR (1 year) in the intervention groups was 0.83 higher (6.03 lower to 7.7 higher)
Function (ODI,0-100) >4 months - Mixed Modality (aerobic+ biomechanical exercise) (1 year)	41 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI,0-100) >4 months - mixed modality (aerobic+ biomechanical exercise) (1 year) in the control groups was 53.2	The mean function (ODI,0-100) >4 months - mixed modality (aerobic biomechanical exercise) (1 year) in the intervention groups was 26.06 lower (47.47 to 4.65 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other Treatment	Risk difference with Spinal Fusion (95% CI)
Function (ODI,0-100) >4 months - 3 element MBR (2 year)	349 (1 study) 2 years	LOW[a] due to risk of bias		The mean function(ODI,0-100) >4 months - 3 element MBR (2 year) in the control groups was 36.1	The mean function(ODI,0-100) >4 months - 3 element MBR (2 year) in the intervention groups was 2.1 lower (6.47 lower to 2.27 higher)
Function (ODI,0-100) >4 months - Mixed Modality (aerobic+ biomechanical exercise) (2 year)	41 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI,0-100) >4 months - mixed modality (aerobic+ biomechanical exercise) (2 year) in the control groups was 40	The mean function (ODI,0-100) >4 months - mixed modality (aerobic+ biomechanical exercise) (2 year) in the intervention groups was 26.59 lower (44.82 to 8.36 lower)
Function (GFS,0-100) >4 months (1 year)	118 (2 studies) 1 years	VERY LOW[a,b,c] due to risk of bias, inconsistency, imprecision		The mean function (gfs,0-100) >4 months (1 year) in the control groups was 19.95	The mean function (gfs,0-100) >4 months (1 year) in the intervention groups was 0.93 higher (10.12 lower to 11.97 higher)
Function (Japanese Orthopaedic Association Score, JOAS,0-3) >4 months - 1 year (Mixed Modality: Aerobic+ biomechanical exercise)	41 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (Japanese orthopaedic association score, joas,0-3) >4 months - 1 year (mixed modality: aerobic+ biomechanical exercise) in the control groups was 0.9	The mean function (Japanese orthopaedic association score, joas,0-3) >4 months - 1 year (mixed modality: aerobic+ biomechanical exercise) in the intervention groups was 0.96 higher (0.36 to 1.56 higher)
Function (Japanese Orthopaedic Association Score, JOAS,0-3) >4 months - 2 year(Mixed Modality: Aerobic+ biomechanical exercise)	41 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (Japanese orthopaedic association score,joas,0-3) >4 months - 2 year(mixed modality: aerobic+ biomechanical exercise) in	The mean function (association score,joas,0-3) >4 months - 1 year (mixed modality: aerobic+ biomechanical exercise) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other Treatment	Risk difference with Spinal Fusion (95% CI)
				the control groups was 1.2	1.16 higher (0.4 to 1.92 higher)
Quality of life, SF-36, 0-100 (2 years) - Physical component score, PCS	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - physical component score, pcs in the control groups was 27.6	The mean quality of life, sf-36, 0-100 (2 years) - physical component score, pcs in the intervention groups was 1.2 higher (2.5 lower to 4.9 higher)
Quality of life, SF-36, 0-100 (2 years) - Mental component score, MSC	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - mental component score, msc in the control groups was 48.1	The mean quality of life, sf-36, 0-100 (2 years) - mental component score, msc in the intervention groups was 0.7 lower (3.79 lower to 2.39 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-General health perception	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-general health perception in the control groups was 53.8	The mean quality of life, sf-36, 0-100 (2 years) - domain-general health perception in the intervention groups was 3.9 higher (2.12 lower to 9.92 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-Physical functioning	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-physical functioning in the control groups was 49.8	The mean quality of life, sf-36, 0-100 (2 years) - domain-physical functioning in the intervention groups was 0.2 higher (6.92 lower to 7.32 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-Role limitation(physical)	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-role limitation(physical) in the control groups was 38.6	The mean quality of life, sf-36, 0-100 (2 years) - domain-role limitation(physical) in the intervention groups was 1 higher (9.61 lower to 11.61 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other Treatment	Risk difference with Spinal Fusion (95% CI)
Quality of life, SF-36, 0-100 (2 years) - Domain-Role limitation (emotional)	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-role limitation(emotional) in the control groups was 65.4	The mean quality of life, sf-36, 0-100 (2 years) - domain-role limitation(emotional) in the intervention groups was 0.2 lower (10.98 lower to 10.58 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-Pain	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-pain in the control groups was 44.9	The mean quality of life, sf-36, 0-100 (2 years) - domain-pain in the intervention groups was 3.2 higher (3.26 lower to 9.66 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-Social functioning	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-social functioning in the control groups was 55.6	The mean quality of life, sf-36, 0-100 (2 years) - domain-social functioning in the intervention groups was 2 lower (8.56 lower to 4.56 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-Mental Health	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-mental health in the control groups was 68.4	The mean quality of life, sf-36, 0-100 (2 years) - domain-mental health in the intervention groups was 1.9 lower (7.48 lower to 3.68 higher)
Quality of life, SF-36, 0-100 (2 years) - Domain-Energy and vitality	246 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 (2 years) - domain-energy and vitality in the control groups was 46.4	The mean quality of life, sf-36, 0-100 (2 years) - domain-energy and vitality in the intervention groups was 0.3 higher (5.66 lower to 6.26 higher)
Healthcare Utilisation (unplanned hospital admissions for spinal surgery)	349 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean healthcare utilisation(unplanned hospital admissions for spinal surgery) in the control groups was 0.31	The mean healthcare utilisation(unplanned hospital admissions for spinal surgery) in the intervention groups was 0.24 lower (0.32 to 0.16 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other Treatment	Risk difference with Spinal Fusion (95% CI)
Healthcare Utilisation (GP consultations) (2 year)	349 (1 study) 2 years	LOW[a] due to risk of bias		The mean healthcare utilisation(gp consultations) (2 year) in the control groups was 6.81	The mean healthcare utilisation (gp consultations) (2 year) in the intervention groups was 0.57 higher (1.29 lower to 2.43 higher)
Healthcare Utilisation (Practice Nurse consultations) (2 year)	349 (1 study)	LOW[a] due to risk of bias		The mean healthcare utilisation(practice nurse consultations) (2 year) in the control groups was 0.62	The mean healthcare utilisation (practice nurse consultations) (2 year) in the intervention groups was 0.24 higher (0.17 lower to 0.65 higher)
Healthcare Utilisation (GP home visits) (2 year)	349 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean healthcare utilisation (gp home visits) (2 year) in the control groups was 0.31	The mean healthcare utilisation (gp home visits) (2 year) in the intervention groups was 0.38 higher (0.07 to 0.69 higher)
Healthcare Utilisation (Practise nurse home visits) (2 year)	349 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean healthcare utilisation (practise nurse home visits) (2 year) in the control groups was 0.24	The mean healthcare utilisation (practise nurse home visits) (2 year) in the intervention groups was 0.37 higher (0.02 to 0.72 higher)
Healthcare Utilisation (Prescriptions) (2 year)	349 (1 study) 2 years	LOW[a] due to risk of bias		The mean healthcare utilisation (prescriptions) (2 year) in the control groups was 13.43	The mean healthcare utilisation (prescriptions) (2 year) in the intervention groups was 0.8 higher (4.21 lower to 5.81 higher)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

[c] Downgraded by 1 or 2 increments because of Heterogeneity, I^2=50%, p=0.04, unexplained by subgroup analysis.

Table 84: Clinical evidence summary: Fusion versus Different type of surgery

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Different types of surgery	Risk difference with Spinal Fusion (95% CI)
Pain Severity (VAS/NRS,0-10) <4 months (3 months)	577 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (VAS/NRS,0-10) <4 months (3 months) in the control groups was 1.78	The mean pain severity (VAS/NRS,0-10) <4 months (3 months) in the intervention groups was 0.92 higher (0.5 to 1.34 higher)
Pain Severity (VAS/NRS,0-10) >4 months (1 year)	729 (2 studies) 1 years	LOW[a] due to risk of bias		The mean pain severity (VAS/NRS,0-10) >4 months (1 year) in the control groups was 2.155	The mean pain severity (VAS/NRS,0-10) >4 months (1 year) in the intervention groups was 0.73 higher (0.32 to 1.14 higher)
Pain Severity (VAS/NRS,0-10) >4 months (2 years)	729 (2 studies) 2 months	VERY LOW[a,b] due to risk of bias, inconsistency		The mean pain severity (VAS/NRS,0-10) >4 months (2 years) in the control groups was 3.94	The mean pain severity (VAS/NRS,0-10) >4 months (2 years) in the intervention groups was 0.1 lower (0.89 lower to 0.69 higher)
Function (ODI,0-100) <4 months (3 months)	577 (1 study) 3 months	LOW[a] due to risk of bias		The mean function(ODI,0-100) <4 months (3 months) in the control groups was 23.4	The mean function(ODI,0-100) <4 months (3 months) in the intervention groups was 8.6 higher (4.6 to 12.6 higher)
Function (ODI,0-100) >4 months (1 year)	729 (2 studies) 1 years	LOW[a] due to risk of bias		The mean function (ODI,0-100) >4 months (1 year) in the control groups was 19.35	The mean function (ODI,0-100) >4 months (1 year) in the intervention groups was 5.9 higher (2.98 to 8.83 higher)
Function(ODI,0-100) >4 months (2 years)	729 (2 studies) 2 years	LOW[a] due to risk of bias		The mean function (ODI,0-100) >4 months (2 years) in the control groups was 19.7	The mean function (ODI,0-100) >4 months (2 years) in the intervention groups was 4.75 higher (1.74 to 7.77 higher)
Quality of life,SF-36 (Physical Component Score,PCS,0-100) < 4 months	577 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life,sf-36(physical component score,pcs,0-100)< 4 months in the control groups was 41.4	The mean quality of life,sf-36 (physical component score,pcs,0-100)< 4 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Different types of surgery	Risk difference with Spinal Fusion (95% CI)
					4.5 lower (6.22 to 2.78 lower)
Quality of life,SF-36 (Physical Component Score,PCS,0-100) > 4 months - 1 year	577 (1 study) 1 years	LOW[a] due to risk of bias		The mean quality of life,sf-36 (physical component score,pcs,0-100)> 4 months - 1 year in the control groups was 44.7	The mean quality of life,sf-36 (physical component score,pcs,0-100) > 4 months - 1 year in the intervention groups was 3.1 lower (5.19 to 1.01 lower)
Quality of life,SF-36 (Physical Component Score,PCS,0-100) > 4 months - 2 year	577 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life,sf-36 (physical component score,pcs,0-100) > 4 months - 2 year in the control groups was 45.1	The mean quality of life,sf-36 (physical component score,pcs,0-100) > 4 months - 2 year in the intervention groups was 3 lower (5.16 to 0.84 lower)
Quality of life, SF-36(Mental Component Score,MCS,0-100)< 4 months	577 (1 study) 3 months	LOW[a] due to risk of bias		The mean quality of life, sf-36(mental component score,mcs,0-100)< 4 months in the control groups was 51.3	The mean quality of life, sf-36(mental component score,mcs,0-100)< 4 months in the intervention groups was 2.8 lower (4.91 to 0.69 lower)
Quality of life,SF36(Mental Component Score,MCS,0-100)> 4 months - 1 year	577 (1 study) 1 years	LOW[a] due to risk of bias		The mean quality of life,sf36(mental component score,mcs,0-100)> 4 months - 1 year in the control groups was 51.3	The mean quality of life,sf36(mental component score,mcs,0-100)> 4 months - 1 year in the intervention groups was 2 lower (4.05 lower to 0.05 higher)
Quality of life,SF36(Mental Component Score,MCS,0-100)> 4 months - 2 year	577 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life,sf36(mental component score,mcs,0-100)> 4 months - 2 year in the control groups was 51.4	The mean quality of life,sf36(mental component score,mcs,0-100)> 4 months - 2 year in the intervention groups was 1.4 lower (3.36 lower to 0.56 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Different types of surgery	Risk difference with Spinal Fusion (95% CI)
Quality of life,EQ-5D,0-1 >4 months - 1 year	152 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life,eq-5d,0-1 >4 months - 1 year in the control groups was 0.71	The mean quality of life,eq-5d,0-1 >4 months - 1 year in the intervention groups was 0.08 lower (0.17 lower to 0.01 higher)
Quality of life,EQ-5D,0-1 >4 months - 2 year	152 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life,eq-5d,0-1 >4 months - 2 year in the control groups was 0.67	The mean quality of life,eq-5d,0-1 >4 months - 2 year in the intervention groups was 0.02 higher (0.07 lower to 0.11 higher)
Adverse events-Mortality	577 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.27 (0.13 to 12.16)	Moderate	
				6 per 1000	2 more per 1000 (from 5 fewer to 67 more)
Adverse events-Complications - 2 year	729 (2 studies) 2 years	LOW[a] due to risk of bias	RR 0.97 (0.9 to 1.05)	Moderate	
				532 per 1000	16 fewer per 1000 (from 53 fewer to 27 more)
Adverse events-Complications - 5 year	152 (1 study) 5 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.77 (0.35 to 1.69)	Moderate	
				163 per 1000	37 fewer per 1000 (from 106 fewer to 112 more)
Adverse events-surgery at adjacent level at 2 years	152 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 6.67 (0.82 to 54.06)	Moderate	
				13 per 1000	74 more per 1000 (from 2 fewer to 690 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Different types of surgery	Risk difference with Spinal Fusion (95% CI)
Reoperations - 2 year	152 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.97 (0.37 to 2.55)	Moderate	
				100 per 1000	3 fewer per 1000 (from 63 fewer to 155 more)
Reoperations - 5 year	152 (1 study) 5 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.86 (0.34 to 2.2)	Moderate	
				113 per 1000	16 fewer per 1000 (from 75 fewer to 136 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

[c] Downgraded by 1 or 2 increments because of Heterogeneity, I^2=50%, p=0.04, unexplained by subgroup analysis.

27.4 Economic evidence

Published literature

Two economic evaluations were identified that included spinal fusion as a comparator and have been included in this review. [121,151] These are summarised in the economic evidence profile below (**Table 85** and **Table 86**) and the economic evidence table in Appendix I.

See also the economic article selection flow chart in Appendix F.

Table 85: Economic evidence profile: Spinal fusion versus other surgery (total disc replacement)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Fritzell 2011[121,140] (Sweden)	Partially applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial (RCT, associated clinical paper Berg 2011) • Cost-utility analysis (QALYs) • Population: Adults with low back pain with/without sciatica. • Two comparators in full analysis: 1. Total disc replacement surgery 2. Fusion(either ALIF or PLIF according to surgeon preference) • Follow-up: 2 years	2−1: £1,587 [(c)]	2−1: -0.01 QALYs [(d)]	Intervention 1 dominates intervention 2 (lower costs and higher QALYs)	Bootstrapping of ICER conducted but only from a societal perspective not a health care provider perspective. Therefore this is not reported here. Two additional sensitivity analyses were conducted. - The costs were discounted at 3%, this did not impact the total cost difference between the 2 comparators. - Reoperation costs were excluded from total healthcare costs. The total costs (mean per patient) were: Intervention 1: £9,710 Intervention 2: £10,235 Incremental (2−1): £525 (95% CI: -£827 to £1,710; p=NR)

(a) Swedish resource use data (2002-2005) and unit costs (2006) may not reflect current NHS context. No discounting applied in base case analysis, discounting of costs at 3% applied in sensitivity analysis, however this is not in line with NICE reference case.

(b) Within-trial analysis and so does not reflect full body of available evidence for this comparison; Berg 2009 is 1 of 2 studies included in the clinical review for spinal fusion versus other surgery. Bootstrapping of ICER not undertaken from a healthcare payer perspective. Potential conflict of interest, study funded by manufacturers of surgical devices.

(c) 2006 Swedish Krona converted using 2006 purchasing power parities[110]. Cost components include: Intervention cost (index procedure for surgery), post-surgery hospital cost (including re-operation costs), primary care costs (including private care) and back-related drug costs.

(d) EQ-5D collected pre-operatively, 1 year and 2 years follow-up. QALYs were calculated using the area under the curve approach adjusted for baseline utility.

Table 86: Economic evidence profile: Spinal fusion versus other treatment (Intensive rehabilitation programme-3 element MBR programme)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Rivero-Arias 2005[151] (UK)	Partially applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial (RCT, associated clinical paper Fairbank 2005) • Cost-utility analysis (QALYs) • Population: Adults with chronic low back pain • Two comparators in full analysis: 1. Intensive rehabilitation programme-3 element MBR programme (paced exercise and education programme based on cognitive behavioural approaches). 2. Fusion(technique based on surgeon preference) • Follow-up: 2 years	2−1: £3,299 [(c)]	2−1: 0.068 QALYs [(d)]	£48,515 per QALY gained	Bootstrapping of ICER conducted but only using a total costs including patient-related costs (broader perspective) not a NHS perspective. Probability Intervention 2 cost-effective (£20K): ~5% (reading from graph) Sensitivity analyses were conducted assuming different surgical technique costs: - posterolateral technique (least expensive procedure): ICER 2 versus 1 = £35,338 per QALY - 360 degree fusion (most expensive procedure): ICER 2 versus 1 = £60,765 per QALY Further sensitivity analysis by varying the time horizon to 4 years (assuming treatment differences for utilities were maintained): ICER = £25,398 per QALY. Finally, they examined impact of patients receiving other interventions subsequent to allocated intervention (at 2 years 45 patients had received both interventions) by assuming that people in each arm continued to receive both treatments in years 3,4 and 5 at rates observed in year

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
							1 and 2: ICER =£16,824 per QALY. The same sensitivity analysis was done but assuming half the rate observed at year 1 and 2 applied: ICER = £31,838 per QALY. Note, these were all conducted using the broader perspective (including patient-related costs).

(a) UK NHS resource use data (1996-2002) and unit cost (2002-2003) may not reflect current NHS context.

(b) Within-trial analysis and so does not reflect full body of available evidence for this comparison; Fairbank 2005 is 1 of 4 studies included in the clinical review for spinal fusion versus other treatments. Sensitivity analyses were conducted using a broader perspective which included patient-related costs.

(c) 2002/3 UK pounds. Cost components include: Intervention costs (including staff time and other resource use such as surgical implants and equipment) and other back pain related NHS contacts up to 24 months (including surgical follow-up appointments, physiotherapy outpatient appointments, unplanned or other back-related hospital admission, HCP contacts, prescriptions).

(d) EQ-5D collected baseline, 6, 12 and 24 months follow-up. QALYs were calculated using the area under the curve approach adjusted for baseline utility

27.4.1 Unit costs

These HRG codes include the following spinal fusion procedures (OPCS codes):

HRG code HC01:

- V333: ALIF (>1 level)
- V336 + V551: ALIF + PLF (1 level)
- V385 + V551: PLIF (1 level)
- V386 + V551/2/3: TLIF

HRG code HC02:

- V402, V403, V404: Posterior instrumented fusion
- V333 + V551: ALIF (1 level)

Table 87: Spinal fusion surgery unit costs

Reference cost HRG	Activity	National average unit cost
Extradural Spine Major 2 with CC Score 5+ (HC01A); as recorded for Total HRG	273	£14,686
Extradural Spine Major 2 with CC Score 2-4 (HC01B); as recorded for Total HRG	1060	£8,968
Extradural Spine Major 2 with CC Score 0-1 (HC01C); as recorded for Total HRG	2428	£7,464
Extradural Spine Major 1 with CC Score 5+ (HC02D); as recorded for Total HRG	311	£13,028
Extradural Spine Major 1 with CC Score 2-4 (HC02E); as recorded for Total HRG	1300	£6,999
Extradural Spine Major 1 with CC Score 0-1 (HC02F); as recorded for Total HRG	2956	£5,518
Weighted for complications and co morbidities	**8328**	**£7,337**

Source: NHS reference costs 2013/2014[57,58]

27.5 Evidence statements

27.5.1 Clinical

27.5.1.1 Fusion versus usual care

Evidence from 1 randomised study demonstrated clinical benefit of spinal fusion compared to usual care for pain at greater than 4 months (very low quality, n=264) and for function measured by the General Function Score (GFS) and Million VAS (MVAS) and in the long term (very low and low quality, n=264). However, function measured by the ODI at greater than 4 months follow-up demonstrated no clinical difference between fusion and usual care(very low quality, n=264). Evidence from a non-randomised study for the same comparison suggested no clinical difference between fusion and

usual care for any of the reported outcomes for quality of life, pain and function (very low quality, n=96).

27.5.1.2 Fusion versus other treatment

Evidence from 3 studies showed there to be no clinical difference between spinal fusion and 3 element MBR in pain and function (low-very low quality, n=467). Overall, there was no clinical difference between the 2 interventions for the majority of the quality of life domains of the SF-36 as well as the composite mental and physical scores, however a clinical benefit favouring spinal fusion was demonstrated in the domains of general health perception (low quality, n=246) and the domain pain (low quality, n=246). In addition there was no difference between spinal fusion and 3 element MBR in any reported healthcare utilisation measure (1 study, very low quality, n=349).

Evidence from a single study comparing spinal fusion with mixed modality exercise demonstrated clinical benefit for fusion in both pain and function (measured by ODI and JOAS) at both the 4 months to 1 year follow up and at 1 and 2 years (low to very low quality, n=41).

27.5.1.3 Fusion versus different type of surgery

Evidence from 2 studies comparing spinal fusion with disc replacement demonstrated spinal fusion to be less effective than disc replacement in terms of improving quality of life measures such as EQ-5D at greater than 4 months (1 study, very low quality, n=152) and the physical component score of the SF-36 at the all follow-up points reported (1 study, low-very low quality, n=577). There was no difference between the 2 surgical treatments for the mental component score of the SF-36 at any follow-up period as well for EQ-5D at the 2 years follow up. Similarly, no clinical difference between spinal fusion and disc replacement was reported for pain and function in either the short or long term either (2 studies, low-very low quality, n=729).

There was slightly conflicting evidence for adverse events reported from 2 studies with the majority of evidence demonstrating no clinical difference between spinal fusion and disc replacement for mortality, complications and reoperation rates at 2 years and 5 year follow up for re-operation rate). However, clinical benefit for fusion in comparison to disc replacement was reported for complications at 5 years in evidence from a single study (low quality, n=152). In contrast, fusion was demonstrated to result in more occurrences of surgery at adjacent level at 2 years compared to disc replacement (1 study, very low quality, n=152).

27.5.2 Economic

- One cost–utility analysis found that spinal fusion was dominated (more costly and less effective) compared to total disc replacement surgery for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost–utility analysis found that spinal fusion was not cost-effective compared to a 3-element MBR programme for treating low back pain with or without sciatica (ICER: £48,515 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.
- No economic analyses were identified comparing spinal fusion to no surgery or usual care.

27.6 Recommendations and link to evidence

Recommendations	**The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations**
Research recommendations	**The current research recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations-for-research**
Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Adverse events, revision rate, failure rate and healthcare utilisation were also considered as important. Evidence was reported for all of the critical outcomes except for psychological distress. Failure rate was the only important outcome for which there was no evidence from studies included in this review. The GDG felt there was sufficient evidence for all of the outcomes that were considered important for this review.
Trade-off between clinical benefits and harms	**Spinal fusion versus usual care** Low and very low quality randomised evidence from a single large trial suggested a clinical benefit in favour of spinal fusion in terms of pain (VAS) in the longer term follow up (4 months - 1 year) however there was uncertainty in this effect. The GDG discussed that the difference in pain scores at the end of 2 years between the surgical and non-surgical group was not very pronounced. However, this study reported a marked decrease in pain severity in the first 6 months after surgery in graphical form. The GDG considered this useful data although it could not be included in this meta-analysis. The GDG discussed that the short term relief in pain could be as a result of the application of a rigid plastic brace restricting the individuals' movement after surgery. A long term benefit in function (measured on three different scales) was also shown to favour fusion. The GDG also noted the 17% complication rate and 8% reoperation rate for spinal fusion and that there was significant potential harm to patients. **Spinal fusion versus other treatment** Clinical benefit in pain (assessed by VAS and Japanese Orthopaedic Association Score (JOAS)) and function (assessed by ODI and General Function Score) favouring spinal fusion was observed in the longer term follow up with serious uncertainty. This long term benefit in pain severity and function was observed in evidence from 1 small study comparing minimally treated patients as the control group to surgery. It was considered unlikely that improvements would be seen in the group receiving minimal treatment. The 3 larger studies in this comparison incorporated more rigorous MBR programmes as their comparator treatment; no clinically important difference in either pain or function was observed with this comparator. The GDG noted that 1 study had a very intensive MBR programme that involved 75 hours of intervention per week compared to 25 hours per week in the other 2 studies. However, evidence was consistent across all 3 studies, suggesting that the outcomes for people receiving MBR programmes were no different those receiving surgery. No clinically important difference in quality of life (assessed by SF-36) or healthcare utilisation (with some uncertainty) was seen between treatments in the long term follow-up for this comparison. The data for these 2 outcomes was taken from 1

	study in which a high number of patients randomised to rehabilitation underwent surgical stabilisation of the spine; 10 subjects opted for this instead of rehabilitation, and 38 subjects in addition to rehabilitation, contributing to a >40% cross-over rate for patients who had both treatments. Overall it appeared that MBR programmes perform as well as spinal fusion in terms of improving pain, function and quality of life, but are associated with a low risk of harm. **Spinal fusion versus different types of surgery** Evidence from 2 large trials demonstrated no clinically important difference in either pain (VAS) or function (ODI) between spinal fusion and disc replacement either in the short or the long term follow-up. A clinical benefit favouring disc replacement was demonstrated when assessed by the physical component of the SF-36 in both the and long term. However, no clinically important difference in the mental component of the SF-36 was observed at any time point. Very low quality evidence suggested a clinical benefit favouring disc replacement in terms of quality of life assessed by EQ-5D at the long term time point of 1 year which was not maintained at the 2 year follow-up. No clinically important difference between spinal fusion and disc replacement was seen in terms of adverse events (mortality and complications). The GDG noted that there was a high rate of serious complications associated with both treatments, for example 1 study reported that 345 out of 405 people experienced adverse events at 2 years following fusion surgery. However, it was noted that intraoperative rates of serious complications differed at 14.6% for disc replacement compared to 8.7% for spinal fusion; the higher rate in disc replacement possibly attributed to its more invasive nature. The GDG understood there to be a roughly 10–20% rate of complications across trials, with approximately 4-5% serious complications. As a result, they did not feel that the clinical benefit favouring disc replacement assessed by the physical component of the SF-36 in both the short term and long term was significant enough to outweigh the potential harms associated with the procedure despite the effect being maintained at 1 and 2 year follow-up. Very low quality evidence demonstrated a clinical benefit favouring disc replacement for further surgery required at an adjacent level at 2 years. However, the study did not report treatment effect at different levels, so the GDG did not feel that this information was useful for decision making. Furthermore, data from the same study suggested no clinically important difference between spinal fusion and disc replacement for revision rate (reoperations) at the long term time points of 2 and 5 years. **Summary** Overall the GDG considered that there was no consistent benefit of spinal fusion over comparator treatments and evidence of potential harm. Given this and the limited number of studies from which data could be evaluated, the GDG agreed that there was a lack of evidence of clinical effectiveness to recommend spinal fusion for people with low back pain other than in the context of a randomised controlled trial.
Trade-off between net clinical effects and costs	Two cost–utility analyses were identified for spinal fusion. The first analysis, Fritzell 2011, was a within-trial analysis (associated RCT: Berg 2009) which found that spinal fusion was dominated (more costly and less effective) compared to total disc replacement in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations. It was noted that all cost elements were higher for the spinal fusion group and that 1 of the key cost drivers was the higher rate of re-operations in the spinal fusion surgery group.

	The second analysis, Rivero-Arias 2005, was a within-trial analysis (associated RCT: Fairbank 2005) which found that spinal fusion was not cost-effective compared to a 3-element MBR programme (ICER: £48,515 per QALY gained). This study was partially applicable with potentially serious limitations. The GDG discussed the high cross-over between treatment arms reported in the trial, resulting in a large proportion of the trial participants receiving both interventions by the end of the 2 year follow-up. The unit cost for spinal fusion surgery was estimated to be £7,337 per patient. This cost is based on the weighted average for complications and co-morbidities of the following HRG codes: Extradural Spine Major 2 with CC Score 5+ (HC01A); Extradural Spine Major 2 with CC Score 2-4 (HC01B); Extradural Spine Major 2 with CC Score 0-1 (HC01C); Extradural Spine Major 1 with CC Score 5+ (HC02D); Extradural Spine Major 1 with CC Score 2-4 (HC02E); Extradural Spine Major 1 with CC Score 0-1 (HC02F). The cost of total disc replacement surgery was also discussed by the GDG. This surgical procedure is included in the same HRG codes as spinal fusion and therefore the 2 surgeries do not differ in unit cost. Taking into account the overall body of clinical effectiveness evidence for spinal fusion, the GDG concluded there was no consistent benefit of spinal fusion over comparator treatments and there was considerable evidence of harm. When combined with the cost-effectiveness evidence which indicated that spinal fusion was not a cost-effective intervention for the treatment of low back pain, the GDG agreed that spinal fusion should not be routinely recommended for people with low back pain.
Quality of evidence	**Spinal fusion versus usual care** Evidence for this comparison was from 1 large study which reported pain, function, adverse events and revision rate. The evidence was rated as low-very low quality due to the risk of bias and uncertainty of the effect size. The population was recruited by invitation to specialist spine centres and subsequent randomisation to more of the same treatment (physiotherapy and advice), or surgery. The GDG discussed that the control group appeared to be a severely disadvantaged group that had not been offered a new treatment and had been selected on the grounds of strict inclusion criteria of mandatory sick leave or equivalent disability for a year, as well as previous failure of non-surgical treatments. The GDG felt that this could result in a risk of bias due to a 'negative contextual effect' and also raised concerns that the study only reported outcomes at 2 years. The surgical group in this study was also much larger than the usual care group; 211 patients underwent surgery whereas 72 patients usual care treatment. It was also noted that Million Visual Analogue Scale (MVAS) used to measure function in the study reported a final score of 0-100 whereas commonly the MVAS comprises of 15 questions with a scale of 0-150. **Spinal fusion versus other treatment** There were 4 studies included in this comparison and the majority of evidence was of very low quality due to risk of bias and imprecision. "Other treatment" was defined as an MBR programme of varying intensity in 3 studies and aerobic and biomechanical exercise in 1 study. One study in particular was noted by the GDG to be a very small trial and used a less intensive comparator than the other trials. The GDG were not convinced by the small benefit in pain and function favouring spinal fusion reported in this study, which was not observed in the larger studies with more intensive comparator interventions. **Spinal fusion versus different types of surgery** Evidence for this comparison was from 2 large randomised studies which both compared disc replacement to spinal fusion. Evidence was low-very low quality due

	to very high risk of bias attributed to selection bias, lack of blinding and incomplete data at follow-up. There was also imprecision on many of the results reported. The larger of the 2 studies was an industry funded investigational device exemption trial for an artificial lumbar disc and had an incomplete outcome data rate of 15.1% in the control arm compared to 5.7% in the disc replacement group which cast doubt on the results reported.
Other considerations	The GDG agreed there were causes of low back pain for which spinal fusion might be an appropriate treatment which were beyond the scope of this guideline. The GDG noted that if spinal fusion was being undertaken, patient outcome information should be submitted to a national registry. The GDG were aware of NICE Interventional procedures guidance for Non rigid stabilisation techniques for the treatment of low back pain, IP366 which recommend normal arrangements for clinical governance, consent and audit for this procedure. The GDG were also aware of existing NICE interventional procedure guidance for Transaxial interbody lumbosacral fusion (IPG 387) and Lateral (including extreme, extra and direct lateral) interbody fusion in the lumbar spine (IPG321) which both recommend special arrangement for clinical governance, consent, audit and research. These procedures were excluded from the review and if considered for people with low back pain, the existing guidance should be followed. **Research recommendation** **Why this is important:** Low back pain affects a large number of individuals in UK. The condition has a huge cost to the individual, society and the country's economy. Over the past 2 decades, increasing number of procedures have been proposed for the surgical management of LBP. These include but are not limited to surgical fixation with internal metal-work applied from the back, front, side or any combination of the three routes. The costs of these operations have escalated, andas well as the monetary cost, there are complications associated with the surgical approaches with some studies reporting around 20% complication rate in the short to medium term. There have been several studies looking at the clinical effectiveness of spinal fusion versus usual care, no surgery, different surgeries, and other treatments. The studies collectively fail to show clear advantage of fusion but do show some modest benefit in some elements of pain, function and quality of life as well a reduction in healthcare utilisation. It is not known what treatments should have been tried prior to the consideration of surgery. Some patients who respond positively to surgery demonstrate a large treatment effect and the ability to predict responders would improve options available to patients. The studies generally suffer from low number of patients, large cross over and in case selection bias. We therefore propose a large, multi- centre randomized trial with sufficient power to answer these important questions.

28 Spinal decompression for sciatica

28.1 Introduction

Spinal decompression refers to removal of pressure from the nervous structures within the spinal column. This circumferential structure consists of vertebral body, disc and ligaments at the front, facet joints and foramen at the sides, and the lamina and ligaments at the back. Compression may be due to an abnormality of any of these structures and their removal results in spinal decompression.

An example of spinal decompression, laminectomy, is the removal of the lamina either unilaterally (hemi-laminectomy) or bilaterally, which is usually accompanied by the removal of the attached yellow ligament (*ligamentum flavum*). This can also include enlarging the foramen (foraminotomy) or undercutting facetectomy (trimming of the overgrown facets) and/or discectomy. The ultimate aim is to make more room for the neural elements.

The most common cause of the narrowing of the spinal canal is degenerative lumbar disease otherwise known as spondylosis. The symptoms associated with degenerative lumbar disease are leg symptoms (often pain, but also numbness and weakness) usually made worse by prolonged standing and walking. This is known as neurogenic claudication. At a very late stage of the condition people can develop bladder and bowel incontinence. In contrast to this, disc prolapse usually causes leg pain and sciatica. These 2 conditions often coexist in people suffering from back pain.

There have been several advances in the techniques of laminectomy and discectomy. With the improvements in optics and illumination, surgical loops, microscopes and endoscopes, the procedures are thought to be less invasive. There has also been the introduction of different methods of removing disc material including laser, thermo-coagulation radiofrequency and many others. Despite controversy surrounding the best method for discectomy, we have not reviewed the comparative effectiveness of these methods and suggest that this be determined by the individual surgeon and by clinical appropriateness.

28.2 Review question: What is the clinical and cost effectiveness of spinal decompression in people with sciatica?

For full details see review protocol in Appendix C.

Table 88: PICO characteristics of review question

Population	People aged 16 or above with sciatica • Populations with neurogenic claudication causing leg pain will be included
Intervention	Spinal decompression • Laminectomy • Discectomy
Comparisons	• Usual care • Other treatment (interventions listed in our guideline review protocols)
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).

	• Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index).
	• Psychological distress (HADS, GHQ, BPI, BDI, STAI)
	Important
	• Responder criteria (>30% improvement in pain or function)
	• Adverse events:
	  ○ Morbidity
	  ○ Mortality
	• Revision rate
	• Failure rate
	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)
	
	• Outcomes to be recorded at:
	  ○ Short term (≤4 months) (8 weeks to 4 months)
	  ○ Long-term:
	  - > 4 months (4 months to 1 year) for all outcomes
	  - 1-2 years for critical outcomes
	  - 0-10 years for failure rates and revision rates (recurrence / repeat surgery at adjacent segments or at the same segment, will be reported narratively only, for GDG

Study design	RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found, non-randomised studies will be included.

28.3 Clinical evidence

Nine RCT's (published in 14 papers) were included in the review.[157-173]

The search was extended to cohort studies for comparisons where there was insufficient evidence (specific forms of decompression versus a valid comparator) and 4 further studies were included (published in 6 papers).[13 ,155 ,167 ,174-179]

Two Cochrane reviews were identified by searches but could not be included for the following reasons:

- the review included studies on surgery techniques in disc prolapse and not just spinal decompression [180];
- the review compared different types of spinal decompression techniques and was therefore not relevant to the review protocol [181].

The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol.

The included studies have been summarised in **Table 89** below. Evidence from these studies is summarised in the GRADE clinical evidence profile/clinical evidence summary below (**Table 94** to **Table 101**). See also the study selection flow chart in Appendix E, study evidence tables in Appendix H, forest plots in Appendix K, GRADE tables in Appendix J and excluded studies list in Appendix L.

For the comparison of discectomy versus usual care, there was substantial heterogeneity between studies when they were meta-analysed for the outcome leg pain severity at up to 4 months. Pre-

specified subgroup analyses to compare people who had discectomy as a procedure to those who had laminectomy could not be applied as the only decompression procedure being investigated was discectomy. A random effects meta-analysis was therefore applied to this outcome, and the evidence was downgraded for inconsistency in GRADE.

28.3.1 Summary of included studies

Table 89: Summary of RCTs included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Cao 2014[13,178] Retrospective cohort study	Discectomy (inter-laminar fenestration and prolapse removed) Fusion	Low back pain with sciatica Lumbar disc herniation N=91 18 months follow-up China	Adverse events - complications	No details reported of concurrent treatment
Erginousakis 2011[157]	Spinal decompression (PDD) Usual care: 6 weeks planned of supervised conservative therapy - actual mean duration was 22 days (analgesics, anti-inflammatory drugs, muscle relaxants, and physiotherapy; included counselling and education. Personal communication once/ week).	Sciatica (with or without low back pain) Invertebral disc herniation n=62 1 year and 2 years follow up Greece	Pain (VAS) Adverse events-Complications	No details reported of concurrent treatment
Gerszten 2010[158]	Spinal decompression (using the Coblation DLR or DLG Spine Wand surgical device) Epidural steroid injection (at the site of disc protrusion. Steroid used in most patients was methylprednisolone).	Sciatica Lumbar disc protrusion N=90 6 months follow-up USA	Pain (VAS) Function (ODI) Adverse events (procedure-related)	Concurrent treatment: both groups allowed to receive additional conservative therapies including bed rest, physical therapy, narcotic analgesics or NSAIDs at the discretion of the treating investigator
Kim 2015[155,179]	Spinal decompression (microsurgical	Sciatica lumbar foraminal stenosis	Pain (VAS) Function (ODI)	No details reported of concurrent treatment

Study	Intervention and comparison	Population	Outcomes	Comments
Prospective cohort study	extraforaminal decompression / discectomy) Fusion (posterior lumbar interbody fusion) following the decompression procedures, including laminectomy and facetectomy	n=55 12 months follow-up Korea	Quality of life (SF-36) Revision rate	
Mcmorland 2010[159]	Microdiscectomy (both sequestrectomy and intrannular discectomy were performed to ensure adequate nerve root decompression) Combination non-invasive interventions: manual therapy+ biomechanical exercise + self-management. Manual therapy (spinal manipulation) plus Cryotherapy or thermotherapy was used on as needed basis during treatment sessions to increase patient ability to tolerate treatment. Patients were moved from passive care to active and then finally self-directed care. This involved providing patient with an education/information pack and introducing them to rehabilitative exercise. Patients also participated in a supervised rehabilitative (core stability) exercise	Sciatica Lumbar disc herniation N=40 1 year follow-up Canada	Pain (McGill) Function (RMDQ) Quality of life (SF-36)	No details reported of concurrent treatment

Study	Intervention and comparison	Population	Outcomes	Comments
	regimen. Treatments typically required 2-3 treatments per week for the first 4 weeks reducing to 1-2 visits per week for the next 3-4 weeks. At the 8 week mark, follow up visits were scheduled based on patients symptoms and initial treatment holiday was given for 2 weeks, Upon follow up if the patients symptoms had not deteriorated, no treatment was given at the follow up and the next treatment holiday time doubled with another follow-up visit scheduled a month later. If the patient's symptoms had worsened at follow-up, treatment was administered and another 2 week holiday was scheduled. This process of treatment withdrawal and follow-up visits was continued until the patient's symptoms were deemed stable			
Osterman 2006[160]	Microdiscectomy Usual care (physiotherapeutic instructions initially and continued with isometric exercises after randomisation)	Sciatica Herniated invertebral disc n=56 2 year follow-up Finland	Pain (VAS) Function (ODI) Quality of Life (SF-36) Healthcare utilisation (additional physiotherapy) Revision rate (reoperations)	39% of patients in the control group crossed over to surgery eventually Concurrent treatment: analgesia was prescribed according to individual requirements
Peul 2007[161] (Peul 2007[161,163],	Microdiscectomy (herniation removed by minimal unilateral	Sciatica Herniated disc	Pain (VAS) Function (RMDQ)	No details reported of concurrent treatment

Study	Intervention and comparison	Population	Outcomes	Comments
Peul 2008[161,162])Vandenhout 2008[164]	transflaval approach. Annular fenestration, curettage, and removal of loose degenerated disc material from the disc space, using a rongeur, without attempting to perform a subtotal discectomy) Usual care (Prolonged conservative treatment (surgery offered at 6 months if needed): intended 6 months of conservative treatment. provided by GPs. informed about their favourable prognosis and invited to visit the trial website (provided info about the natural course of their illness and the expectation of successful recovery, irrespective of initial intensity of pain). Treatment aimed mainly at enabling patients to resume daily activities. If needed, prescription of pain medication was adjusted according to clinical guidelines. Patients fearful of moving were referred to a physiotherapist.)	N=283 1 year and 2 year follow-up The Netherlands	Quality of Life (SF-36 and EQ-5D) Responder criteria (Recovery: complete or nearly complete disappearance of symptoms)	NOTE: if sciatica persisted for 6 months after the patient underwent randomisation, discectomy was offered. Surgery was offered earlier than 6 months after randomisation if patients had increasing leg pain not responsive to medication, or progressive neurologic deficits.
SPORT trial: Weinstein 2006A[167,168]	Discectomy (standard, open) Usual care (at least physical therapy, education and counselling with	Sciatica Intervertebral disc herniation N=1191 (3 studies) 1 year follow-up USA	Pain (Sciatica bothersomeness) Function (ODI) Quality of Life (SF-36 and EQ-5D)-EQ-5D data reported	Back pain data from analyses adjusted for most key confounders High rate of cross-over from the control group

Study	Intervention and comparison	Population	Outcomes	Comments
	home exercise instruction and non-steroidal anti-inflammatory drugs if tolerated. Physicians were instructed to individualise non-operative treatment and explore a wide range of non-operative options)		graphically and as QALY's therefore not usable for reviewing purposes Adverse events (inadvertent durotomy, wound infection)	arm into the discectomy group No details reported of concurrent treatment
SPORT trial: Weinstein 2006[167]Pearson 2008[177] (Kerr 2015[175,176], Lurie 2014[174] Tosteson 2008 [170]Tosteson 2008A[170,171] Prospective cohort study	As above for SPORT trial	As above for SPORT trial	Pain (Back pain bothersomeness Adverse events (inadvertent durotomy, wound infection) Healthcare utilisation(number of physical therapy visits and medication use)	Data from the observational cohort trial reported separately as well as combined with the RCT data. High rate of cross-over from the control group arm into the discectomy group No details reported of concurrent treatment
SPORT trial: Weinstein 2008[167,169]	Laminectomy(posterior decompressive laminectomy) Usual Care (recommended to include at least active physical therapy, education or counselling with home exercise instruction, and the administration of non-steroidal anti-inflammatory drugs if tolerated.	Sciatica Lumbar spinal stenosis at 1 or more levels N=654 2 year follow-up USA	Pain (Sciatica bothersomeness and low back pain bothersomeness) Function (ODI) Quality of Life (SF-36)	High rate of crossover in the study in both treatment arms No details reported of concurrent treatment
Weber 1983[172,173]	Decompression surgery (type not specified) Usual Care (conservative treatment)	N=567 N=1191 (3 studies) 1 year follow-up USA	No outcomes of interest reported in the study	No details reported of concurrent treatment

28.3.2 Data unsuitable for meta-analysis

Table 90: Discectomy versus usual care

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Weinstein 2006A[167,168]	Adverse events(intraoperative complications) at 2 year follow-up	The most common intraoperative complication was dural tear which occurred in 4% of patients. There were 10 events of dural tear/spinal fluid leak, 1 event of vascular injury and 2 events of other complications. There were no complications reported in 230 patients (95%)				Very high
Weinstein 2006A[167,168]	Adverse events(postoperative complications) at 2 year follow-up	There were 4 events of wound infection and 9 events of other postoperative complications. No complications were reported in 226 (95%) of patients.				Very high
Weinstein 2006A[167,168]Osterman 2006[160]	Reoperations at 1 year follow up	Weinstein 2006A reported 9 cases of additional surgery (4%) within 1 year of initial surgery. These included 5 reoperations due to recurrent herniation (2%) and 4 reoperations due to complication or other reasons (2%) Osterman 2006 reported 2 reoperations because of recurring symptoms on the same side and level. The reoperations took place at 6 weeks and 19 months after initial surgery				Very high
Weinstein 2006A[167,168]	Reoperations at 2 year follow up	There were 13 cases of additional surgery (5%) patients within 2 year of initial surgery. These included 8 reoperations due to recurrent herniation (3%) and 4 reoperations due to complication or other reasons (2%)				Very high
Weinstein 2006[167]	Adverse events(complications) at 2 year follow-up	The most common surgical complication was dural tear in 2% of cases				Very high
Weinstein 2006[167]	Reoperations at 1 and 2 year follow-up	Reoperation occurred in 7% of cases by 1 year and in 9% of cases at 2 years; more than half were recurrent herniation at the same level				Very high
Pearson 2008[177]	Adverse events (complications) at 2 year follow-up	Inadvertent durotomy and wound infection were the most common complications, occurring in 23 (3%) of patients and 18 (2%) of patients respectively				Very high

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Pearson 2008[177]	Reoperations at 1 year and 2 year follow- up	36 patients underwent reoperation within 1 year including 26 for reherniation. By 2 years, 48 patients had undergone reoperation, 38 of whom had suffered reherniation.				Very high
Pearson 2008[177]	Reoperations at 8 year follow- up	The rates of reoperation were bot significantly different between the randomised and observational cohorts.87 of the 119 re-operations noted the type of re-operation; approximately 85% of these (74/87) were listed as recurrent herniation at the same level				Very high

Table 91: Laminectomy versus usual care

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Weinstein 2008[167,169]	Adverse events	The most common surgical complication was dural tear in 9% of cases				Very high
Weinstein 2008[167,169]	Reoperations	At 2 years, reoperation had occurred in 8% of patients; fewer than half of these operations were for recurrent stenosis				Very high

Table 92: Percutaneous decompression versus usual care

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Erginousakis 2011[157]	Adverse events	There were no adverse events in either the treatment groups				Very high

Table 93: Discectomy versus fusion for sciatica

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Kim 2015[155,179]	Leg pain (VAS 0-10), at >4 months - 1 year	No significant difference between the 2 groups (p=0.909).				Very high
Kim 2015[155,179]	Back pain (VAS 0-10), at >4 months - 1 year	No significant difference between the 2 groups (p=0.626).				Very high
Kim 2015[155,179]	Quality of life (SF-36 physical component) at >4 months - 1 year	No significant difference between groups (p=0.643).				Very high

Study	Outcome	Intervention results	Intervention group (n)	Comparison results	Comparison group (n)	Risk of bias
Kim 2015[155,179]	Quality of life (SF-36 mental component) at >4 months - 1 year	No significant difference between groups (p=0.818).				Very high

28.3.3 Clinical Evidence Summary

Table 94: Discectomy versus Usual Care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Bodily pain	690 (2 studies) ≤4 month	VERY LOW[a,c] due to risk of bias, inconsistency		The mean quality of life, sf-36, 0-100 ≤4 months - domain-bodily pain in the control groups was 41	The mean quality of life, sf-36, 0-100 ≤4 months - domain-bodily pain in the intervention groups was 8.35 higher (7.87 to 8.83 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Physical functioning	690 (2 studies) ≤4 months	VERY LOW[a,c] due to risk of bias, inconsistency		The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical functioning in the control groups was 43.4	The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical functioning in the intervention groups was 9.26 higher (8.84 to 9.68 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Social functioning	281 (1 study) ≤4 months	LOW[a,b] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-social functioning in the control groups was 67.6	The mean quality of life, sf-36, 0-100 ≤4 months - domain-social functioning in the intervention groups was 2.3 higher (1.76 to 2.84 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Physical role	281 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical role in the control groups was 29.3	The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical role in the intervention groups was 0.2 higher (0.54 lower to 0.94 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Emotional role	281 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-emotional role in the control groups was 66.2	The mean quality of life, sf-36, 0-100 ≤4 months - domain-emotional role in the intervention groups was 3.1 higher (2.26 to 3.94 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Mental health index	281 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-mental health index in the control groups was 73.0	The mean quality of life, sf-36, 0-100 ≤4 months - domain-mental health index in the intervention groups was 9.1 higher (8.75 to 9.45 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Vitality	281 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-vitality in the control groups was 57.1	The mean quality of life, sf-36, 0-100 ≤4 months - domain-vitality in the intervention groups was 10.4 higher (10 to 10.8 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-General health perception	281 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-general health perception in the control groups was 65.2	The mean quality of life, sf-36, 0-100 ≤4 months - domain-general health perception in the intervention groups was 10.5 higher (10.14 to 10.86 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Bodily pain	696 (2 studies) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-bodily pain in the control groups was 54.85	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-bodily pain in the intervention groups was 3.3 higher (2.94 to 3.66 higher
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Physical functioning	696 (2 studies) >4 months - 1 year	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-physical functioning in the control groups was 56.4	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-physical functioning in the intervention groups was 1.5 higher (1.08 to 1.92 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Social functioning	281 (1 study) >4 months - 1 year	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-social functioning in the control groups was 82.4	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-social functioning in the intervention groups was 4.5 higher (4.07 to 4.93 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Physical role	281 (1 study) >4 months - 1 year	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-physical role in the control groups was 61.9	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-physical role in the intervention groups was 7.2 higher (6.37 to 8.03 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Emotional role	281 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-emotional role in the control groups was 81	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-emotional role in the intervention groups was 3.9 higher (3.23 to 4.57 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Mental health index	281 (1 study) 4 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-mental health index in the control groups was 80.5	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-mental health index in the intervention groups was 2.7 higher (2.37 to 3.03 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-Vitality	281 (1 study) >4 months - 1 year	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-vitality in the control groups was 68.5	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-vitality in the intervention groups was 3.2 higher (2.84 to 3.56 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year - Domain-General health perception	281 (1 study) >4	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-general health perception in the control	The mean quality of life, sf-36, 0-100 >4 months - 1 year - domain-general health perception in the intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
	months - 1 year			groups was 71.6	groups was 2.5 higher (2.11 to 2.89 higher)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Bodily pain	373 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months(2 year) - domain-bodily pain in the control groups was 37.1	The mean quality of life, sf-36, 0-100 >4 months(2 year) - domain-bodily pain in the intervention groups was 3.2 higher (2.07 lower to 8.47 higher)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Physical functioning	373 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months(2 year) - domain-physical functioning in the control groups was 35.9	The mean quality of life, sf-36, 0-100 >4 months(2 year) - domain-physical functioning in the intervention groups was 0 higher (5.41 lower to 5.41 higher)
Quality of life, EQ-5D, 0-1 ≤4 months (3 months)	283 (1 study) 3 months	LOW[a] due to risk of bias		The mean quality of life, eq-5d, 0-1 ≤4 months(3 months) in the control groups was 0.57	The mean quality of life, eq-5d, 0-1 ≤4 months(3 months) in the intervention groups was 0.06 higher (0.01 to 0.11 higher)
Quality of life, EQ-5D, 0-1 >4 months - 1 year (1 year)	283 (1 study) 1 years	LOW[a] due to risk of bias		The mean quality of life, eq-5d, 0-1 >4 months - 1 year(1 year) in the control groups was 0.82	The mean quality of life, eq-5d, 0-1 >4 months - 1 year(1 year) in the intervention groups was 0.02 higher (0.02 lower to 0.06 higher)
Leg Pain Severity (VAS,0-10) ≤4 months	333 (2 studies) ≤4 months	VERY LOW [a,b,c] due to risk of bias, inconsistency, imprecision		The mean leg pain severity(VAS,0-10) ≤4 months in the control groups was 2.195	The mean leg pain severity(VAS,0-10) ≤4 months in the intervention groups was 1.39 lower (2.39 to 0.39 lower)
Leg Pain Severity (VAS,0-10) >4 months - 1 year	333 (2 studies) >4	LOW[a] due to risk of bias		The mean leg pain severity(VAS,0-10) >4 months - 1 year in the control groups was 1.175	The mean leg pain severity(VAS,0-10) >4 months - 1 year in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
	months - 1 year				0.57 lower (0.87 to 0.28 lower)
Leg Pain Severity (VAS,0-10) >4 months (2 years)	50 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean leg pain severity(VAS,0-10) >4 months(2 year) in the control groups was 1.5	The mean leg pain severity(VAS,0-10) >4 months(2 year) in the intervention groups was 0.9 lower (1.95 lower to 0.15 higher)
Back Pain Severity (VAS,0-10) ≤4 months	333 (2 studies) ≤4 months	LOW[a] due to risk of bias		The mean back pain severity(VAS,0-10) ≤4 months in the control groups was 2.385	The mean back pain severity(VAS,0-10) ≤4 months in the intervention groups was 1.13 lower (1.18 to 1.08 lower)
Back Pain Severity (VAS,0-10) >4 months - 1 year	332 (2 studies) >4 months - 1 year	LOW[a] due to risk of bias		The mean back pain severity(VAS,0-10) >4 months - 1 year in the control groups was 1.74	The mean back pain severity(VAS,0-10) >4 months - 1 year in the intervention groups was 0.23 lower (0.28 to 0.18 lower)
Back Pain Severity (VAS,0-10) >4 months (2 year)	50 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean back pain severity(VAS,0-10) >4 months (2 year) in the control groups was 2.1	The mean back pain severity(VAS,0-10) >4 months (2 year) in the intervention groups was 1 lower (2.28 lower to 0.28 higher)
Pain Severity (Sciatica bothersomeness, change score,0-6) ≤4 months	409 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(back pain bothersomeness, change score,0-6) ≤4 months in the control groups was -6.8	The mean pain severity(back pain bothersomeness, change score,0-6) ≤4 months in the intervention groups was 2.2 lower (3.46 to 0.94 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
Pain Severity (Sciatica bothersomeness, change score,0-6) >4 months - 1 year (1 year)	413 (1 study) 1 years	LOW [a,b] due to risk of bias		The mean pain severity(back pain bothersomeness,change score,0-6) >4 months - 1 year (1 year) in the control groups was -8.7	The mean pain severity(back pain bothersomeness, change score,0-6) >4 months - 1 year (1 year) in the intervention groups was 1.6 lower (2.86 to 0.34 lower)
Pain Severity (Sciatica bothersomeness, change score,0-6) >4 months (2 years)	373 (1 study) 2 years	LOW[a] due to risk of bias		The mean pain severity(back pain bothersomeness, change score,0-6) >4 months (2 year) in the control groups was -8.5	The mean pain severity(back pain bothersomeness, change score,0-6) >4 months (2 year) in the intervention groups was 1.6 lower (2.92 to 0.28 lower)
Function (RMDQ, final score) ≤4 months	281 (1 study) ≤4 months	LOW[a] due to risk of bias		The mean function(RMDQ, final score) ≤4 months in the control groups was 9.2	The mean function(RMDQ, final score) ≤4 months in the intervention groups was 3.1 lower (3.22 to 2.98 lower)
Function (RMDQ final score) >4 months - 1 year	281 (1 study) >4 months - 1 year	LOW[a] due to risk of bias		The mean function(RMDQ final score) >4 months - 1 year in the control groups was 4.8	The mean function(RMDQ final score) >4 months - 1 year in the intervention groups was 0.8 lower (0.92 to 0.68 lower)
Function (ODI change score) ≤4 months	461 (2 studies) ≤4 months	LOW[a] due to risk of bias		The mean function(,ODI change score) ≤4 months in the control groups was -17.65	The mean function(,ODI change score) ≤4 months in the intervention groups was 5.1 lower (8.91 to 1.3 lower)
Function (ODI change score) >4 months - 1 year	467 (2 studies) >4	LOW[a] due to risk of bias		The mean function(ODI change score) >4 months - 1 year in the control groups was -19.2	The mean function(,ODI change score) >4 months - 1 year in the intervention groups was 2.58 lower (6.47 lower to 1.3 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
	months - 1 year				
Function (ODI change score) >4 months (2 years)	423 (2 studies) 2 years	LOW[a] due to risk of bias		The mean function(ODI change score) >4 months (2 year) in the control groups was -19.85	The mean function(,ODI change score) >4 months (2 year) in the intervention groups was 3.38 lower (7.33 lower to 0.58 higher)
Responder criteria (complete or nearly complete disappearance of symptoms) ≤ 4 months (8 weeks)	281 (1 study) 8 weeks	LOW[a] due to risk of bias	RR 1.97 (1.49 to 2.6)	Moderate	
				312 per 1000	303 more per 1000 (from 153 more to 499 more)
Responder criteria (complete or nearly complete disappearance of symptoms) > 4 months (26 weeks)	281 (1 study) 26 weeks	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.38 (1.21 to 1.57)	Moderate	
				660 per 1000	251 more per 1000 (from 139 more to 376 more)
Healthcare Utilisation (Number of patients with additional physical therapy visits) > 4 months (2 years)	50 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.49 (0.26 to 0.95)	Moderate	
				625 per 1000	319 fewer per 1000 (from 31 fewer to 463 fewer)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 or 2 increments because of Heterogeneity, I^2=50%, p=0.04, unexplained by subgroup analysis.

[c] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 95: Discectomy versus usual care (cohort and RCT+ cohort)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Sciatica due to herniated disc- Discectomy (95% CI)
Quality of life, SF-36, 0-100 ≤4 months (3 month) - Domain-Bodily pain	656 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months(3 month) - domain-bodily pain in the control groups was 25.3	The mean quality of life, sf-36, 0-100 ≤4 months (3 month) - domain-bodily pain in the intervention groups was 14.9 higher (10.77 to 19.03 higher)
Quality of life, SF-36, 0-100 ≤4 months (3 month) - Domain-Physical functioning	656 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months(3 month) - domain-physical functioning in the control groups was 26	The mean quality of life, sf-36, 0-100 ≤4 months (3 month) - domain-physical functioning in the intervention groups was 15.4 higher (11.53 to 19.27 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year (1 year) - Domain-Bodily pain	631 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months - 1 year(1 year) - domain-bodily pain in the control groups was 29.2	The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-bodily pain in the intervention groups was 10.8 higher (6.5 to 15.1 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year (1 year) - Domain-Physical functioning	631 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months - 1 year(1 year) - domain-physical functioning in the control groups was 32	The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-physical functioning in the intervention groups was 15.1 higher (10.9 to 19.3 higher)
Quality of life, SF-36, 0-100 >4 months (2 years) - Domain-Bodily pain	621 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months(2 year) - domain-bodily pain in the control groups was 31.9	The mean quality of life, sf-36, 0-100 >4 months (2 years) - domain-bodily pain in the intervention groups was 10.2 higher (5.9 to 14.5 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Sciatica due to herniated disc- Discectomy (95% CI)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Physical functioning	621 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months(2 year) - domain-physical functioning in the control groups was 32.4	The mean quality of life, sf-36, 0-100 >4 months (2 years) - domain-physical functioning in the intervention groups was 12 higher (7.8 to 16.2 higher)
Pain Severity (Sciatica bothersomeness index, change score,0-24) ≤4 months (3 months)	656 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(sciatica bothersomeness index, change score,0-24) ≤4 months (3 months) in the control groups was -7.5	The mean pain severity (sciatica bothersomeness index, change score,0-24) ≤4 months (3 months) in the intervention groups was 3.9 lower (4.93 to 2.87 lower)
Pain Severity (Sciatica bothersomeness index, change score,0-24) >4 months - 1 year (1 year)	631 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (sciatica bothersomeness index, change score,0-24) >4 months - 1 year (1 year) in the control groups was -8.6	The mean pain severity (sciatica bothersomeness index, change score,0-24) >4 months - 1 year (1 year) in the intervention groups was 2.6 lower (3.67 to 1.53 lower)
Pain Severity (Sciatica bothersomeness index, change score, 0-24) >4 months (2 year)	621 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (sciatica bothersomeness index, change score,0-24) >4 months (2 year) in the control groups was -8.7	The mean pain severity (sciatica bothersomeness index, change score,0-24) >4 months (2 year) in the intervention groups was 2.1 lower (3.17 to 1.03 lower)
Function (ODI change score) ≤4 months	656 (1 study) 3 months	VERY LOW[a] due to risk of bias		The mean function (ODI change score) ≤4 months in the control groups was -20.9	The mean function (ODI change score) ≤4 months in the intervention groups was 15.2 lower (18.6 to 11.8 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Sciatica due to herniated disc- Discectomy (95% CI)
Function (ODI change score) 4 months (1 year)	631 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean function(ODI change score) 4 months (1 year) in the control groups was -22.4	The mean function (ODI change score) 4 months (1 year) in the intervention groups was 15.3 lower (19.03 to 11.57 lower)
Function (ODI change score) ≤4 months (2 years)	621 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI change score) ≤4 months (2 years) in the control groups was -24.2	The mean function (ODI change score) ≤4 months (2 years) in the intervention groups was 13.4 lower (17.13 to 9.67 lower)
Pain Severity (Back Pain bothersomeness, 0-6) ≤4 months	1191 (1 study)	VERY LOW[a] due to risk of bias		The mean pain severity (back pain bothersomeness, 0-6) ≤4 months in the control groups was -1.3	The mean pain severity (back pain bothersomeness, 0-6) ≤4 months in the intervention groups was 0.9 lower (0.91 to 0.89 lower)
Pain Severity (Back Pain bothersomeness, 0-6) >4 months - 1 year (1 year)	1191 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean pain severity (back pain bothersomeness, 0-6) >4 months - 1 year (1 year) in the control groups was -1.4	The mean pain severity (back pain bothersomeness, 0-6) >4 months - 1 year (1 year) in the intervention groups was 0.7 lower (0.71 to 0.69 lower)
Pain Severity (Back Pain bothersomeness, 0-6) >4 months (2 year)	1191 (1 study) 2 years	VERY LOW[a] due to risk of bias		The mean pain severity (back pain bothersomeness, 0-6) >4 months (2 year) in the control groups was -1.5	The mean pain severity (back pain bothersomeness, 0-6) >4 months (2 year) in the intervention groups was 0.5 lower (0.51 to 0.49 lower)
Healthcare Utilisation (Number of patients with more reported diagnostic test use) > 4 months (2 years)	1191 (1 study) 2 years	LOW[a] due to risk of bias	RR 1.56 (1.34 to 1.81)	Moderate	
				339 per 1000	190 more per 1000 (from 115 more to 275 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Sciatica due to herniated disc- Discectomy (95% CI)
Healthcare Utilisation (Number of patients with additional physical therapy visits) > 4 months (2 years)	1191 (1 study) 2 years	VERY LOW[a] due to risk of bias	RR 1.12 (0.99 to 1.28)	Moderate	
				440 per 1000	53 more per 1000 (from 4 fewer to 123 more)
Healthcare Utilisation (Number of patients with reported healthcare visits) > 4 months (2 years)	1191 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision	RR 1.02 (0.98 to 1.07)	Moderate	
				880 per 1000	18 more per 1000 (from 18 fewer to 62 more)
Healthcare Utilisation (Medication use) > 4 months (2 years)	1191 (1 study) 2 years	VERY LOW[a] due to risk of bias	RR 1.08 (1.04 to 1.12)	Moderate	
				889 per 1000	71 more per 1000 (from 36 more to 107 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 96: Discectomy versus combination treatment (manual therapy+ biomechanical exercise + self-management)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Manual therapy+ biomechanical exercise + self-management	Risk difference with Sciatica due to herniated intervertebral disc- Discectomy (95% CI)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Bodily pain	40 (1 study) 12 weeks	LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-bodily pain in the control groups was 47.1	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-bodily pain in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Manual therapy+ biomechanical exercise + self-management	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
					10.3 higher (2.37 lower to 22.97 higher)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Physical role	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-physical role in the control groups was 32.5	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-physical role in the intervention groups was 3.7 lower (27.1 lower to 19.7 higher)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Emotional role	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-emotional role in the control groups was 74.5	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-emotional role in the intervention groups was 9.5 lower (34.49 lower to 15.49 higher)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Vitality	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-vitality in the control groups was 59.0	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-vitality in the intervention groups was 8.20 higher (3.37 lower to 19.77 higher)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Physical function	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-physical function in the control groups was 73.6	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-physical function in the intervention groups was 6.80 higher (9.64 lower to 23.24 higher)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Social function	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-social function in the control groups was 73.6	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-social function in the intervention groups was 6.30 lower (23.79 lower to 11.19 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Manual therapy+ biomechanical exercise + self-management	Risk difference with Sciatica due to herniated intervertebral disc-Discectomy (95% CI)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-Mental health	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-mental health in the control groups was 82.8	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-mental health in the intervention groups was 0.40 higher (5.61 lower to 6.41 higher)
Quality of life, SF-36, 0-100 ≤4 months (12 weeks) - Domain-General health	40 (1 study) 12 weeks	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-mental health in the control groups was 77.8	The mean quality of life, sf-36, 0-100 ≤4 months (12 weeks) - domain-mental health in the intervention groups was 5.40 higher (-3.40 lower to 14.20 higher)
Pain Severity(McGill, 0-78) ≤ 4 months (12 weeks)	40 (1 study) 12 weeks	LOW[a,b] due to risk of bias, imprecision		The mean pain severity (McGill, 0-78) ≤ 4 months (12 weeks) in the control groups was 19.4	The mean pain severity (McGill, 0-78) ≤ 4 months (12 weeks) in the intervention groups was 6.4 lower (15.9 lower to 3.1 higher)
Function (RMDQ,0-24) ≤4 months	40 (1 study) 12 weeks	LOW[a,b] due to risk of bias, imprecision		The mean function (RMDQ,0-24) ≤4 months in the control groups was 9.0	The mean function (RMDQ,0-24) ≤4 months in the intervention groups was 1.8 lower (5.87 lower to 2.27 higher)

[a]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b]Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 97: Percutaneous disc decompression versus Usual Care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual Care	Risk difference with Sciatica due to herniated intervertebral disc- Percutaneous disc decompression (95% CI)
Pain Severity (Leg Pain NVS,0-10) ≤4 months (3 months)	62 (1 study) 3 months	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (leg pain nvs,0-10) ≤4 months (3 months) in the control groups was 6	The mean pain severity (leg pain nvs,0-10) ≤4 months (3 months) in the intervention groups was 1.6 lower (2.95 to 0.25 lower)
Pain Severity (Leg Pain NVS,0-10) >4 months - 1 year (1 year)	62 (1 study) 1 years	LOW[a] due to risk of bias		The mean pain severity (leg pain nvs,0-10) >4 months - 1 year (1 year) in the control groups was -2.9	The mean pain severity (leg pain nvs,0-10) >4 months - 1 year (1 year) in the intervention groups was 2.8 lower (4.02 to 1.58 lower)
Pain Severity (Leg Pain NVS,0-10) >4 months (2 years)	62 (1 study) 2 years	LOW[a] due to risk of bias		The mean pain severity (leg pain nvs,0-10) >4 months (2 years) in the control groups was -2.8	The mean pain severity (leg pain nvs,0-10) >4 months (2 years) in the intervention groups was 3.10 lower (4.45 to 1.75 lower)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 98: Plasma disc decompression versus other treatment (epidural steroid injection)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other treatment (Transforaminal epidural steroid injections)	Risk difference with Sciatica due to herniated intervertebral disc- Plasma disc decompression (95% CI)
Pain Severity (Leg Pain VAS,0-10) ≤4 months (3 months)	85 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision		The mean pain severity (leg pain VAS, 0-10) ≤4 months (3 months) in the control groups was -1.8	The mean pain severity(leg pain VAS,0-10) ≤4 months (3 months) in the intervention groups was 1.8 lower (3.05 to 0.55 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Other treatment (Transforaminal epidural steroid injections)	Risk difference with Sciatica due to herniated intervertebral disc- Plasma disc decompression (95% CI)
Pain Severity (Leg Pain VAS,0-10) >4 months - 1 year (6 months)	85 (1 study) 6 months	LOW[a,b] due to risk of bias, imprecision		The mean pain severity (leg pain VAS,0-10) >4 months - 1 year(6 months) in the control groups was -1.6	The mean pain severity (leg pain VAS,0-10) >4 months - 1 year (6 months) in the intervention groups was 1.8 lower (3.05 to 0.55 lower)
Pain Severity (Back Pain VAS,0-10) ≤4 months (3 months)	85 (1 study) 3 months	MODERATE[a] due to risk of bias		The mean pain severity (back pain VAS,0-10) ≤4 months (3 months) in the control groups was 0.7	The mean pain severity (back pain VAS,0-10) ≤4 months (3 months) in the intervention groups was 2.2 lower (3.18 to 1.22 lower)
Pain Severity (Back Pain VAS,0-10) >4 months - 1 year (6 months)	85 (1 study) 6 months	LOW[a,b] due to risk of bias, imprecision		The mean pain severity (back pain VAS,0-10) >4 months - 1 year (6 months) in the control groups was 0.02	The mean pain severity (back pain VAS,0-10) >4 months - 1 year (6 months) in the intervention groups was 1.62 lower (2.73 to 0.51 lower)
Function ODI, 0-100 ≤4 months (3 months)	85 (1 study) 3 months	LOW[a,b] due to risk of bias, imprecision		The mean function ODI, 0-100 ≤4 months (3 months) in the control groups was 0.2	The mean function ODI, 0-100 ≤4 months (3 months) in the intervention groups was 1.2 lower (1.91 to 0.49 lower)
Function (ODI,0-100) >4 months - 1 year (6 months)	85 (1 study) 6 months	MODERATE[a] due to risk of bias		The mean function (ODI,0-100) >4 months - 1 year (6 months) in the control groups was 0.4	The mean function (ODI, 0-100) >4 months - 1 year (6 months) in the intervention groups was 1.6 lower (2.31 to 0.89 lower)
Procedure related adverse events> 4 months – 1 year (6 months)	85 (1 study) 6 months	VERY LOW[a,b] due to risk of bias, imprecision	RR 0.63 (0.22 to 1.84)	Moderate	
				175 per 1000	65 fewer per 1000 (from 137 fewer to 147 more)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 99: Discectomy versus fusion (cohort)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Fusion	Risk difference with Sciatica due to herniated disc- Discectomy (95% CI)
Function (ODI 0-100) >4 months - 1 year	55 (1 study) >4 months - 1 year	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI 0-100) >4 months - 1 year in the control groups was 27.2	The mean function (ODI 0-100) >4 months - 1 year in the intervention groups was 1.52 lower (8.76 lower to 5.72 higher)
Revision surgery >4 months - 1 year	55 (1 study) >4 months - 1 year	VERY LOW[a] due to risk of bias	OR 9.82 (0.97 to 99.53)	Moderate	
				0 per 1000	-

[a] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

[b] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

Table 100: Laminectomy versus usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)- Laminectomy versus Usual Care (95% CI)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Bodily pain	251 (1 study) 3 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-bodily pain in the control groups was 11.1	The mean quality of life, sf-36, 0-100 ≤4 months - domain-bodily pain in the intervention groups was 2.5 higher (4.16 lower to 9.16 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Physical functioning	251 (1 study) 3 months	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical functioning in the control groups was 11.6	The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical functioning in the intervention groups was 4.2 lower (10.86 lower to 2.46 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)- Laminectomy versus Usual Care (95% CI)
Quality of life, SF-36, 0-100 >4 months - 1 year (1 year) - Domain-Bodily pain	246 (1 study) 1 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-bodily pain in the control groups was 17.5	The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-bodily pain in the intervention groups was 5.5 higher (0.74 lower to 11.74 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year (1 year) - Domain-Physical functioning	246 (1 study) 1 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-physical functioning in the control groups was 16.4	The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-physical functioning in the intervention groups was 1.6 higher (4.64 lower to 7.84 higher)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Bodily pain	221 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-bodily pain in the control groups was 15.6	The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-bodily pain in the intervention groups was 7.8 higher (1.56 to 14.04 higher)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Physical functioning	221 (1 study) 2 years	LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-physical functioning in the control groups was 17.1	The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-physical functioning in the intervention groups was 0 higher (6.52 lower to 6.52 higher)
Pain Severity (Low Back Pain bothersomeness, change score,0-24) ≤4 months	251 (1 study) 3 months	LOW[a] due to risk of bias		The mean pain severity (low back pain bothersomeness, change score,0-24) ≤4 months in the control groups was -1	The mean pain severity (low back pain bothersomeness, change score,0-24) ≤4 months in the intervention groups was 0.4 higher (0.15 lower to 0.95 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)-Laminectomy versus Usual Care (95% CI)
Pain Severity (Low Back Pain bothersomeness, change score,0-24) >4 months - 1 year	246 (1 study) 1 years	LOW[a] due to risk of bias		The mean pain severity (low back pain bothersomeness, change score,0-24) >4 months - 1 year in the control groups was -1.3	The mean pain severity (low back pain bothersomeness, change score,0-24) >4 months - 1 year in the intervention groups was 0 higher (0.55 lower to 0.55 higher)
Pain Severity (Low Back Pain bothersomeness, change score,0-24) >4 months (2 year)	221 (1 study) 2 years	LOW[a] due to risk of bias		The mean pain severity (low back pain bothersomeness, change score,0-24) >4 months (2 year) in the control groups was -1.6	The mean pain severity (low back pain bothersomeness, change score,0-24) >4 months (2 year) in the intervention groups was 0.3 higher (0.26 lower to 0.86 higher)
Pain Severity (Sciatica Pain bothersomeness, change score,0-24) ≤4 months	251 (1 study) 3 months	LOW[a] due to risk of bias		The mean pain severity (sciatica pain bothersomeness, change score,0-24) ≤4 months in the control groups was -1.2	The mean pain severity (sciatica pain bothersomeness, change score,0-24) ≤4 months in the intervention groups was 0.3 lower (1.01 lower to 0.41 higher)
Pain Severity (Sciatica Pain bothersomeness, change score,0-24) >4 months - 1 year (1 year)	246 (1 study) 1 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity (sciatica pain bothersomeness, change score,0-24) >4 months - 1 year (1 year) in the control groups was -1.7	The mean pain severity (sciatica pain bothersomeness, change score,0-24) >4 months - 1 year (1 year) in the intervention groups was 0.6 lower (1.15 to 0.05 lower)
Pain Severity (Sciatica Pain bothersomeness, change score,0-24) >4 months (2 year)	221 (1 study) 2 years	LOW[a] due to risk of bias		The mean pain severity (sciatica pain bothersomeness, change score,0-24) >4 months (2 year) in the control groups was -1.8	The mean pain severity (sciatica pain bothersomeness, change score,0-24) >4 months (2 year) in the intervention groups was 0.4 lower (0.96 lower to 0.16 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)- Laminectomy versus Usual Care (95% CI)
Function (ODI change score) ≤4 months	251 (1 study) 3 months	LOW[a] due to risk of bias		The mean function (ODI change score) ≤4 months in the control groups was -8.1	The mean function (ODI change score) ≤4 months in the intervention groups was 0.5 higher (5.05 lower to 6.05 higher)
Function (ODI change score) >4 months - 1 year	246 (1 study) 1 years	LOW[a] due to risk of bias		The mean function (ODI change score) >4 months - 1 year in the control groups was -12.7	The mean function (ODI change score) >4 months - 1 year in the intervention groups was 2.2 lower (7.33 lower to 2.93 higher)
Function (ODI change score) >4 months (2 year)	221 (1 study) 2 years	LOW[a] due to risk of bias		The mean function (ODI change score) >4 months (2 year) in the control groups was -12.9	The mean function (ODI change score) >4 months (2 year) in the intervention groups was 3.5 lower (8.63 lower to 1.63 higher)

[a]Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[b]Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 101: Laminectomy versus usual care (cohort and RCT+ cohort)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)- Laminectomy versus Usual Care (95% CI)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Bodily pain	691 (1 study) 3 months	VERY LOW[a,b] due to risk		The mean quality of life, sf-36, 0-100 ≤4 months - domain-bodily pain in	The mean quality of life, sf-36, 0-100 ≤4 months - domain-bodily pain in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)- Laminectomy versus Usual Care (95% CI)
		of bias, imprecision		the control groups was 11.8	16.1 higher (12.91 to 19.29 higher)
Quality of life, SF-36, 0-100 ≤4 months - Domain-Physical functioning	691 (1 study) 3 months	VERY LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical functioning in the control groups was 10	The mean quality of life, sf-36, 0-100 ≤4 months - domain-physical functioning in the intervention groups was 14.8 higher (11.48 to 18.12 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year (1 year) - Domain-Bodily pain	532 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-bodily pain in the control groups was 13.5	The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-bodily pain in the intervention groups was 14.5 higher (10.89 to 18.11 higher)
Quality of life, SF-36, 0-100 >4 months - 1 year (1 year) - Domain-Physical functioning	532 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-physical functioning in the control groups was 10.5	The mean quality of life, sf-36, 0-100 >4 months - 1 year (1 year) - domain-physical functioning in the intervention groups was 16 higher (12.39 to 19.61 higher)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Bodily pain	533 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-bodily pain in the control groups was 13.3	The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-bodily pain in the intervention groups was 13.6 higher (9.99 to 17.21 higher)
Quality of life, SF-36, 0-100 >4 months (2 year) - Domain-Physical functioning	448 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-physical functioning in the control groups was 11.8	The mean quality of life, sf-36, 0-100 >4 months (2 year) - domain-physical functioning in the intervention groups was 11.2 higher (6.76 to 15.64 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)-Laminectomy versus Usual Care (95% CI)
Pain Severity(Low Back Pain bothersomeness, change score,0-24) ≤4 months	691 (1 study) 3 months	VERY LOW[a] due to risk of bias		The mean pain severity(low back pain bothersomeness, change score,0-24) ≤4 months in the control groups was -0.8	The mean pain severity(low back pain bothersomeness, change score,0-24) ≤4 months in the intervention groups was 1.2 lower (1.48 to 0.92 lower)
Pain Severity(Low Back Pain bothersomeness, change score,0-24) >4 months - 1 year	532 (1 study) 1 years	LOW[a] due to risk of bias		The mean pain severity(low back pain bothersomeness, change score,0-24) >4 months - 1 year in the control groups was 1	The mean pain severity(low back pain bothersomeness, change score,0-24) >4 months - 1 year in the intervention groups was 3.0 lower (3.28 to 2.72 lower)
Pain Severity(Low Back Pain bothersomeness, change score,0-24) >4 months (2 year)	533 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(low back pain bothersomeness, change score,0-24) >4 months (2 year) in the control groups was -1.1	The mean pain severity(low back pain bothersomeness change score,0-24) >4 months (2 year) in the intervention groups was 0.9 lower (1.18 to 0.62 lower)
Pain Severity(Sciatica Pain bothersomeness, change score,0-24) ≤4 months	691 (1 study) 3 months	VERY LOW[a] due to risk of bias		The mean pain severity(sciatica pain bothersomeness, change score,0-24) ≤4 months in the control groups was -0.9	The mean pain severity(sciatica pain bothersomeness, change score,0-24) ≤4 months in the intervention groups was 1.8 lower (2.08 to 1.52 lower)
Pain Severity(Sciatica Pain bothersomeness, change score,0-24) >4 months - 1 year (1 year)	532 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean pain severity(sciatica pain bothersomeness, change score,0-24) >4 months - 1 year (1 year) in the control groups was -1.4	The mean pain severity(sciatica pain bothersomeness, change score,0-24) >4 months - 1 year (1 year) in the intervention groups was 1.2 lower (1.48 to 0.92 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sciatica due to stenosis (foraminal and/or canal)-Laminectomy versus Usual Care (95% CI)
Pain Severity(Sciatica Pain bothersomeness, change score,0-24) >4 months (2 year)	533 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean pain severity(sciatica pain bothersomeness, change score,0-24) >4 months (2 year) in the control groups was -1.4	The mean pain severity(sciatica pain bothersomeness, change score,0-24) >4 months (2 year) in the intervention groups was 1.1 lower (1.38 to 0.82 lower)
Function (ODI change score) ≤4 months	691 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean function (ODI change score) ≤4 months in the control groups was -7.6	The mean function (ODI change score) ≤4 months in the intervention groups was 13.8 lower (16.44 to 11.16 lower)
Function (ODI change score) >4 months - 1 year	532 (1 study) 1 years	VERY LOW[a] due to risk of bias		The mean function (ODI change score) >4 months - 1 year in the control groups was -8.9	The mean function (ODI change score) >4 months - 1 year in the intervention groups was 12.5 lower (15.41 to 9.59 lower)
Function (ODI change score) >4 months (2 years)	533 (1 study) 2 years	VERY LOW[a,b] due to risk of bias, imprecision		The mean function (ODI change score) >4 months (2 years) in the control groups was -9.3	The mean function (ODI change score) >4 months (2 years) in the intervention groups was 11.2 lower (14.26 to 8.14 lower)

[a] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and 2 increments if the majority of the evidence was at very high risk of bias

[b] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

28.4 Economic evidence

Published literature

Three economic evaluations were identified with the relevant comparison and have been included in this review.[164,170,171] These are summarised in the economic evidence profile below and the economic evidence tables in Appendix I.

Three economic evaluations relating to this review question were identified but selectively excluded.[182,183,109,184] This is reported in Appendix M, with reasons for exclusion given.

See also the economic article selection flow chart in Appendix F.

Table 102: Economic evidence profile: surgery versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost (£)	Incremental effects (QALYs)	Cost effectiveness (ICER)	Uncertainty
Tosteson 2008[170] (USA)	Partially applicable[(a)]	Potentially serious limitations	• Based on both randomised and observational cohorts of the SPORT trial combined and analysed according to treatment received using regression models. • Population: Adults with a diagnosis of intervertebral disc herniation. • Two comparators in full analysis: 1. Standard open laminotomy/laminectomy with removal of the herniation and examination of the involved nerve root. Surgeons only performed other procedures when it was deemed necessary. 2. Usual care as decided by the physician • Follow-up was 2 years.	9,133	0.21	£43,490 per QALY gained	Probabilistic analysis only reported for total costs which include indirect costs. No other sensitivity analyses conducted.
Tosteson 2008A [170,171] (USA)	Partially applicable[(a)]	Potentially serious limitations	• Based on both randomised and observational cohorts of the SPORT trial combined and analysed according to treatment received using regression models. • Population: Adults with symptoms for at least 12 weeks and image-confirmed diagnosis of spinal	6,661	0.17	£44,865 per QALY gained	95% CI: 31,617 – 66,191 Indirect costs were included in all the sensitivity analyses conducted: observational and randomised cohorts were analysed separately and no major difference between the 2 ICERs was observed; adjusting for observed mortality decreased the ICER only

Study	Applicability	Limitations	Other comments	Incremental cost (£)	Incremental effects (QALYs)	Cost effectiveness (ICER)	Uncertainty
			stenosis without degenerative spondylolisthesis. • Two comparators in full analysis: 1. Standard posterior laminectomy. 2. Usual care as chosen by the patient and physician • Follow-up was 2 years.				slightly; the ICER increased when QALYs were estimated with SF-6D and when higher surgery cost was used.
Van den Hout 2008[164] (Netherlands)	Partially applicable[(f)]	Potentially serious limitations	• Within-trial analysis (associated clinical paper Peul 2008[161,162]) • Population: patients aged 18 to 65 with a radiologically confirmed disc herniation and lumbosacral radicular syndrome that had lasted for 6 to 12 weeks. • Two comparators in full analysis: 1. Early surgery to remove disc herniation. 2. Usual care - prolonged conservative care provided by the GP; if sciatica persisted at 6 months, microdiscectomy was offered. • Increasing leg pain not responsive to drugs and progressive neurological deficit were reasons for performing surgery earlier than 6 months. • Follow-up was 1 year.	1,405	0.044	£31,932 per QALY gained	95% CI: 10,817 – 332,249 When SF-6D was used as an alternative utility measure the QALY difference was 0.024, resulting in an ICER of £58,541.

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) Study conducted in the USA; discount rate is 3%

(b) Outcomes were based also on observational data, not on RCT only, it was not clear how many individuals were form the RCTs and how many from the observational study; costs from US Medicare payments which may not reflect actual costs; resource use was based on patient-reported data which may not be accurate; unclear what parameters at baseline were used to adjust EQ5D data; no sensitivity analyses were conducted and the 95% CI of the ICER was reported only for the total costs (direct and indirect too).

(c) 2004 US dollars converted to UK pounds.[110] Cost components incorporated: surgery, health care visits, diagnostic test, medications, and other health care services. Indirect costs were included but analysed separately and not reported here.

(d) QALYs estimated using the EQ5D US tariff.

(e) Outcomes were based also on observational data, not on RCT; costs from US Medicare payments which may not reflect actual costs; resource use was based on patient-reported data which may not be accurate; sensitivity analyses were conducted using both direct and indirect costs.

(f) Study conducted in the Netherlands. Intervention not described in detail in this paper. Patients in the usual care group could have surgery after the initial 6 months and outcomes were collected up to 1 year.

(g) Short time horizon; resource use was based on patient-reported data which may not be accurate; hospital prices were used.[110] Cost components incorporated: surgery with admissions to hospital, physical therapy, visits, homecare, drugs and aids.

(h) Indirect and societal costs were included but analysed separately and not reported here.

(i) QALYs estimated using the EQ5D UK tariff

The studies from the USA reported a higher incremental cost for surgery compared to the study conducted in the Netherlands. The unit cost of surgery used in the USA study was $12,754 for surgery with no complications, which is equal to £8,071 using the purchasing power parities.[110] This figure is very high compared to the cost reported in the NHS Reference Cost (£3,582) for the HRG code HC04F – Extradural Spine Intermediate 1, which includes spinal decompression surgery.

If a lower cost estimate for surgery was used in the analysis, the estimated ICER would be lower too.

28.5 Evidence statements

28.5.1 Clinical

28.5.1.1 Discectomy versus usual care

In people with sciatica due to herniated disc, there was clinical benefit for discectomy compared with usual care for quality of life demonstrated in evidence from 2 studies at less than or equal to 4 months for the SF-36 domains of bodily pain and physical functioning (very low quality, n=696) as well as in mental health, vitality and general health from 1 study (low quality, n=281). Evidence for greater than 4 months' time point of 1 year from 2 studies demonstrated a clinical benefit for discectomy compared to usual care in quality of life for the majority of domains of the SF-36 apart from physical functioning and mental health for which there was no clinical difference between treatments. Evidence of quality of life measured by the SF-36 at the 2 year follow-up demonstrated a clinical benefit for discectomy compared to usual care for the SF-36 domain bodily pain but not for physical function(very low quality, n=373). Evidence for quality of life measured by the EQ-5D demonstrated clinical benefit for discectomy compared to usual care at the less than 4 months' and no difference between treatments at 1 year (1 study, low quality, n=283).

Conflicting evidence demonstrated a clinical benefit of discectomy compared with usual care for both leg and back pain measured by VAS in the short term but no difference between treatments at 1 and 2 years (2 studies, very low-low quality, n=333). Further evidence demonstrated no benefit in pain measured by sciatica bothersomeness index at any time point (low quality, n=413). Benefit in function measured by the RMDQ was seen for discectomy compared to usual care at less than four months' but not when assessed by the ODI. There was no difference in treatments in function assessed by either scale in the long term.

Clinical benefit for discectomy compared to usual care was also demonstrated in evidence from 1 study for responders to complete disappearance of symptoms at both the less than and greater than four month follow up.

Non-randomised evidence demonstrated clinical benefit for discectomy compared with usual care for all quality of life domains measured by the SF-36 at both short and long term follow-up (1 study, very low quality, n=631). Evidence from 2 non-randomised studies suggested clinical benefit in leg pain measured by the sciatica bothersomeness index and back pain assessed with back pain bothersomeness index for discectomy compared to usual care in the short term and long term follow-up of 1 year but not at 2 years (very low quality, n=656 and n=1191). Additionally when compared with usual care, benefit for discectomy for function on the ODI was demonstrated at both short and long term follow up in 1 study (n=656, very low quality). There was non-randomised evidence of a poorer outcome with discectomy when compared to usual care for healthcare utilisation assessed by number of patients with more reported diagnostic test use but no clinical difference between treatments for any other healthcare utilisation measure (1 study, low quality, n=1191).

28.5.1.2 Discectomy versus combination treatment (manual therapy + biomechanical exercise + self-management)

Conflicting evidence from 1 study for quality of life at less than 4 months follow up showed clinical benefit for discectomy compared to combination treatment for the SF-36 domains of bodily pain, vitality and physical function but clinical harm for discectomy for the domains of physical role, emotional role and social function. There was no difference between treatments for the domain of mental health (very low quality, n=40). Evidence from the same study demonstrated no difference in pain and function between discectomy and the combination treatment at the short term follow up of less than 4 months (low quality, n=40).

28.5.1.3 Percutaneous disc decompression versus usual care

Evidence from 1 study demonstrated clinical benefit in pain for percutaneous disc decompression when compared to usual care at both the short term and long term follow up (low to very low quality, n=62).

28.5.1.4 Plasma disc decompression versus epidural steroid injection

Evidence from a single study demonstrated clinical benefit in both leg and back pain for plasma disc decompression when compared to epidural steroid injections at both short term and long term follow up (moderate to low quality, n=85). However, there was no clinical difference between treatments for function (low to moderate quality, n=85) at any time point or procedure related adverse events at the greater than 4 months follow up (very low quality, n=85).

28.5.1.5 Discectomy versus fusion (cohort)

Evidence from a single study showed no clinical benefit in function for discectomy when compared with spinal fusion at the greater than 4 months follow up (very low quality, n=55).

28.5.1.6 Laminectomy versus usual care

Conflicting evidence from 1 study for quality of life at less than 4 months follow up showed laminectomy to be less effective than usual care for the SF-36 domain of physical functioning but clinical benefit with laminectomy compared to usual care was seen for the domain of bodily pain at the long term follow up of 1 and 2 years (low quality, n=246). The same study demonstrated no clinical difference in pain (both back pain and sciatica) and function when laminectomy was compared to usual care at both the less than and greater than 4 months follow-ups low to very low quality, n=251).

Non-randomised evidence from a single study demonstrated a clinical benefit of laminectomy compared to usual care for quality of life assessed by the SF-36 in the domains of bodily pain and physical functioning at both the short term and long term follow ups (very low quality, n=533). A clinical benefit of laminectomy compared to usual care for back pain was seen at the greater than 4 month time point of 1 year but not at any other follow up period (low quality, n=691). There was no difference between treatments in leg pain assessed by the sciatica bothersomeness index reported in the same study. Additionally, when compared with usual care, a clinical benefit with laminectomy was seen for function at both the less than and greater than 4 months follow up periods (1 study, very low quality, n=532).

28.5.2 Economic

- Three cost–utility analyses found that spinal decompression was not cost-effective compared to usual care treating patients with disc herniation or spinal stenosis. These analyses were assessed as partially applicable with potentially serious limitations.

28.6 Recommendations and link to evidence

Recommendations	The current recommendations can be found at https://www.nice.org.uk/guidance/ng59/chapter/Recommendations
Relative values of different outcomes	The GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Responder criteria for pain and function, adverse events, revision rate, failure rate and healthcare utilisation were also considered as important. Evidence was reported for all of the critical outcomes except for psychological distress. Failure rate was the only important outcome for which there was no evidence from studies included in this review. The GDG felt there was sufficient evidence for all of the other outcomes that were considered important for this review.
Trade-off between clinical benefits and harms	**Discectomy versus usual care** Overall, the evidence suggested a clinical benefit in favour of discectomy when performed in people with sciatica due to a herniated intervertebral disc for quality of life assessed by the SF-36 in the domains of bodily pain, physical functioning, mental health index, vitality and general health perception in the short term. This benefit was also supported by EQ-5D data at the short term follow-up. Some benefit for discectomy was also seen at the long term follow up of 1 year in the SF-36 domains of bodily pain, social functioning, physical/emotional role and vitality as well. As with quality of life data, clinical benefit favouring discectomy was observed for both back and leg pain in the short term. The GDG noted that although the benefits were maintained in the long term, the between group difference was not. The GDG noted that sciatic symptoms usually improve over the course of the first 3 months in the majority of people without treatment but this evidence suggested people undergoing discectomy improve quicker. The GDG agreed that in some individuals the pain severity may warrant an earlier intervention. In terms of function, the randomised evidence showed no difference between treatments, although the non-randomised data suggested a clinically important difference favouring discectomy in both the short and long term. In terms of healthcare utilisation, there was no evidence for a difference other than a suggestion that more diagnostic tests were required in those undergoing discectomy; however the GDG agreed that this did not outweigh the possible short term benefits observed. The group noted that discectomy was a relatively safe procedure, and that the most common surgical complication in the discectomy group was a dural tear. The GDG thought this could possibly increase hospital length of stay, and that a tear may result in CNS infection. Reoperation rates were low with discectomy, and mainly due to recurrent disc herniation. The GDG noted that re-operations may not be considered as adverse events following surgery, but may be a natural history of the condition, since about 5% of patients will suffer from a recurrence of disc prolapse. The GDG noted that there was a high rate of cross-over from the control group arm into the discectomy group in the included trials, and those that crossed over had high pain scores post usual care treatment. Results were usually reported as intention to treat analysis and therefore the effects seen in the usual care group may

have been over-estimated. This was noted as an inevitable consequence of surgical trials that do not utilise a placebo control. If cross-over isn't offered as an option in a trial, a high drop-out rate from the usual care arm would also be expected. It was also considered that had the people who crossed over to receive discectomy been removed from the analysis, the effect size in favour of discectomy would likely have been larger than observed, though the GDG recognised that this introduces a risk of bias. There was also concern raised about the uncertainty surrounding the amount of physiotherapy sessions received by the treatment groups in 1 study. It was unclear if this treatment was offered at baseline or as additional sessions. Equally, It was not possible to establish whether the proportion of patients referred for additional physiotherapy was the same in the discectomy and the control groups. The GDG felt this could have affected the outcomes of pain and function reported and therefore did not have much confidence in the effects reported.

The GDG agreed that although there was concern about the reliability of the evidence due to a high cross-over rate, the cross-over of patients was more predominant in 1 arm of the trial (from the usual care group to surgery), and occurred mostly after the short term outcome data was collected. This gave the GDG some confidence in the results reported as the benefit seen in the discectomy group would have been even larger had the usual care cross-over patients not been considered in this arm. However as this very low quality evidence was from a single trial with a small sample size, it did not contribute significantly to informing the recommendation.

Discectomy versus combination treatment (manual therapy + biomechanical exercise + self-management)

Contrasting results were seen amongst the individual domains of quality of life (assessed by the SF-36) in the short term. There were no obvious baseline differences between the arms for these domains that may have explained this.

Evidence for pain (assessed by McGill) and function (assessed by RMDQ) showed no clinically important difference between the 2 groups. The GDG noted that the study reported baseline pain scores and the "present pain intensity" values separately with 2 values for each group varying significantly from each other. The present pain intensity scores were reported to be ~2.5 for both the discectomy and combination treatment groups (baseline McGill scores were reported as ~30). The GDG considered this to be an anomaly and therefore interpreted the results with caution.

Percutaneous disc decompression versus usual care

The evidence showed a clinically important difference favouring percutaneous disc decompression for the outcome of pain in both the short term (≤ 4 months) and long term (> 4 months; at both 1 year and 2 year follow up). However as this finding came from a single, low quality study with a small sample size, the GDG could not be confident enough to make a recommendation based on this limited evidence.

Plasma disc decompression versus epidural steroid injection

A clinical benefit in pain (assessed by VAS) favouring decompression was reported for both leg and back pain in the short term and long term. However, no clinically important difference between treatments was seen in function (assessed by ODI) at either time-point. The GDG noted that 1 of the criteria for inclusion in the trial was that the participants had to have failed a previous epidural injection for the same symptoms between 3 weeks to 6 months previously. They considered this to be a serious flaw of the trial, which lowered their confidence in the evidence reported.

When weighing up the balance between benefits and harms, the GDG considered the adverse events associated with plasma decompression. The evidence showed that there was no clinically important difference in adverse events reported between the 2 treatment groups. The group felt that the majority of adverse events reported were not a cause for concern, except possibly increased weakness seen in the decompression group. However, as this was a single event and there was no additional information provided; the GDG could not derive conclusive evidence of harm from the study.

	Discectomy versus fusion The GDG discussed that the majority of the evidence was in favour of discectomy in terms of quality of life and pain in the short term, however these effects were not always maintained at long term followed up. The evidence also showed no clinically important difference between the 2 surgical treatments for function (assessed by ODI) in the long term. **Summary** The GDG considered that discectomy for people suffering from sciatica offered a good prognosis and was successful in providing long-term pain relief. However, they also noted that sciatic symptoms tend to improve naturally with time without treatment. Despite the good long term prognosis with or without treatment, the GDG felt that earlier symptom resolution with surgical intervention should be an option for people. It was agreed that there was sufficient evidence to suggest that discectomy should be considered for a subgroup of people with sciatica who had failed to respond to conservative management of their symptoms.
Trade-off between net clinical effects and costs	Three economic studies were included which compared spinal decompression with usual care.[164,170,171] The first 2were USA studies based on both randomised and observational cohorts of the SPORT trial; [170,171] in the first study the population was adults with a diagnosis of intervertebral disc herniation, while in the second the population was adults with spinal stenosis without degenerative spondylolisthesis (the study presented results separately for people with and without degenerative spondylolisthesis but we only focused on the latter). In both studies surgery was more effective but more costly than usual care with a resulting ICER of more than £40,000 per QALY. In the second study, a probabilistic sensitivity analysis resulted in 95% confidence interval around the ICER of £31,617 to £66,191 per QALY gained. The third study was a within-trial analysis (associated clinical paper Peul 2008[162]) conducted in the Netherlands on a population with disc herniation and lumbosacral radicular syndrome where early micro-discectomy was compared to prolonged conservative care provided by the GP followed by surgery if sciatica persisted at 6 months.[164] However, people in the conservative care group could also receive surgery earlier than 6 months if they had increasing leg pain that was not responsive to drugs and progressive neurological deficit. Again, in this study surgery was more effective but more costly than usual care, with an ICER of £31,932 per QALY gained. The 95% confidence interval around the ICER was £10,817 to £332,249 per QALY gained. It was noted that in the first 2 studies conducted in the USA the cost of surgery was significantly higher compared to the cost reported in the study from the Netherlands. The unit cost of surgery in the USA studies (£8,071) was also compared to the NHS Reference cost of spinal decompression surgery in the UK (£3,582). Conducting a simple threshold analysis using the intervention cost of £3,582 reported in the NHS Reference Cost; spinal decompression surgery would need to generate at least an additional 0.179 QALYs compared to no surgery for it to be considered cost effective at the £20,000 per QALY threshold. The observed QALY gain in the USA studies was 0.21 and 0.17. However, in the European study, the effectiveness was much lower compared to the USA studies (0.044 QALYs). The GDG discussed this evidence and concluded that this could be due to a high cross-over between arms in this study: during the first year surgery was performed in 89% of patients in the early surgery group and 40% of the prolonged conservative care group. If the effectiveness was similar to that reported in the USA studies then spinal decompression is likely to be cost-effective. The GDG concluded that there was a high uncertainty around the conclusions of the economic studies as the cost of surgery is overestimated in the USA studies and the effectiveness is likely to be underestimated in the European study. Therefore overall the GDG concluded that decompression surgery is likely to be cost effective in patients with sciatica when other treatments have failed.

Quality of evidence	The evidence for all comparisons and all outcomes was rated as low or very low quality, mainly due to risk of bias (and sometimes due to additional imprecision). The evidence from randomised studies was considered to be at high risk of bias mainly due to lack of appropriate blinding to the key confounders that could influence the outcome. However, the group noted that a limitation of surgery trials that do not utilise a placebo control is that it is often not possible to carry out adequate blinding, but that lack of blinding still would mean there is a risk of bias in interpreting the results. The majority of low quality evidence for the discectomy versus usual care comparison was derived from 2 trials with large sample sizes. Both trials had a high rate of cross-over in both arms, which the GDG agreed would affect their confidence in interpreting the data that was reported. The evidence for all other comparisons in the review was of low quality and came from single studies with relatively small sample sizes. The non-randomised evidence was rated as very low quality, due to inherent selection bias in non-randomised studies as well as a lack of appropriate blinding. This meant it was considered to be at serious risk of bias and therefore the group placed low confidence in the effects reported.
Other considerations	The issue regarding optimal time to offer spinal decompression was discussed. Whilst the GDG agreed that in the majority of cases, sciatic symptoms would improve naturally with time, they recognised that the option for earlier pain relief should be available for a subset of patients that suffer from severe, acute sciatic pain. The group agreed that surgical intervention following a period of conservative management for around 6 weeks would be reasonable. However, it was noted that there was little evidence to support this time-point and that the 6 week conservative treatment interval was largely historical and consensus based. The GDG agreed that as non-surgical management should be pursued prior to surgery, this would negate the need to specify a specific time point in the recommendation as it is likely that it would be at least 3-6 months before surgery was offered. The GDG discussed the need of imaging prior to spinal decompression. The GDG observed that prior imaging was an inclusion criteria for all the studies included in the review. The GDG was also aware that operating without concordant imaging would carry a significant risk of harm, because such patients would be exposed to the risks of surgery and general anaesthetics with little chance of any benefit. The GDG decided it was therefore appropriate to restrict the use of spinal decompression in people in whom radiological findings are concordant with sciatic symptoms. The GDG noted that if spinal decompression was being performed, patient outcome information should be submitted to a national registry. The GDG agreed that this recommendation would equally apply for pregnant women and this should be considered on a case by case basis. The GDG were aware of the NICE clinical guideline for pharmacological management of neuropathic pain (CG173) which covers the pharmacological management of sciatica and therefore was outside of the remit for this guideline to do a systematic review of the evidence for this. Conservative management for sciatica should therefore be guided by the recommendations set in CG173 before discectomy is considered as an option. It was also noted that in the non-randomised study included in the review, patients had to pay for their own treatment which the group agreed was a serious limitation of the trial, since the costs of spinal fusion far outweigh those of discectomy. This could potentially skew the results in favour of the cheaper surgical option. The GDG were aware of existing NICE interventional procedure guidance for Interspinous distraction procedures for lumbar spinal stenosis causing neurogenic claudication (IPG365) and Percutaneous intradiscal laser ablation in the lumbar spine

	(IPG 357) which recommend normal arrangements for clinical governance, consent and audit. This specific procedure was excluded from this review and therefore this existing guidance should be followed for people with sciatica. Interventional procedure guidance also exists for Percutaneous intradiscal laser ablation in the lumbar spine (IPG357) which recommends normal arrangements for clinical governance, consent and audit, Automated percutaneous mechanical lumbar discectomy (IPG141), Endoscopic laser foraminoplasty (IPG31) Insertion of an annular disc implant lumbar discectomy (IPG506) and Percutaneous endoscopic laser lumbar discectomy (IPG300) which all recommend special arrangements for clinical governance, consent, audit and research. These procedures were excluded from the review due to being inappropriate to pool with decompression techniques in general, and therefore if being considered for people with sciatica, existing guidance should be followed. The GDG were also aware of IPG guidance for Percutaneous coblation of the intervertebral disc for low back pain and sciatica (IPG543) which recommends normal arrangements, however it was noted that this review considered different evidence and followed different methodology to that included within this review. At the time of consultation IPG300 was being updated. Information on the update is available here: http://www.nice.org.uk/guidance/indevelopment/gid-ip2806.

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30 Acronyms and abbreviations

Acronym or abbreviation	Description
ACT	Acceptance and Commitment Therapy
ADL	Activities of daily living
ALBP	Aberdeen Low Back Pain
ALBPSQ	Acute low back pain screening questionnaire (alternative name for OMPQ)
APTA	American Physical Therapy Association
ATEAM	Alexander technique lessons, technology and massage
AUC	Area under curve
BDI	Beck depression inventory
BPI	Brief Pain Inventory
CFT	Compassion Focused Therapy
CI	Confidence interval
CPG	Clinical Practice Guidelines
CPR	Clinical prediction rule
CTIP	Cognitive treatment of illness perception
CUA	Cost-utility analysis
DRAM	Distress and Risk Assessment Method
EIFEL	French version of the Roland Morris disability questionnaire
EMG	Electromyographic
FABQ	Fear Avoidance Beliefs Questionnaire
FRI	Functional Rating Index
GDG	Guideline Development Group
GHQ	General Health Quality
GPR	Global Posture Re-education
HADS	Hospital Anxiety and Depression Scale
HILT	High Intensity Laser Therapy
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
iLSO	Inextensible lumbosacral orthotics
IQR	Interquartile range
LBP	Low back pain
MET	Muscle energy technique
MBR	Multi-disciplinary biopsychosocial rehabilitation
MBSR	Mindfulness-Based Stress Reduction
MCS	Mental Component Score
MID	Minimum important difference
MODI	Modified Oswestry disability index
MPQ	McGill Pain Questionnaire
MVAS	Million Visual Analogue Scale
NICE	National Institute for Health and Care Excellence
NIOSH	National Institute for Occupational Safety and Health
NRS	Numeric pain rating scale

Acronym or abbreviation	Description
NR	Not reported
NRS	Numeric rating scale
NSAID	Non-steroidal anti-inflammatory drug
ODI	Oswestry disability index
OECD	Organisation for Economic Co-operation and Development
ÖMPQ	Örebro musculoskeletal pain questionnaire
OMSQ	Modified Orebro Musculoskeletal Screening Questionnaire
PACE	Paracetamol for Low Back Pain
PCS	Physical Component Score
PDI	Pain disability index
PENS	Percutaneous electrical nerve stimulation
PGIC	Patient's global impression of change
PICO	Population, intervention, comparator, outcome
PT	Physical therapists
QALY	Quality-adjusted life year
QBPDQ	Quebec Back Pain Disability Questionnaire
QOL	Quality of life
RCT	Randomised controlled trial
RMDQ	Roland Morris disability questionnaire
ROC	Receiver operator characteristic
SBT	STarT Back Screening Tool
SFI	Spine functional index
SIP	Sickness impact profile
SR	Systematic review
STAI	State –Trait Anxiety Inventory
TENS	Transcutaneous electrical nerve stimulation
TSK	Tampa scale of kinesiophobia
UC	Usual care
VAS	Visual analogue scale

31 Glossary

The NICE Glossary can be found at www.nice.org.uk/glossary.

31.1 Guideline-specific terms

Term	Definition
Acceptance and commitment therapy (ACT)	An empirically-based psychological intervention that uses acceptance and mindfulness strategies, with commitment and behaviour change strategies, to increase psychological flexibility.
Acupuncture	Acupuncture is a treatment derived from ancient Chinese medicine in which fine needles are inserted at certain sites in the body for therapeutic or preventative purposes
Behavioural therapies	Treatment to help change potentially self-destructing behaviours in people with chronic low back pain.
Cognitive behavioural approaches	Cognitive approaches are aimed at altering unhelpful or inappropriate beliefs as a basis for changing behaviour, such as fear-avoidance.
Disc replacement	Also known as spinal arthroplasty, disc replacement is a surgical procedure to relieve low back pain. It involves replacing invertebral units with artificial discs that can act as a functional prosthetic replacement. The pain relief stems from removal of the painful disc.
Electrotherapies	Umbrella term consisting of TENS, PENS, interferential therapy, LLLT, and therapeutic ultrasound, involving the application of forms of energy to the body with the goal of improving symptoms or recovery of low back pain.
Epidural injections	An injection into the epidural space within the spine, using either corticosteroids or anti-TNF agents for their anti-inflammatory and immunosuppressant properties.
Exercise therapies	A wide variation of physical exercise to prevent or treat low back pain. These can be performed on a one-to-one basis or in a group environment. The guideline covers biomechanical, aerobic, mind-body and mixed modality exercise.
Imaging	Radiographic techniques to produce images of the spinal column to assist clinical decision-making when assessing people with low back pain with or without sciatica. These are defined in the guideline by X-rays, CT scans and MRI scans.
Low back pain	Pain in the back between the bottom of the rib cage and the buttock creases.
Manual therapies	Active or passive movements delivered usually by a GP to the neuromusculoskeletal system focussing on joints and soft tissues to improve mobility and function, and to decrease pain. These are reviewed in the guideline by soft tissue techniques, traction, manipulation or mobilisation and mixed modality manual therapy.
Mindfulness therapy	Therapy to make patient aware of the present moment, and non-judgmentally to the unfolding of experience moment by moment to alter behaviours towards low back pain.
Multidisciplinary biopsychosocial rehabilitation programmes	An intervention that involves a physical component (such as specific exercise modalities, mobilisation, massage) and at least 1 other element from a biopsychosocial approach, that is psychological or social and occupational or educational (defined educational intervention e.g. education on anatomy, psychology, imaging, coping, medication, family, work and social life). The different components of the intervention had to be offered as an integrated programme involving communication between the providers responsible for the different components. These programmes may include various components delivered by 1 individual, or by a number of people, such as the

Term	Definition
	multi-disciplinary aspect applies to the interventions included in the package (across disciplines), not to the number of people / disciplines delivering this.
Multi-modal treatment package	Exercise alongside at least one of self-management, manual therapy or psychological therapy (for example, cognitive behavioural therapy).
Orthotics and appliances	Generic or bespoke insoles, corsets, belts or supports aiming to reduce the impact or provide support to the lower back and pelvic muscles.
Pharmacological interventions	Oral/sublingual, rectal, intra-muscular and transdermal drug treatments to relieve low back pain with or without sciatica. This does not include pharmacological treatment for the management of sciatica alone.
Postural therapies	Postural therapies aim to prevent or reduce low back pain by focusing on the correction of postures that are theorised to be suboptimal and place excessive or damaging loads upon the spine.
Radiofrequency denervation	A minimally invasive and percutaneous procedure performed under local anaesthesia or light intravenous sedation. Radiofrequency energy is delivered along an insulated needle in contact with the target nerves to denature the nerve.
Risk assessment tools	Tools developed to support clinical decision-making. These include: the Örebro Musculoskeletal Pain Screening Questionnaire (ÖMSPQ), the STarT Back Screening Tool and the Distress and Risk Assessment Method (DRAM).
Risk stratification	Risk stratified care strategies were developed in order to avoid a 'one size fits all' approach. There are many different stratifications and it is appreciated that there can be overlap between groups.
Self-management	Programmes to assist people with low back pain and sciatica returning to normal activities. This includes education and advice for staying active.
Spinal decompression	Removal of pressure from the nervous structures within the spinal column. This guideline covers the following procedures: laminectomy, discectomy, facetectomy, foraminotomy, fenestration, spinal decompression, sequestration and laminotomy.
Spinal fusion	Spinal fusion is an operation performed to achieve solid bone union between spinal vertebrae to prevent movement, using either the patient's own bone or artificial bone substitutes.
Spinal injections	Variations of injected agents which aim to either reduce inflammation in tissue or induce inflammation to stimulate healthy tissue regrowth. These include facet joint injections, medial branch blocks, intradiscal therapy and prolotherapy.

31.2 General terms

Term	Definition
Abstract	Summary of a study, which may be published alone or as an introduction to a full scientific paper.
Algorithm (in guidelines)	A flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows.
Allocation concealment	The process used to prevent advance knowledge of group assignment in an RCT. The allocation process should be impervious to any influence by the individual making the allocation, by being administered by someone who is not responsible for recruiting participants.
Applicability	How well the results of a study or NICE evidence review can answer a clinical question or be applied to the population being considered.
Arm (of a clinical study)	Subsection of individuals within a study who receive 1 particular intervention, for example placebo arm.

Term	Definition
Association	Statistical relationship between 2 or more events, characteristics or other variables. The relationship may or may not be causal.
Base case analysis	In an economic evaluation, this is the main analysis based on the most plausible estimate of each input. In contrast, see Sensitivity analysis.
Baseline	The initial set of measurements at the beginning of a study (after run-in period where applicable), with which subsequent results are compared.
Bias	Influences on a study that can make the results look better or worse than they really are. (Bias can even make it look as if a treatment works when it does not.) Bias can occur by chance, deliberately or as a result of systematic errors in the design and execution of a study. It can also occur at different stages in the research process, for example, during the collection, analysis, interpretation, publication or review of research data. For examples see selection bias, performance bias, information bias, confounding factor, and publication bias.
Blinding	A way to prevent researchers, doctors and patients in a clinical trial from knowing which study group each patient is in so they cannot influence the results. The best way to do this is by sorting patients into study groups randomly. The purpose of 'blinding' or 'masking' is to protect against bias. A single-blinded study is one in which patients do not know which study group they are in (for example whether they are taking the experimental drug or a placebo). A double-blinded study is one in which neither patients nor the researchers and doctors know which study group the patients are in. A triple blind study is one in which neither the patients, clinicians or the people carrying out the statistical analysis know which treatment patients received.
Carer (caregiver)	Someone who looks after family, partners or friends in need of help because they are ill, frail or have a disability.
Clinical effectiveness	How well a specific test or treatment works when used in the 'real world' (for example, when used by a doctor with a patient at home), rather than in a carefully controlled clinical trial. Trials that assess clinical effectiveness are sometimes called management trials. Clinical effectiveness is not the same as efficacy.
Clinician	A healthcare professional who provides patient care. For example, a doctor, nurse or physiotherapist.
Cochrane Review	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of randomised controlled trials prepared by the Cochrane Collaboration).
Cohort study	A study with 2 or more groups of people – cohorts – with similar characteristics. One group receives a treatment, is exposed to a risk factor or has a particular symptom and the other group does not. The study follows their progress over time and records what happens. See also observational study.
Comparability	Similarity of the groups in characteristics likely to affect the study results (such as health status or age).
Confidence interval (CI)	There is always some uncertainty in research. This is because a small group of patients is studied to predict the effects of a treatment on the wider population. The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. The CI is usually stated as '95% CI', which means that the range of values has a 95 in a 100 chance of including the 'true' value. For example, a study may state that "based on our sample findings, we are 95% certain that the

Term	Definition
	'true' population blood pressure is not higher than 150 and not lower than 110". In such a case the 95% CI would be 110 to 150. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment – often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example, if a large number of patients have been studied).
Control group	A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. The aim is to check for any differences. Ideally, the people in the control group should be as similar as possible to those in the treatment group, to make it as easy as possible to detect any effects due to the treatment.
Cost-consequences analysis (CCA)	Cost-consequences analysis is one of the tools used to carry out an economic evaluation. This compares the costs (such as treatment and hospital care) and the consequences (such as health outcomes) of a test or treatment with a suitable alternative. Unlike cost-benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (like the quality-adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out.
Cost-effectiveness analysis (CEA)	Cost-effectiveness analysis is one of the tools used to carry out an economic evaluation. The benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which life is extended as a result of the intervention).
Cost-effectiveness model	An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.
Cost-utility analysis (CUA)	Cost-utility analysis is one of the tools used to carry out an economic evaluation. The benefits are assessed in terms of both quality and duration of life, and expressed as quality-adjusted life years (QALYs). See also utility.
Discounting	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Dominance	A health economics term. When comparing tests or treatments, an option that is both less effective and costs more is said to be 'dominated' by the alternative.
Drop-out	A participant who withdraws from a trial before the end.
Economic evaluation	An economic evaluation is used to assess the cost-effectiveness of healthcare interventions (that is, to compare the costs and benefits of a healthcare intervention to assess whether it is worth doing). The aim of an economic evaluation is to maximise the level of benefits – health effects – relative to the resources available. It should be used to inform and support the decision-making process; it is not supposed to replace the judgement of healthcare professionals. There are several types of economic evaluation: cost-benefit analysis, cost-consequences analysis, cost-effectiveness analysis, cost-minimisation analysis and cost-utility analysis. They use similar methods to define and

Term	Definition
	evaluate costs, but differ in the way they estimate the benefits of a particular drug, programme or intervention.
Effect (as in effect measure, treatment effect, estimate of effect, effect size)	A measure that shows the magnitude of the outcome in one group compared with that in a control group. For example, if the absolute risk reduction is shown to be 5% and it is the outcome of interest, the effect size is 5%. The effect size is usually tested, using statistics, to find out how likely it is that the effect is a result of the treatment and has not just happened by chance (that is, to see if it is statistically significant).
Effectiveness	How beneficial a test or treatment is under usual or everyday conditions, compared with doing nothing or opting for another type of care.
Efficacy	How beneficial a test, treatment or public health intervention is under ideal conditions (for example, in a laboratory), compared with doing nothing or opting for another type of care.
EQ-5D (EuroQol 5 dimensions)	A standardised instrument used to measure health-related quality of life. It provides a single index value for health status.
Evidence	Information on which a decision or guidance is based. Evidence is obtained from a range of sources including randomised controlled trials, observational studies, expert opinion (of clinical professionals or patients).
Exclusion criteria (literature review)	Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.
Exclusion criteria (clinical study)	Criteria that define who is not eligible to participate in a clinical study.
Extended dominance	If Option A is both more clinically effective than Option B and has a lower cost per unit of effect, when both are compared with a do-nothing alternative then Option A is said to have extended dominance over Option B. Option A is therefore cost-effective and should be preferred, other things remaining equal.
Extrapolation	An assumption that the results of studies of a specific population will also hold true for another population with similar characteristics.
Follow-up	Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.
Generalisability	The extent to which the results of a study hold true for groups that did not participate in the research. See also external validity.
GRADE, GRADE profile	A system developed by the GRADE Working Group to address the shortcomings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence. The results of applying the GRADE system to clinical trial data are displayed in a table known as a GRADE profile.
Harms	Adverse effects of an intervention.
Health economics	Study or analysis of the cost of using and distributing healthcare resources.
Health-related quality of life (HRQoL)	A measure of the effects of an illness to see how it affects someone's day-to-day life.
Heterogeneity or Lack of homogeneity	The term is used in meta-analyses and systematic reviews to describe when the results of a test or treatment (or estimates of its effect) differ significantly in different studies. Such differences may occur as a result of differences in the populations studied, the outcome measures used or because of different definitions of the variables involved. It is the opposite of homogeneity.

Term	Definition
Imprecision	Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of effect.
Inclusion criteria (literature review)	Explicit criteria used to decide which studies should be considered as potential sources of evidence.
Incremental analysis	The analysis of additional costs and additional clinical outcomes with different interventions.
Incremental cost	The extra cost linked to using one test or treatment rather than another. Or the additional cost of doing a test or providing a treatment more frequently.
Incremental cost-effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for one treatment compared with another.
Indirectness	The available evidence is different to the review question being addressed, in terms of PICO (population, intervention, comparison and outcome).
Intention-to-treat analysis (ITT)	An assessment of the people taking part in a clinical trial, based on the group they were initially (and randomly) allocated to. This is regardless of whether or not they dropped out, fully complied with the treatment or switched to an alternative treatment. Intention-to-treat analyses are often used to assess clinical effectiveness because they mirror actual practice: that is, not everyone complies with treatment and the treatment people receive may be changed according to how they respond to it.
Intervention	In medical terms this could be a drug treatment, surgical procedure, diagnostic or psychological therapy. Examples of public health interventions could include action to help someone to be physically active or to eat a more healthy diet.
Length of stay	The total number of days a participant stays in hospital.
Licence	See 'Product licence'.
Life years gained	Mean average years of life gained per person as a result of the intervention compared with an alternative intervention.
Likelihood ratio	The likelihood ratio combines information about the sensitivity and specificity. It tells you how much a positive or negative result changes the likelihood that a patient would have the disease. The likelihood ratio of a positive test result (LR+) is sensitivity divided by (1 minus specificity).
Long-term care	Residential care in a home that may include skilled nursing care and help with everyday activities. This includes nursing homes and residential homes.
Loss to follow-up	A patient, or the proportion of patients, actively participating in a clinical trial at the beginning, but whom the researchers were unable to trace or contact by the point of follow-up in the trial
Meta-analysis	A method often used in systematic reviews. Results from several studies of the same test or treatment are combined to estimate the overall effect of the treatment.
Multivariate model	A statistical model for analysis of the relationship between 2 or more predictor (independent) variables and the outcome (dependent) variable.
Observational study	Individuals or groups are observed or certain factors are measured. No attempt is made to affect the outcome. For example, an observational study of a disease or treatment would allow 'nature' or usual medical care to take its course. Changes or differences in one characteristic (for example, whether or not people received a specific treatment or intervention) are studied without intervening.

Term	Definition
	There is a greater risk of selection bias than in experimental studies.
Odds ratio	Odds are a way to represent how likely it is that something will happen (the probability). An odds ratio compares the probability of something in one group with the probability of the same thing in another. An odds ratio of 1 between 2 groups would show that the probability of the event (for example a person developing a disease, or a treatment working) is the same for both. An odds ratio greater than 1 means the event is more likely in the first group. An odds ratio less than 1 means that the event is less likely in the first group. Sometimes probability can be compared across more than 2 groups – in this case, one of the groups is chosen as the 'reference category', and the odds ratio is calculated for each group compared with the reference category. For example, to compare the risk of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. Odds ratios would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. See also confidence interval, risk ratio.
Opportunity cost	The loss of other healthcare programmes displaced by investment in or introduction of another intervention. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Outcome	The impact that a test, treatment, policy, programme or other intervention has on a person, group or population. Outcomes from interventions to improve the public's health could include changes in knowledge and behaviour related to health, societal changes (for example, a reduction in crime rates) and a change in people's health and wellbeing or health status. In clinical terms, outcomes could include the number of patients who fully recover from an illness or the number of hospital admissions, and an improvement or deterioration in someone's health, functional ability, symptoms or situation. Researchers should decide what outcomes to measure before a study begins.
P value	The p value is a statistical measure that indicates whether or not an effect is statistically significant. For example, if a study comparing 2 treatments found that one seems more effective than the other, the p value is the probability of obtaining these results by chance. By convention, if the p value is below 0.05 (that is, there is less than a 5% probability that the results occurred by chance) it is considered that there probably is a real difference between treatments. If the p value is 0.001 or less (less than a 1% probability that the results occurred by chance), the result is seen as highly significant. If the p value shows that there is likely to be a difference between treatments, the confidence interval describes how big the difference in effect might be.
Placebo	A fake (or dummy) treatment given to participants in the control group of a clinical trial. It is indistinguishable from the actual treatment (which is given to participants in the experimental group). The aim is to determine what effect the experimental treatment has had – over and above any placebo effect caused because someone has received (or thinks they have received) care or attention.
Postoperative	Pertaining to the period after patients leave the operating theatre, following surgery.
Power (statistical)	The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.

Term	Definition
Preoperative	The period before surgery commences.
Primary care	Healthcare delivered outside hospitals. It includes a range of services provided by GPs, nurses, health visitors, midwives and other healthcare professionals and allied health professionals such as dentists, pharmacists and opticians.
Primary outcome	The outcome of greatest importance, usually the one in a study that the power calculation is based on.
Probabilistic analysis	In economic evaluation, this is an analysis that uses a probability distribution for each input. In contrast, see Deterministic analysis.
Product licence	An authorisation from the MHRA to market a medicinal product.
Prognosis	A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.
Publication bias	Publication bias occurs when researchers publish the results of studies showing that a treatment works well and don't publish those showing it did not have any effect. If this happens, analysis of the published results will not give an accurate idea of how well the treatment works. This type of bias can be assessed by a funnel plot.
Quality of life	See 'Health-related quality of life'.
Quality-adjusted life year (QALY)	A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health. QALYS are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality of life score (on a scale of 0 to 1). It is often measured in terms of the person's ability to perform the activities of daily life, freedom from pain and mental disturbance.
Randomisation	Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, it could involve using a random numbers table or a computer-generated random sequence. It means that each individual (or each group in the case of cluster randomisation) has the same chance of receiving each intervention.
Randomised controlled trial (RCT)	A study in which a number of similar people are randomly assigned to 2 (or more) groups to test a specific drug or treatment. One group (the experimental group) receives the treatment being tested, the other (the comparison or control group) receives an alternative treatment, a dummy treatment (placebo) or no treatment at all. The groups are followed up to see how effective the experimental treatment was. Outcomes are measured at specific times and any difference in response between the groups is assessed statistically. This method is also used to reduce bias.
RCT	See 'Randomised controlled trial'.
Receiver operated characteristic (ROC) curve	A graphical method of assessing the accuracy of a diagnostic test. Sensitivity is plotted against 1 minus specificity. A perfect test will have a positive, vertical linear slope starting at the origin. A good test will be somewhere close to this ideal.
Reference standard	The test that is considered to be the best available method to establish the presence or absence of the outcome – this may not be the one that is routinely used in practice.
Reporting bias	See 'Publication bias'.

Term	Definition
Retrospective study	A research study that focuses on the past and present. The study examines past exposure to suspected risk factors for the disease or condition. Unlike prospective studies, it does not cover events that occur after the study group is selected.
Review question	In guideline development, this term refers to the questions about treatment and care that are formulated to guide the development of evidence-based recommendations.
Risk ratio (RR)	The ratio of the risk of disease or death among those exposed to certain conditions compared with the risk for those who are not exposed to the same conditions (for example, the risk of people who smoke getting lung cancer compared with the risk for people who do not smoke). If both groups face the same level of risk, the risk ratio is 1. If the first group had a risk ratio of 2, subjects in that group would be twice as likely to have the event happen. A risk ratio of less than 1 means the outcome is less likely in the first group. The risk ratio is sometimes referred to as relative risk.
Secondary outcome	An outcome used to evaluate additional effects of the intervention deemed a priori as being less important than the primary outcomes.
Selection bias	Selection bias occurs if: a) The characteristics of the people selected for a study differ from the wider population from which they have been drawn, or b) There are differences between groups of participants in a study in terms of how likely they are to get better.
Sensitivity	How well a test detects the thing it is testing for. If a diagnostic test for a disease has high sensitivity, it is likely to pick up all cases of the disease in people who have it (that is, give a 'true positive' result). But if a test is too sensitive it will sometimes also give a positive result in people who don't have the disease (that is, give a 'false positive'). For example, if a test were developed to detect if a woman is 6 months pregnant, a very sensitive test would detect everyone who was 6 months pregnant, but would probably also include those who are 5 and 7 months pregnant. If the same test were more specific (sometimes referred to as having higher specificity), it would detect only those who are 6 months pregnant, and someone who was 5 months pregnant would get a negative result (a 'true negative'). But it would probably also miss some people who were 6 months pregnant (that is, give a 'false negative'). Breast screening is a 'real-life' example. The number of women who are recalled for a second breast screening test is relatively high because the test is very sensitive. If it were made more specific, people who don't have the disease would be less likely to be called back for a second test but more women who have the disease would be missed.
Sensitivity analysis	A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. One-way simple sensitivity analysis (univariate analysis): each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study. Multi-way simple sensitivity analysis (scenario analysis): 2 or more parameters are varied at the same time and the overall effect on the results is evaluated.

Term	Definition
	Threshold sensitivity analysis: the critical value of parameters above or below which the conclusions of the study will change are identified. Probabilistic sensitivity analysis: probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example, Monte Carlo simulation).
Specificity	The proportion of true negatives that are correctly identified as such. For example in diagnostic testing the specificity is the proportion of non-cases correctly diagnosed as non-cases. See related term 'Sensitivity'. In terms of literature searching a highly specific search is generally narrow and aimed at picking up the key papers in a field and avoiding a wide range of papers.
Stakeholder	An organisation with an interest in a topic that NICE is developing a clinical guideline or piece of public health guidance on. Organisations that register as stakeholders can comment on the draft scope and the draft guidance. Stakeholders may be: • manufacturers of drugs or equipment • national patient and carer organisations • NHS organisations • organisations representing healthcare professionals.
Systematic review	A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. It may include a meta-analysis.
Time horizon	The time span over which costs and health outcomes are considered in a decision analysis or economic evaluation.
Transition probability	In a state transition model (Markov model), this is the probability of moving from one health state to another over a specific period of time.
Univariate	Analysis which separately explores each variable in a data set.
Utility	In health economics, a 'utility' is the measure of the preference or value that an individual or society places upon a particular health state. It is generally a number between 0 (representing death) and 1 (perfect health). The most widely used measure of benefit in cost–utility analysis is the quality-adjusted life year, but other measures include disability-adjusted life years (DALYs) and healthy year equivalents (HYEs).