Radiofrequency denervation for chronic low back pain (Review)

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ABSTRACT

Introduction Radiofrequency (RF) denervation, an invasive treatment for chronic low back pain (CLBP), is used most often for pain suspected to arise from facet joints, sacroiliac (SI) joints or discs. Many (uncontrolled) studies have shown substantial variation in its use between countries and continued uncertainty regarding its effectiveness. The objective of this review is to assess the effectiveness of RF denervation procedures for the treatment of patients with CLBP. The current review is an update of the review conducted in 2003.

Methods We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, three other databases, two clinical trials registries and the reference lists of included studies from inception to May 2014 for randomised controlled trials (RCTs) fulfilling the inclusion criteria. We updated this search in June 2015, but we have not yet incorporated these results. We included RCTs of RF denervation for patients with CLBP who had a positive response to a diagnostic block or discography. We applied no language or date restrictions. Pairs of review authors independently selected RCTs, extracted data and assessed risk of bias (RoB) and clinical relevance using standardised forms. We performed meta-analyses with clinically homogeneous studies and assessed the quality of evidence for each outcome using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach.

Results In total, we included 23 RCTs (N=1309), 13 of which (56%) had low RoB. We included both men and women with a mean age of 50.6 years. We assessed the overall quality of the evidence as very low to moderate. Twelve studies examined suspected facet joint pain, five studies disc pain, two studies SI-joint pain, two studies radicular CLBP, one study suspected radiating low back pain and one study CLBP with or without suspected radiation. Overall, moderate evidence suggests that facet joint RF denervation has a greater effect on pain compared with placebo over the short term (mean difference (MD) -1.47, 95% confidence interval (CI) -2.28 to -0.67). Low-quality evidence indicates that facet joint RF denervation is more effective than placebo for function over the short term (MD - 5.53, 95% CI -8.66 to -2.40) and over the long term (MD -3.70, 95% CI -6.94 to -0.47). Evidence of very low to low quality shows that facet joint RF denervation is more effective for pain than steroid injections over the short (MD -2.23, 95% CI -2.38 to -2.08), intermediate (MD -2.13, 95% CI -3.45 to -0.81), and long term (MD -2.65, 95% CI -3.43 to -1.88). RF denervation used for disc pain produces conflicting results, with no effects for
RF denervation compared with placebo over the short and intermediate term, and small effects for RF denervation over the long term for pain relief (MD -1.63, 95% CI -2.58 to -0.68) and improved function (MD -6.75, 95% CI -13.42 to -0.09). Lack of evidence of short-term effectiveness undermines the clinical plausibility of intermediate-term or long-term effectiveness. When RF denervation is used for SI-joint pain, low-quality evidence reveals no differences from placebo in effects on pain (MD -2.12, 95% CI -5.45 to 1.21) and function (MD -14.06, 95% CI -30.42 to 2.30) over the short term, and one study shows a small effect on both pain and function over the intermediate term. RF denervation is an invasive procedure that can cause a variety of complications. The quality and size of original studies were inadequate to permit assessment of how often complications occur.

**Conclusions** The review authors found no high-quality evidence suggesting that RF denervation provides pain relief for patients with CLBP. Similarly, we identified no convincing evidence to show that this treatment improves function. Overall, the current evidence for RF denervation for CLBP is very low to moderate in quality; high-quality evidence is lacking. High-quality RCTs with larger patient samples are needed, as are data on long-term effects.
INTRODUCTION

Description of the condition
A major proportion of the adult population has low back pain at some stage of life. Although most patients are treated successfully with conservative treatment or without treatment, a substantial group of patients develop chronic pain symptoms (lasting longer than three months).¹ Patients with chronic low back pain (CLBP) account for most reported healthcare and socioeconomic costs.¹ Among low back pain diagnoses, about 85% are defined as non-specific low back pain, that is, low back pain not attributable to a recognisable, known specific pathology or anatomical structure (e.g. infection, tumour, osteoporosis, fracture).²⁻⁴ Suspected sources of back pain include lumbar facet (zygapophysial) joints, sacroiliac (SI) joints and degenerated intervertebral discs.⁵⁻⁸ No gold standard is known for diagnosing facet joint, SI-joint or disc pain. Such pain cannot be diagnosed clinically or radiologically.⁹,¹⁰ Little evidence is available for using diagnostic blocks, which locally anaesthetise medial branch nerves that innervate the painful joint.¹¹⁻¹⁴ Despite lack of validity and the chance of false-positive test results, these diagnostic blocks are used frequently in diagnosing facet joint pain, SI-joint pain or disc pain, and in predicting the success of radiofrequency (RF) denervation procedures. However, it should be noted that “nerve blocks” are invalidated methods of diagnosing the source or sources of CLBP.¹⁵

Radiofrequency denervation is one of the treatment options for patients with CLBP. In RF denervation, an RF generator produces an alternating current (frequency, 250 to 500 kHz) through an electrode, thereby inducing ionic movements in the tissue directly surrounding the active tip. This leads to molecular friction and heating of the tissue within a limited distance of the electrode.¹⁶ Since Shealy published his article on RF denervation of the lumbar facet joint in 1976, RF denervation procedures have been modified and now are used frequently for low back pain.¹³,¹⁷⁻²⁰ For example, they are used in the management of SI-joint pain and disc pain.²¹⁻²³ RF denervation is a technique that attempts to modulate neural transmission of nociceptive stimuli to reduce spinal pain. It aims to de-activate the nerves suspected of contributing to pain by applying an electrical current to coagulate the sensory nerves and prevent conduction of nociceptive impulses.¹⁶,²⁴ Radiofrequency lesioning is used to produce a partial lesion in the nerves supplying the painful structure.

The current review will be an update of the review conducted in 2003.²⁵ The original
review studied the effects of RF denervation procedures in chronic low back and neck pain. Only four trials evaluating RF denervation procedures in CLBP were selected (one studying discogenic low back pain and three studying facet joint pain). The review produced conflicting evidence on the effectiveness of RF denervation for facet joint pain. Limited evidence suggested that intra discal RF denervation may not be effective in relieving discogenic low back pain. Convincing evidence was lacking. The current review was split into separate reviews for chronic neck pain and CLBP, and the literature search was updated until May 2014. This review focusses on CLBP.

The objective of this review is to assess the effectiveness of RF denervation procedures for the treatment of patients with CLBP.

METHODS

Types of studies
We included only randomised controlled trials (RCTs). We imposed no language or date restrictions.

Types of participants
We included patients with CLBP (longer than three months) who had a positive response to diagnostic block or discography. We excluded patients with acute trauma, fracture, malignancy and inflammatory disease.

Types of interventions
Trials had to examine the effects of RF denervation compared with other treatments or placebo. We applied no limits on the temperature used, and we included both continuous and pulsed RF. We included and reported on additional treatments.

Types of outcome measures
Primary outcomes considered were pain, functional status (disorder-specific and generic), global improvement, health-related quality of life and complications. Secondary outcomes consisted of ability to work and satisfaction with treatment. We evaluated these outcomes at short- (less than one month), intermediate- (one to six months) and long-term (longer than six months) follow-up.
Search methods for identification of studies
The search strategy was based on current recommendations of the Cochrane Back and Neck (CBN) Review Group and built on the literature search of the original review.\textsuperscript{26,27} We searched the following databases from inception to 2014 May 29.

- Cochrane Central Register of Controlled Trials (CENTRAL).
- MEDLINE (Ovid SP, 1946 to May Week 3 2014).
- MEDLINE In-Process & Other Non-Indexed Citations (Ovid SP, 2014 May 29).
- EMBASE (Ovid SP, 1947 to Week 21 2014).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO, from 1981 to 2014 May 30).
- PsycINFO (Ovid SP, 1806 to May Week 4 2014).
- ClinicalTrials.gov.
- World Health Organization (WHO) International Clinical Trials Registry Platform.

For this update, searches were run annually since 2010. Complete search strategies for the eight databases are available on request of the author. We performed a further search in June 2015 and added one trial report\textsuperscript{28} to ‘Studies awaiting classification’ and determined that three additional studies are ongoing.\textsuperscript{29-31} Results of ‘Studies awaiting classification’ and ‘Ongoing studies’ will be incorporated into the review at the next update. We checked the references of identified relevant articles and reviews. Furthermore, we consulted experts in the field of RF denervation treatment to identify potentially relevant studies that might have been missed.

Data collection and analysis
Methods used for this systematic review are based on current recommendations of the CBN review group and the Cochrane Handbook for Systematic Reviews of Interventions.\textsuperscript{26,32}

Selection of studies
Pairs of review authors independently selected the trials. They reviewed included studies from the original review and titles, keywords and abstracts of identified references initially screened by the trials search co-ordinator of the CBN review group, to determine whether the study potentially met the inclusion criteria regarding design, participants and interventions. We retrieved full-text articles on studies that appeared to be relevant and on studies that provided insufficient information to allow a decision. The same pairs
of review authors assessed pairwise full-text articles revealed by this literature search and trials that were included in the original review to make a final decision on which articles should be included in this review. We discussed disagreements, and if consensus could not be reached, we consulted a third review author.

**Data extraction and management**

Pairs of review authors independently extracted the data, using a standardised form that had been developed by the CBN review group. We extracted the following data: characteristics of study design, population, intervention, control, duration of follow-up, outcomes and results. We used a consensus method to resolve disagreements, consulting with a third review author if disagreements persisted.

**Assessment of risk of bias in included studies**

We assessed risk of bias (RoB) of RCTs using the 12 criteria recommended by the CBN review group. In pairs of two, three review authors (MvT, RO, EM) independently assessed RoB. We used a consensus method to resolve disagreements and consulted the third review author if disagreements persisted. We scored the criteria as ‘high risk’, ‘low risk’ or ‘unclear risk’. Low RoB was defined as a trial meeting at least six criteria and having no fatal flaws.

**Measures of treatment effect**

We defined outcome measures from individual trials through meta-analysis when clinically and methodologically homogeneous. We sent comparisons to an international panel of eight anaesthesiologists, who rated the clinical homogeneity of study populations and interventions within each comparison. The review team assessed homogeneity in comparison treatments, outcomes, measurement instruments and timing of outcomes. An $I^2$ value greater than 70% might show considerable heterogeneity between studies. We used fixed effects with an $I^2$ value less than 25%, which indicates statistical homogeneity. We calculated mean differences (MDs) for pain and functional status. We converted all visual analogue scale (VAS) or numerical rating scale (NRS) scores to scales ranging from zero to 10, when necessary. We expressed precision with 95% confidence intervals (95% CIs). If standard deviations (SDs) were not reported, we calculated these using reported values of the CI. If the CI was not available, we used SDs of baseline scores, or estimations of SDs based on other studies with the same population, treatment and score.
Unit of analysis issues
In the study comparing two interventions with a single control group,\textsuperscript{33} the number of participants in the control group was divided by two to avoid double counting of participants.

Data synthesis
If a meta-analysis was not possible, we described results from clinically comparable trials in the text. We assessed the overall quality of evidence for each primary outcome by using an adapted GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach,\textsuperscript{34} as recommended by the CBN review group.\textsuperscript{26} The quality of evidence on a specific outcome is based on the following domains and is downgraded by one level for each of the factors encountered.

- Limitations in design (> 25% of participants from studies with high RoB).
- Inconsistency of results (severe heterogeneity ($I^2 > 50\%$) or inconsistent findings among studies).
- Indirectness in targeted populations, interventions or outcomes that differ from those in which we are interested.
- Imprecision of results across all studies that measure that particular outcome (total number of participants < 400 for each outcome).
- Publication bias.

We considered comparisons including one RCT with fewer than 400 participants as inconsistent and imprecise and as yielding ‘low quality evidence’, which we could further downgrade to ‘very low quality evidence’ if we found limitations in design (i.e. high RoB), indirectness or other considerations. We applied the following grading of evidence.\textsuperscript{34}

- High quality: Further research is very unlikely to change the quality of evidence that is based on consistent findings from at least two RCTs with low RoB and is generalizable to the population in question. Data are sufficient and include narrow CIs. No reporting biases are known or suspected.
- Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate; one domain is not met.
- Low quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change it; two domains are not met.
• Very low quality: Great uncertainty surrounds the estimate; three domains are not met.

Assessment of clinical relevance
Assessment of clinical relevance included whether characteristics of participants, interventions and treatment settings were described precisely enough to be comparable with those in practice. Further, we assessed whether clinically relevant outcomes were measured, if their effects were clinically important and if treatment benefits were worth the potential harms.\textsuperscript{26,35}

Subgroup analysis and investigation of heterogeneity
Subgroups were based on patient selection. We analysed separately participants with pain suspected to originate from the facet joints, SI-joints or discs, and those with another type of CLBP. Furthermore, comparisons were based on types of interventions and comparisons, outcomes and timing of outcomes. We assessed heterogeneity using the Chi\textsuperscript{2} test, I\textsuperscript{2} and visual inspection of forest plots. If Chi\textsuperscript{2} was not statistically significant, if I\textsuperscript{2} was below 50\% and if confidence intervals were overlapping, we considered the data statistically homogeneous.

Sensitivity analysis
We performed sensitivity analyses if uncertainty remained concerning the clinically homogeneity of studies compared.

RESULTS

Database searching yielded 746 individual studies. We included two studies after reference searching and full screening of a total of 36 studies. Five studies were still ongoing and were excluded.\textsuperscript{36–40} We assessed the remaining 31 studies by reviewing full-text articles. We excluded eight studies for various reasons, resulting in a total of 23 included studies (Figure 1). Following the updated search in June 2015, we determined that three additional studies are ongoing.\textsuperscript{28,29,30}
Included studies
The 23 included studies consisted of 1309 participants, and the sample size of each study ranged from 20 to 120 participants. Baseline characteristics of all participants were similar with regard to age, sex and duration of pain for all except two studies, in which these were not described precisely or were different. Studies included both men and women with a mean age of 50.6 years. Twelve studies examined suspected facet joint pain, five studies disc pain, two studies SI-joint pain, two studies radicular CLBP, one study radiating low back pain and one study CLBP with or without radiation. Full characteristics of included studies are available upon request.
Facet joint pain
We included 12 RCTs on suspected chronic facet joint pain.33,41,43-52 These studies included participants with CLBP longer than three months to longer than 12 months. All participants reacted positively to local anaesthetic injections; criteria ranged from a description of ‘good or equivocal response to local anaesthetic injection into and around the appropriate painful joints’ to ‘at least 80% of pain relief of at least one component of their pain after three separate diagnostic blocks with a local anaesthetic solution’. For RF denervation, one study used the original Shealy technique.41 The other studies used modified versions, but all researchers induced an RF lesion at 80°C to 85°C for 60 to 90 seconds. In five studies, placebo was used for control and electrodes were used in the RF lesion group, but no RF lesion was induced.41,47,49,51,52 The study by Kroll et al compared continuous RF (CRF) denervation (80°C, 75 seconds) versus pulsed RF denervation (PRF) (42°C, 120 seconds).45 The study by Tekin et al compared CRF (80°C, 90 seconds) versus PRF denervation (42°C, 240 seconds) using a sham group.33 Two studies compared different methods of RF denervation; the study of Sanders et al compared intra-articular versus extra-articular lumbar facet joint denervation, and the study of Moon et al compared the RF facet denervation distal approach versus the tunnel vision approach.48,50 Three studies used steroid injections in the control group.43,44,46

Discogenic low back pain
We included five RCTs on suspected discogenic CLBP, which included participants with duration of low back pain between six months and longer than two years.21,53-56 These trials included only participants with positive response to either analgesic21,56 or provocative discography.53-55 The intervention consisted of percutaneous intra discal RF thermocoagulation (PIRFT) in four studies.21,53-55 One study evaluated RF denervation of the ramus communicans nerve (this denervation is performed outside the intervertebral disc) in participants who failed to respond to intra discal electrothermic therapy (IDET).56 Four studies were placebo-controlled.21,54-56 One study compared high-intensity PIRFT versus low-intensity PIRFT.53

Sacroiliac joint pain
We included two RCTs57,58 studying suspected SI-joint pain. Both studies included participants with axial low back or buttock pain lasting six months or longer. One study used pain relief of 75% or greater after a single diagnostic SI-joint injection as confirmation
of SI-joint pain. The other study performed a dual lateral branch block, in which participants had to have 75% pain relief. In the study of Cohen et al, the intervention consisted of RF denervation of 90-second 80°C RF of L4-L5 primary dorsal rami and S1-S3 lateral branch RF using cooling probe technology. The other study applied RF energy for 150 seconds at 60°C on L5, then delivered RF energy for 150 seconds at 60°C on S1, S2 and S3. Both studies were placebo controlled.

**Spinal dorsal root ganglion - lumbosacral radicular pain**

We included three RCTs performing RF denervation of the dorsal root ganglion (DRG) for suspected lumbosacral radicular pain. Two studies included participants with lumbosacral radicular pain for longer than six months with 75% pain reduction after three separate diagnostic blocks or complete relief of radicular symptoms following low-volume segmental nerve block. The other study included participants with a history of chronic lumbar radicular pain for at least four months with clinical features and computed tomography/magnetic resonance imaging findings of lumbosacral radicular pain. Two studies used RF denervation as treatment, and one study used pulsed RF denervation as treatment. Two studies compared treatment versus placebo, and the other study used PRF plus CRF denervation for comparison.

**Low back pain with or without radiation**

We included one RCT on CLBP for longer than six months with or without radiation. This study compared PRF denervation on DRG versus electro-acupuncture therapy, and versus conservative treatment with medication.

**Excluded studies**

For this update, we fully screened 36 studies. Five studies were ongoing and were excluded. Eight studies were retrieved in full text and were eventually excluded. Reasons for exclusion included no randomised controlled trial as study design and no direct measurement of the effectiveness of RF denervation. Additional details of the excluded studies are available upon request.

**Risk of bias in included studies**

Figure 2 shows results of the RoB assessment. Thirteen studies (56%) had low RoB.
### Figure 2. Risk of bias summary: review authors’ judgements about each risk of bias item for each included study.

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Allocation
Nine studies (40%) described an adequate randomisation procedure in combination with adequate concealment of treatment allocation. Method of randomisation remained unclear in seven studies (30%). Treatment allocation remained unclear in 14 studies (61%).

Blinding
Care providers, participants and outcome assessors were blinded in nine studies (47%).

Incomplete outcome data
Fourteen studies (61%) had acceptable dropout rates. Dropout rates were unclear in eight studies, and in one study the dropout rate was high. Three studies did not perform intention-to-treat analysis.

Selective reporting
Whether selective reporting occurred remained unclear in all but one study. All studies included core outcomes (pain and function), and we identified no protocols for all but one study.\(^{60}\)

Other potential sources of bias
Groups were similar at baseline in 17 studies (74%) regarding demographic factors and most important prognostic factors. The description of possible co-interventions was unclear in 20 studies, co-interventions were avoided in two studies and co-interventions could have introduced bias in one study. Two studies did not adequately describe compliance, showing unclear risk of bias. Timing of outcome assessments was similar between studies.

Effects of interventions
Summary effect estimates are presented when there was no substantial heterogeneity. Findings are summarized in Tables 1-4.

Feasibility of statistical pooling
We considered statistical pooling only if subgroups of studies were clinically homogeneous, and if study authors provided sufficient information on study characteristics, outcome
measures and study results. Review of included study characteristics revealed that four treatment subgroups were sufficiently clinically homogeneous to permit statistical pooling, as shown in the summary of findings tables 1-4.

Comparisons considering facet joint pain

Facet joint: RF denervation versus placebo

For short-term outcomes (<one month), three RCTs measured pain on a visual analogue scale (VAS).\textsuperscript{33,41,47} We considered the studies in this comparison as statistically homogeneous (MD \( -1.47, 95\%\text{CI} -2.28 \text{ to } -0.67 \)) (Analysis 1.1). Moderate-quality evidence (three RCTs; N=160; imprecision) suggests that facet joint RF denervation is more effective than placebo for pain relief over the short term. For intermediate-term outcomes (one to six months), three RCTs measured pain on a VAS.\textsuperscript{47,51,52} One study reported outcomes in a different direction from the others. However, because of clinical homogeneity, we performed pooling, with pooled MD of \(-0.71 \ (95\%\text{CI} -2.25 \text{ to } 0.84)\) (Analysis 1.2). Low-quality evidence (three RCTs; N=182; inconsistency; imprecision) suggests that facet joint RF denervation is no more effective than placebo for pain relief over the intermediate term.

For long-term outcomes (> six months), three RCTs measured pain on a VAS and showed statistical homogeneity.\textsuperscript{33,41,49} The pooled MD was \(-0.70 \ (95\%\text{CI} -1.48 \text{ to } 0.08)\) (Analysis 1.3). Moderate-quality evidence (three RCTs; N=130; imprecision) suggests that facet joint RF denervation is no more effective than placebo for pain relief over the long term. When we removed the comparison of pulsed RF denervation versus placebo in the study of Tekin from the analysis (as recommended by one of the clinicians on the advisory team), the pooled MD for pain intensity was \(-1.51 \ (95\%\text{CI} -2.79 \text{ to } -0.23)\) over the short term (Analysis 1.1; sensitivity analysis) and \(-1.06 \ (95\%\text{CI} -2.23 \text{ to } 0.11)\) over the long term (Analysis 1.3; sensitivity analysis). Removal of this study component from the comparisons slightly altered the pooled MD; the long-term effect became somewhat larger but less precise (moderate quality of evidence).
Table 1. Facet joint: radiofrequency denervation versus placebo

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI) (studies)</th>
<th>Number of participants</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient or population:</strong> patients with chronic low back pain</td>
<td><strong>Settings:</strong> secondary care</td>
<td><strong>Intervention:</strong> facet joint radiofrequency denervation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Comparison:</strong> placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain 1 month post treatment (VAS 0 to 10)</td>
<td>Placebo Mean pain score ranged across control groups from 4.3 to 6.0</td>
<td>Mean pain score in intervention groups was on average 1.5 lower (2.3 to 0.7 lower)</td>
<td>160 (3 studies)</td>
<td>++++</td>
</tr>
<tr>
<td>Pain 1 to 6 months post treatment (VAS 0 to 10)</td>
<td>Placebo Mean pain score ranged across control groups from 4.4 to 4.9</td>
<td>Mean pain score in intervention groups was on average 0.7 lower (2.3 lower to 0.8 higher)</td>
<td>182 (3 studies)</td>
<td>⊕⊕⊕</td>
</tr>
<tr>
<td>Pain &gt; 6 months post treatment (VAS 0 to 10)</td>
<td>Placebo Mean pain score ranged across control groups from 3.1 to 7.0</td>
<td>Mean pain score in intervention groups was on average 0.7 lower (1.5 lower to 0.1 higher)</td>
<td>140 (3 studies)</td>
<td>⊕⊕⊕</td>
</tr>
<tr>
<td>Function 1 month post treatment (ODI 0 to 100)</td>
<td>Functional status in control group was 30.5</td>
<td>Mean functioning in intervention groups was on average 5.5 lower (8.7 to 2.4 lower)</td>
<td>60 (1 study)</td>
<td>⊕⊕⊕</td>
</tr>
<tr>
<td>Function &gt; 6 months post treatment (ODI 0 to 100)</td>
<td>Functional status in control group was 28.9</td>
<td>Mean function in intervention groups was on average 3.7 lower (6.9 to 0.5 lower)</td>
<td>60 (1 study)</td>
<td>⊕⊕⊕</td>
</tr>
<tr>
<td>Complications</td>
<td>Not estimable</td>
<td>Not estimable</td>
<td>0</td>
<td>No evidence</td>
</tr>
</tbody>
</table>

CI: Confidence interval; VAS: Visual analogue scale.

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

a Results of the main analyses are presented.
b Downgraded when fewer than 400 participants.
c $I^2 = 82\%, P value = 0.0004$, CIs hardly overlap, although the deviating study does not show significant results.
Table 2. Facet joint: radiofrequency denervation versus steroid injections

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>Number of participants</th>
<th>Quality of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed risk</td>
<td>Corresponding risk</td>
<td>(studies)</td>
<td>(GRADE)</td>
</tr>
<tr>
<td>Pain 1 month post treatment (VAS 0 to 10)</td>
<td>Mean pain score ranged across control groups from 4.4 to 5.4</td>
<td>Mean pain score in intervention groups was on average 2.2 lower (2.4 to 2.1 lower)</td>
<td>180 (2 studies)</td>
<td>☼☼☼ ⊝ ⊝ Low a,b</td>
</tr>
<tr>
<td>Pain 6 months post treatment (VAS 0 to 10)</td>
<td>Mean pain score ranged across control groups from 4.4 to 6.5</td>
<td>Mean pain score in intervention groups was on average 2.1 lower (3.5 to 0.8 lower)</td>
<td>232 (3 studies)</td>
<td>☼☼☼☼ ⊝ ⊝ ⊝ ⊝ Very low a,b,c</td>
</tr>
<tr>
<td>Pain 12 months post treatment (VAS 0 to 10)</td>
<td>Mean pain score ranged across control groups from 4.9 to 7.0</td>
<td>Mean pain score in intervention groups was on average 2.7 lower (3.4 to 1.9 lower)</td>
<td>180 (2 studies)</td>
<td>☼☼☼☼ ⊝ ⊝ ⊝ ⊝ Very low a,b,c</td>
</tr>
</tbody>
</table>

CI: Confidence interval; VAS: Visual analogue scale.

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

a Fewer than 6 out of 12 items low risk of bias.
b Fewer than 400 participants included.
c I² higher than 50%.
**Table 3. Discs: radiofrequency denervation versus placebo**

- **Patient or population:** patients with chronic low back pain
- **Settings:** secondary care
- **Intervention:** discs: radiofrequency denervation
- **Comparison:** placebo

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>Number of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain 1 month post treatment (VAS 0 to 10)</strong></td>
<td>placebo: pain score in control group was 5.7</td>
<td>Pain score in intervention groups was 0.4 lower (1.5 lower to 0.7 higher)</td>
<td>56 (1 study)</td>
<td>⊕⊕⊕⊝ Low a,b</td>
</tr>
<tr>
<td><strong>Pain 1 to 6 months post treatment (VAS 0 to 10)</strong></td>
<td>mean pain score ranged across control groups from 4.4 to 5.9</td>
<td>mean pain score in intervention groups was on average 0.3 higher (2.3 lower to 2.8 higher)</td>
<td>84 (2 studies)</td>
<td>⊕⊕⊝⊝ Low b,c</td>
</tr>
<tr>
<td><strong>Pain &gt; 6 months post treatment (VAS 0 to 10)</strong></td>
<td>mean pain score ranged across control groups from 5.3 to 6.6</td>
<td>mean pain score in intervention groups was on average 0.8 lower (1.2 to 0.3 lower)</td>
<td>75 (2 studies)</td>
<td>⊕⊕⊕⊝ Moderate b</td>
</tr>
<tr>
<td><strong>Function 1 month post treatment (ODI 0 to 100)</strong></td>
<td>functional status in control group was 39.9</td>
<td>mean function in intervention groups was on average 1.0 higher (6.9 lower to 8.9 higher)</td>
<td>57 (1 study)</td>
<td>⊕⊕⊝⊝ Low a,b</td>
</tr>
<tr>
<td><strong>Function 1 to 6 months post treatment (ODI 0 to 100)</strong></td>
<td>mean functional status ranged across control groups from 36.7 to 40.4</td>
<td>mean functioning in intervention groups was on average 0.9 higher (6.4 lower to 8.1 higher)</td>
<td>85 (2 studies)</td>
<td>⊕⊕⊝⊝ Moderate b</td>
</tr>
<tr>
<td><strong>Function &gt; 6 months post treatment (ODI 0 to 100)</strong></td>
<td>mean functional status ranged across control groups from 28.2 to 41.2</td>
<td>mean functioning in intervention groups was on average 6.8 lower (13.4 to 0.1 lower)</td>
<td>76 (2 studies)</td>
<td>⊕⊕⊝⊝ Moderate b</td>
</tr>
</tbody>
</table>

**CI:** Confidence interval; **VAS:** Visual analogue scale.

**GRADE Working Group grades of evidence.**

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- **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
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- **Very low quality:** We are very uncertain about the estimate.

- a Single study, in any case inconsistent.
- b Fewer than 400 participants included.
- c I² > 50%.
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>Number of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Mean pain score ranged across control groups from 3.9 to 6.3</td>
<td>Mean pain score in intervention groups was on average 2.1 lower (5.5 lower to 1.2 higher)</td>
<td>79 (2 studies)</td>
<td>⊗⊗⊗⊗ Very low&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>SI-joint radiofrequency denervation</td>
<td>Pain 1 month post treatment (VAS 0 to 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>Pain score in control group was 5.0</td>
<td>Mean pain score in intervention groups was on average 1.3 lower (2.1 to 0.5 lower)</td>
<td>51 (1 study)</td>
<td>⊗⊗⊗⊗ Low&lt;sup&gt;b,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>SI-joint radiofrequency denervation</td>
<td>Pain 1 to 6 months post treatment (VAS 0 to 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>Mean pain score ranged across control groups from 31.0 to 43.6</td>
<td>Mean pain score in intervention groups was on average 14.1 lower (30.4 lower to 2.3 higher)</td>
<td>75 (2 studies)</td>
<td>⊗⊗⊗⊗ Very low&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>SI-joint radiofrequency denervation</td>
<td>Function 1 month post treatment (ODI 0 to 100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>Pain score in control group was 37.0</td>
<td>Mean pain score in intervention groups was on average 11.0 lower (17.9 to 4.1 lower)</td>
<td>49 (1 study)</td>
<td>⊗⊗⊗⊗ Low&lt;sup&gt;b,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>SI-joint radiofrequency denervation</td>
<td>Function 1 to 6 months post treatment (ODI 0 to 100)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI: Confidence interval; VAS: Visual analogue scale

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

<sup>a</sup> Fewer than 6 out of 12 items low risk of bias.
<sup>b</sup> Fewer than 400 participants included.
<sup>c</sup> $I^2 > 50%$.
<sup>d</sup> Single study, in any case inconsistent.
### Analysis 1.1 Comparison 1 Facet joint Radiofrequency denervation versus placebo, Pain intensity (VAS 0-10), Outcome 1 VAS 1 month

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>RF denervation Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallagher 1994</td>
<td>3.4</td>
<td>2.9</td>
<td>18</td>
<td>6.3</td>
<td>3.4</td>
<td>12</td>
<td>9.6%</td>
<td>-2.60 [-4.94, -0.26]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leclaire 2001</td>
<td>4.8</td>
<td>2.5</td>
<td>36</td>
<td>5.2</td>
<td>2.1</td>
<td>34</td>
<td>26.8%</td>
<td>-0.40 [-1.48, 0.68]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tekin 2007</td>
<td>2.3</td>
<td>1.4</td>
<td>20</td>
<td>4.3</td>
<td>1</td>
<td>10</td>
<td>32.2%</td>
<td>-2.00 [-2.87, -1.13]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tekin 2007</td>
<td>2.8</td>
<td>1.5</td>
<td>20</td>
<td>4.3</td>
<td>1</td>
<td>10</td>
<td>31.3%</td>
<td>-1.50 [-2.40, -0.60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>74</td>
<td></td>
<td>66</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>-1.47 [-2.28, -0.67]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 0.33; \chi^2 = 6.09, df = 3 (P = 0.11); I^2 = 51\%

Test for overall effect: \( Z = 3.58 (P = 0.0003) \)

1.1.2 Sensitivity analysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>RF denervation Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallagher 1994</td>
<td>3.4</td>
<td>2.9</td>
<td>18</td>
<td>6.3</td>
<td>3.4</td>
<td>12</td>
<td>18.8%</td>
<td>-2.60 [-4.94, -0.26]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leclaire 2001</td>
<td>4.8</td>
<td>2.5</td>
<td>36</td>
<td>5.2</td>
<td>2.1</td>
<td>34</td>
<td>37.6%</td>
<td>-0.40 [-1.48, 0.68]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tekin 2007</td>
<td>2.3</td>
<td>1.4</td>
<td>20</td>
<td>4.3</td>
<td>1</td>
<td>10</td>
<td>43.6%</td>
<td>-2.00 [-2.75, -1.25]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>74</td>
<td></td>
<td>66</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>-1.51 [-2.79, -0.23]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 0.83; \chi^2 = 6.50, df = 2 (P = 0.04); I^2 = 69\%

Test for overall effect: \( Z = 2.32 (P = 0.02) \)

Test for subgroup differences: \( \chi^2 = 0.00, df = 1 (P = 0.96), I^2 = 0\%

### Analysis 1.2 Comparison 1 Facet joint Radiofrequency denervation versus placebo, Pain intensity (VAS 0-10), Outcome 2 VAS 1-6 months

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>RF denervation Mean</th>
<th>SD</th>
<th>Total</th>
<th>Placebo Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leclaire 2001</td>
<td>5.2</td>
<td>2.7</td>
<td>36</td>
<td>4.4</td>
<td>1.8</td>
<td>34</td>
<td>34.8%</td>
<td>0.80 [-0.27, 1.87]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Kleef 1999</td>
<td>2.83</td>
<td>2.4</td>
<td>15</td>
<td>4.77</td>
<td>2.5</td>
<td>16</td>
<td>27.5%</td>
<td>-1.94 [-3.67, -0.21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Wijk 2005</td>
<td>3.7</td>
<td>1.8</td>
<td>40</td>
<td>4.9</td>
<td>1.8</td>
<td>41</td>
<td>37.7%</td>
<td>-1.20 [-1.98, -0.42]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>91</td>
<td></td>
<td>91</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>-0.71 [-2.25, 0.84]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 1.48; \chi^2 = 11.09, df = 2 (P = 0.004); I^2 = 82\%

Test for overall effect: \( Z = 0.90 (P = 0.37) \)
One RCT with two intervention groups measured functional status on the Oswestry Disability Index (ODI) (zero to 100) over the short term. Low-quality evidence (one RCT; N=60; inconsistency, imprecision) suggests that facet joint RF denervation is more effective than placebo for functional status over the short term (MD -5.53, 95% CI -8.66 to -2.40). None of the included studies measured functional status over the intermediate term. For long-term outcomes (>six months), one RCT with two intervention groups measured functional status on the ODI (zero to 100). Low-quality evidence (one RCT; N=60; inconsistency, imprecision) suggests that facet joint RF denervation is more effective than placebo for functional status over the long term (MD -3.70, 95% CI -6.94 to -0.47). One RCT that compared two intervention groups (PRF and CRF) versus placebo measured patient satisfaction on a four-point scale. Low-quality evidence (one RCT; N=60; inconsistency, imprecision) suggests that both interventions are more effective than placebo in achieving patient satisfaction. Timing of measurement and MDs between groups were not stated.
**Facet joint: continuous RF denervation versus pulsed RF denervation**

One RCT compared continuous facet RF denervation versus pulsed RF denervation.\textsuperscript{45} Investigators reported no significant results for pain three months after treatment. Very low quality evidence (one RCT; N=26; serious RoB; inconsistency, imprecision) suggests that continuous RF denervation is no more effective than pulsed RF denervation (MD 0.07, 95% CI -1.82 to 1.96).

**Facet joint: percutaneous intra-articular denervation versus percutaneous extra-articular denervation**

One RCT compared facet percutaneous intra-articular RF denervation versus percutaneous extra-articular RF denervation.\textsuperscript{50} Very low-quality evidence (one RCT; N=34; serious RoB; inconsistency, imprecision) suggests that intra-articular RF denervation is more effective than extra-articular RF denervation for pain relief three months after the intervention (MD - 2.20, 95% CI -3.69 to -0.71).

**Facet joint: RF denervation: distal approach versus tunnel vision approach**

One RCT compared the distal approach versus the tunnel vision approach to performing facet joint RF denervation.\textsuperscript{48} Researchers observed no significant results for pain one month (MD -0.20, 95% CI -1.21 to 0.81) and longer than six months after treatment (MD 0.00, 95% CI -1.08 to 1.08). Very low quality evidence (one RCT; N=68; serious RoB; inconsistency, imprecision) suggests that the distal approach is no more effective than the tunnel vision approach. For functional status, no significant results were found one month (MD 2.20, 95% CI -2.28 to 6.68) and longer than six months after treatment (MD 2.90, 95% CI -1.71 to 7.51). Very low quality evidence (one RCT; N=68; serious RoB; inconsistency, imprecision) suggests that the distal approach is no more effective than the tunnel vision approach.

**Facet joint: RF denervation versus steroid injections**

For short-term outcomes (< one month) when RF denervation was compared with steroid injections, two RCTs measured pain on a VAS and reported statistical homogeneity. When these studies were pooled, the MD was -2.23 (95%CI -2.38 to -2.08) (Analysis 2.1).\textsuperscript{43,44} Low-quality evidence (two RCTs; N=180; serious RoB; imprecision) suggests that facet joint RF denervation is more effective than steroid injections for pain relief over the short term.
For intermediate-term outcomes (one to six months), three RCTs measured pain on a VAS.\textsuperscript{43,44,46} On the basis of \( \chi^2 \), \( I^2 \) and confidence intervals, the studies were deemed statistically heterogeneous, in large part because of the small SDs, which were difficult to extract from the study of Civelek.\textsuperscript{43} Confidence intervals were hardly overlapping, but because of clinical homogeneity, and because all effects were noted to be in the same direction, we decided to pool the results of these studies. The MD was -2.13 (95% CI -3.45 to -0.81) (Analysis 2.2). Very low-quality evidence (three RCTs; N=132; serious RoB; imprecision, inconsistency) suggests that facet joint RF denervation is more effective than steroid injection for pain relief over the intermediate term.

For long-term outcomes (> six months), two RCTs measured pain on a VAS.\textsuperscript{43,44} For the same reason as in Analysis 2.2, statistical pooling was performed unless limitations in this approach were noted. The MD was -2.65 (95% CI -3.45 to -1.88) (Analysis 2.3). Very low-quality evidence (three RCTs; N=180; serious RoB; imprecision, inconsistency) suggests that facet joint RF denervation is more effective than steroid injection for pain relief over the intermediate term.

**Analysis 2.1 Facet joint Radiofrequency denervation versus steroid injections, Pain intensity (VAS 0-10), 1 month**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Radiofrequency Mean (SD)</th>
<th>Injections Mean (SD)</th>
<th>Mean Difference Mean (SD)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civelek 2012</td>
<td>2.2 (0.3)</td>
<td>4.4 (0.5)</td>
<td>-2.20 (-2.36 -2.04)</td>
<td>88.8%</td>
</tr>
<tr>
<td>Duger 2012</td>
<td>2.9 (0.79)</td>
<td>5.36 (1.24)</td>
<td>-2.46 (-2.92 -2.00)</td>
<td>11.2%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>90.0 (50)</td>
<td>90.0 (50)</td>
<td>-2.23 (-2.38 -2.08)</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: \( \chi^2 = 1.11, \text{df} = 1 (P = 0.29); I^2 = 10\%

Test for overall effect, \( Z = 28.68 \) (\( P < 0.00001 \))

**Analysis 2.2 Facet joint Radiofrequency denervation versus steroid injections, Pain intensity (VAS 0-10), 6 months**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Radiofrequency Mean (SD)</th>
<th>Injections Mean (SD)</th>
<th>Mean Difference Mean (SD)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civelek 2012</td>
<td>2.5 (0.4)</td>
<td>4.4 (0.7)</td>
<td>-1.90 (-2.12 -1.68)</td>
<td>36.5%</td>
</tr>
<tr>
<td>Duger 2012</td>
<td>2.97 (0.72)</td>
<td>6.46 (1.21)</td>
<td>-3.49 (-3.93 -3.05)</td>
<td>35.5%</td>
</tr>
<tr>
<td>Lakemeier 2013</td>
<td>4.7 (2.4)</td>
<td>5.4 (2.1)</td>
<td>-0.70 (-1.93 0.53)</td>
<td>28.0%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>116.0 (50)</td>
<td>116.0 (50)</td>
<td>-2.13 (-3.45 -0.81)</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: \( \tau^2 = 1.22; \chi^2 = 46.24, \text{df} = 2 (P = 0.00001); I^2 = 96\% \)

Test for overall effect, \( Z = 3.17 \) (\( P = 0.002 \))
### Analysis 2.3 Facet joint Radiofrequency denervation versus steroid injections, Pain intensity (VAS 0-10), 12 months

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Radiofrequency Mean</th>
<th>SD</th>
<th>Total</th>
<th>Injections Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civelek 2012</td>
<td>2.6</td>
<td>0.4</td>
<td>50</td>
<td>4.9</td>
<td>0.7</td>
<td>50</td>
<td>55.1%</td>
<td>-2.30</td>
<td>[-2.52, -2.08]</td>
</tr>
<tr>
<td>Duger 2012</td>
<td>3.94</td>
<td>1.25</td>
<td>40</td>
<td>7.03</td>
<td>1.22</td>
<td>40</td>
<td>44.9%</td>
<td>-3.09</td>
<td>[-3.63, -2.55]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>90</td>
<td></td>
<td></td>
<td>90</td>
<td>100.0%</td>
<td>-2.65</td>
<td>[-3.43, -1.88]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.27; Chi² = 6.99, df = 1 (P = 0.008); I² = 86%
Test for overall effect: Z = 6.76 (P < 0.00001)

One RCT compared RF denervation versus steroid injections and measured function. Investigators reported no significant results for function six months after treatment (MD -5.00, 95% CI -15.19 to 5.19). Very low-quality evidence (one RCT; N=52; serious RoB; inconsistency, imprecision) suggests that RF denervation is no more effective than steroid injections over the long term. One RCT compared RF denervation versus steroid injections and measured participant satisfaction. Low-quality evidence (one RCT; N= 80; serious RoB; inconsistency, imprecision) suggests that facet joint RF denervation is more effective than steroid injection for participant satisfaction over the short, intermediate and long term.

### Comparisons considering the discs

#### 120-Second disc RF denervation versus 360-second RF denervation

One study compared 360-second RF denervation versus 120-second RF denervation. Researchers found no significant differences in pain and function between groups at any follow-up assessment. Very low-quality evidence (one RCT; N=37; serious RoB; imprecision) suggests that 360-second RF denervation is no more effective for pain and function than 120-second RF denervation over the short, intermediate and long term.

#### Disc: RF denervation versus lidocaine

One study compared the effects of RF denervation versus lidocaine in participants with disc pain. Investigators reported no significant results for pain four months after the procedure. Very low-quality evidence (one RCT; N=49; serious RoB; inconsistency, imprecision) suggests that RF denervation is more effective than lidocaine four months post treatment.
**Disc: RF denervation versus placebo**

One study compared RF denervation versus placebo and reported short-term outcomes. Low-quality evidence (one RCT; \(N = 56\); inconsistency, imprecision) suggests that RF denervation is no more effective than placebo for pain and function over the short term.\(^{54}\) Two studies compared RF denervation versus placebo and reported outcome measures for pain and function. Researchers reported no significant results for pain and function one to six months after the intervention.\(^{21,54}\) Low-quality evidence (two RCTs; \(N = 84\); imprecision, inconsistency) suggests that RF denervation is no more effective than placebo for pain (MD 0.27, 95% CI -2.25 to 2.79) (Analysis 3.1) and function over the intermediate term (MD 0.86, 95% CI -6.37 to 8.10) (Analysis 4.1). Over the long term, two studies showed small significant results for pain and function six and 12 months after treatment. Moderate-quality evidence (two RCTs; \(N = 75\); imprecision) suggests that RF denervation is more effective than placebo for pain (MD -1.63, 95% CI -2.58 to -0.68) (Analysis 3.2) and function over the long term (MD -6.75, 95% CI -13.42 to -0.09) (Analysis 4.2).\(^{54,55}\)

**Analysis 3.1 Disc: Radiofrequency denervation versus placebo, Pain intensity (VAS 0-10), 1-6 months**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barendse 2001</td>
<td>5.89</td>
<td>1.3</td>
<td>13</td>
<td>4.36</td>
<td>1.1</td>
<td>15</td>
<td>51.0%</td>
<td>1.53</td>
<td>[0.63, 2.43]</td>
</tr>
<tr>
<td>Kapural 2013</td>
<td>4.94</td>
<td>2.05</td>
<td>27</td>
<td>5.98</td>
<td>2.36</td>
<td>29</td>
<td>49.0%</td>
<td>-1.04</td>
<td>[-2.20, 0.12]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>40</td>
<td></td>
<td>44</td>
<td></td>
<td></td>
<td>100.0%</td>
<td></td>
<td>0.27</td>
<td>[-2.25, 2.79]</td>
</tr>
</tbody>
</table>

Heterogeneity: \(\tau^2 = 3.02\); \(\chi^2 = 11.83\), df = 1 (\(P = 0.0006\)); \(I^2 = 92\%

Test for overall effect: \(Z = 0.21\) (\(P = 0.83\))

**Analysis 3.2 Disc: Radiofrequency denervation versus placebo, Pain intensity (VAS 0-10), 6 months**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kapural 2013</td>
<td>4.94</td>
<td>2.15</td>
<td>27</td>
<td>6.58</td>
<td>2.11</td>
<td>29</td>
<td>72.2%</td>
<td>-1.64</td>
<td>[-2.76, -0.52]</td>
</tr>
<tr>
<td>Kvarstein 2009</td>
<td>3.7</td>
<td>2.2</td>
<td>10</td>
<td>5.3</td>
<td>1.8</td>
<td>9</td>
<td>27.8%</td>
<td>-1.60</td>
<td>[-3.40, 0.20]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>37</td>
<td></td>
<td>38</td>
<td></td>
<td></td>
<td>100.0%</td>
<td></td>
<td>-1.63</td>
<td>[-2.58, -0.68]</td>
</tr>
</tbody>
</table>

Heterogeneity: \(\chi^2 = 0.00\), df = 1 (\(P = 0.97\)); \(I^2 = 0\%

Test for overall effect: \(Z = 3.36\) (\(P = 0.0008\))
Comparison considering SI-joint pain

**SI-joint: RF denervation versus placebo**

Two low-quality studies (N=79; serious RoB; imprecision, inconsistency) compared RF denervation versus placebo over the short term. Very low-quality evidence suggests that RF denervation is no more effective than placebo for pain (MD -2.12, 95% CI -5.45 to 1.21) (Analysis 5.1) and function (MD -14.06, 95%CI -30.42 to 2.30) (Analysis 5.2) one month post treatment.\(^{57,58}\) One low-quality study (one RCT; N=51; inconsistency, imprecision) showed a smaller effect of RF denervation compared with placebo for pain and function one to six months after the intervention.\(^{58}\)

Comparisons considering the dorsal root ganglion

**Radiating low back pain: pulsed RF denervation versus pulsed RF denervation and continuous RF denervation.**

In one study (N=76; serious RoB; inconsistency, imprecision), very low-quality evidence suggests that PRF denervation versus PRF and CRF has no effect three months after treatment on pain relief, functional improvement or health-related quality of life;\(^{61}\) and that PRF is not more or less effective for pain relief than PRF and CRF denervation over the short term (two months). Low-quality evidence suggests that RF denervation causes no serious complications.
Dorsal root ganglion: RF denervation versus placebo

One study compared RF denervation versus placebo.\(^5^9\) Investigators reported no significant results for pain three months after the procedure. Low-quality evidence (one RCT; N=80; imprecision) suggests that RF denervation is no more effective than placebo three months post treatment. Researchers presented no other results for VAS leg, daily physical activities scores, numerical analgesics rating scale scores, global subjective efficacy ratings and Short Form (SF)-36 scores. Adverse events and complications did not differ between treatments, and no serious complications or side effects occurred in either group.

Dorsal root ganglion: pulsed RF denervation versus placebo

One study provided low-quality evidence showing that pulsed RF denervation is no more effective than placebo in the dorsal root ganglion over the short term. Long-term data or data considering functional status could not be extracted, but the study reports no statistically significant differences in pain and function between PRF and placebo until three months after the intervention.\(^6^0\)
Low back pain with or without radiation

In one study, very low-quality evidence (one RCT; N=100; serious RoB; inconsistency, imprecision) suggests that PRF denervation on dorsal root ganglion compared with either electro-acupuncture or sham offers better short-term effects for pain relief and health-related quality of life but not for functional improvement among individuals suffering from CLBP.42

Clinical relevance of included studies

Most studies described the study population (91%) and the interventions and settings (87%) well enough for comparison with clinical practice. Seventeen studies (74%) measured clinically relevant outcomes (pain and function). When assessing the clinically important size of the effect, researchers considered 30% reduction on VAS/NRS for pain or 8% to 12% improvement in function on the ODI over the short term as clinically important. Only seven studies (30%) showed clinically relevant effects on one of these outcomes.33,44,51,52,56,57 All included studies had small sample sizes, and most poorly described side effects or other complications. Therefore, whether treatment benefits were worth the potential harms remains unclear in all studies.

DISCUSSION

Summary of main results

The objective of this systematic review was to assess the effectiveness of radiofrequency (RF) denervation procedures for treatment of chronic low back pain (CLBP) on the basis of information provided by randomised controlled trials (RCTs). We included 23 RCTs, 13 (56%) of which were considered to have low risk of bias (RoB), even though all had deficiencies, as discussed below. Reviewed studies provided evidence of low to moderate quality suggesting that RF denervation of the facet joint could offer greater pain relief (visual analogue scale (VAS)) (short term) and small improvement in function (Oswestry Disability Index (ODI)) (short and long term) when compared with placebo and steroid injections. For suspected discogenic lumbar pain, evidence of low to very low quality suggests that RF denervation has no effect beyond placebo over the short term, and evidence of moderate quality suggests that RF denervation when compared with placebo has a smaller effect on pain (Numerical Rating Scale (NRS)) and function (ODI)
over the long term. For suspected sacroiliac (SI) joint pain, low-quality evidence shows small effects over the intermediate term and no effects over the short term. For other sources of pain, evidence of low to very low quality shows no effects of RF denervation.

**Overall completeness and applicability of evidence**
The overall number of participants in all 23 studies (N=1309) makes the number of participants included in each individual trial small. This methodological shortcoming contributes to the overall low quality of the evidence. From a clinical perspective, because of the specialised invasiveness of the technique and exposure to x-ray, the small number of participants was understandable. However, it should be pointed out that these interventions were tested in highly selected groups that had undergone diagnostic blocks, and the results must therefore be interpreted with care. Furthermore, no reliable data can be found on the diagnostic accuracy or clinical utility of diagnostic facet joint, SI-joint or selective nerve root blocks.¹²

**Outcome measures**
Five studies did not fulfil the two main clinically relevant outcome measures: pain and disorder-specific disability. The studies of Gallagher, Duger, and Simopoulos used pain as the only outcome measure. In this review, we did not consider “ability to work” as an imperative criterion, as it is not always relevant among individuals with CLBP. Only one study assessed treatment-related costs.²²

**Follow-up**
Follow-up time for intention-to-treat analysis varied from one month to one year. However, only one study included follow-up measurement one year after the start of treatment. In six studies, the blinding code was broken in cases of treatment failure, and an escape treatment was offered. Longer follow-up periods are needed - not only to prove efficacy in RF denervation, but also to track eventual long-term adverse effects.

**Adverse effects**
No adverse effects were reported in 10 studies. Two studies reported subsiding pain associated with the procedure. The study of Oh reported complaints of mild lower limb weakness that dissipated completely. Cohen reported transient non-
painful paraesthesias that resolved without therapy.\textsuperscript{57} Symptoms were more common and lasted longer in the RF denervation group. However, no permanent complications were reported. Two studies found no statistically significant differences between groups.\textsuperscript{52,59} In one study, two actively treated and three sham-treated participants experienced increased pain.\textsuperscript{55} For ethical reasons, inclusion of new participants was therefore discontinued. Three studies reported complications (change in pain characteristics, exacerbation of pain, small superficial burns after RF denervation) that did not last longer than one month.\textsuperscript{43,48,54} Furthermore, most RCTs were small and were not designed to evaluate adverse events, so no clear conclusion can be drawn regarding risks of RF denervation.

Quality of the evidence

Thirteen studies (56\%) had an overall low RoB. The RoB items ‘compliance’ and ‘similar timing of outcome assessment’ were scored best with both 22 studies that complied to these items. However, compliance was in most of the studies irrelevant because it was a single session intervention. Selective reporting and the avoidance or similarity of co-interventions was scored worst, with respectively one and two studies which complied to this item. Selective reporting was scored unclear if no study protocol was published. Most studies included core outcomes (pain and function), but protocols could not be identified in all but one study.\textsuperscript{60} In most studies it was not reported clearly if co-interventions were avoided or similar. Especially these RoB items need improvement in future studies. The RoB item ‘patient blinding’ was scored ‘Yes’ if the intervention and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.\textsuperscript{26} However, blinding the RF denervation procedure is very difficult and debatable. For future reviews it can be discussed if this item should be scored ‘yes’ if blinding was described as indistinguishable for patients but was not tested.

Potential biases in the review process

The primary limitation of this review - lack of studies with low RoB - is encountered in many systematic reviews. Methodologically well-conducted studies with an appropriate sample size undertaken to examine the effectiveness of RF denervation remain scarce. Also, many included studies had no published protocol and, to our knowledge, had not been registered in any of the trial registries. Another limitation is the possibility
of publication bias, which we attempted to minimise by conducting an extensive database search. This search is up-to-date until May 2014; the fact that one study is not incorporated may be a source of potential bias. The influence of publication bias on the results was impossible to assess because a small number of studies contributed to each pooled estimate.

**Agreements and disagreements with other studies or reviews**

Since the original review was published in 2003, 19 new studies about RF denervation for CLBP have been exported. The original review showed conflicting evidence for the effectiveness of facet joint RF denervation. This evidence remains conflicting; however, we found moderate-quality evidence for effects favouring RF denervation over placebo for pain (short term), and low-quality evidence supports RF denervation for functional improvement (over the short, intermediate and long term). In 2003, Niemisto et al reported limited evidence that intradiscal RF denervation may not be effective for discogenic pain. This review supports these results over the short and intermediate term, but moderate-quality evidence shows small positive results over the long term. The current review found greater variation among control groups, most of which did not show significant differences. Only low-quality evidence was found to favour the effects of RF denervation over steroid injections for pain. In 2010, Henschke et al published a systematic review on injection therapy and denervation procedures for CLBP. They concluded that only low-quality to very low-quality evidence could support the use of injection and denervation procedures over placebo and other treatments. The only possible beneficial treatment effect reported by these review authors was facet joint RF denervation. The current review supports this conclusion. Henschke et al showed the same limited results for injection therapy, as did the systematic review of Staal et al, which concluded that evidence was insufficient to support use of injection therapy for sub-acute and chronic low back pain. This finding was consistent with our results (although based on low quality evidence) suggesting that RF denervation is more effective than steroid injections for facet joint pain. Poetscher et al concluded that facet joint RF denervation was more effective than placebo for pain control and functional improvement and was possibly more effective than steroid injections for pain control. These results are supported by evidence of low to moderate quality and show similarities with our results. All previously published reviews state that adverse effects were not sufficiently reported.
CONCLUSIONS

Implications for practice
In general, all conclusions concerning the effects of continuous radiofrequency (CRF) or pulsed radiofrequency (PRF) denervation on CLBP are based on evidence of very low, low or moderate quality. Given this overall quality of evidence, it is recommended that practitioners should be careful when making the decision to use RF denervation in routine clinical practice until rigorous, high quality studies on effectiveness and cost-effectiveness have been performed. As the original studies were not of adequate quality and size to permit assessment of how often complications of RF denervation occur, RF denervation for suspected facet joint pain may have smaller effects in reducing pain (short term) and improving function (short term and long term) in comparison with placebo, but valid evidence on harms is lacking. For suspected discogenic pain, evidence of low to moderate quality shows no short-term and intermediate-term effects. This undermines the clinical plausibility of moderate evidence for small effects favouring RF denervation over the long term. For suspected SI-joint pain, low-quality evidence suggests that RF denervation may not provide short term effects on pain and functional improvement, and may confer small effects over the long term. For other CLBP, the evidence is low in quality and is too sparse to allow any conclusions.

Implications for research
Additional high-quality registered RCTs with larger patient samples, careful pre-selection of patients with diagnostic blocks, longer follow-ups and meaningful standardised outcomes are needed, as are trials on indications for which RF denervation is now used without scientific evidence of efficacy.

Acknowledgements
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