

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Radiofrequency denervation for chronic back pain: a systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035540
Article Type:	Original research
Date Submitted by the Author:	05-Nov-2019
Complete List of Authors:	Chappell, Mary; Cambridgeshire County Council, Public Health Directorate Lakshman, Raj; Cambridgeshire County Council, Public Health Directorate; University of Cambridge, Medical Research Council Epidemiology Unit Trotter, Patrick; Cambridge University Hospitals NHS Foundation Trust Abrahams, Mark; Cambridge University Hospitals NHS Foundation Trust Lee, Michael; University of Cambridge, Division of Anaesthesia
Keywords:	Back pain < ORTHOPAEDIC & TRAUMA SURGERY, Rheumatology < INTERNAL MEDICINE, Neurology < INTERNAL MEDICINE, PAIN MANAGEMENT

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **Radiofrequency denervation for chronic back pain: a systematic review and**
4 **meta-analysis**
5
6
7

8 Mary E Chappell¹, Raj Lakshman^{1,2}, Patrick Trotter³, Mark J Abrahams³, Michael C
9 Lee⁴
10
11

12
13 ¹Public Health Directorate, Cambridgeshire County Council, Cambridge, UK
14

15
16 ²Medical Research Council Epidemiology Unit, University of Cambridge, Cambridge
17
18 UK
19

20
21 ³Cambridge University Hospitals NHS Foundation trust, Cambridge, UK
22

23
24 ⁴Division of Anaesthesia, University of Cambridge, Cambridge, UK
25
26
27
28

29
30 Correspondence to: Mary E Chappell, Public Health Directorate, Cambridgeshire
31
32 County Council, Cambridge CB3 0AP, UK. Tel. 01223 729037
33

34
35 Email mary.chappell@cambridgeshire.gov.uk
36
37
38
39

40
41 Word count:

42
43 Abstract 205
44

45
46 Main text 4,080
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To assess the effectiveness of radiofrequency denervation of lumbosacral anatomical targets for the management of chronic back pain.

Design: Systematic review and meta-analysis of randomised controlled trials.

Methods: A database search (Medline, Medline in Process, Embase, CINHAL and the Cochrane library) was conducted to April 2019 for placebo or no-treatment controlled trials of radiofrequency denervation for the management of chronic back pain. Included trials were quality assessed using the Cochrane risk of bias tool and the quality of outcomes assessed using the GRADE approach. Meta-analysis was conducted to calculate mean difference in post-treatment pain score.

Results: Nineteen randomised controlled trials were included in the review. There appears to be short-term effectiveness (3-6 months) of radiofrequency denervation for a number of indications (facet joint, sacroiliac joint and inter-vertebral discs) but the placebo effect is large, additional intervention effect size is small (<1 on a 11 point (0-10) pain scale). Longer-term effectiveness is uncertain.

Conclusions: Radiofrequency denervation of lumbosacral targets is likely to have a small positive effect for the management of patients with chronic back pain. The quality of evidence for the majority of outcomes is low or very low quality and there is still a degree of uncertainty, particularly around the duration of effect.

1
2
3 Strengths and limitations of this study:
4
5

- 6 • This review brings together a number of recent trials with earlier trials so that
7
8 there is a sizable sum of evidence on which to assess the effectiveness of
9
10 radiofrequency denervation for back pain.
11
12
- 13 • Due to the invasive nature of the procedure, it is difficult to perform truly
14
15 patient or provider blinded trials and this brings some uncertainty around
16
17 findings.
18
19
- 20 • There is limited reporting of long-term outcomes for the effectiveness of
21
22 radiofrequency denervation.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Back pain is an extremely common symptom experienced by people of all ages, and can be attributed to a wide variety of disease processes.^{1,2} Low back pain is now the leading cause of disability worldwide and back pain is associated with a substantial economic burden, with high medical and societal costs.³ Studies have shown that a large proportion of medical costs come from hospital admissions and physical therapy for the management of back pain.⁴ However, there are also indirect costs associated with chronic or recurrent back pain that are difficult to quantify relating to work absenteeism and related productivity.^{1,3,4} In many cases, back pain is non-specific, or structural pathology amenable to surgical correction cannot be identified.⁵⁻⁷ Hence, patients and practitioners continue to seek non-surgical alternatives for the management of back pain.

Radiofrequency denervation (RD) involves the application of an alternating electric current (250 to 500kHz) via a needle probe to induce a highly localised rise in tissue temperature at the needle tip.⁸ The needle tip is usually placed under fluoroscopic guidance to enable selective ablation of sensory nerve branches that supply facet joints, sacroiliac joint or other structures that comprise the lumbosacral spine. RD would therefore offer relief of pain by attenuating sensory signals from the lumbosacral spine.⁹

Despite its use for over 20 years,¹⁰ the effectiveness of RD targeted at the anatomy of lumbosacral spine is not yet established, with randomised controlled trials (RCTs) continuing to be performed. A number of trials have been published since the publication of the last high quality review in 2015¹¹ and our systematic review aimed to bring together this evidence in an attempt to evaluate whether RD is an effective intervention for the management of chronic non-specific back pain.

Materials and Methods

Search strategy

A search was conducted in Medline, Medline in Process, Embase, CINHAL and the Cochrane library from January 2014 to April 2019 (Appendix 1). Previous systematic reviews were used to obtain additional relevant studies published pre 2014.

Inclusion criteria

RCTs comparing RD of the spine with a control in patients with back pain with or without sciatica were included. Only trials of radiofrequency procedures for the purpose of ablating or denaturing sensory nerve branches or nociceptors that supply the lumbosacral spine were considered for inclusion. Trials of pulsed RF,¹² or other forms of 'neuromodulatory' procedures that do not aim to ablate or denature these targets, were excluded from the review. Control groups where there was no active treatment were considered for inclusion but trials with potentially effective comparators e.g. corticosteroid injections, were excluded. Only trials of patients with back pain without a definite or surgically remediable cause (chronic non-specific back pain) were included in the review. The outcome for the review was patient-reported pain score e.g. Visual Analogue Scale or Numeric Rating Scale.

Data collection and quality assessment

Trial characteristics were recorded from included studies. Study results were extracted independently by two authors (MC, PT), with any disagreements resolved by consensus. The overall strength of evidence was assessed using the GRADE approach.¹³ Risk of bias was assessed using the Cochrane Risk of Bias tool.¹⁴ Any outcome where more than half of trials were considered to have a high or unclear risk of bias was downgraded. Outcomes were also downgraded where heterogeneity

1
2
3 in the meta-analysis was greater than 50%. Optimal sample size was taken to be 85
4
5 participants per study arm (as calculated in the Juch 2017 trial¹⁵) and studies with
6
7 less than 170 participants, and/or where the 95% confidence intervals included the
8
9 line of no effect, were downgraded for imprecision. Publication bias was assessed
10
11 using funnel plots and outcomes downgraded where there was a high certainty of
12
13 publication bias.
14
15

16 17 *Data analysis*

18
19
20 Meta-analyses were conducted in RevMan with fixed effects models. Pain score data
21
22 were reported on a 0-10 point scale (Visual Analogue Scale or Numeric Rating
23
24 Scale) in all studies and the mean difference was therefore calculated without
25
26 standardisation as done in the previous Cochrane review.¹¹ Studies with different
27
28 spinal targets e.g. facet joints, sacroiliac joints or inter-vertebrae disc, were
29
30 separated in the analysis. For facet joint pain, a plot of treatment versus no
31
32 treatment/sham was produced by fixed effects meta-analysis of scores for each arm.
33
34 A sensitivity analysis was conducted to check the validity of findings by removing
35
36 studies considered to have a particularly high risk of bias. Subgroup analysis to
37
38 explore study heterogeneity was not conducted because of the small number of
39
40 studies and high likelihood of reaching spurious conclusions.
41
42
43
44
45

46 **Results**

47 48 *Study characteristics*

49
50
51 The search identified 922 citations of which 229 were duplicates. Studies were
52
53 excluded as shown in figure 1. Of the 693 citations reviewed 8 new trials were
54
55 identified as well as 11 from a previous Cochrane review.¹¹ Exclusions were made
56
57 as shown in figure 1. Nineteen trials were included in the review and their
58
59
60

1
2
3 characteristics are shown in appendix 2. Trials investigated the effectiveness of RD
4 of the facet joint (supplied by medial branch of the dorsal spinal ramus),^{15–23} the
5 sacroiliac joints,^{15,24–27} the intervertebral discs^{28–32}, or vertebrae end-plate (supplied
6 by the basivertebral nerve).³³ The majority of trials used a sham control group but
7 one large trial compared RD with no treatment (both groups received an exercise
8 program) and one small trial compared RD plus conventional medical with
9 conventional medical management alone (including self-care, medications and
10 physical and cognitive therapy).
11
12
13
14
15
16
17
18
19
20
21

22 *Study quality*

23
24 Sham-controlled trials generally appear to have conducted adequate randomisation
25 but allocation concealment was often unclear. Processes were in place to blind
26 patients and providers and outcome assessors. In some trials maintenance of
27 blinding was unclear as it was evident that patients undergoing sham procedures
28 were offered RD in case of sham treatment failure. In these cases, blinding would
29 have been broken. Most trials did not report dropouts and there was unclear risk of
30 attrition bias. The outcome for this review was pain score and this was reported in all
31 trials and reporting bias was not considered to be an issue in the review. Four trials
32 were identified as having high risk of bias and were removed in the sensitivity
33 analysis.^{16,18,23,24}
34
35
36
37
38
39
40
41
42
43
44
45
46
47

48 *Overall quality of the evidence*

49
50 The majority of outcomes were graded down for imprecision and all outcomes were
51 downgraded for potential risk of bias. Consequently almost all outcomes were
52 graded as low quality. However, in some cases, high heterogeneity was also present
53 and these outcomes were graded as very low quality. Publication bias was
54
55
56
57
58
59
60

1
2
3 suggested by asymmetry in a number of the funnel plots. However, there was
4
5 uncertainty due to the small numbers of studies and outcomes were not graded
6
7 down for publication bias.
8
9

10 *Study findings*

11
12
13 Results of the meta-analyses are shown in table 1.
14
15

16 *RD of the facet joints*

17
18
19 Meta-analysis of pain scores at 1-3 months post procedure (longest time point used
20
21 for studies with multiple time points) (marked on a 0-10 scale) is shown in figure 2
22
23 and table 1. The effect size was significant and similar when all trials were included
24
25 (7 trials, MD -0.48, CI -0.81, -0.15) or where just the sham-controlled trials were
26
27 included (6 trials, MD -0.51, CI -0.90, -0.11). At six and twelve months after the
28
29 procedure, there was still a significant effect but the effect size was lower for all trials
30
31 compared with sham-controlled trials only (table 1). A plot of change in meta-
32
33 analysed pain score over time after the procedure for facet joint RD and control
34
35 groups is shown in figure 3. When this was plotted with sham-controlled trials alone,
36
37 a similar pattern was observed (available on request).
38
39
40
41

42 *RD of the sacroiliac joints*

43
44
45 Figure 4 shows the meta-analysis of trials for pain score at 1-3 months (longest time
46
47 point used for studies with multiple time points). There was a significant effect of RD
48
49 for the analysis including all trials (5 trials, MD -0.97, CI -1.38, -0.57) or just sham-
50
51 controlled trials (4 trials, MD -1.13, CI -1.63, -0.63). Only one trial¹⁵ assessed
52
53 outcome at later time points and this showed no significant difference compared to a
54
55 no treatment control (table 1).
56
57
58
59
60

RD of the intervertebral discs

Pain score at 1-3 months post-treatment was significantly lower for RD compared with control in all trials (4 trials, MD -0.98, CI -1.62, -0.33) or just sham-controlled trials (3 trials, MD -0.63, CI -1.36, 0.10) (figure 5). The effect was still significant at 6 months (table 1).

RD of the vertebrae body and end plate

One recent trial of RD for vertebrae body and end plate (basivertebral nerve ablation)³³ did not show significant benefits of RD compared with sham at 3, 6 or 12 months (table 1).

Sensitivity analysis

Four studies were removed in the sensitivity analysis due to a high risk of methodological bias^{16,18,23,24} and the two non-sham controlled trials were also removed.^{15,31} The removal of these trials did not largely affect outcome at 1-3 months for facet joint sham trials (4 trials, MD -0.59, CI -1.10, -0.08) or sacroiliac sham trials (3 trials, MD -0.84, CI -1.37, -0.32) but the facet joint sham trial outcome at 6 months became non-significant (1 trial, MD 0.18, CI -2.80, 3.16).

Discussion

Main findings

This systematic review presents evidence suggesting that RD of the lumbosacral spine is likely to have a small positive effect in patients with chronic back pain. The quality of evidence for the majority of findings is low or very low quality and there is still a degree of uncertainty around this assertion, particularly around the duration of effect. The size of benefit appears to be small (<1 point on a 0-10 pain scale) and there is limited evidence investigating effectiveness at more than 6 months. These

1
2
3 assertions apply to RD for facet and sacroiliac joints, whereas evidence for benefit to
4 other targets is more limited. There is a suggestion that there may be a benefit of RD
5 for intervertebral discs but there is some inconsistency, with short-term outcomes
6 showing insignificant effect.
7
8
9
10

11
12 What is also clear from the review is that both treatment and sham/no treatment
13 groups improved during the trials e.g. in the facet joint trials shown in figure 2. In the
14 sham controlled studies, this may, in part, be due to placebo effect. However, the
15 large trial by Juch et al¹⁵ used a “no additional treatment” control (both groups
16 received an exercise program) but all study arms improved over time. This may be
17 because a high proportion of control study participants actually received RD (~30%)
18 due to cross-over during the trial. However, this may also be explained by self-
19 selection of participants who volunteer for research trials,³⁴ and hence are likely to
20 make more of an active effort to manage their back pain. Such participants may be
21 more likely to engage with, and be diligent in, exercise programs and seek medical
22 assistance where needed.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37

38 In the trial by Juch et al., control group improvements may also be explained by the
39 conservative management that they received. The exercise program employed was
40 multi-disciplinary and comprised individual sessions over 8-12 hours focused on
41 quality of movement and behaviour, with access to psychological care. There is
42 evidence suggesting that patients with chronic back pain can benefit from pain
43 management programs that are of sufficient quality and duration.³⁵ Where patients
44 have not received an adequate trial of conservative therapy, they may benefit from
45 further exercise programs and other conservative management. It remains unclear
46 whether patients who are either unable or unwilling to engage with conservative
47 approaches to pain management would benefit from RD based interventions as a
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 first-line or isolated modality of treatment. Hence, there should be some reservation
4
5 when considering the use of RD treatment as a first-line, or isolated modality of pain
6
7 management.
8
9

10 Regression to the mean may also have played a role in control group improvements
11
12 since patients in the trial were recruited with elevated pain, responsive to an
13
14 anaesthetic block. Back pain has been shown to have a varied aetiology, with some
15
16 patients experiencing fluctuating levels of pain over time, whilst other experience
17
18 constant high levels of pain.^{36,37} For the majority of trials that reported it, duration of
19
20 back pain in participants prior to enrolment was 2-5 years and a proportion of these
21
22 were likely to have had high levels of constant pain. Some, however, may have been
23
24 experiencing fluctuating or recurrent pain within this period since the actual inclusion
25
26 criteria for most trials was pain for >3 or 6 months based on patient recall. If they
27
28 were recruited at a point where their pain had flared acutely, there would be a natural
29
30 tendency for that painful episode to resolve over time.
31
32
33
34

35 36 *Strengths and limitations* 37 38

39 A major strength of this review is that it collates a larger body of evidence than
40
41 previous systematic reviews, with the addition of a number of recent trials and
42
43 thorough assessment of the quality of the evidence. The review is able to tentatively
44
45 answer the question about the effectiveness of RD for back pain; an assertion that,
46
47 to date, has proved to be very difficult due a paucity of evidence in this field.
48
49

50
51 This review utilises evidence from a previous Cochrane review¹¹ but the inclusion
52
53 criteria for our review had a narrower scope (included only sham- or conservative
54
55 management-controlled trials of conventional neuro-ablative RD). Since the previous
56
57
58
59
60

1
2
3 review appears to be of high quality, and we updated it with a thorough search of the
4 literature to date, there is assurance that all relevant trials were included.
5
6
7

8 A limitation of this review is that it was difficult to truly assess risk of bias in trials
9 included in the review. Trial integrity rested heavily on the blinding of participants and
10 the outcome was likely to be highly subject to patients' preconceptions of the
11 different interventions given. Most trials did not report information that providers gave
12 patients about the different possible treatment arms e.g. did providers suggest to
13 patients that RD was the effective treatment and that sham or no treatment would be
14 ineffective? Where blinding was broken, these viewpoints may have influenced
15 patients' response. In some of the sham-controlled studies this was clearly evident.
16 For example, in some studies, before randomisation, patients were told that, if
17 randomised to sham, they could receive RD if they gained no benefit. Where blinding
18 was broken, these opinions were likely to influence patients' perception of their pain.
19 In other studies information from providers was not reported and it is difficult to
20 assess whether this type of bias occurred.
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38

39 The review may also be limited in its ability to ascertain the technical quality of
40 individual research trials. Even when examining the reported trial methodology, it is
41 difficult to conclusively identify trials that employed procedures that may be more or
42 less successful in denervating the specific lumbosacral anatomy. Some aspects of
43 RD procedures in earlier trials are considered outdated^{38,39} but the advantages of
44 more recent procedures for RD remain unproven, and there is no clear evidence of
45 their superiority. Sensitivity analysis based on technical quality was therefore
46 considered unhelpful and not performed.
47
48
49
50
51
52
53
54
55
56

57 The review is also limited by the lack of long term data from trials. Most studies do
58 not attempt to blind patients for more than 3 months and the longer follow up
59
60

1
2
3 outcomes are considered to be at higher risk of bias. It is still therefore unclear
4
5 whether RD of lumbosacral anatomy has long-term benefits for back pain.
6
7

8 Finally, the review is limited in its ability to identify any aspects of patient or
9
10 intervention characteristics that may make RD treatment more likely to be beneficial.
11

12
13 There is to date no reliable predictor of benefit on back pain for RD procedures
14
15 based on clinical or imaging findings or diagnostic injections.⁴⁰ The relative
16
17 advantages of different RD technologies used in included trials (e.g. 'cooled'^{24,25,31}
18
19 and 'bipolar'^{29,31} RD) remains to be established. Due to the small number of studies
20
21 at each time point, sub-group analysis was not considered appropriate. However, the
22
23 publication of more sham-controlled trials and trials comparing different RD
24
25 technologies may make this type of investigation possible. Technical advances and
26
27 advances in knowledge and experience may allow RD to become a more effective
28
29 treatment and it is important that these developments are formally assessed and
30
31 published.
32
33
34

35
36 In conclusion, despite the limitations in this review and the published literature, it is
37
38 possible to conclude that there is likely to be a beneficial effect of RD of selected
39
40 lumbosacral anatomical targets for chronic back pain. However, the mean size of
41
42 effect appears to be small and, overall, clinical significance may be marginal. Hence,
43
44 chronic back pain remains a highly challenging condition to treat.
45
46
47
48
49
50

51 **Acknowledgements** Thanks to Julie Aikens and Kerry Herbert at Hinchingsbrooke
52
53 Healthcare Library for their assistance in designing and running the search strategies
54
55 for the review.
56
57
58
59
60

1
2
3 **Contributors:** MC contributed to the planning of this work, selected articles for
4 inclusion, extracted data, quality assessed studies and drafted and re-drafted the
5 manuscript. RL contributed to the planning of this work, reviewed the manuscript and
6 approved the final version. PT extracted data from the trials, reviewed the
7 manuscript and approved the final version. MA contributed to the planning of this
8 work, reviewed the manuscript and approved the final version. ML contributed to the
9 planning of this work, reviewed the manuscript and approved the final version.

10
11
12
13
14
15
16
17
18
19
20 **Funding** This research received no specific grant from any funding agency in the
21 public, commercial or not-for-profit sectors. RL is supported by the Medical Research
22 Council (MC_UU_12015/2). MCL is supported by AABGI Foundation project grant
23 (RCZB/071).

24
25
26
27
28
29 **Competing interests** None declared.

30
31
32 **Patient consent for publication** Not required.

33
34
35 **Provenance and peer review** Not commissioned; externally peer reviewed.

36
37
38 **Data availability statement** All data relevant to the study are included in the article
39 or uploaded as supplementary information.

40
41
42
43 **Patient and Public Involvement** This research was done without patient
44 involvement.

45
46
47
48 **Open access** This is an open access article distributed in accordance with the
49 Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which
50 permits others to distribute, remix, adapt, build upon this work non-commercially, and
51 license their derivative works on different terms, provided the original work is
52 properly cited, appropriate credit is given, any changes made indicated, and the use
53 is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

References

- 1 Hartvigsen J, Hancock MJ, Kongsted A, *et al*. What low back pain is and why we need to pay attention. *Lancet* 2018;391:2356–67. doi:10.1016/S0140-6736(18)30480-X
- 2 Hoy D, Bain C, Williams G, *et al*. A systematic review of the global prevalence of low back pain. *Arthritis Rheum* 2012;64:2028–37. doi:10.1002/art.34347
- 3 Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain* 2000;84:95–103. doi:10.1016/S0304-3959(99)00187-6
- 4 Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *Spine J* 2008;8:8–20. doi:10.1016/j.spinee.2007.10.005
- 5 National Institute of Health and Care Excellence. Low back pain and sciatica in over 16s: assessment and management. 2016.
- 6 Chou R, Baisden J, Carragee EJ, *et al*. Surgery for Low Back Pain: A Review of the Evidence for an American Pain Society Clinical Practice Guideline. *Spine (Phila Pa 1976)* 2009;34:1094–109.
- 7 Chou R, Loeser JD, Owens DK, *et al*. Interventional Therapies, Surgery, and Interdisciplinary Rehabilitation for Low Back Pain: An Evidence-Based Clinical Practice Guideline From the American Pain Society. *Spine (Phila Pa 1976)* 2009;34:1066–77. doi:10.1097/BRS.0b013e3181a1390d
- 8 Kline M. Radiofrequency techniques in clinical practice. In: *Waldman SD, Winnie AP, eds. Interventional Pain Management. Philadelphia, PA: Saunders. 1996.*

- 1
2
3 9 Wray JK, Dixon B, Przkora R. *Radiofrequency Ablation*. 2019.
4
5
6 10 Manchikanti L, Hirsch J, Pampati V, *et al*. Utilization of Facet Joint and
7
8 Sacroiliac Joint Interventions in Medicare Population from 2000 to 2014:
9
10 Explosive Growth Continues! *Curr Pain Headache Rep* 2016;20:58.
11
12
13 11 Maas E, Ostelo R, Niemisto L, *et al*. Radiofrequency denervation for chronic
14
15 low back pain. *Cochrane Database Syst Rev* 2015;:Art. No.: CD008572.
16
17 doi:10.1001/jama.2017.16386
18
19
20
21 12 Brandon R, Cohen D, Edward T, *et al*. Pulsed Radiofrequency
22
23 Neuromodulation in Interventional Pain Management—A Growing Technology.
24
25 *J Radiol Nurs* 2018;37:181–7.
26
27
28 13 Schünemann H, Brożek J, Guyatt G, *et al.*, editors. *GRADE Handbook:*
29
30 *Handbook for grading the quality of evidence and the strength of*
31
32 *recommendations using the GRADE approach*.
33
34
35 14 Higgins JP, Savovic J, Page MJ, *et al.*, editors. *Revised Cochrane risk-of-bias*
36
37 *tool for randomized trials (RoB 2)*. 2019.
38
39
40
41 15 Juch JNS, Maas ET, Ostelo RWJG, *et al*. Effect of Radiofrequency
42
43 Denervation on Pain Intensity Among Patients With Chronic Low Back Pain.
44
45 *JAMA* 2017;318:68–81.
46
47
48 16 Gallagher J, Petriccione di Vadi P, Wedley J, *et al*. Radiofrequency facet joint
49
50 denervation in the treatment of low back pain: a prospective controlled double-
51
52 blind study to assess its efficacy. *Pain Clin* 1994;7:193–8.
53
54
55 17 Leclaire R, Fortin L, Lambert R, *et al*. Radiofrequency Facet Joint Denervation
56
57 in the Treatment of Low Back Pain: A Placebo-Controlled Clinical Trial to
58
59 Assess Efficacy. *Spine (Phila Pa 1976)* 2001;26:1411–6.
60

- 1
2
3 doi:10.1097/00007632-200107010-00003
4
5
6 18 Moussa WMM, Khedr W. Percutaneous radiofrequency facet capsule
7
8 denervation as an alternative target in lumbar facet syndrome. *Clin Neurol*
9
10 *Neurosurg* 2016;150:96–104. doi:10.1016/j.clineuro.2016.09.004
11
12
13 19 van Kleef M, Barendse GAM, Kessels A, *et al.* Randomised trial of
14
15 radiofrequency lumbar facet denervation for chronic low back pain. *Spine*
16
17 *(Phila Pa 1976)* 1999;24:1937–42.
18
19
20 20 Van Tilburg CWJ, Schuurmans FA, Stronks DL, *et al.* Randomized sham-
21
22 controlled double-blind multicenter clinical trial to ascertain the effect of
23
24 percutaneous radiofrequency treatment for sacroiliac joint pain: Three-month
25
26 results. *Clin J Pain* 2016;32:921–6. doi:10.1097/AJP.0000000000000351
27
28
29
30 21 Van Wijk RMAW, Geurts JWM, Wynne HJ, *et al.* Radiofrequency denervation
31
32 of lumbar facet joints in the treatment of chronic low back pain: A randomized,
33
34 double-blind, sham lesion-controlled trial. *Clin J Pain* 2005;21:335–44.
35
36
37
38 22 Nath S, Nath CA, Pettersson K. Percutaneous Lumbar Zygapophysial (Facet)
39
40 Joint Neurotomy Using Radiofrequency Current, in the Management of
41
42 Chronic Low Back Pain. *Spine (Phila Pa 1976)* 2008;33:1291–1297.
43
44 doi:10.1109/ICCGI.2010.42
45
46
47 23 Tekin I, Mirzai H, Ok G, *et al.* A comparison of conventional and pulsed
48
49 radiofrequency denervation in the treatment of chronic facet joint pain. *Clin J*
50
51 *Pain* 2007;23:524–9. doi:10.1097/AJP.0b013e318074c99c
52
53
54
55 24 Cohen SP, Hurley RW, Buckenmaier CC, *et al.* Randomized Placebo-
56
57 Controlled Study Evaluating Lateral Branch Radiofrequency Denervation for
58
59 Sacroiliac Joint Pain. *Anesthesiology* 2008;109:279–88.
60

- 1
2
3 doi:10.1038/mp.2011.182.doi
4
5
6 25 Patel N, Gross A, Brown L, *et al.* A Randomized, Placebo-Controlled Study to
7 Assess the Efficacy of Lateral Branch Neurotomy for Chronic Sacroiliac Joint
8 Pain. *Pain Med* 2012;13:383–98. doi:10.1111/j.1526-4637.2012.01328.x
9
10
11
12
13 26 Van Tilburg C, Stronks D, Groeneweg J, *et al.* Randomised sham-controlled
14 double-blind multicentre clinical trial to ascertain the effect of percutaneous
15 radiofrequency treatment for lumbar facet joint pain. *Spine (Phila Pa 1976)*
16 2016;98-B:1526–33.
17
18
19
20
21
22
23 27 Mehta V, Poply K, Husband M, *et al.* The Effects of Radiofrequency
24 Neurotomy Using a Strip-Lesioning Device on Patients with Sacroiliac Joint
25 Pain: Results from a Single-Center, Randomized, Sham-Controlled Trial. *Pain*
26 *Physician* 2018;21:607–18.
27
28
29
30
31
32
33 28 Barendse GAM, van den Berg SGM, Kessels AHF, *et al.* Randomized
34 Controlled Trial of Percutaneous Intradiscal Radiofrequency
35 Thermocoagulation for Chronic Discogenic Back Pain. Lack of Effect From a
36 90-Second 70 C Lesion. *Spine (Phila Pa 1976)* 2001;26:287–92.
37
38
39
40
41
42 doi:10.1097/00007632-200102010-00014
43
44
45 29 Kapural L, Vrooman B, Sarwar S, *et al.* A Randomized, Placebo-Controlled
46 Trial of Transdiscal Radiofrequency, Biacuplasty for Treatment of Discogenic
47 Lower Back Pain. *Pain Med* 2013;14:362–73. doi:10.1111/pme.12023
48
49
50
51
52 30 van Tilburg CWJ, Stronks DL, Groeneweg JG, *et al.* Randomized sham-
53 controlled, double-blind, multicenter clinical trial on the effect of percutaneous
54 radiofrequency at the ramus communicans for lumbar disc pain. *Eur J Pain*
55 2017;21:520–9. doi:10.1002/ejp.945
56
57
58
59
60

- 1
2
3 31 Desai MJ, Kapural L, Petersohn JD, *et al.* A prospective, randomized,
4 multicenter, open-label clinical trial comparing intradiscal biacuplasty to
5 conventional medical management for discogenic lumbar back pain. *Spine*
6 *(Phila Pa 1976)* 2016;41:1065–74. doi:10.1097/BRS.0000000000001412
7
8
9
10
11
12 32 Kvarstein G, Måwe L, Indahl A, *et al.* A randomized double-blind controlled trial
13 of intra-annular radiofrequency thermal disc therapy - A 12-month follow-up.
14 *Pain* 2009;145:279–86. doi:10.1016/j.pain.2009.05.001
15
16
17
18
19 33 Fischgrund JS, Rhyne A, Franke J, *et al.* Intraosseous basivertebral nerve
20 ablation for the treatment of chronic low back pain: a prospective randomized
21 double-blind sham-controlled multi-center study. *Eur Spine J* 2018;27:1146–
22 56. doi:10.1007/s00586-018-5496-1
23
24
25
26
27
28
29 34 The Cochrane Collaboration. Introduction to sources of bias in clinical trials. In:
30 *Cochrane Handbook for Systematic Reviews of Interventions*. 2011.
31
32
33
34 35 Morley S, Williams A, Hussain S. Estimating the clinical effectiveness of
35 cognitive behavioural therapy in the clinic: Evaluation of a CBT informed pain
36 management programme. *Pain* 2008;137:670–80.
37
38
39
40
41
42 36 Dunn K, Croft P. Epidemiology and natural history of low back pain. *Eura*
43 *Medicophys* 2004;40:9–13.
44
45
46
47 37 Dunn K, Jordan K, Croft P. Characterizing the course of low back pain: a latent
48 class analysis. *Am J Epidemiol* 2006;63:754–61.
49
50
51
52 38 Dreyfuss P, Baker R. Comment on: Radiofrequency facet joint denervation in
53 the treatment of low back pain: a placebo-controlled clinical trial to assess
54 efficacy. *Spine (Phila Pa 1976)* 2002;27:556–7.
55
56
57
58
59 39 Kapural L, Provenzano D, Narouze S. RE: Juch JNS, *et al.* Effect of

1
2
3 Radiofrequency Denervation on Pain Intensity Among Patients With Chronic
4
5 Low Back Pain: The Mint Randomized Clinical Trials. *JAMA* 2017;318(1):68–
6
7 81. *Neuromodulation* 2017;20:844. doi:10.1111/ner.12729
8
9

- 10 40 Cohen SP, Julie JH, Brummett C. Facet joint pain-advances in patient
11
12 selection and treatment. *Nat Rev Rheumatol* 2013;9:101–16.
13
14
15 doi:10.1038/nrrheum.2012.198
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Table 1 Results of the meta-analyses of randomised controlled trials

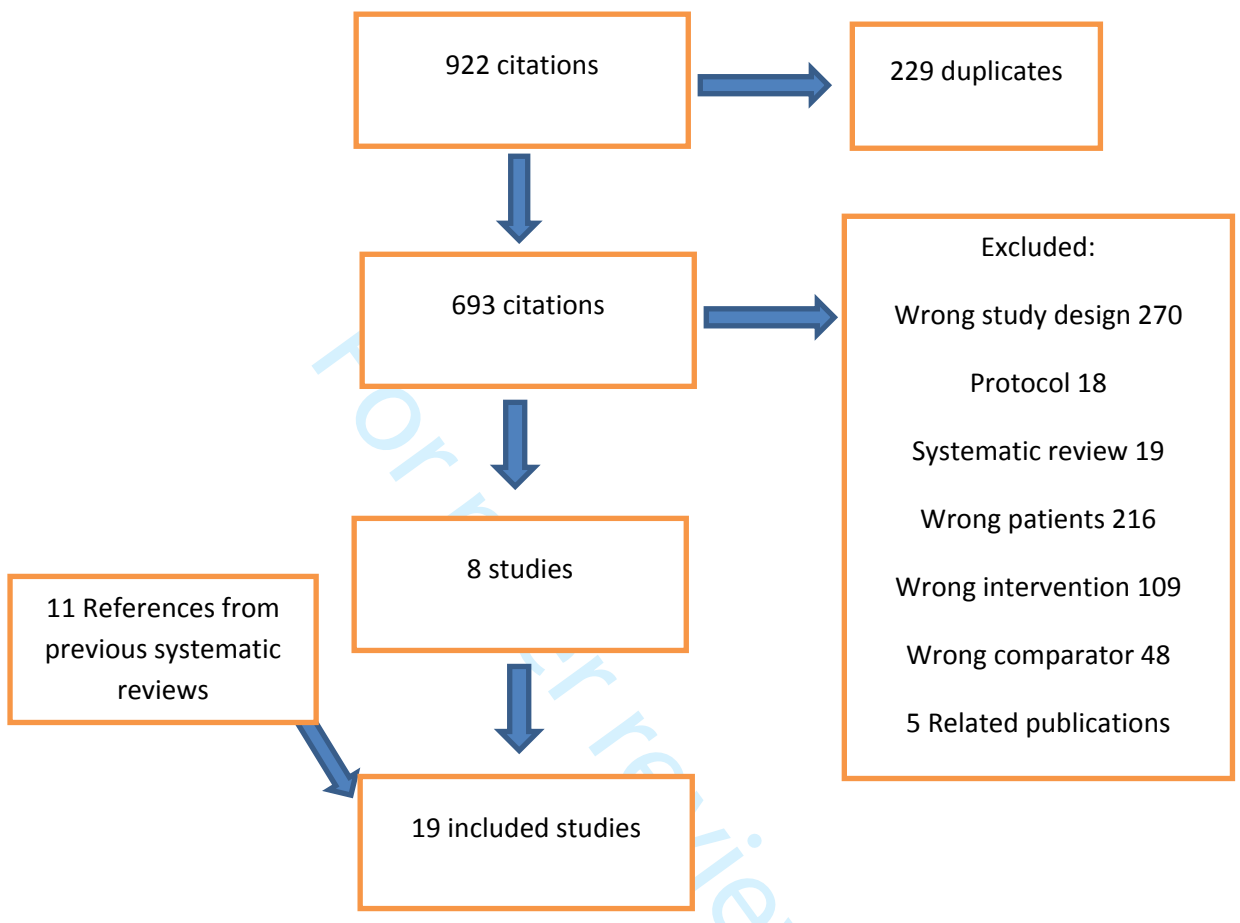
	All trials					Sham controlled trials				
	k	N	MD (95% CI)	I ²	GRADE*	k	N	MD (95% CI)	I ²	GRADE*
RD of the facet joints										
1-3 months	7	599	-0.48 (-0.81, -0.15)	59%	Low	6	348	-0.51 (-0.90, -0.11)	66%	Low
1 month	4	411	-0.64 (-1.08, -0.21)	22%	Moderate	3	160	-0.48 (-1.17, 0.21)	43%	Low
2 months	2	282	-0.83 (-1.36, -0.30)	44%	Low	1	31	-1.94 (-3.65, -0.23)	NA	Very low
3 months	4	478	-0.41 (-0.76, -0.03)	64%	Low	3	127	-0.37 (-0.83, 0.08)	76%	Very low (R, H, I)
6 months	4	361	-0.57 (-1.01, -0.13)	42%	Low	3	110	-0.90 (-1.53, -0.28)	32%	Low (R, I)
1 year	2	291	-0.71 (-1.20, -0.21)	89%	Very low	1	40	-1.50 (-2.21, -0.79)	NA	Very low
RD of the sacroiliac joints										
1-3 months	5	384	-0.97 (-1.38, -0.57)	83%	Low	4	156	-1.13 (-1.63, -0.63)	87%	Very low
1 month	4	367	-0.91 (-1.32, -0.51)	82%	Low	3	139	-0.81 (-1.36, -0.26)	88%	Very low
2 months	1	228	-0.47 (-1.04, 0.10)	NA	Low					
3 months	4	356	-0.78 (-1.20, -0.37)	73%	Low	3	128	-0.84 (-1.37, -0.32)	81%	Very low
6 months	1	228	-0.28 (-1.00, 0.44)	NA	Low					
12 months	1	228	-0.19 (-0.92, 0.54)	NA	Low					
RD of the intervertebral discs										
1-3 months	4	200	-0.98 (-1.62, -0.33)	40%	Low	3	144	-0.63 (-1.36, 0.10)	0%	Low
1 month	3	176	-0.61 (-1.31, 0.09)	61%	Low	2	116	-0.16 (-0.97, 0.65)	0%	Low (R,I)
2 months	1	28	0.28 (-1.95, 2.51)	NA	Very low	1	28	0.28 (-1.95, 2.51)	NA	Very low
3 months	3	172	-1.09 (-1.76, -0.42)	45%	Low	2	116	-0.74 (-1.51, 0.03)	0%	Low
6 months	3	127	-1.74 (-2.58, -0.91)	0%	Low	2	75	-1.63 (-2.58, -0.68)	0%	Low
12 months	1	20	-1.70 (-3.63, 0.23)	NA	Very low	1	20	-1.70 (-3.63, 0.23)	NA	Very low
RD of the vertebrae body and endplate										
3 months	1	205	-0.34 (-1.09, 0.41)	NA	Moderate	1	205	-0.34 (-1.09, 0.41)	NA	Moderate
6 months	1	205	-0.67 (-1.44, 0.10)	NA	Moderate	1	205	-0.67 (-1.44, 0.10)	NA	Moderate
12 months	1	205	-0.50 (-1.29, 0.29)	NA	Moderate	1	205	-0.50 (-1.29, 0.29)	NA	Moderate

k, number of trials; N, number of participants; MD, Mean difference.

*GRADE assessment of the quality of the evidence

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1 PRISMA flow diagram



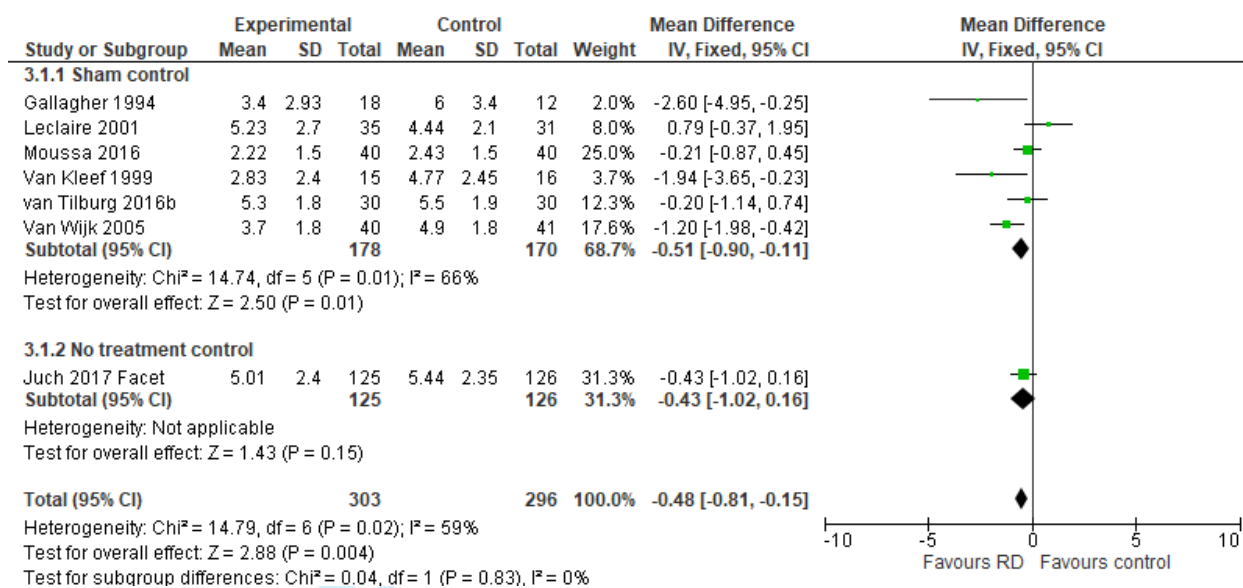


Figure 2 Post treatment pain score for radiofrequency denervation of the facet joints versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

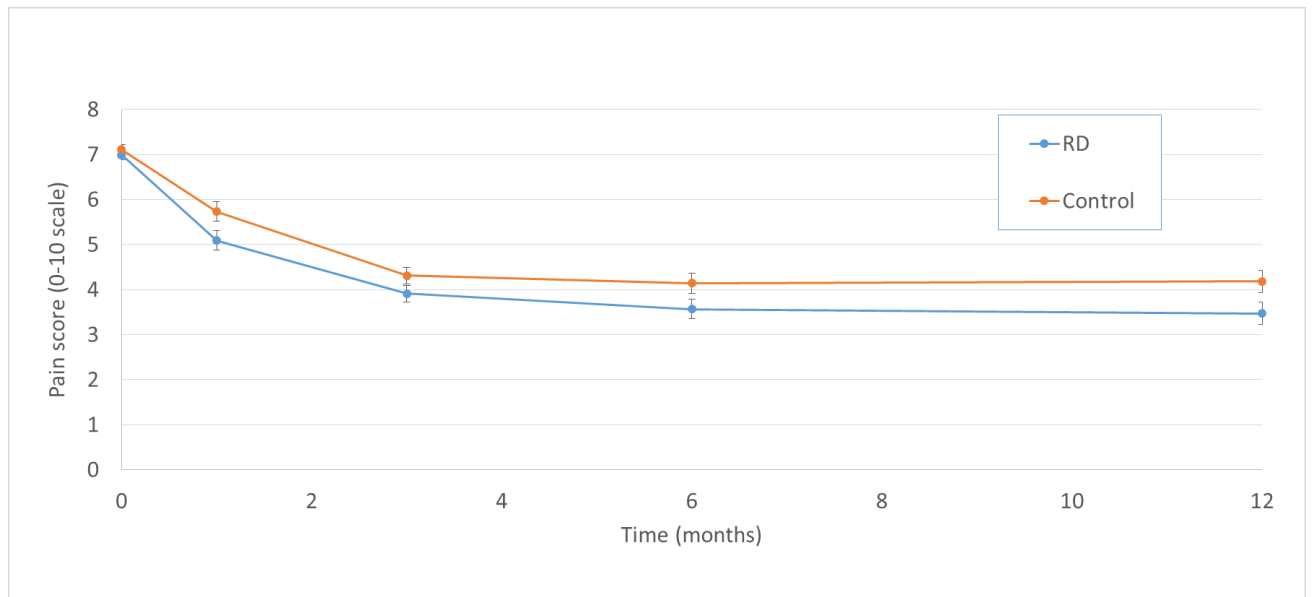


Figure 3 Change in back pain score (closed bound 0-10 scale) for patients with facet joint pain following radiofrequency denervation or control treatment

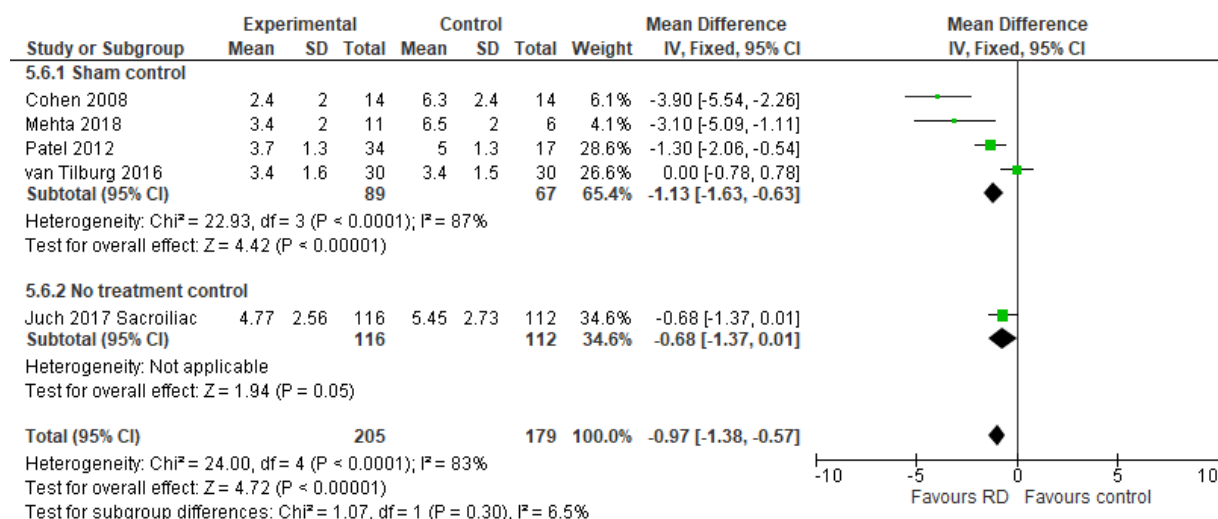


Figure 4 Post treatment pain score for radiofrequency denervation of the sacroiliac joints versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

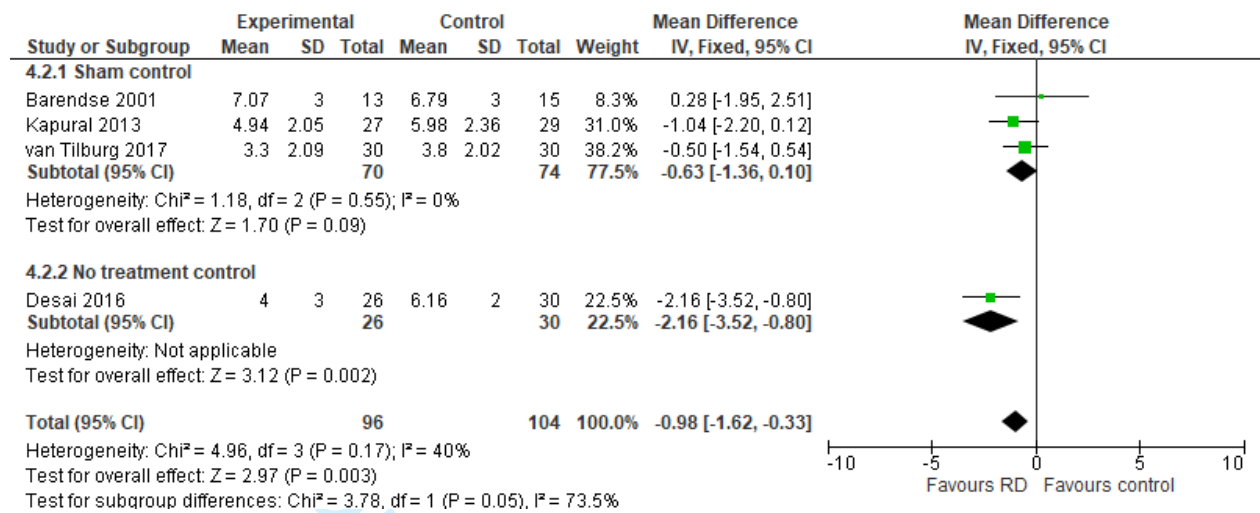


Figure 5 Post treatment pain score for radiofrequency denervation of the intervertebral discs versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

Appendix 1 Search strategies

Medline and Embase

#	Database	Search term
1	Medline	(randomized controlled trial).pt
2	Medline	(controlled clinical trial).pt
3	Medline	(randomi*ed).ab
4	Medline	(placebo).ti,ab
5	Medline	(drug therapy).fs
6	Medline	(randomly).ti,ab
7	Medline	(trial).ti,ab
8	Medline	(groups).ti,ab
9	Medline	(1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)
10	Medline	(animals NOT (humans AND animals)).su
11	Medline	9 not 10
12	Medline	(dorsalgia).ti,ab
13	Medline	exp "BACK PAIN"/
14	Medline	(backache).ti,ab
15	Medline	(lumbar ADJ pain).ti,ab
16	Medline	(coccyx).ti,ab
17	Medline	(coccydynia).ti,ab
18	Medline	(sciatica).ti,ab
19	Medline	"SCIATIC NEUROPATHY"/

1			
2			
3	20	Medline	(spondylosis).ti,ab
4			
5	21	Medline	(lumbago).ti,ab
6			
7			
8	22	Medline	(12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20
9			OR 21)
10			
11	23	Medline	exp SPINE/
12			
13			
14	24	Medline	(discitis).ti,ab
15			
16			
17	25	Medline	exp "SPINAL DISEASES"/
18			
19	26	Medline	(disc ADJ degeneration).ti,ab
20			
21			
22	27	Medline	(disc ADJ prolapse).ti,ab
23			
24			
25	28	Medline	(disc ADJ herniation).ti,ab
26			
27			
28	29	Medline	(spinal fusion).su
29			
30	30	Medline	(facet ADJ joints).ti,ab
31			
32			
33	31	Medline	(intervertebral disc).su
34			
35	32	Medline	(postlaminectomy).ti,ab
36			
37			
38	33	Medline	(arachnoiditis).ti,ab
39			
40			
41	34	Medline	(failed ADJ back).ti,ab
42			
43	35	Medline	(23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31
44			OR 32 OR 33 OR 34)
45			
46	36	Medline	(22 OR 35)
47			
48			
49	37	Medline	exp "RADIO WAVES"/
50			
51			
52	38	Medline	exp "PULSED RADIOFREQUENCY TREATMENT"/
53			
54	39	Medline	(radiofrequency).af
55			
56			
57	40	Medline	(radio frequency).af
58			
59			
60			

- 1
2
3 41 Medline exp ELECTROCOAGULATION/
4
5
6 42 Medline (electrocoag*).af
7
8 43 Medline (thermocoag*).af
9
10
11 44 Medline neurotom* OR (neuroly*).af
12
13 45 Medline (37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44)
14
15
16 46 Medline (11 AND 36 AND 45)
17
18 47 EMBASE "CLINICAL TRIAL"/
19
20
21 48 EMBASE "CONTROLLED CLINICAL TRIAL"/
22
23
24 49 EMBASE "CONTROLLED STUDY"/
25
26
27 50 EMBASE "RANDOMIZED CONTROLLED TRIAL"/
28
29
30 51 EMBASE "DOUBLE BLIND PROCEDURE"/
31
32
33 52 EMBASE "SINGLE BLIND PROCEDURE"/
34
35
36 53 EMBASE "CROSSOVER PROCEDURE"/
37
38
39 54 EMBASE PLACEBO/
40
41 55 EMBASE (allocat*).ti,ab
42
43 56 EMBASE (assign*).ti,ab
44
45 57 EMBASE (blind*).ti,ab
46
47 58 EMBASE (clinic* ADJ25 (study OR trial)).ti,ab
48
49
50 59 EMBASE (crossover OR cross-over).ti,ab
51
52
53 60 EMBASE (factorial*).ti,ab
54
55
56 61 EMBASE (followup OR follow-up).ti,ab
57
58 62 EMBASE (prospectiv*).ti,ab
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 63 EMBASE (placebo*).ti,ab
- 64 EMBASE (random*).ti,ab
- 65 EMBASE ((singl* OR doubl* OR trebl* OR trip*) ADJ25 (blind* OR mask*)).ti,ab
- 66 EMBASE (volunteer*).ti,ab
- 67 EMBASE (47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66)
- 68 EMBASE exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
- 69 EMBASE exp ANIMALS/
- 70 EMBASE exp INVERTEBRATE/
- 71 EMBASE ANIMAL EXPERIMENT/
- 72 EMBASE ANIMAL MODEL/
- 73 EMBASE ANIMAL TISSUE/
- 74 EMBASE ANIMAL CELL/
- 75 EMBASE NONHUMAN/
- 76 EMBASE 71 or 72 or 73 or 74 or 75
- 77 EMBASE exp ANIMALS/
- 78 EMBASE exp INVERTEBRATE/
- 79 EMBASE (76 OR 77 OR 78)
- 80 EMBASE 77 or 78
- 81 EMBASE HUMAN/ OR NORMAL HUMAN/ OR HUMAN CELL/
- 82 EMBASE (76 AND 77 AND 78 AND 81)

- 1
2
3 83 EMBASE (dorsalgia).ti,ab
4
5
6 84 EMBASE (back pain).ti,ab
7
8 85 EMBASE exp BACKACHE/
9
10
11 86 EMBASE (lumbar ADJ pain).ti,ab
12
13
14 87 EMBASE (coccyx).ti,ab
15
16 88 EMBASE (coccydynia).ti,ab
17
18
19 89 EMBASE (sciatica).ti,ab
20
21 90 EMBASE ISCHIALGIA/
22
23
24 91 EMBASE (spondylosis).ti,ab
25
26 92 EMBASE (lumbago).ti,ab
27
28
29 93 EMBASE (back disorder*).ti,ab
30
31
32 94 EMBASE (83 OR 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90 OR 91
33 OR 92 OR 93)
34
35 95 EMBASE exp SPINE/
36
37
38 96 EMBASE (discitis OR diskitis).ti,ab
39
40
41 97 EMBASE exp "SPINE DISEASE"/
42
43 98 EMBASE (disc ADJ degeneration).ti,ab
44
45
46 99 EMBASE (disc ADJ prolapse).ti,ab
47
48
49 100 EMBASE (disc ADJ herniation).ti,ab
50
51 101 EMBASE (spinal fusion).ti,ab
52
53 102 EMBASE (facet ADJ joints).ti,ab
54
55
56 103 EMBASE (intervertebral disk OR Intervertebral disc).ti,ab
57
58
59 104 EMBASE (postlaminectomy).ti,ab
60

1		
2		
3	105	EMBASE (arachnoiditis).ti,ab
4		
5	106	EMBASE (failed ADJ back).ti,ab
6		
7		
8	107	EMBASE (95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102 OR
9		103 OR 104 OR 105 OR 106)
10		
11	108	EMBASE 94 or 107
12		
13		
14	109	EMBASE exp PULSED RADIOFREQUENCY TREATMENT/
15		
16		
17	110	EMBASE exp RADIOFREQUENCY/
18		
19	111	EMBASE exp RADIOFREQUENCY RADIATION/
20		
21		
22	112	EMBASE (radiofrequency OR radio-frequency).ti,ab
23		
24		
25	113	EMBASE exp THERMOCOAGULATION/ OR thermocoag*
26		
27	114	EMBASE exp ELECTROCOAGULATION/ OR electrocoag*
28		
29		
30	115	EMBASE (neurotom* OR neuroly*).ti,ab
31		
32	116	EMBASE (109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115)
33		
34		
35	117	EMBASE (108 AND 116)
36		
37		
38	118	Medline 46 [DT 2014-2019]
39		
40		
41		

Medline in process

#	Database	Search term
1	Medline	("randomi*ed controlled trial").ti,ab
2	Medline	("controlled clinical trial").ti,ab
3	Medline	("randomi*ed").ab
4	Medline	(placebo).ti,ab
5	Medline	("drug therapy").fs

- 1
2
3 6 Medline (randomly).ti,ab
4
5
6 7 Medline (trial).ti,ab
7
8 8 Medline (groups).ti,ab
9
10
11 9 Medline (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)
12
13 10 Medline (dorsalgia).ti,ab
14
15
16 11 Medline ("back pain").ti,ab
17
18
19 12 Medline (backache).ti,ab
20
21 13 Medline ("lumber pain").ti,ab
22
23
24 14 Medline (coccyx).ti,ab
25
26 15 Medline (coccydynia).ti,ab
27
28
29 16 Medline (sciatica*).ti,ab
30
31
32 17 Medline (spondylosis).ti,ab
33
34 18 Medline (lumbago).ti,ab
35
36
37 19 Medline (10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
38 OR 18)
39
40 20 Medline (spine OR sacrum OR "lumber vertebrae" OR
41 "intervertebral disc*").ti,ab
42
43
44 21 Medline (discitis).ti,ab
45
46
47 22 Medline ("disc degeneration").ti,ab
48
49 23 Medline ("disc prolapse").ti,ab
50
51
52 24 Medline ("disc herniation").ti,ab
53
54 25 Medline ("spinal fusion").ti,ab
55
56
57 26 Medline ("facet joints").ti,ab
58
59
60

1		
2		
3	27	Medline (postlaminectomy).ti,ab
4		
5	28	Medline (arachnoiditis).ti,ab
6		
7		
8	29	Medline ("failed back").ti,ab
9		
10		
11	30	Medline (20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29)
12		
13		
14	31	Medline (19 OR 30)
15		
16		
17	32	Medline (radiowave* OR "radio wave*").ti,ab
18		
19		
20	33	Medline (radiofrequency OR "radio frequency").ti,ab
21		
22	34	Medline (electrocoag*).ti,ab
23		
24		
25	35	Medline (thermocoag*).ti,ab
26		
27		
28	36	Medline (neurotom* OR neuroloy*).ti,ab
29		
30	37	Medline (32 OR 33 OR 34 OR 35 OR 36)
31		
32		
33	38	Medline (9 AND 31 AND 37)
34		
35	39	Medline 38 [Document status In Data Review OR In Process OR PubMed not MEDLINE OR Publisher]
36		
37		
38		
39		

Cinahl

#	Database	Search term
41		
42		
43		
44		
45	1	CINAHL exp "CLINICAL TRIALS"/
46		
47		
48	2	CINAHL ("randomi*ed controlled trial*").ti,ab
49		
50		
51	3	CINAHL (clinical ADJ3 trial).ti,ab
52		
53		
54	4	CINAHL (double-blind).ti,ab
55		
56	5	CINAHL (single-blind).ti,ab
57		
58		
59	6	CINAHL (triple-blind).ti,ab
60		

- 1
2
3 7 CINAHL (1 OR 2 OR 3 OR 4 OR 5 OR 6)
4
5
6 8 CINAHL "PLACEBO EFFECT"/
7
8 9 CINAHL PLACEBOS/
9
10
11 10 CINAHL (placebo*).ti,ab
12
13 11 CINAHL (random*).ti,ab
14
15
16 12 CINAHL (8 OR 9 OR 10 OR 11)
17
18
19 13 CINAHL "RANDOM SAMPLE"/
20
21 14 CINAHL exp "STUDY DESIGN"/
22
23
24 15 CINAHL (latin square).ti,ab
25
26 16 CINAHL exp "COMPARATIVE STUDIES"/
27
28
29 17 CINAHL exp "EVALUATION RESEARCH"/
30
31
32 18 CINAHL exp "PROSPECTIVE STUDIES"/
33
34 19 CINAHL (13 OR 14 OR 15 OR 16 OR 17 OR 18)
35
36
37 20 CINAHL (follow-up stud*).ti,ab
38
39 21 CINAHL (followup stud*).ti,ab
40
41
42 22 CINAHL (control*).ti,ab
43
44
45 23 CINAHL (prospectiv*).ti,ab
46
47 24 CINAHL (volunteer*).ti,ab
48
49
50 25 CINAHL (20 OR 21 OR 22 OR 23 OR 24)
51
52 26 CINAHL (7 OR 12 OR 19 OR 25)
53
54
55 27 CINAHL ANIMALS/
56
57
58 28 CINAHL 26 not 27
59
60

1
2
3 29 CINAHL ("dorsalgia").ti,ab
4
5
6 30 CINAHL exp "BACK PAIN"/
7
8 31 CINAHL "LOW BACK PAIN"/
9
10
11 32 CINAHL ("backache").ti,ab
12
13
14 33 CINAHL (lumbar ADJ1 pain).ti,ab
15
16 34 CINAHL (lumbar ADJ5 pain).ti,ab
17
18
19 35 CINAHL (29 OR 30 OR 31 OR 32 OR 33 OR 34)
20
21 36 CINAHL COCCYX/
22
23
24 37 CINAHL SCIATICA/
25
26 38 CINAHL (sciatica).ti,ab
27
28
29 39 CINAHL (coccyx).ti,ab
30
31
32 40 CINAHL (coccydynia).ti,ab
33
34 41 CINAHL "LUMBAR VERTEBRAE"/
35
36
37 42 CINAHL (lumbar ADJ2 vertebra).ti,ab
38
39
40 43 CINAHL (36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42)
41
42 44 CINAHL "THORACIC VERTEBRAE"/
43
44
45 45 CINAHL exp SPONDYLOLYSIS/
46
47 46 CINAHL (lumbago).ti,ab
48
49
50 47 CINAHL (44 OR 45 OR 46)
51
52 48 CINAHL (35 OR 43 OR 47)
53
54
55 49 CINAHL (28 AND 48)
56
57
58 50 CINAHL (radiofrequency OR radio-frequency).ti,ab
59
60

1		
2		
3	51	CINAHL
4		(thermocoag*).ti,ab
5		
6	52	CINAHL
7		exp ELECTROCOAGULATION/ OR electrocoag*
8		
9	53	CINAHL
10		(neurotom* OR neuroly*).ti,ab
11		
12	54	CINAHL
13		"RADIO WAVES"/
14		
15	55	CINAHL
16		(50 OR 51 OR 52 OR 53 OR 54)
17		
18	56	CINAHL
19		(49 AND 55)
20		
21	57	CINAHL
22		56 [DT 2014-2019]

Cochrane

#	Database	Search term
23		
24		
25		
26		
27		
28	1	Cochrane
29		MeSH descriptor: [Back Pain] explode all trees
30		
31	2	Cochrane
32		dorsalgia
33		
34	3	Cochrane
35		backache
36		
37	4	Cochrane
38		MeSH descriptor: [Low Back Pain] explode all trees
39		
40	5	Cochrane
41		lumbar next pain or coccyx or coccydynia or spondylosis
42		
43	6	Cochrane
44		MeSH descriptor: [Spine] explode all trees
45		
46	7	Cochrane
47		MeSH descriptor: [Spinal Diseases] explode all trees
48		
49	8	Cochrane
50		lumbago OR discitis OR disc near degeneration OR disc near prolapse OR disc near herniation
51		
52	9	Cochrane
53		spinal fusion
54		
55	10	Cochrane
56		facet near joints
57		
58	11	Cochrane
59		MeSH descriptor: [Intervertebral Disk] explode all trees
60		
	12	Cochrane
		postlaminectomy

1			
2			
3	13	Cochrane	arachnoiditis
4			
5	14	Cochrane	failed near back
6			
7			
8	15	Cochrane	MeSH descriptor: [Cauda Equina] explode all trees
9			
10			
11	16	Cochrane	lumbar near vertebra*
12			
13	17	Cochrane	spinal near stenosis
14			
15			
16	18	Cochrane	slipped near (disc* or disk*)
17			
18			
19	19	Cochrane	degenerat* near (disc* or disk*)
20			
21	20	Cochrane	stenosis near (spine or root or spinal)
22			
23			
24	21	Cochrane	displace* near (disc* or disk*)
25			
26	22	Cochrane	prolap* near (disc* or disk*)
27			
28			
29	23	Cochrane	MeSH descriptor: [Sciatic Neuropathy] explode all trees
30			
31			
32	24	Cochrane	sciatic*
33			
34	25	Cochrane	back disorder*
35			
36			
37	26	Cochrane	back near pain
38			
39			
40	27	Cochrane	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
41			
42			
43			
44	28	Cochrane	MeSH descriptor: [Radio Waves] explode all trees
45			
46			
47	29	Cochrane	MeSH descriptor: [Pulsed Radiofrequency Treatment] explode all trees
48			
49			
50	30	Cochrane	radiofrequency
51			
52			
53	31	Cochrane	radio frequency or radio-frequency
54			
55			
56	32	Cochrane	MeSH descriptor: [Electrocoagulation] explode all trees
57			
58	33	Cochrane	electrocoag*
59			
60			

- 1
2
3 34 Cochrane thermocoag*
4
5
6 35 Cochrane neurotom* or neuroly*
7
8 36 Cochrane #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35
9
10
11 37 Cochrane #27 and #36 in Trials
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Appendix 2 Study characteristics

Study	N	Inclusion criteria		Mean age (SD)	Mean pain score (SD)	Intervention	Control	Funding
RD of the facet joints								
Gallagher 1994	41	Low back pain >3 months duration with symptoms typical of facet joint pain	Improvement (n=30) or equivocal (n=11) response to anaesthetic block	NR	VAS RD 5.8 (1.78); Sham 7.2 (1.94)	Nerves above and below painful joint denervated at 80° for 90 seconds.	Nerves also identified with stimulation but no heat lesion made	NR
Juch 2017	251	Low back pain without response to conservative management and considered to be related to the facet joint	Positive response to anaesthetic block (reported 50% pain relief 30-90 minutes after block)	RD 53.0 (11.5); Control 52.6 (10.8)	NRS RD 7.14 (1.38) Control 7.19 (1.29)	Denervation at 90° for 90s of L3-4, L4-5 or L5-S1 with exercise program	Exercise program	The Netherlands Organization for Health Research and Development, by the Dutch Society for Anesthesiology, and the Dutch health insurance companies
Leclaire 2001	70	Low back pain for >3 months	“Significant” relief of back pain for >24h following facet injections	RD 46.7 (9.3); Sham 46.4 (9.8)	VAS RD 5.19 (2.67); Sham 5.15 (2.08)	RD with fluoroscopic guidance at 80°C for 90s of at least 2 levels	Nerves also identified with stimulation but electrode only heated to 37°C	Institut de recherche en sante´ and se´curite´ du travail du Que´bec
Moussa 2016	80	Low back pain for >1 year without response to conservative management	Complete or near complete reduction of CLBP on VAS 30 min after 2	RD capsule 58.1 (NR); RD conventional 56.5 (NR);	VAS RD 8.22 (NR); Sham 7.83 (NR)	RD of facet capsule on medial and lateral aspect or	Same procedure without elect current turned on	No funding received

			injections separated by >2 weeks	Sham 55.9 (NR)		conventional RD at 85°C for 90s		
Nath 2008	40	Low back pain for >2 years, not responded to previous treatment, pain attributable to lumbar facet joints	80% pain relief on 3 medial branch blocks	56 (range, 36–79)	VAS RD 5.98 (NR); Sham 4.38 (NR)	RD at 85°C for 60s with additional lesions just lateral and medial to the target nerve	Same procedure as RD but electrode tip remained at body temperature	No funding received
Tekin 2007	40	Back pain for >6 months with focal pain over the facet joints and unresponsive to conservative treatments	>50% reduction in VAS pain 30 minutes after diagnostic medial branch block	RD 60.5 (8.5); Sham 57.9 (9.3)	VAS RD 6.5 (1.5); Sham 6.8 (1.6)	RD at same levels as diagnostic blocks at 80°C for 90s.	Same procedure as RD but with current switched off	Not reported
Van Kleef 1999	32	Low back pain of >12 months duration, failure of conservative management	>50% reduction in pain following diagnostic nerve block of L3-L5 Baseline VAS score of >4	RD 46.6 (7.4); Sham 41.4 (7.5)	VAS RD 5.2 (1.7); Sham 5.2 (1.6)	RD at 80°C for 60s	Same procedure as RD but with current switched off	The Nederlandse organisatie voor wetenschappelijk
Van Tilburg 2016	60	Low back pain for >3 months and failure of conservative management	Decrease of >2 on medial branch block	RD 65 (12); Sham 58 (12)	NRS RD 7.2 (1.4); Sham 7.4 (0.8)	RD at 80°C for 60s per level for three steps with physiotherapy	Same procedure as RD but with current switched off with physiotherapy	No funding from a commercial party
Van Wijk 2005	81	Low back pain for >6 months	≥50% reduction on	RD 46.9 (11.5);	VAS RD 5.8 (1.8);	RD 80°C for 60 seconds	Same procedure as	Grant from the Dutch Health

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

diagnostic block Sham 48.1 (12.6) Sham 6.5 (1.8) at the levels concerned RD but with current switched off Insurance Council

RD of the sacroiliac joints

Cohen 2008	28	Axial low back or buttock pain ≥ 6 months, tenderness overlying the sacroiliac joint(s), failure to respond to conservative therapy	≥ 75% pain relief for ≥3h following diagnostic sacroiliac joint injection, but back near baseline within 2 months	RD 51.9 (13.6); Sham 51.8 (13.1)	VAS RD 6.1 (1.8); Sham 6.5 (1.9)	RD 80°C for 90 seconds using cooling probe technology (Cooled RD)	Same procedure as RD but no current applied	John P. Murtha Neuroscience and Pain Institute, the Army Regional Anesthesia & Pain Medicine Initiative, and National Institutes of Health grant # MH075884
Juch 2017	228	Low back pain without response to conservative management, considered to be related to the sacroiliac joint.	Positive response to anaesthetic block (reported 50% pain relief 30-90 minutes after block)	RD 51.6 (10.9); Control 51.1 (12.2)	NRS RD 7.17 (1.65); Control 7.06 (1.43)	RD - 60° for 2.5 min per lesion of S1, S2 and S3 with exercise program	Exercise program	The Netherlands Organization for Health Research and Development, by the Dutch Society for Anesthesiology, and the Dutch health insurance companies
Mehta 2018	17	CLBP for >6 months. >5 on NRS	>80% pain reduction on 2 diagnostic blocks	RD 56.6 (NR); Sham 62.6 (NR)	VAS RD 8.1 (0.8); Sham 7.3 (0.8)	RD of the L5 medial branch of the primary dorsal root nerve and strip lesioning of the lateral branches	Identical to active RD treatment except that no RF energy was applied	None

						of the S1, 2, and 3 nerve roots		
Patel 2012	51	Pain for ≥6 months, 3-day average NRS between 4 and 8, failure of conservative management	≥75% pain reduction for 4h-7 days on two sets of anaesthetic blocks and back to baseline by start of the study	RD 56 (15); Sham 64 (14)	NRS RD 6.1 (1.3); Sham 5.8 (1.3)	RD at 60°C for 150s of L5 dorsal ramus and then acral lateral branches of S1, S2 and S3 (cooled RD)	Same procedure as RD but RF energy was not delivered.	Baylis Medical
Van Tilburg 2016	60	Sacroiliac joint pain for >3 months, failure of conservative management	Decrease of ≥2 on NRS following diagnostic block	RD 59.5 (27); Sham 62 (18)	NRS RD 7.2 (1.4); Sham 7.5 (1.2)	85°C each step for 90s, total of 5 steps	Same procedure as RD but no heat lesions made	Not reported
RD of the intervertebral discs								
Barendse 2001	28	Non-specific LBP for >1y, failure of conservative management	>50% pain relief 30 minutes after an analgesic discography at L4–L5 and L5–S1. Patients with multilevel pain excluded	RD 40.8 (7.5); Sham 45.2 (8.4)	VAS RD 6.5 (1.3); Sham 5.5 (1.1)	70°C for 90s without anaesthetic	Same procedure as RD but no current applied	Not reported
Desai 2016	63	Lumbar discogenic pain for ≥6 months, unresponsive to conservative management	Diagnosed via provocation discography - definite single-level concordant	Mean age 41 (11); Control 43 (11)	VAS RD 6.7 (NR); Sham 7 (NR)	RD at 50°C for 15 minutes and then 60°C for 2.5 min (bopolar cooled RD) with conventional	Conventional medical management	Halyard Health, Inc. (formerly Kimberly-Clark Health Care)

			pain on manometry			medical management		
Kapural 2013	55	CLBP unresponsive to conservative management for ≥6 months; no surgical interventions within previous 3 months	Single-level degenerative disc disease or two-level disease without evidence of additional degenerative changes in other disc spaces on MRI	RD 40.4 (10.3); Sham 38.4 (10.4)	VAS RD 7.13 (1.61); Sham 7.18 (1.98)	RD at 45°C bipolar for 15 minutes or 50°C bipolar for 15 minutes and monopolar at 60°C for 2.5 minutes	Mimicked active treatment, except that introducers and electrodes positioned just outside of the disc, and no RF energy delivered	Baylis Medical
Kvarstein 2009	20	Unremitting low back pain for more than 6 months; Pain intensity ≥5 /10 and low back pain greater than leg pain; Failure on conservative treatment	Positive one-level pain provocation discography	RD 44.7 (10.1); Sham 39.6 (8.9)	NRS RD 4.6 (1.8); Sham 5.5 (2.0)	RD increased by 5°C every second minute to 4-min interval at 65°C (from 50°C)	Exposed to a similar intervention, but the annulus was not exposed to RF heating	Radionics, TYCO Healthcare Group provided the discTRODE probes
Van Tilburg 2017	60	Low back pain >3 months and symptoms suggestive of lumbar disc problem	Reduction of ≥2 on a numerical rating scale (0–10) after a diagnostic ramus communicans test block	RD 50.5 (13.9); Sham 50.1 (12.3)	NRS 7.8 (1.05); Sham 7.8 (1.05)	RD treatment at 80 °C for 60s per level	Same procedure but without RF treatment	No support received that influenced submitted work
RD of the vertebrae body and endplate								

1									
2									
3	Fischgrund	225	CLBP ≥6 months,	No diagnostic	RD 46.9	VAS RD 6.73	Thermal	Same	Not reported
4	2018		not responded to	block for	(range 26–	(1.38);	ablation at	procedure as	
5			conservative	inclusion	69); Sham	Sham 6.64	the terminus of	RD but only	
6			treatment, Type 1 or		47.1 (range	(1.34)	the basivertebral	docking	
7			Type 2 Modic		25–69)		nerve 85°C for	introducer	
8			changes required				15 min	cannula 1–2	
9			at the proposed					mm	
10			treatment levels					into the	
11								pedicle and	
12								simulating RD	
13									
14									
15									
16									
17									
18									
19									
20									
21									
22									
23									
24									
25									
26									
27									
28									
29									
30									
31									
32									
33									
34									
35									
36									
37									
38									
39									
40									
41									
42									
43									
44									
45									
46									

CLBP, chronic low back pain; N, number of trials; NRS, numeric rating scale; RD, radiofrequency denervation; SD, standard deviation; VAS, visual analogue scale.

BMJ Open

Radiofrequency denervation for chronic back pain: a systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035540.R1
Article Type:	Original research
Date Submitted by the Author:	02-May-2020
Complete List of Authors:	Chappell, Mary; Cambridgeshire County Council, Public Health Directorate Lakshman, Raj; Cambridgeshire County Council, Public Health Directorate; University of Cambridge, Medical Research Council Epidemiology Unit Trotter, Patrick; Cambridge University Hospitals NHS Foundation Trust Abrahams, Mark; Cambridge University Hospitals NHS Foundation Trust Lee, Michael; University of Cambridge, Division of Anaesthesia
Primary Subject Heading:	Rheumatology
Secondary Subject Heading:	Neurology
Keywords:	Back pain < ORTHOPAEDIC & TRAUMA SURGERY, Rheumatology < INTERNAL MEDICINE, Neurology < INTERNAL MEDICINE, PAIN MANAGEMENT

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **Radiofrequency denervation for chronic back pain: a systematic review and**
4 **meta-analysis**
5
6

7
8 Mary E Chappell¹, Raj Lakshman^{1,2}, Patrick Trotter³, Mark J Abrahams³, Michael C
9 Lee⁴
10

11
12
13 ¹Public Health Directorate, Cambridgeshire County Council, Cambridge, UK
14

15
16 ²Medical Research Council Epidemiology Unit, University of Cambridge, Cambridge
17
18 UK
19

20
21 ³Cambridge University Hospitals NHS Foundation trust, Cambridge, UK
22

23
24 ⁴Division of Anaesthesia, University of Cambridge, Cambridge, UK
25
26
27
28

29
30 Correspondence to: Mary E Chappell, Public Health Directorate, Cambridgeshire
31
32 County Council, Cambridge CB3 0AP, UK. Tel. 01223 729037
33

34
35 Email mary.chappell@cambridgeshire.gov.uk
36
37
38
39

40
41 Word count:

42
43 Abstract 204
44

45
46 Main text 4,080
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To assess the effectiveness of radiofrequency denervation of lumbosacral anatomical targets for the management of chronic back pain.

Design: Systematic review and meta-analysis of randomised controlled trials.

Methods: A database search (Medline, Medline in Process, Embase, CINAHL and the Cochrane library) was conducted to April 2019 for placebo or no-treatment controlled trials of radiofrequency denervation for the management of chronic back pain. Included trials were quality assessed using the Cochrane risk of bias tool and the quality of outcomes assessed using the GRADE approach. Meta-analysis was conducted to calculate mean difference in post-treatment pain score.

Results: Nineteen randomised controlled trials were included in the review. There appears to be short-term pain relief (1-3 months) provided by radiofrequency denervation of sacroiliac joint and inter-vertebral discs but the placebo effect is large and additional intervention effect size is small (<1 on a 11 point (0-10) pain scale). Longer-term effectiveness is uncertain.

Conclusions: Radiofrequency denervation of selected lumbosacral targets appears to have a small, short-term, positive effect for the management of patients with chronic back pain. However, the quality of evidence for the majority of outcomes is low or very low quality and there is still a degree of uncertainty, particularly around the duration of effect.

1
2
3
4
5
6 Strengths and limitations of this study:
7
8

- 9
- 10 • This review brings together a number of recent trials with earlier trials so that
11 there is a sizable sum of evidence on which to assess the effectiveness of
12 radiofrequency denervation for back pain.
13
 - 14 • Due to the invasive nature of the procedure, it is difficult to perform truly
15 patient or provider blinded trials and this brings some uncertainty around
16 findings.
17
 - 18 • There is limited reporting of long-term outcomes for the effectiveness of
19 radiofrequency denervation.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Back pain is an extremely common symptom experienced by people of all ages, and can be attributed to a wide variety of disease processes.^{1,2} Low back pain is now the leading cause of disability worldwide and back pain is associated with a substantial economic burden, with high medical and societal costs.³ Studies have shown that a large proportion of medical costs come from hospital admissions and physical therapy for the management of back pain.⁴ However, there are also indirect costs associated with chronic or recurrent back pain that are difficult to quantify relating to work absenteeism and related productivity.^{1,3,4} In many cases, back pain is non-specific, or structural pathology amenable to surgical correction cannot be identified.⁵⁻⁷ Hence, patients and practitioners continue to seek non-surgical alternatives for the management of back pain.

Radiofrequency denervation (RD) involves the application of an alternating electric current (250 to 500kHz) via a needle probe to induce a highly localised rise in tissue temperature at the needle tip.⁸ The needle tip is usually placed under fluoroscopic guidance to enable selective ablation of sensory nerve branches that supply facet joints, sacroiliac joint or other structures that comprise the lumbosacral spine. RD would therefore offer relief of pain by attenuating sensory signals from the lumbosacral spine.⁹

Despite its use for over 20 years,¹⁰ the effectiveness of RD targeted at the anatomy of lumbosacral spine is not yet established, with randomised controlled trials (RCTs) continuing to be performed. A number of trials have been published since the publication of the last high quality review in 2015¹¹ and our systematic review aimed to bring together this evidence in an attempt to evaluate whether RD is an effective intervention for the management of chronic non-specific back pain.

Materials and Methods

Search strategy

A search was conducted in Medline, Medline in Process, Embase, CINHALL and the Cochrane library from January 2014 to April 2019 (Appendix 1). Previous systematic reviews were used to obtain additional relevant studies published pre 2014.

Inclusion criteria

RCTs comparing RD of the spine with a control in patients with back pain with or without sciatica were included. Only trials of radiofrequency procedures for the purpose of ablating or denaturing sensory nerve branches or nociceptors that supply the lumbosacral spine were considered for inclusion. Trials of pulsed RF,¹² or other forms of 'neuromodulatory' procedures that do not aim to ablate or denature these targets, were excluded from the review. Control groups where there was no active treatment were considered for inclusion but trials with potentially effective comparators e.g. corticosteroid injections, were excluded. Only trials of patients with back pain without a definite or surgically remediable cause (chronic non-specific back pain) were included in the review. The outcome for the review was patient-reported pain score e.g. Visual Analogue Scale or Numeric Rating Scale.

Data collection and quality assessment

Trial characteristics were recorded from included studies. Study results were extracted independently by two authors (MC, PT), with any disagreements resolved by consensus. The overall strength of evidence was assessed using the GRADE approach.¹³ Risk of bias was assessed using the Cochrane Risk of Bias tool.¹⁴ Any outcome where more than half of trials were considered to have a high or unclear risk of bias was downgraded. Outcomes were also downgraded where heterogeneity

1
2
3 in the meta-analysis was greater than 50%. Optimal sample size was taken to be 85
4
5 participants per study arm (as calculated in the Juch 2017 trial¹⁵) and studies with
6
7 less than 170 participants, and/or where the 95% confidence intervals included the
8
9 line of no effect, were downgraded for imprecision. Publication bias was assessed
10
11 using funnel plots and outcomes downgraded where there was a high certainty of
12
13 publication bias.
14
15

16 17 *Data analysis*

18
19
20 Meta-analyses were conducted in RevMan¹⁶ with random effects models since the
21
22 included studies investigated effectiveness in different population groups with
23
24 varying intervention and control group treatments. Pain score at 1-3 months was
25
26 taken as the primary outcome (longest time point used for studies reporting multiple
27
28 time points), allowing outcome from a larger number of studies to be combined. Pain
29
30 score data were reported on a 0-10 point scale (Visual Analogue Scale or Numeric
31
32 Rating Scale) in all studies and the mean difference was therefore calculated without
33
34 standardisation as done in the previous Cochrane review.¹¹ Studies with different
35
36 spinal targets e.g. facet joints, sacroiliac joints or inter-vertebrae disc, were
37
38 separated in the analysis. For facet joint pain, a plot of treatment versus no
39
40 treatment/sham was produced by fixed effects meta-analysis of scores for each arm.
41
42
43 A sensitivity analysis was conducted to check the validity of findings by removing
44
45 studies considered to have a particularly high risk of bias. Subgroup analysis to
46
47 explore study heterogeneity was not conducted because of the small number of
48
49 studies and high likelihood of reaching spurious conclusions.
50
51
52
53

54 55 **Results**

56 57 58 *Study characteristics*

59
60

1
2
3 The search identified 922 citations of which 229 were duplicates. Studies were
4 excluded as shown in figure 1. Of the 693 citations reviewed 8 new trials were
5 identified as well as 11 from a previous Cochrane review.¹¹ Exclusions were made
6 as shown in figure 1. Nineteen trials were included in the review and their
7 characteristics are shown in appendix 2. Trials investigated the effectiveness of RD
8 of the facet joint (supplied by medial branch of the dorsal spinal ramus),^{15,17-24} the
9 sacroiliac joints,^{15,25-28} the intervertebral discs²⁹⁻³³, or vertebrae end-plate (supplied
10 by the basivertebral nerve).³⁴ The majority of trials used a sham control group but
11 one large trial compared RD with no treatment (both groups received an exercise
12 program) and one small trial compared RD plus conventional medical with
13 conventional medical management alone (including self-care, medications and
14 physical and cognitive therapy).

31 *Study quality*

32 Sham-controlled trials generally appear to have conducted adequate randomisation
33 but allocation concealment was often unclear. Processes were in place to blind
34 patients and providers and outcome assessors. In some trials maintenance of
35 blinding was unclear as it was evident that patients undergoing sham procedures
36 were offered RD in case of sham treatment failure. In these cases, blinding would
37 have been broken. Most trials did not report dropouts and there was unclear risk of
38 attrition bias. The outcome for this review was pain score and this was reported in all
39 trials and reporting bias was not considered to be an issue in the review. Four trials
40 were identified as having high risk of bias and were removed in the sensitivity
41 analysis.^{17,19,24,25}

57 *Overall quality of the evidence*

1
2
3 The majority of outcomes were graded down for imprecision and all outcomes were
4
5 downgraded for potential risk of bias. Consequently almost all outcomes were
6
7 graded as low quality. However, in some cases, high heterogeneity was also present
8
9 and these outcomes were graded as very low quality. Publication bias was
10
11 suggested by asymmetry in a number of the funnel plots. However, there was
12
13 uncertainty due to the small numbers of studies and outcomes were not graded
14
15 down for publication bias.
16
17

18 19 *Study findings*

20
21
22 Results of the meta-analyses are shown in table 1.
23

24 25 *RD of the facet joints*

26
27
28 Meta-analysis of pain scores at 1-3 months post procedure (longest time point used
29
30 for studies with multiple time points) (marked on a 0-10 scale) was performed to
31
32 allow combination of data from the maximum number of studies, and results are
33
34 shown in figure 2 and table 1. The effect size was similar when all trials were
35
36 included (7 trials, MD -0.56, CI -1.13, 0.01) or where just the sham-controlled trials
37
38 were included (6 trials, MD -0.63, CI -1.39, 0.12) but the effect was not significant for
39
40 either. We also considered outcomes at 6 and 12 months, where data were available
41
42 to explore longer term outcomes, but did not find any significant effect (table 1).
43
44
45

46 47 *RD of the sacroiliac joints*

48
49
50 Figure 3 shows the meta-analysis of trials for pain score at 1-3 months (longest time
51
52 point used for studies with multiple time points). There was a significant effect of RD
53
54 for the analysis including all trials (5 trials, MD -1.53, CI -2.62, -0.45) or just sham-
55
56 controlled trials (4 trials, MD -1.89, CI -3.45, -0.34). Only one trial¹⁵ assessed
57
58
59
60

1
2
3 outcome at later time points and this showed no significant difference compared to a
4 no treatment control (table 1).
5
6

7 8 *RD of the intervertebral discs* 9

10 Pain score at 1-3 months post-treatment was significantly lower for RD compared
11 with control in all trials (4 trials, MD -0.98, CI -1.84, -0.12) but not for sham-controlled
12 trials alone (3 trials, MD -0.63, CI -1.36, 0.10) (figure 4). Pain score was significantly
13 lower for RD when all trials and sham-controlled trials were considered at 6 months
14 but, for one trial assessing outcome at one year, it was not (table 1).
15
16
17
18
19
20
21

22 23 *RD of the vertebrae body and end plate* 24

25 One recent trial of RD for vertebrae body and end plate (basivertebral nerve
26 ablation)³⁴ did not show significant benefits of RD compared with sham at 3, 6 or 12
27 months (table 1).
28
29
30
31

32 33 *Sensitivity analysis* 34

35 Four studies were removed in the sensitivity analysis due to a high risk of
36 methodological bias^{17,19,24,25} and the two non-sham controlled trials were also
37 removed.^{15,32} After the removal of these trials, outcome at 1-3 months for facet joint
38 sham trials was still not significant (4 trials, MD -0.57, CI -1.60, 0.46) and 1-3 month
39 outcome for sacroiliac sham trials became non-significant (3 trials, MD -1.21, CI -
40 2.59, 0.16). The facet joint sham trial outcome at 6 months also became non-
41 significant (1 trial, MD 0.18, CI -2.80, 3.16).
42
43
44
45
46
47
48
49
50
51

52 **Discussion** 53

54 55 *Main findings* 56 57 58 59 60

1
2
3 This systematic review presents evidence suggesting that RD of the lumbosacral
4 spine may have a small positive but short-lived effect in patients with chronic back
5 pain, depending on the precise part of the anatomy that is being targeted by the
6 procedure. The quality of evidence for the majority of findings is low or very low
7 quality and there is still a degree of uncertainty around this assertion, particularly
8 around the duration of effect. The size of benefit appears to be small (<1 point on a
9 0-10 pain scale) and there is limited data for outcomes beyond 6 months. These
10 assertions apply to RD for sacroiliac joints, whereas evidence for benefit to other
11 targets is more limited. RD for facet joints did not show a significant benefit on 1-3
12 month outcome. There is a suggestion that there may be a benefit of RD for
13 intervertebral discs but there is some inconsistency, with insignificant effect even for
14 short-term outcomes.

15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
What is also clear from the review is that both treatment and sham/no treatment
groups improved during the trials. In the sham controlled studies, this may, in part,
be due to placebo effect. However, the large trial by Juch et al¹⁵ used a “no
additional treatment” control (both groups received an exercise program) but all
study arms improved over time. This may be because a high proportion of control
study participants actually received RD (~30%) due to cross-over during the trial.
However, this may also be explained by self-selection of participants who volunteer
for research trials,³⁵ and hence are likely to make more of an active effort to manage
their back pain. Such participants may be more likely to engage with, and be diligent
in, exercise programs and seek medical assistance where needed.

In the trial by Juch et al., control group improvements may also be explained by the
conservative management that they received. The exercise program employed was
multi-disciplinary and comprised individual sessions over 8-12 hours focused on

1
2
3 quality of movement and behaviour, with access to psychological care. There is
4
5 evidence suggesting that patients with chronic back pain can benefit from pain
6
7 management programs that are of sufficient quality and duration.³⁶ Where patients
8
9 have not received an adequate trial of conservative therapy, they may benefit from
10
11 further exercise programs and other conservative management. It remains unclear
12
13 whether patients who are either unable or unwilling to engage with conservative
14
15 approaches to pain management would benefit from RD based interventions as a
16
17 first-line or isolated modality of treatment. Hence, there should be some reservation
18
19 when considering the use of RD treatment as a first-line, or isolated modality of pain
20
21 management.
22
23
24
25

26
27 Regression to the mean may also have played a role in control group improvements
28
29 since patients in the trial were recruited with elevated pain, responsive to an
30
31 anaesthetic block. Back pain has been shown to have a varied aetiology, with some
32
33 patients experiencing fluctuating levels of pain over time, whilst other experience
34
35 constant high levels of pain.^{37,38} For the majority of trials that reported it, duration of
36
37 back pain in participants prior to enrolment was 2-5 years and a proportion of these
38
39 were likely to have had high levels of constant pain. Some, however, may have been
40
41 experiencing fluctuating or recurrent pain within this period since the actual inclusion
42
43 criteria for most trials was pain for >3 or 6 months based on patient recall. If they
44
45 were recruited at a point where their pain had flared acutely, there would be a natural
46
47 tendency for that painful episode to resolve over time.
48
49
50

51 52 *Strengths and limitations* 53

54
55 A major strength of this review is that it collates a larger body of evidence than
56
57 previous systematic reviews, with the addition of a number of recent trials and
58
59 thorough assessment of the quality of the evidence. The review is able to tentatively
60

1
2
3 answer the question about the effectiveness of RD for back pain; an assertion that,
4
5 to date, has proved to be very difficult due a paucity of evidence in this field.
6
7

8 This review utilises evidence from a previous Cochrane review¹¹ but the inclusion
9
10 criteria for our review had a narrower scope (included only sham- or conservative
11
12 management-controlled trials of conventional neuro-ablative RD). Since the previous
13
14 review appears to be of high quality, and we updated it with a thorough search of the
15
16 literature to date, there is assurance that all relevant trials were included.
17
18

19
20 A limitation of this review is that it was difficult to truly assess risk of bias in trials
21
22 included in the review. Trial integrity rested heavily on the blinding of participants and
23
24 the outcome was likely to be highly subject to patients' preconceptions of the
25
26 different interventions given. Most trials did not report information that providers gave
27
28 patients about the different possible treatment arms e.g. did providers suggest to
29
30 patients that RD was the effective treatment and that sham or no treatment would be
31
32 ineffective? Where blinding was broken, these viewpoints may have influenced
33
34 patients' response. In some of the sham-controlled studies this was clearly evident.
35
36 For example, in some studies, before randomisation, patients were told that, if
37
38 randomised to sham, they could receive RD if they gained no benefit. Where blinding
39
40 was broken, these opinions were likely to influence patients' perception of their pain.
41
42 In other studies information from providers was not reported and it is difficult to
43
44 assess whether this type of bias occurred.
45
46
47
48
49

50 The review may also be limited in its ability to ascertain the technical quality of
51
52 individual research trials. Even when examining the reported trial methodology, it is
53
54 difficult to conclusively identify trials that employed procedures that may be more or
55
56 less successful in denervating the specific lumbosacral anatomy. Some aspects of
57
58 RD procedures in earlier trials are considered outdated^{39,40} but the advantages of
59
60

1
2
3 more recent procedures for RD remain unproven, and there is no clear evidence of
4 their superiority. Sensitivity analysis based on technical quality was therefore
5 considered unhelpful and not performed.
6
7
8
9

10 The review is also limited by the lack of long term data from trials. Most studies do
11 not attempt to blind patients for more than 3 months and the longer follow up
12 outcomes are considered to be at higher risk of bias. It is still therefore unclear
13 whether RD of lumbosacral anatomy has long-term benefits for back pain.
14
15
16
17
18

19 Finally, the review is limited in its ability to identify any aspects of patient or
20 intervention characteristics that may make RD treatment more likely to be beneficial.
21
22

23 There is to date no reliable predictor of benefit on back pain for RD procedures
24 based on clinical or imaging findings or diagnostic injections.⁴¹ The relative
25 advantages of different RD technologies used in included trials (e.g. 'cooled'^{25,26,32}
26 and 'bipolar'^{30,32} RD) remains to be established. Due to the small number of studies
27 at each time point, sub-group analysis was not considered appropriate. However, the
28 publication of more sham-controlled trials and trials comparing different RD
29 technologies may make this type of investigation possible. Technical advances and
30 advances in knowledge and experience may allow for better selection of anatomical
31 targets and patients for RD and hence improve clinical outcomes: it is important that
32 these developments are formally assessed and published.
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

48 In conclusion, within the limitations in this review and the published literature, there
49 appears to be at least short-term benefit from RD of selected lumbosacral
50 anatomical targets for chronic back pain. However, the mean size of effect appears
51 to be small and, overall, clinical significance may be marginal. Hence, chronic back
52 pain remains a highly challenging condition to treat.
53
54
55
56
57
58
59
60

1
2
3
4
5
6 **Acknowledgements** Thanks to Julie Aikens and Kerry Herbert at Hinchingsbrooke
7
8 Healthcare Library for their assistance in designing and running the search strategies
9
10 for the review.
11
12

13 **Contributors:** MC contributed to the planning of this work, selected articles for
14
15 inclusion, extracted data, quality assessed studies and drafted and re-drafted the
16
17 manuscript. RL contributed to the planning of this work, reviewed the manuscript and
18
19 approved the final version. PT extracted data from the trials, reviewed the
20
21 manuscript and approved the final version. MA contributed to the planning of this
22
23 work, reviewed the manuscript and approved the final version. ML contributed to the
24
25 planning of this work, reviewed the manuscript and approved the final version.
26
27
28
29

30 **Funding** This research received no specific grant from any funding agency in the
31
32 public, commercial or not-for-profit sectors. RL is supported by the Medical Research
33
34 Council (MC_UU_12015/2). MCL is supported by AABGI Foundation project grant
35
36 (RCZB/071).
37
38
39

40 **Competing interests** None declared.
41

42 **Patient consent for publication** Not required.
43
44

45 **Provenance and peer review** Not commissioned; externally peer reviewed.
46
47

48 **Data availability statement** All data relevant to the study are included in the article
49
50 or uploaded as supplementary information.
51
52

53 **Patient and Public Involvement** This research was done without patient
54
55 involvement.
56
57
58
59
60

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

References

- 1 Hartvigsen J, Hancock MJ, Kongsted A, *et al*. What low back pain is and why we need to pay attention. *Lancet* 2018;**391**:2356–67. doi:10.1016/S0140-6736(18)30480-X
- 2 Hoy D, Bain C, Williams G, *et al*. A systematic review of the global prevalence of low back pain. *Arthritis Rheum* 2012;**64**:2028–37. doi:10.1002/art.34347
- 3 Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain* 2000;**84**:95–103. doi:10.1016/S0304-3959(99)00187-6
- 4 Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *Spine J* 2008;**8**:8–20. doi:10.1016/j.spinee.2007.10.005
- 5 National Institute of Health and Care Excellence. Low back pain and sciatica in over 16s: assessment and management. 2016.
- 6 Chou R, Baisden J, Carragee EJ, *et al*. Surgery for Low Back Pain: A Review of the Evidence for an American Pain Society Clinical Practice Guideline. *Spine (Phila Pa 1976)* 2009;**34**:1094–109.
- 7 Chou R, Loeser JD, Owens DK, *et al*. Interventional Therapies, Surgery, and Interdisciplinary Rehabilitation for Low Back Pain: An Evidence-Based Clinical

- 1
2
3 Practice Guideline From the American Pain Society. *Spine (Phila Pa 1976)*
4
5 2009;**34**:1066–77. doi:10.1097/BRS.0b013e3181a1390d
6
7
- 8 8 Kline M. Radiofrequency techniques in clinical practice. In: *Waldman SD,*
9
10 *Winnie AP, eds. Interventional Pain Management. Philadelphia, PA: Saunders.*
11
12 1996.
13
14
- 15 9 Wray JK, Dixon B, Przkora R. *Radiofrequency Ablation*. 2019.
16
17
- 18 10 Manchikanti L, Hirsch J, Pampati V, *et al*. Utilization of Facet Joint and
19
20 Sacroiliac Joint Interventions in Medicare Population from 2000 to 2014:
21
22 Explosive Growth Continues! *Curr Pain Headache Rep* 2016;**20**:58.
23
24
25
- 26 11 Maas E, Ostelo R, Niemisto L, *et al*. Radiofrequency denervation for chronic
27
28 low back pain. *Cochrane Database Syst Rev* 2015;:Art. No.: CD008572.
29
30 doi:10.1001/jama.2017.16386
31
32
- 33 12 Brandon R, Cohen D, Edward T, *et al*. Pulsed Radiofrequency
34
35 Neuromodulation in Interventional Pain Management—A Growing Technology.
36
37 *J Radiol Nurs* 2018;**37**:181–7.
38
39
- 40 13 Schünemann H, Brožek J, Guyatt G, *et al.*, editors. *GRADE Handbook:*
41
42 *Handbook for grading the quality of evidence and the strength of*
43
44 *recommendations using the GRADE approach*.
45
46
47
- 48 14 Higgins JP, Savovic J, Page MJ, *et al.*, editors. *Revised Cochrane risk-of-bias*
49
50 *tool for randomized trials (RoB 2)*. 2019.
51
52
- 53 15 Juch JNS, Maas ET, Ostelo RWJG, *et al*. Effect of Radiofrequency
54
55 Denervation on Pain Intensity Among Patients With Chronic Low Back Pain.
56
57 *JAMA* 2017;**318**:68–81.
58
59
60

- 1
2
3 16 Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen:
4 The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
5
6
7
8 17 Gallagher J, Petriccione di Vadi P, Wedley J, *et al*. Radiofrequency facet joint
9 denervation in the treatment of low back pain: a prospective controlled double-
10 blind study to assess its efficacy. *Pain Clin* 1994;**7**:193–8.
11
12
13
14
15 18 Leclaire R, Fortin L, Lambert R, *et al*. Radiofrequency Facet Joint Denervation
16 in the Treatment of Low Back Pain: A Placebo-Controlled Clinical Trial to
17 Assess Efficacy. *Spine (Phila Pa 1976)* 2001;**26**:1411–6.
18
19
20
21
22
23
24
25
26 19 Moussa WMM, Khedr W. Percutaneous radiofrequency facet capsule
27 denervation as an alternative target in lumbar facet syndrome. *Clin Neurol*
28
29
30
31
32
33 20 van Kleef M, Barendse GAM, Kessels A, *et al*. Randomised trial of
34 radiofrequency lumbar facet denervation for chronic low back pain. *Spine*
35
36
37
38
39
40 21 Van Tilburg CWJ, Schuurmans FA, Stronks DL, *et al*. Randomized sham-
41 controlled double-blind multicenter clinical trial to ascertain the effect of
42 percutaneous radiofrequency treatment for sacroiliac joint pain: Three-month
43 results. *Clin J Pain* 2016;**32**:921–6. doi:10.1097/AJP.0000000000000351
44
45
46
47
48
49
50 22 Van Wijk RMAW, Geurts JWM, Wynne HJ, *et al*. Radiofrequency denervation
51 of lumbar facet joints in the treatment of chronic low back pain: A randomized,
52 double-blind, sham lesion-controlled trial. *Clin J Pain* 2005;**21**:335–44.
53
54
55
56
57 23 Nath S, Nath CA, Pettersson K. Percutaneous Lumbar Zygapophysial (Facet)
58 Joint Neurotomy Using Radiofrequency Current, in the Management of
59
60

- 1
2
3 Chronic Low Back Pain. *Spine (Phila Pa 1976)* 2008;**33**:1291–1297.
4
5 doi:10.1109/ICCGI.2010.42
6
7
- 8 24 Tekin I, Mirzai H, Ok G, *et al.* A comparison of conventional and pulsed
9 radiofrequency denervation in the treatment of chronic facet joint pain. *Clin J*
10 *Pain* 2007;**23**:524–9. doi:10.1097/AJP.0b013e318074c99c
11
12
13
14
15 25 Cohen SP, Hurley RW, Buckenmaier CC, *et al.* Randomized Placebo-
16 Controlled Study Evaluating Lateral Branch Radiofrequency Denervation for
17 Sacroiliac Joint Pain. *Anesthesiology* 2008;**109**:279–88.
18
19
20
21
22
23
24
25
26 26 Patel N, Gross A, Brown L, *et al.* A Randomized, Placebo-Controlled Study to
27 Assess the Efficacy of Lateral Branch Neurotomy for Chronic Sacroiliac Joint
28 Pain. *Pain Med* 2012;**13**:383–98. doi:10.1111/j.1526-4637.2012.01328.x
29
30
31
32
33 27 Van Tilburg C, Stronks D, Groeneweg J, *et al.* Randomised sham-controlled
34 double-blind multicentre clinical trial to ascertain the effect of percutaneous
35 radiofrequency treatment for lumbar facet joint pain. *Spine (Phila Pa 1976)*
36
37
38
39
40
41
42
43 28 Mehta V, Poply K, Husband M, *et al.* The Effects of Radiofrequency
44 Neurotomy Using a Strip-Lesioning Device on Patients with Sacroiliac Joint
45 Pain: Results from a Single-Center, Randomized, Sham-Controlled Trial. *Pain*
46 *Physician* 2018;**21**:607–18.
47
48
49
50
51
52
53 29 Barendse GAM, van den Berg SGM, Kessels AHF, *et al.* Randomized
54 Controlled Trial of Percutaneous Intradiscal Radiofrequency
55 Thermocoagulation for Chronic Discogenic Back Pain. Lack of Effect From a
56
57
58
59
60

- 1
2
3 doi:10.1097/00007632-200102010-00014
4
5
6 30 Kapural L, Vrooman B, Sarwar S, *et al.* A Randomized, Placebo-Controlled
7
8 Trial of Transdiscal Radiofrequency, Biacuplasty for Treatment of Discogenic
9
10 Lower Back Pain. *Pain Med* 2013;**14**:362–73. doi:10.1111/pme.12023
11
12
13 31 van Tilburg CWJ, Stronks DL, Groeneweg JG, *et al.* Randomized sham-
14
15 controlled, double-blind, multicenter clinical trial on the effect of percutaneous
16
17 radiofrequency at the ramus communicans for lumbar disc pain. *Eur J Pain*
18
19 2017;**21**:520–9. doi:10.1002/ejp.945
20
21
22
23 32 Desai MJ, Kapural L, Petersohn JD, *et al.* A prospective, randomized,
24
25 multicenter, open-label clinical trial comparing intradiscal biacuplasty to
26
27 conventional medical management for discogenic lumbar back pain. *Spine*
28
29 (*Phila Pa 1976*) 2016;**41**:1065–74. doi:10.1097/BRS.0000000000001412
30
31
32
33 33 Kvarstein G, Måwe L, Indahl A, *et al.* A randomized double-blind controlled trial
34
35 of intra-annular radiofrequency thermal disc therapy - A 12-month follow-up.
36
37 *Pain* 2009;**145**:279–86. doi:10.1016/j.pain.2009.05.001
38
39
40
41 34 Fischgrund JS, Rhyne A, Franke J, *et al.* Intraosseous basivertebral nerve
42
43 ablation for the treatment of chronic low back pain: a prospective randomized
44
45 double-blind sham-controlled multi-center study. *Eur Spine J* 2018;**27**:1146–
46
47 56. doi:10.1007/s00586-018-5496-1
48
49
50 35 The Cochrane Collaboration. Introduction to sources of bias in clinical trials. In:
51
52 *Cochrane Handbook for Systematic Reviews of Interventions*. 2011.
53
54
55 36 Morley S, Williams A, Hussain S. Estimating the clinical effectiveness of
56
57 cognitive behavioural therapy in the clinic: Evaluation of a CBT informed pain
58
59 management programme. *Pain* 2008;**137**:670–80.
60

- 1
2
3 37 Dunn K, Croft P. Epidemiology and natural history of low back pain. *Eura*
4
5 *Medicophys* 2004;**40**:9–13.
6
7
8 38 Dunn K, Jordan K, Croft P. Characterizing the course of low back pain: a latent
9
10 class analysis. *Am J Epidemiol* 2006;**63**:754–61.
11
12
13 39 Dreyfuss P, Baker R. Comment on: Radiofrequency facet joint denervation in
14
15 the treatment of low back pain: a placebo-controlled clinical trial to assess
16
17 efficacy. *Spine (Phila Pa 1976)* 2002;**27**:556–7.
18
19
20 40 Kapural L, Provenzano D, Narouze S. RE: Juch JNS, et al. Effect of
21
22 Radiofrequency Denervation on Pain Intensity Among Patients With Chronic
23
24 Low Back Pain: The Mint Randomized Clinical Trials. *JAMA* 2017;**318**(1):68–
25
26 81. *Neuromodulation* 2017;**20**:844. doi:10.1111/ner.12729
27
28
29 41 Cohen SP, Julie JH, Brummett C. Facet joint pain-advances in patient
30
31 selection and treatment. *Nat Rev Rheumatol* 2013;**9**:101–16.
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1 Results of the meta-analyses of randomised controlled trials

	All trials					Sham controlled trials				
	k	N	MD (95% CI)	I ²	GRADE*	k	N	MD (95% CI)	I ²	GRADE*
RD of the facet joints										
1-3 months	7	599	-0.56 (-1.13, 0.01)	59%	Low	6	348	-0.63 (-1.39, 0.12)	66%	Low
6 months	4	361	-0.66 (-1.37, 0.05)	42%	Low	3	110	-1.05 (-2.21, 0.10)	32%	Low
1 year	2	291	-0.72 (-2.24, 0.80)	89%	Very low	1	40	-1.50 (-2.21, -0.79)	NA	Very low
RD of the sacroiliac joints										
1-3 months	5	384	-1.53 (-2.62, -0.45)	83%	Low	4	156	-1.89 (-3.45, -0.34)	87%	Very low
6 months	1	228	-0.28 (-1.00, 0.44)	NA	Low					
12 months	1	228	-0.19 (-0.92, 0.54)	NA	Low					
RD of the intervertebrae discs										
1-3 months	4	200	-0.98 (-1.84, -0.12)	40%	Low	3	144	-0.63 (-1.36, 0.10)	0%	Low
6 months	3	127	-1.74 (-2.58, -0.91)	0%	Low	2	75	-1.63 (-2.58, -0.68)	0%	Low
12 months	1	20	-1.70 (-3.63, 0.23)	NA	Very low	1	20	-1.70 (-3.63, 0.23)	NA	Very low
RD of the vertebrae body and endplate										
3 months	1	205	-0.34 (-1.09, 0.41)	NA	Moderate	1	205	-0.34 (-1.09, 0.41)	NA	Moderate
6 months	1	205	-0.67 (-1.44, 0.10)	NA	Moderate	1	205	-0.67 (-1.44, 0.10)	NA	Moderate
12 months	1	205	-0.50 (-1.29, 0.29)	NA	Moderate	1	205	-0.50 (-1.29, 0.29)	NA	Moderate

k, number of trials; N, number of participants; MD, Mean difference.

*GRADE assessment of the quality of the evidence

Figure 1 PRISMA flow diagram

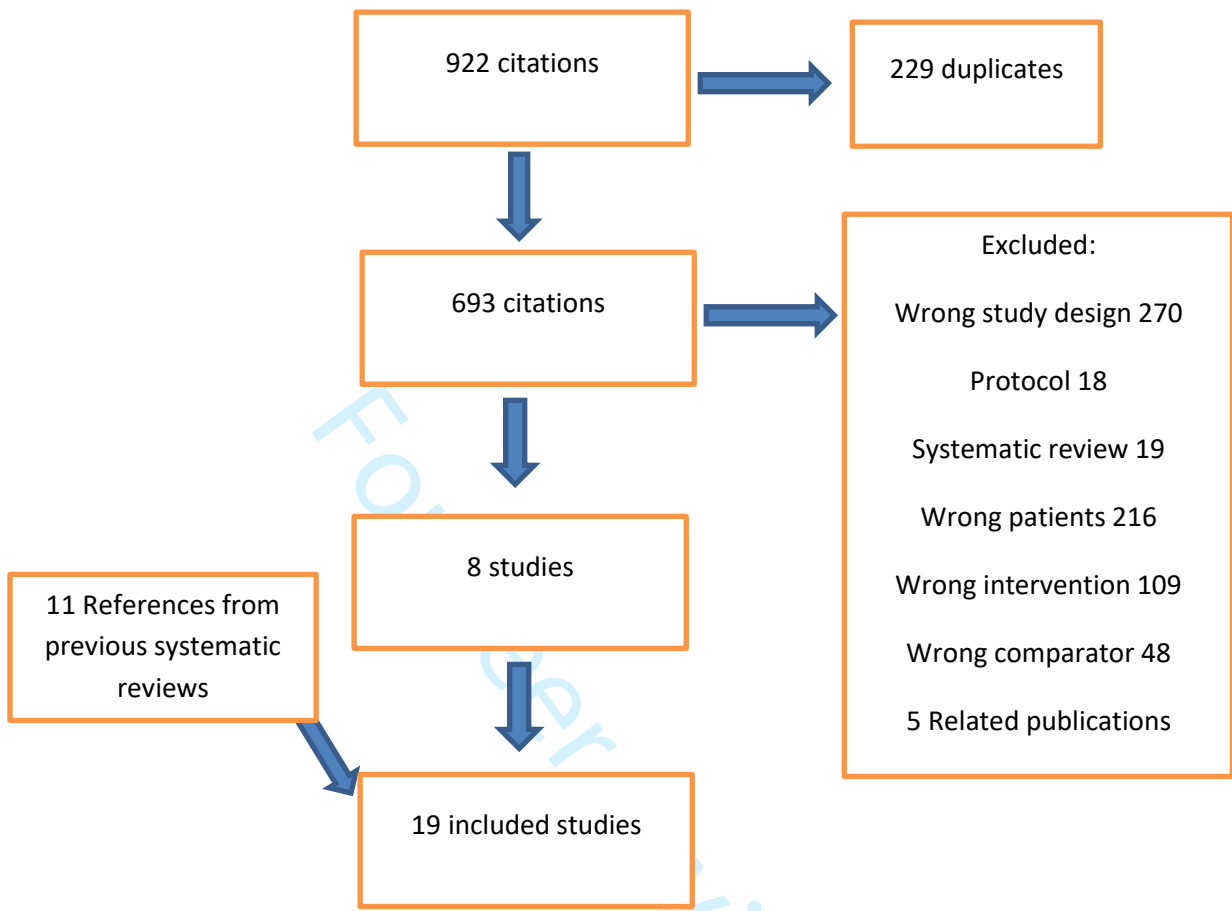
Figure 2 Post treatment pain score for radiofrequency denervation of the facet joints versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

Figure 3 Post treatment pain score for radiofrequency denervation of the sacroiliac joints versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

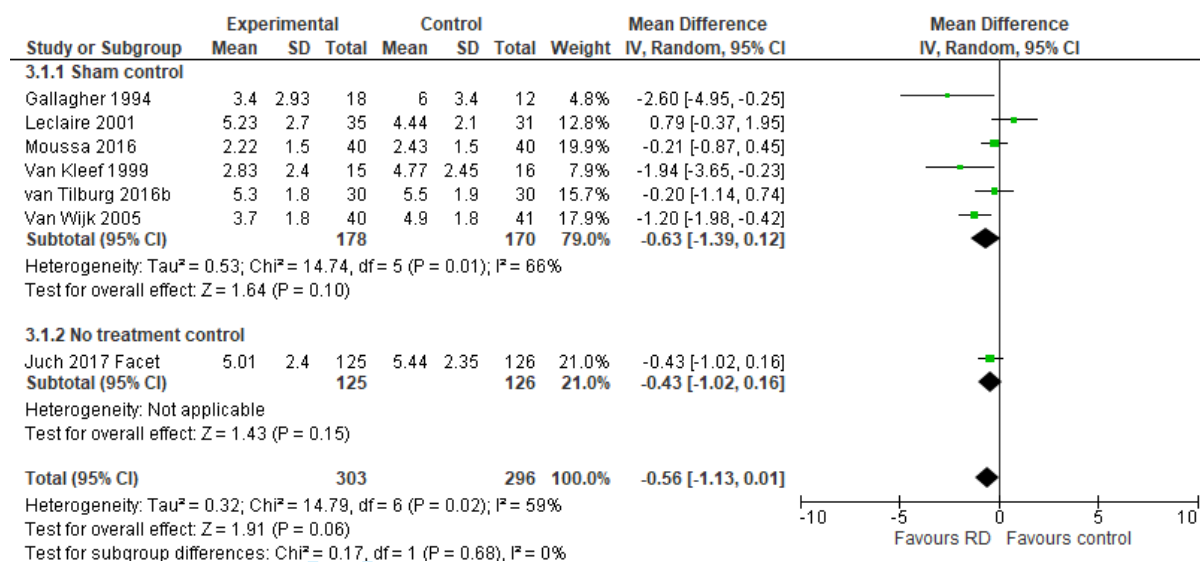
Figure 4 Post treatment pain score for radiofrequency denervation of the intervertebral discs versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

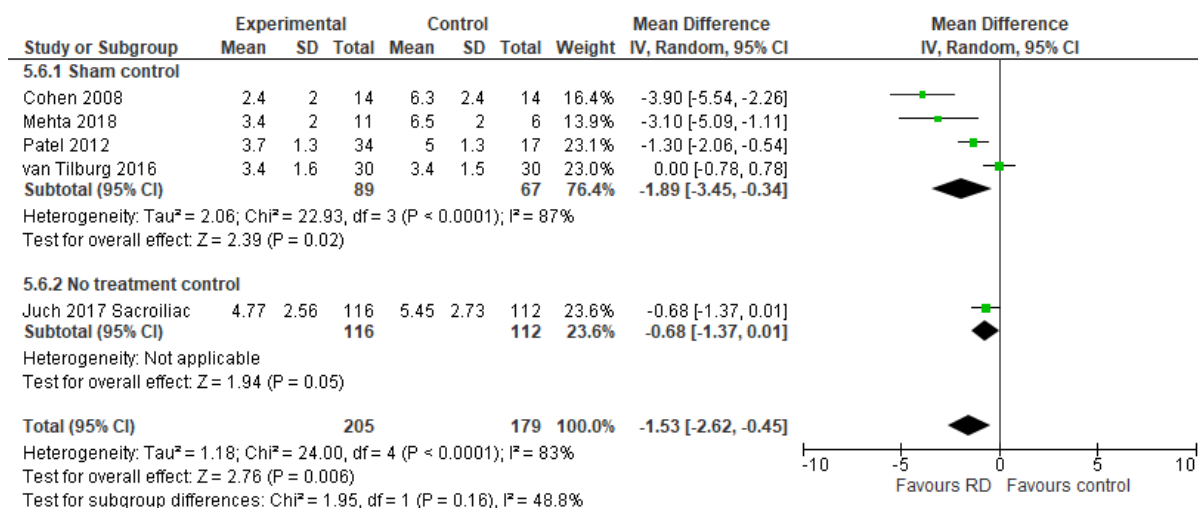
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

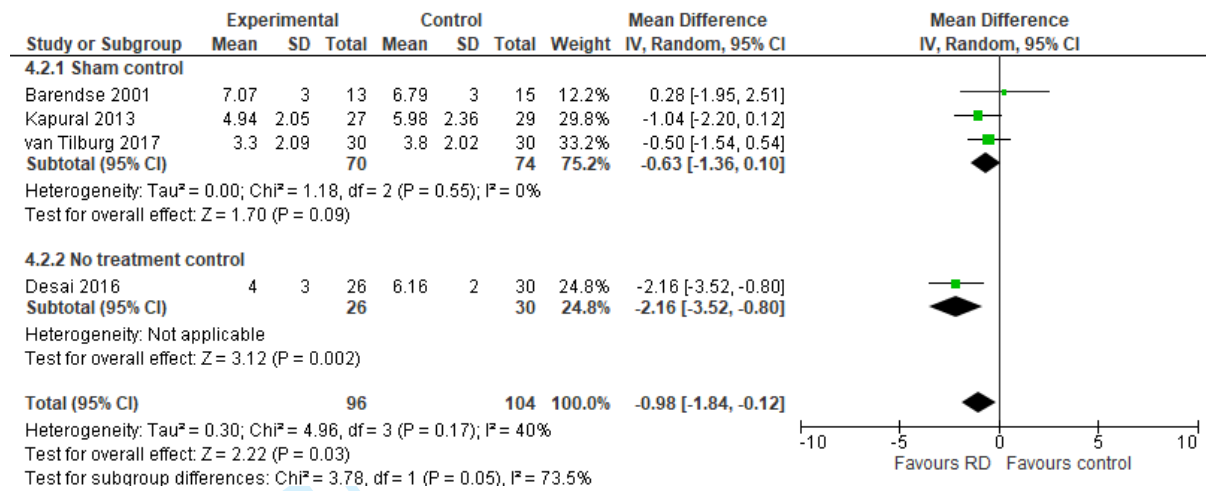
For peer review only



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60







Appendix 1 Search strategies

Medline and Embase

#	Database	Search term
1	Medline	(randomized controlled trial).pt
2	Medline	(controlled clinical trial).pt
3	Medline	(randomi*ed).ab
4	Medline	(placebo).ti,ab
5	Medline	(drug therapy).fs
6	Medline	(randomly).ti,ab
7	Medline	(trial).ti,ab
8	Medline	(groups).ti,ab
9	Medline	(1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)
10	Medline	(animals NOT (humans AND animals)).su
11	Medline	9 not 10
12	Medline	(dorsalgia).ti,ab
13	Medline	exp "BACK PAIN"/
14	Medline	(backache).ti,ab
15	Medline	(lumbar ADJ pain).ti,ab
16	Medline	(coccyx).ti,ab
17	Medline	(coccydynia).ti,ab
18	Medline	(sciatica).ti,ab
19	Medline	"SCIATIC NEUROPATHY"/

1			
2			
3	20	Medline	(spondylosis).ti,ab
4			
5	21	Medline	(lumbago).ti,ab
6			
7			
8	22	Medline	(12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20
9			OR 21)
10			
11	23	Medline	exp SPINE/
12			
13			
14	24	Medline	(discitis).ti,ab
15			
16			
17	25	Medline	exp "SPINAL DISEASES"/
18			
19	26	Medline	(disc ADJ degeneration).ti,ab
20			
21			
22	27	Medline	(disc ADJ prolapse).ti,ab
23			
24			
25	28	Medline	(disc ADJ herniation).ti,ab
26			
27	29	Medline	(spinal fusion).su
28			
29			
30	30	Medline	(facet ADJ joints).ti,ab
31			
32			
33	31	Medline	(intervertebral disc).su
34			
35	32	Medline	(postlaminectomy).ti,ab
36			
37			
38	33	Medline	(arachnoiditis).ti,ab
39			
40			
41	34	Medline	(failed ADJ back).ti,ab
42			
43	35	Medline	(23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31
44			OR 32 OR 33 OR 34)
45			
46	36	Medline	(22 OR 35)
47			
48			
49	37	Medline	exp "RADIO WAVES"/
50			
51			
52	38	Medline	exp "PULSED RADIOFREQUENCY TREATMENT"/
53			
54	39	Medline	(radiofrequency).af
55			
56			
57	40	Medline	(radio frequency).af
58			
59			
60			

- 1
2
3 41 Medline exp ELECTROCOAGULATION/
4
5
6 42 Medline (electrocoag*).af
7
8 43 Medline (thermocoag*).af
9
10
11 44 Medline neurotom* OR (neuroly*).af
12
13 45 Medline (37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44)
14
15
16 46 Medline (11 AND 36 AND 45)
17
18 47 EMBASE "CLINICAL TRIAL"/
19
20
21 48 EMBASE "CONTROLLED CLINICAL TRIAL"/
22
23
24 49 EMBASE "CONTROLLED STUDY"/
25
26
27 50 EMBASE "RANDOMIZED CONTROLLED TRIAL"/
28
29
30 51 EMBASE "DOUBLE BLIND PROCEDURE"/
31
32
33 52 EMBASE "SINGLE BLIND PROCEDURE"/
34
35
36 53 EMBASE "CROSSOVER PROCEDURE"/
37
38
39 54 EMBASE PLACEBO/
40
41 55 EMBASE (allocat*).ti,ab
42
43 56 EMBASE (assign*).ti,ab
44
45 57 EMBASE (blind*).ti,ab
46
47 58 EMBASE (clinic* ADJ25 (study OR trial)).ti,ab
48
49
50 59 EMBASE (crossover OR cross-over).ti,ab
51
52
53 60 EMBASE (factorial*).ti,ab
54
55
56 61 EMBASE (followup OR follow-up).ti,ab
57
58 62 EMBASE (prospectiv*).ti,ab
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 63 EMBASE (placebo*).ti,ab
- 64 EMBASE (random*).ti,ab
- 65 EMBASE ((singl* OR doubl* OR trebl* OR trip*) ADJ25 (blind* OR mask*)).ti,ab
- 66 EMBASE (volunteer*).ti,ab
- 67 EMBASE (47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66)
- 68 EMBASE exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
- 69 EMBASE exp ANIMALS/
- 70 EMBASE exp INVERTEBRATE/
- 71 EMBASE ANIMAL EXPERIMENT/
- 72 EMBASE ANIMAL MODEL/
- 73 EMBASE ANIMAL TISSUE/
- 74 EMBASE ANIMAL CELL/
- 75 EMBASE NONHUMAN/
- 76 EMBASE 71 or 72 or 73 or 74 or 75
- 77 EMBASE exp ANIMALS/
- 78 EMBASE exp INVERTEBRATE/
- 79 EMBASE (76 OR 77 OR 78)
- 80 EMBASE 77 or 78
- 81 EMBASE HUMAN/ OR NORMAL HUMAN/ OR HUMAN CELL/
- 82 EMBASE (76 AND 77 AND 78 AND 81)

- 1
2
3 83 EMBASE (dorsalgia).ti,ab
4
5
6 84 EMBASE (back pain).ti,ab
7
8 85 EMBASE exp BACKACHE/
9
10
11 86 EMBASE (lumbar ADJ pain).ti,ab
12
13
14 87 EMBASE (coccyx).ti,ab
15
16 88 EMBASE (coccydynia).ti,ab
17
18
19 89 EMBASE (sciatica).ti,ab
20
21 90 EMBASE ISCHIALGIA/
22
23
24 91 EMBASE (spondylosis).ti,ab
25
26 92 EMBASE (lumbago).ti,ab
27
28
29 93 EMBASE (back disorder*).ti,ab
30
31
32 94 EMBASE (83 OR 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90 OR 91
33 OR 92 OR 93)
34
35 95 EMBASE exp SPINE/
36
37
38 96 EMBASE (discitis OR diskitis).ti,ab
39
40
41 97 EMBASE exp "SPINE DISEASE"/
42
43 98 EMBASE (disc ADJ degeneration).ti,ab
44
45
46 99 EMBASE (disc ADJ prolapse).ti,ab
47
48
49 100 EMBASE (disc ADJ herniation).ti,ab
50
51 101 EMBASE (spinal fusion).ti,ab
52
53 102 EMBASE (facet ADJ joints).ti,ab
54
55
56 103 EMBASE (intervertebral disk OR Intervertebral disc).ti,ab
57
58
59 104 EMBASE (postlaminectomy).ti,ab
60

1		
2		
3	105	EMBASE (arachnoiditis).ti,ab
4		
5	106	EMBASE (failed ADJ back).ti,ab
6		
7		
8	107	EMBASE (95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102 OR
9		103 OR 104 OR 105 OR 106)
10		
11	108	EMBASE 94 or 107
12		
13		
14	109	EMBASE exp PULSED RADIOFREQUENCY TREATMENT/
15		
16		
17	110	EMBASE exp RADIOFREQUENCY/
18		
19	111	EMBASE exp RADIOFREQUENCY RADIATION/
20		
21		
22	112	EMBASE (radiofrequency OR radio-frequency).ti,ab
23		
24		
25	113	EMBASE exp THERMOCOAGULATION/ OR thermocoag*
26		
27	114	EMBASE exp ELECTROCOAGULATION/ OR electrocoag*
28		
29		
30	115	EMBASE (neurotom* OR neuroly*).ti,ab
31		
32	116	EMBASE (109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115)
33		
34		
35	117	EMBASE (108 AND 116)
36		
37		
38	118	Medline 46 [DT 2014-2019]
39		
40		
41		

Medline in process

#	Database	Search term
44		
45		
46		
47	1	Medline ("randomi*ed controlled trial").ti,ab
48		
49	2	Medline ("controlled clinical trial").ti,ab
50		
51		
52	3	Medline ("randomi*ed").ab
53		
54	4	Medline (placebo).ti,ab
55		
56		
57	5	Medline ("drug therapy").fs
58		
59		
60		

- 1
2
3 6 Medline (randomly).ti,ab
4
5
6 7 Medline (trial).ti,ab
7
8 8 Medline (groups).ti,ab
9
10
11 9 Medline (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)
12
13 10 Medline (dorsalgia).ti,ab
14
15
16 11 Medline ("back pain").ti,ab
17
18
19 12 Medline (backache).ti,ab
20
21 13 Medline ("lumber pain").ti,ab
22
23
24 14 Medline (coccyx).ti,ab
25
26 15 Medline (coccydynia).ti,ab
27
28
29 16 Medline (sciatica*).ti,ab
30
31
32 17 Medline (spondylosis).ti,ab
33
34 18 Medline (lumbago).ti,ab
35
36
37 19 Medline (10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
38 OR 18)
39
40 20 Medline (spine OR sacrum OR "lumber vertebrae" OR
41 "intervertebral disc*").ti,ab
42
43
44 21 Medline (discitis).ti,ab
45
46
47 22 Medline ("disc degeneration").ti,ab
48
49 23 Medline ("disc prolapse").ti,ab
50
51
52 24 Medline ("disc herniation").ti,ab
53
54 25 Medline ("spinal fusion").ti,ab
55
56
57 26 Medline ("facet joints").ti,ab
58
59
60

1		
2		
3	27	Medline (postlaminectomy).ti,ab
4		
5	28	Medline (arachnoiditis).ti,ab
6		
7		
8	29	Medline ("failed back").ti,ab
9		
10		
11	30	Medline (20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27
12		OR 28 OR 29)
13		
14	31	Medline (19 OR 30)
15		
16		
17	32	Medline (radiowave* OR "radio wave*").ti,ab
18		
19		
20	33	Medline (radiofrequency OR "radio frequency").ti,ab
21		
22	34	Medline (electrocoag*).ti,ab
23		
24		
25	35	Medline (thermocoag*).ti,ab
26		
27		
28	36	Medline (neurotom* OR neuroloy*).ti,ab
29		
30	37	Medline (32 OR 33 OR 34 OR 35 OR 36)
31		
32		
33	38	Medline (9 AND 31 AND 37)
34		
35	39	Medline 38 [Document status In Data Review OR In Process
36		OR PubMed not MEDLINE OR Publisher]
37		
38		
39		

Cinahl

#	Database	Search term
41		
42		
43		
44		
45	1	CINAHL exp "CLINICAL TRIALS"/
46		
47		
48	2	CINAHL ("randomi*ed controlled trial*").ti,ab
49		
50		
51	3	CINAHL (clinical ADJ3 trial).ti,ab
52		
53		
54	4	CINAHL (double-blind).ti,ab
55		
56	5	CINAHL (single-blind).ti,ab
57		
58		
59	6	CINAHL (triple-blind).ti,ab
60		

- 1
2
3 7 CINAHL (1 OR 2 OR 3 OR 4 OR 5 OR 6)
4
5
6 8 CINAHL "PLACEBO EFFECT"/
7
8 9 CINAHL PLACEBOS/
9
10
11 10 CINAHL (placebo*).ti,ab
12
13 11 CINAHL (random*).ti,ab
14
15
16 12 CINAHL (8 OR 9 OR 10 OR 11)
17
18
19 13 CINAHL "RANDOM SAMPLE"/
20
21 14 CINAHL exp "STUDY DESIGN"/
22
23
24 15 CINAHL (latin square).ti,ab
25
26 16 CINAHL exp "COMPARATIVE STUDIES"/
27
28
29 17 CINAHL exp "EVALUATION RESEARCH"/
30
31
32 18 CINAHL exp "PROSPECTIVE STUDIES"/
33
34 19 CINAHL (13 OR 14 OR 15 OR 16 OR 17 OR 18)
35
36
37 20 CINAHL (follow-up stud*).ti,ab
38
39 21 CINAHL (followup stud*).ti,ab
40
41
42 22 CINAHL (control*).ti,ab
43
44
45 23 CINAHL (prospectiv*).ti,ab
46
47 24 CINAHL (volunteer*).ti,ab
48
49
50 25 CINAHL (20 OR 21 OR 22 OR 23 OR 24)
51
52 26 CINAHL (7 OR 12 OR 19 OR 25)
53
54
55 27 CINAHL ANIMALS/
56
57 28 CINAHL 26 not 27
58
59
60

- 1
2
3 29 CINAHL ("dorsalgia").ti,ab
4
5
6 30 CINAHL exp "BACK PAIN"/
7
8 31 CINAHL "LOW BACK PAIN"/
9
10
11 32 CINAHL ("backache").ti,ab
12
13 33 CINAHL (lumbar ADJ1 pain).ti,ab
14
15
16 34 CINAHL (lumbar ADJ5 pain).ti,ab
17
18
19 35 CINAHL (29 OR 30 OR 31 OR 32 OR 33 OR 34)
20
21 36 CINAHL COCCYX/
22
23
24 37 CINAHL SCIATICA/
25
26 38 CINAHL (sciatica).ti,ab
27
28
29 39 CINAHL (coccyx).ti,ab
30
31
32 40 CINAHL (coccydynia).ti,ab
33
34 41 CINAHL "LUMBAR VERTEBRAE"/
35
36
37 42 CINAHL (lumbar ADJ2 vertebra).ti,ab
38
39
40 43 CINAHL (36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42)
41
42 44 CINAHL "THORACIC VERTEBRAE"/
43
44
45 45 CINAHL exp SPONDYLOLYSIS/
46
47 46 CINAHL (lumbago).ti,ab
48
49
50 47 CINAHL (44 OR 45 OR 46)
51
52 48 CINAHL (35 OR 43 OR 47)
53
54
55 49 CINAHL (28 AND 48)
56
57
58 50 CINAHL (radiofrequency OR radio-frequency).ti,ab
59
60

1		
2		
3	51	CINAHL
4		(thermocoag*).ti,ab
5		
6	52	CINAHL
7		exp ELECTROCOAGULATION/ OR electrocoag*
8		
9	53	CINAHL
10		(neurotom* OR neuroly*).ti,ab
11		
12	54	CINAHL
13		"RADIO WAVES"/
14		
15	55	CINAHL
16		(50 OR 51 OR 52 OR 53 OR 54)
17		
18	56	CINAHL
19		(49 AND 55)
20		
21	57	CINAHL
22		56 [DT 2014-2019]

Cochrane

#	Database	Search term
23		
24		
25		
26		
27		
28	1	Cochrane
29		MeSH descriptor: [Back Pain] explode all trees
30		
31	2	Cochrane
32		dorsalgia
33		
34	3	Cochrane
35		backache
36		
37	4	Cochrane
38		MeSH descriptor: [Low Back Pain] explode all trees
39		
40	5	Cochrane
41		lumbar next pain or coccyx or coccydynia or spondylosis
42		
43	6	Cochrane
44		MeSH descriptor: [Spine] explode all trees
45		
46	7	Cochrane
47		MeSH descriptor: [Spinal Diseases] explode all trees
48		
49	8	Cochrane
50		lumbago OR discitis OR disc near degeneration OR disc near prolapse OR disc near herniation
51		
52	9	Cochrane
53		spinal fusion
54		
55	10	Cochrane
56		facet near joints
57		
58	11	Cochrane
59		MeSH descriptor: [Intervertebral Disk] explode all trees
60		
	12	Cochrane
		postlaminectomy

1			
2			
3	13	Cochrane	arachnoiditis
4			
5			
6	14	Cochrane	failed near back
7			
8	15	Cochrane	MeSH descriptor: [Cauda Equina] explode all trees
9			
10			
11	16	Cochrane	lumbar near vertebra*
12			
13			
14	17	Cochrane	spinal near stenosis
15			
16	18	Cochrane	slipped near (disc* or disk*)
17			
18			
19	19	Cochrane	degenerat* near (disc* or disk*)
20			
21	20	Cochrane	stenosis near (spine or root or spinal)
22			
23			
24	21	Cochrane	displace* near (disc* or disk*)
25			
26	22	Cochrane	prolap* near (disc* or disk*)
27			
28			
29	23	Cochrane	MeSH descriptor: [Sciatic Neuropathy] explode all trees
30			
31			
32	24	Cochrane	sciatic*
33			
34			
35	25	Cochrane	back disorder*
36			
37	26	Cochrane	back near pain
38			
39			
40	27	Cochrane	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
41			
42			
43			
44	28	Cochrane	MeSH descriptor: [Radio Waves] explode all trees
45			
46			
47	29	Cochrane	MeSH descriptor: [Pulsed Radiofrequency Treatment] explode all trees
48			
49			
50	30	Cochrane	radiofrequency
51			
52			
53	31	Cochrane	radio frequency or radio-frequency
54			
55			
56	32	Cochrane	MeSH descriptor: [Electrocoagulation] explode all trees
57			
58	33	Cochrane	electrocoag*
59			
60			

- 1
2
3 34 Cochrane thermocoag*
4
5
6 35 Cochrane neurotom* or neuroly*
7
8 36 Cochrane #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35
9
10
11 37 Cochrane #27 and #36 in Trials
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Appendix 2 Study characteristics

Study	N	Inclusion criteria		Mean age (SD)	Mean pain score (SD)	Intervention	Control	Funding
RD of the facet joints								
Gallagher 1994	41	Low back pain >3 months duration with symptoms typical of facet joint pain	Improvement (n=30) or equivocal (n=11) response to anaesthetic block	NR	VAS RD 5.8 (1.78); Sham 7.2 (1.94)	Nerves above and below painful joint denervated at 80° for 90 seconds.	Nerves also identified with stimulation but no heat lesion made	NR
Juch 2017	251	Low back pain without response to conservative management and considered to be related to the facet joint	Positive response to anaesthetic block (reported 50% pain relief 30-90 minutes after block)	RD 53.0 (11.5); Control 52.6 (10.8)	NRS RD 7.14 (1.38) Control 7.19 (1.29)	Denervation at 90° for 90s of L3-4, L4-5 or L5-S1 with exercise program	Exercise program	The Netherlands Organization for Health Research and Development, by the Dutch Society for Anesthesiology, and the Dutch health insurance companies
Leclaire 2001	70	Low back pain for >3 months	“Significant” relief of back pain for >24h following facet injections	RD 46.7 (9.3); Sham 46.4 (9.8)	VAS RD 5.19 (2.67); Sham 5.15 (2.08)	RD with fluoroscopic guidance at 80°C for 90s of at least 2 levels	Nerves also identified with stimulation but electrode only heated to 37°C	Institut de recherche en sante´ and se´curite´ du travail du Que´bec
Moussa 2016	80	Low back pain for >1 year without response to conservative management	Complete or near complete reduction of CLBP on VAS 30 min after 2	RD capsule 58.1 (NR); RD conventional 56.5 (NR);	VAS RD 8.22 (NR); Sham 7.83 (NR)	RD of facet capsule on medial and lateral aspect or	Same procedure without elect current turned on	No funding received

			injections separated by >2 weeks	Sham 55.9 (NR)		conventional RD at 85°C for 90s		
Nath 2008	40	Low back pain for >2 years, not responded to previous treatment, pain attributable to lumbar facet joints	80% pain relief on 3 medial branch blocks	56 (range, 36–79)	VAS RD 5.98 (NR); Sham 4.38 (NR)	RD at 85°C for 60s with additional lesions just lateral and medial to the target nerve	Same procedure as RD but electrode tip remained at body temperature	No funding received
Tekin 2007	40	Back pain for >6 months with focal pain over the facet joints and unresponsive to conservative treatments	>50% reduction in VAS pain 30 minutes after diagnostic medial branch block	RD 60.5 (8.5); Sham 57.9 (9.3)	VAS RD 6.5 (1.5); Sham 6.8 (1.6)	RD at same levels as diagnostic blocks at 80°C for 90s.	Same procedure as RD but with current switched off	Not reported
Van Kleef 1999	32	Low back pain of >12 months duration, failure of conservative management	>50% reduction in pain following diagnostic nerve block of L3-L5 Baseline VAS score of >4	RD 46.6 (7.4); Sham 41.4 (7.5)	VAS RD 5.2 (1.7); Sham 5.2 (1.6)	RD at 80°C for 60s	Same procedure as RD but with current switched off	The Nederlandse organisatie voor wetenschappelijk
Van Tilburg 2016	60	Low back pain for >3 months and failure of conservative management	Decrease of >2 on medial branch block	RD 65 (12); Sham 58 (12)	NRS RD 7.2 (1.4); Sham 7.4 (0.8)	RD at 80°C for 60s per level for three steps with physiotherapy	Same procedure as RD but with current switched off with physiotherapy	No funding from a commercial party
Van Wijk 2005	81	Low back pain for >6 months	≥50% reduction on	RD 46.9 (11.5);	VAS RD 5.8 (1.8);	RD 80°C for 60 seconds	Same procedure as	Grant from the Dutch Health

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

diagnostic block Sham 48.1 (12.6) Sham 6.5 (1.8) at the levels concerned RD but with current switched off Insurance Council

RD of the sacroiliac joints

Cohen 2008	28	Axial low back or buttock pain ≥ 6 months, tenderness overlying the sacroiliac joint(s), failure to respond to conservative therapy	≥ 75% pain relief for ≥3h following diagnostic sacroiliac joint injection, but back near baseline within 2 months	RD 51.9 (13.6); Sham 51.8 (13.1)	VAS RD 6.1 (1.8); Sham 6.5 (1.9)	RD 80°C for 90 seconds using cooling probe technology (Cooled RD)	Same procedure as RD but no current applied	John P. Murtha Neuroscience and Pain Institute, the Army Regional Anesthesia & Pain Medicine Initiative, and National Institutes of Health grant # MH075884
Juch 2017	228	Low back pain without response to conservative management, considered to be related to the sacroiliac joint.	Positive response to anaesthetic block (reported 50% pain relief 30-90 minutes after block)	RD 51.6 (10.9); Control 51.1 (12.2)	NRS RD 7.17 (1.65); Control 7.06 (1.43)	RD - 60° for 2.5 min per lesion of S1, S2 and S3 with exercise program	Exercise program	The Netherlands Organization for Health Research and Development, by the Dutch Society for Anesthesiology, and the Dutch health insurance companies
Mehta 2018	17	CLBP for >6 months. >5 on NRS	>80% pain reduction on 2 diagnostic blocks	RD 56.6 (NR); Sham 62.6 (NR)	VAS RD 8.1 (0.8); Sham 7.3 (0.8)	RD of the L5 medial branch of the primary dorsal root nerve and strip lesioning of the lateral branches	Identical to active RD treatment except that no RF energy was applied	None

						of the S1, 2, and 3 nerve roots		
Patel 2012	51	Pain for ≥6 months, 3-day average NRS between 4 and 8, failure of conservative management	≥75% pain reduction for 4h-7 days on two sets of anaesthetic blocks and back to baseline by start of the study	RD 56 (15); Sham 64 (14)	NRS RD 6.1 (1.3); Sham 5.8 (1.3)	RD at 60°C for 150s of L5 dorsal ramus and then acral lateral branches of S1, S2 and S3 (cooled RD)	Same procedure as RD but RF energy was not delivered.	Baylis Medical
Van Tilburg 2016	60	Sacroiliac joint pain for >3 months, failure of conservative management	Decrease of ≥2 on NRS following diagnostic block	RD 59.5 (27); Sham 62 (18)	NRS RD 7.2 (1.4); Sham 7.5 (1.2)	85°C each step for 90s, total of 5 steps	Same procedure as RD but no heat lesions made	Not reported
RD of the intervertebral discs								
Barendse 2001	28	Non-specific LBP for >1y, failure of conservative management	>50% pain relief 30 minutes after an analgesic discography at L4–L5 and L5–S1. Patients with multilevel pain excluded	RD 40.8 (7.5); Sham 45.2 (8.4)	VAS RD 6.5 (1.3); Sham 5.5 (1.1)	70°C for 90s without anaesthetic	Same procedure as RD but no current applied	Not reported
Desai 2016	63	Lumbar discogenic pain for ≥6 months, unresponsive to conservative management	Diagnosed via provocation discography - definite single-level concordant	Mean age 41 (11); Control 43 (11)	VAS RD 6.7 (NR); Sham 7 (NR)	RD at 50°C for 15 minutes and then 60°C for 2.5 min (bopolar cooled RD) with conventional	Conventional medical management	Halyard Health, Inc. (formerly Kimberly-Clark Health Care)

			pain on manometry			medical management		
Kapural 2013	55	CLBP unresponsive to conservative management for ≥6 months; no surgical interventions within previous 3 months	Single-level degenerative disc disease or two-level disease without evidence of additional degenerative changes in other disc spaces on MRI	RD 40.4 (10.3); Sham 38.4 (10.4)	VAS RD 7.13 (1.61); Sham 7.18 (1.98)	RD at 45°C bipolar for 15 minutes or 50°C bipolar for 15 minutes and monopolar at 60°C for 2.5 minutes	Mimicked active treatment, except that introducers and electrodes positioned just outside of the disc, and no RF energy delivered	Baylis Medical
Kvarstein 2009	20	Unremitting low back pain for more than 6 months; Pain intensity ≥5 /10 and low back pain greater than leg pain; Failure on conservative treatment	Positive one-level pain provocation discography	RD 44.7 (10.1); Sham 39.6 (8.9)	NRS RD 4.6 (1.8); Sham 5.5 (2.0)	RD increased by 5°C every second minute to 4-min interval at 65°C (from 50°C)	Exposed to a similar intervention, but the annulus was not exposed to RF heating	Radionics, TYCO Healthcare Group provided the discTRODE probes
Van Tilburg 2017	60	Low back pain >3 months and symptoms suggestive of lumbar disc problem	Reduction of ≥2 on a numerical rating scale (0–10) after a diagnostic ramus communicans test block	RD 50.5 (13.9); Sham 50.1 (12.3)	NRS 7.8 (1.05); Sham 7.8 (1.05)	RD treatment at 80 °C for 60s per level	Same procedure but without RF treatment	No support received that influenced submitted work
RD of the vertebrae body and endplate								

1									
2									
3	Fischgrund	225	CLBP ≥6 months,	No diagnostic	RD 46.9	VAS RD 6.73	Thermal	Same	Not reported
4	2018		not responded to	block for	(range 26–	(1.38);	ablation at	procedure as	
5			conservative	inclusion	69); Sham	Sham 6.64	the terminus of	RD but only	
6			treatment, Type 1 or		47.1 (range	(1.34)	the basivertebral	docking	
7			Type 2 Modic		25–69)		nerve 85°C for	introducer	
8			changes required				15 min	cannula 1–2	
9			at the proposed					mm	
10			treatment levels					into the	
11								pedicle and	
12								simulating RD	
13									
14									
15									
16									
17									
18									
19									
20									
21									
22									
23									
24									
25									
26									
27									
28									
29									
30									
31									
32									
33									
34									
35									
36									
37									
38									
39									
40									
41									
42									
43									
44									
45									
46									

CLBP, chronic low back pain; N, number of trials; NRS, numeric rating scale; RD, radiofrequency denervation; SD, standard deviation; VAS, visual analogue scale.

BMJ Open

Radiofrequency denervation for chronic back pain: a systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035540.R2
Article Type:	Original research
Date Submitted by the Author:	15-May-2020
Complete List of Authors:	Chappell, Mary; Cambridgeshire County Council, Public Health Directorate Lakshman, Raj; Cambridgeshire County Council, Public Health Directorate; University of Cambridge, Medical Research Council Epidemiology Unit Trotter, Patrick; Cambridge University Hospitals NHS Foundation Trust Abrahams, Mark; Cambridge University Hospitals NHS Foundation Trust Lee, Michael; University of Cambridge, Division of Anaesthesia
Primary Subject Heading:	Rheumatology
Secondary Subject Heading:	Neurology
Keywords:	Back pain < ORTHOPAEDIC & TRAUMA SURGERY, Rheumatology < INTERNAL MEDICINE, Neurology < INTERNAL MEDICINE, PAIN MANAGEMENT

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **Radiofrequency denervation for chronic back pain: a systematic review and**
4 **meta-analysis**
5
6

7
8 Mary E Chappell¹, Raj Lakshman^{1,2}, Patrick Trotter³, Mark J Abrahams³, Michael C
9 Lee⁴
10

11
12
13 ¹Public Health Directorate, Cambridgeshire County Council, Cambridge, UK
14

15
16 ²Medical Research Council Epidemiology Unit, University of Cambridge, Cambridge
17
18 UK
19

20
21 ³Cambridge University Hospitals NHS Foundation trust, Cambridge, UK
22

23
24 ⁴Division of Anaesthesia, University of Cambridge, Cambridge, UK
25
26
27
28

29
30 Correspondence to: Mary E Chappell, Public Health Directorate, Cambridgeshire
31
32 County Council, Cambridge CB3 0AP, UK. Tel. 01223 729037
33

34
35 Email mary.chappell@cambridgeshire.gov.uk
36
37
38
39

40
41 Word count:

42
43 Abstract 221
44

45
46 Main text 4,188
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To assess the effectiveness of radiofrequency denervation of lumbosacral anatomical targets for the management of chronic back pain.

Design: Systematic review and meta-analysis of randomised controlled trials.

Methods: A database search (Medline, Medline in Process, Embase, CINHAL and the Cochrane library) was conducted to April 2019 for placebo or no-treatment controlled trials of radiofrequency denervation for the management of chronic back pain. Included trials were quality assessed using the Cochrane risk of bias tool and the quality of outcomes assessed using the GRADE approach. Meta-analysis was conducted to calculate mean difference in post-treatment pain score.

Results: Nineteen randomised controlled trials were included in the review. There appears to be short-term pain relief (1-3 months) provided by radiofrequency denervation of the sacroiliac joint (5 trials, MD -1.53, CI -2.62, -0.45) and intervertebral discs (4 trials, MD -0.98, CI -1.84, -0.12) but the placebo effect is large and additional intervention effect size is small (<1 on a 11 point (0-10) pain scale). Longer-term effectiveness (>6 months) is uncertain.

Conclusions: Radiofrequency denervation of selected lumbosacral targets appears to have a small, short-term, positive effect for the management of patients with chronic back pain. However, the quality of evidence for the majority of outcomes is low or very low quality and there is still a degree of uncertainty, particularly around the duration of effect.

1
2
3
4
5
6 Strengths and limitations of this study:
7
8

- 9
- 10 • This review brings together a number of recent trials with earlier trials so that
11 there is a sizable sum of evidence on which to assess the effectiveness of
12 radiofrequency denervation for back pain.
13
 - 14 • Due to the invasive nature of the procedure, it is difficult to perform truly
15 patient or provider blinded trials and this brings some uncertainty around
16 findings.
17
 - 18 • There is limited reporting of long-term outcomes (>6 months) for the
19 effectiveness of radiofrequency denervation.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Back pain is an extremely common symptom experienced by people of all ages, and can be attributed to a wide variety of disease processes.^{1,2} Low back pain is now the leading cause of disability worldwide and back pain is associated with a substantial economic burden, with high medical and societal costs.³ Studies have shown that a large proportion of medical costs come from hospital admissions and physical therapy for the management of back pain.⁴ However, there are also indirect costs associated with chronic or recurrent back pain that are difficult to quantify relating to work absenteeism and related productivity.^{1,3,4} In many cases, back pain is non-specific, or structural pathology amenable to surgical correction cannot be identified.⁵⁻⁷ Hence, patients and practitioners continue to seek non-surgical alternatives for the management of back pain.

Radiofrequency denervation (RD) involves the application of an alternating electric current (250 to 500kHz) via a needle probe to induce a highly localised rise in tissue temperature at the needle tip.⁸ The needle tip is usually placed under fluoroscopic guidance to enable selective ablation of sensory nerve branches that supply facet joints, sacroiliac joint or other structures that comprise the lumbosacral spine. RD would therefore offer relief of pain by attenuating sensory signals from the lumbosacral spine.⁹

Despite its use for over 20 years,¹⁰ the effectiveness of RD targeted at the anatomy of the lumbosacral spine is not yet established, with randomised controlled trials (RCTs) continuing to be performed. A number of trials have been published since the publication of the last high quality review in 2015¹¹ and our systematic review aimed to bring together this evidence in an attempt to evaluate whether RD is an effective intervention for the management of chronic non-specific back pain.

Materials and Methods

Search strategy

A search was conducted in Medline, Medline in Process, Embase, CINHAL and the Cochrane library from January 2014 to April 2019 (Appendix 1). Previous systematic reviews were used to obtain additional relevant studies published pre 2014.

Inclusion criteria

RCTs comparing RD of the spine with a control in patients with back pain with or without sciatica were included. Only trials of radiofrequency procedures for the purpose of ablating or denaturing sensory nerve branches or nociceptors that supply the lumbosacral spine were considered for inclusion. Trials of pulsed RF,¹² or other forms of 'neuromodulatory' procedures that do not aim to ablate or denature these targets, were excluded from the review. Control groups where there was no active treatment were considered for inclusion but trials with potentially effective comparators e.g. corticosteroid injections, were excluded. Only trials of patients with back pain without a definite or surgically remediable cause (chronic non-specific back pain) were included in the review. The outcome for the review was patient-reported pain score e.g. Visual Analogue Scale or Numeric Rating Scale.

Data collection and quality assessment

Trial characteristics were recorded from included studies. Study results were extracted independently by two authors (MC, PT), with any disagreements resolved by consensus. The overall strength of evidence was assessed using the GRADE approach.¹³ Risk of bias was assessed using the Cochrane Risk of Bias tool.¹⁴ Any outcome where more than half of trials were considered to have a high or unclear risk of bias was downgraded. Outcomes were also downgraded where heterogeneity

1
2
3 in the meta-analysis was greater than 50%. Optimal sample size was taken to be 85
4
5 participants per study arm (as calculated in the Juch 2017 trial¹⁵) and studies with
6
7 less than 170 participants, and/or where the 95% confidence intervals included the
8
9 line of no effect, were downgraded for imprecision. Publication bias was assessed
10
11 using funnel plots and outcomes downgraded where there was a high certainty of
12
13 publication bias.
14
15

16 17 *Data analysis*

18
19
20 Meta-analyses were conducted in RevMan¹⁶ with random effects models since the
21
22 included studies investigated effectiveness in different population groups with
23
24 varying intervention and control group treatments. Pain score at 1-3 months was
25
26 taken as the primary outcome (longest time point used for studies reporting multiple
27
28 time points), allowing outcome from a larger number of studies to be combined. Pain
29
30 score data were reported on a 0-10 point scale (Visual Analogue Scale or Numeric
31
32 Rating Scale) in all studies and the mean difference was therefore calculated without
33
34 standardisation as done in the previous Cochrane review.¹¹ Studies with different
35
36 spinal targets e.g. facet joints, sacroiliac joints or inter-vertebrae disc, were
37
38 separated in the analysis. A sensitivity analysis was conducted to check the validity
39
40 of findings by removing studies considered to have a particularly high risk of bias.
41
42 Subgroup analysis to explore study heterogeneity was not conducted because of the
43
44 small number of studies and high likelihood of reaching spurious conclusions.
45
46
47
48
49

50 **Results**

51 52 53 *Study characteristics*

54
55
56 The search identified 922 citations of which 229 were duplicates. Studies were
57
58 excluded as shown in figure 1. Of the 693 citations reviewed, 8 new trials were
59
60

1
2
3 identified as well as 11 from a previous Cochrane review.¹¹ Exclusions were made
4 as shown in figure 1. Nineteen trials were included in the review and their
5 characteristics are shown in appendix 2. Trials investigated the effectiveness of RD
6 of the facet joint (supplied by medial branch of the dorsal spinal ramus),^{15,17–24} the
7 sacroiliac joints,^{15,25–28} the intervertebral discs,^{29–33} or vertebrae end-plate (supplied
8 by the basivertebral nerve).³⁴ The majority of trials used a sham control group but
9 one large trial compared RD with no treatment (both groups received an exercise
10 program) and one small trial compared RD plus conventional medical with
11 conventional medical management alone (including self-care, medications and
12 physical and cognitive therapy).
13
14
15
16
17
18
19
20
21
22
23
24
25

26 *Study quality*

27
28 Sham-controlled trials generally appear to have conducted adequate randomisation
29 but allocation concealment was often unclear. Processes were in place to blind
30 patients and providers and outcome assessors. In some trials, maintenance of
31 blinding was unclear as it was evident that patients undergoing sham procedures
32 were offered RD in case of sham treatment failure. In these cases, blinding would
33 have been broken. Most trials did not report dropouts and there was unclear risk of
34 attrition bias. The outcome for this review was pain score and this was reported in all
35 trials and reporting bias was not considered to be an issue in the review. Four trials
36 were identified as having high risk of bias and were removed in the sensitivity
37 analysis.^{17,19,24,25}
38
39
40
41
42
43
44
45
46
47
48
49
50
51

52 *Overall quality of the evidence*

53
54 The majority of outcomes were graded down for imprecision and all outcomes were
55 downgraded for potential risk of bias. Consequently, almost all outcomes were
56
57
58
59
60

1
2
3 graded as low quality. However, in some cases, high heterogeneity was also present
4
5 and these outcomes were graded as very low quality. Publication bias was
6
7 suggested by asymmetry in a number of the funnel plots. However, there was
8
9 uncertainty due to the small numbers of studies and outcomes were not graded
10
11 down for publication bias.
12
13

14 15 *Study findings*

16
17
18 Results of the meta-analyses are shown in table 1.
19

20 21 *RD of the facet joints*

22
23 Meta-analysis of pain scores at 1-3 months post procedure (longest time point used
24
25 for studies with multiple time points) (marked on a 0-10 scale) is shown in figure 2
26
27 and table 1. The effect size was similar when all trials were included (7 trials, MD -
28
29 0.56, CI -1.13, 0.01) or where just the sham-controlled trials were included (6 trials,
30
31 MD -0.63, CI -1.39, 0.12) but the effect was not significant for either. We also
32
33 considered outcomes at 6 and 12 months, where data were available to explore
34
35 longer term outcomes, but did not find any significant effect (table 1).
36
37
38
39

40 41 *RD of the sacroiliac joints*

42
43 Figure 3 shows the meta-analysis of trials for pain score at 1-3 months (longest time
44
45 point used for studies with multiple time points). There was a significant effect of RD
46
47 for the analysis including all trials (5 trials, MD -1.53, CI -2.62, -0.45) or just sham-
48
49 controlled trials (4 trials, MD -1.89, CI -3.45, -0.34). Only one trial¹⁵ assessed
50
51 outcome at later time points and this showed no significant difference compared to a
52
53 no treatment control (table 1).
54
55

56 57 *RD of the intervertebral discs*

1
2
3 Pain score at 1-3 months post-treatment was significantly lower for RD compared
4 with control in all trials (4 trials, MD -0.98, CI -1.84, -0.12) but not for sham-controlled
5 trials alone (3 trials, MD -0.63, CI -1.36, 0.10) (figure 4). Pain score was significantly
6 lower for RD when all trials and sham-controlled trials were considered at 6 months
7 but, for one trial assessing outcome at one year, it was not (table 1).

15 *RD of the vertebrae body and end plate*

16
17 One trial of RD for vertebrae body and end plate (basivertebral nerve ablation)³⁴ did
18 not show significant benefits of RD compared with sham at 3, 6 or 12 months (table
19 1).

25 *Sensitivity analysis*

26
27 Four studies were removed in the sensitivity analysis due to a high risk of
28 methodological bias^{17,19,24,25} and the two non-sham controlled trials were also
29 removed.^{15,32} After the removal of these trials, outcome at 1-3 months for facet joint
30 sham trials was still not significant (4 trials, MD -0.57, CI -1.60, 0.46) and 1-3 month
31 outcome for sacroiliac sham trials became non-significant (3 trials, MD -1.21, CI -
32 2.59, 0.16). The facet joint sham trial outcome at 6 months also became non-
33 significant (1 trial, MD 0.18, CI -2.80, 3.16).

44 **Discussion**

47 *Main findings*

48
49 This systematic review presents evidence suggesting that RD of the lumbosacral
50 spine may have a small positive but short-lived effect in patients with chronic back
51 pain, depending on the precise part of the anatomy that is being targeted by the
52 procedure. The quality of evidence for the majority of findings is low or very low
53 quality and there is still a degree of uncertainty around this assertion, particularly
54
55
56
57
58
59
60

1
2
3 around the duration of effect. The size of benefit appears to be small (<1 point on a
4 0-10 pain scale) and there is limited data for outcomes beyond 6 months. These
5 assertions apply to RD for sacroiliac joints, whereas evidence for benefit to other
6 targets is more limited. RD for facet joints did not show a significant benefit on 1-3
7 month outcome. There is a suggestion that there may be a benefit of RD for
8 intervertebral discs but there is some inconsistency, with insignificant effect for short-
9 term outcomes.

10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
What is also clear from the review is that both treatment and sham/no treatment
groups improved during the trials. In the sham controlled trials, this may, in part, be
due to placebo effect. However, the large trial by Juch et al¹⁵ used a “no additional
treatment” control (both groups received an exercise program) but all study arms
improved over time. This may be because a high proportion of control study
participants actually received RD (~30%) due to cross-over during the trial. However,
this may also be explained by self-selection of participants who volunteer for
research trials,³⁵ and hence are likely to make more of an active effort to manage
their back pain. Such participants may be more likely to engage with, and be diligent
in, exercise programs and seek medical assistance where needed.

In the trial by Juch et al., control group improvements may also be explained by the
conservative management that they received. The exercise program employed was
multi-disciplinary and comprised individual sessions over 8-12 hours focused on
quality of movement and behaviour, with access to psychological care. There is
evidence suggesting that patients with chronic back pain can benefit from pain
management programs that are of sufficient quality and duration.³⁶ Where patients
have not received an adequate trial of conservative therapy, they may benefit from
further exercise programs and other conservative management. It remains unclear

1
2
3 whether patients who are either unable or unwilling to engage with conservative
4 approaches to pain management would benefit from RD based interventions as a
5 first-line or isolated modality of treatment. Hence, there should be some reservation
6 when considering the use of RD treatment as a first-line, or isolated modality of pain
7 management.
8
9

10
11
12 Regression to the mean may also have played a role in control group improvements
13 since patients in the trial were recruited with elevated pain, responsive to an
14 anaesthetic block. Back pain has been shown to have a varied aetiology, with some
15 patients experiencing fluctuating levels of pain over time, whilst other experience
16 constant high levels of pain.^{37,38} For the majority of trials that reported it, duration of
17 back pain in participants prior to enrolment was 2-5 years and a proportion of these
18 were likely to have had high levels of constant pain. Some, however, may have been
19 experiencing fluctuating or recurrent pain within this period since the actual inclusion
20 criteria for most trials was pain for >3 or 6 months based on patient recall. If they
21 were recruited at a point where their pain had flared acutely, there would be a natural
22 tendency for that painful episode to resolve over time.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

40 41 *Strengths and limitations*

42
43 A major strength of this review is that it collates a larger body of evidence than
44 previous systematic reviews, with the addition of a number of recent trials and
45 thorough assessment of the quality of the evidence. The review is able to tentatively
46 answer the question about the effectiveness of RD for back pain; an assertion that,
47 to date, has proved to be very difficult due a paucity of evidence in this field.
48
49
50
51
52
53
54

55 This review utilises evidence from a previous Cochrane review¹¹ but the inclusion
56 criteria for our review had a narrower scope (included only sham- or conservative
57
58
59
60

1
2
3 management-controlled trials of conventional neuro-ablative RD). Since the previous
4 review appears to be of high quality, and we updated it with a thorough search of the
5 literature to date, there is assurance that all relevant trials were included.
6
7
8
9

10 A limitation of this review is that it was difficult to truly assess risk of bias in trials
11 included in the review. Trial integrity rested heavily on the blinding of participants and
12 the outcome was likely to be highly subject to patients' preconceptions of the
13 different interventions given. Most trials did not report information that providers gave
14 patients about the different possible treatment arms e.g. did providers suggest to
15 patients that RD was the effective treatment and that sham or no treatment would be
16 ineffective? Where blinding was broken, these viewpoints may have influenced
17 patients' response. In some of the sham-controlled studies this was clearly evident.
18 For example, in some studies, before randomisation, patients were told that, if
19 randomised to sham, they could receive RD if they gained no benefit. Where blinding
20 was broken, these opinions were likely to influence patients' perception of their pain.
21 In other studies information from providers was not reported and it is difficult to
22 assess whether this type of bias occurred.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

41 The review may also be limited in its ability to ascertain the technical quality of
42 individual research trials. Even when examining the reported trial methodology, it is
43 difficult to conclusively identify trials that employed procedures that may be more or
44 less successful in denervating the specific lumbosacral anatomy. Some aspects of
45 RD procedures in earlier trials are considered outdated^{39,40} but the advantages of
46 more recent procedures for RD remain unproven, and there is no clear evidence of
47 their superiority. Sensitivity analysis based on technical quality was therefore
48 considered unhelpful and not performed.
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 The review is also limited by the lack of long term data from trials. Most studies do
4 not attempt to blind patients for more than 3 months and the longer follow up
5 outcomes are considered to be at higher risk of bias. It is still therefore unclear
6 whether RD of lumbosacral anatomy has long-term benefits for back pain.
7
8
9
10
11

12
13 Finally, the review is limited in its ability to identify any aspects of patient or
14 intervention characteristics that may make RD treatment more likely to be beneficial.
15

16
17 There is to date no reliable predictor of benefit on back pain for RD procedures
18 based on clinical or imaging findings or diagnostic injections.⁴¹ The relative
19 advantages of different RD technologies used in included trials (e.g. 'cooled'^{25,26,32}
20 and 'bipolar'^{30,32} RD) remains to be established. Due to the small number of studies
21 at each time point, sub-group analysis was not considered appropriate. However, the
22 publication of more sham-controlled trials and trials comparing different RD
23 technologies may make this type of investigation possible. Technical advances and
24 advances in knowledge and experience may allow for better selection of anatomical
25 targets and patients for RD and hence improve clinical outcomes. It is important that
26 these developments are formally assessed and published.
27
28
29
30
31
32
33
34
35
36
37
38
39
40

41 In conclusion, within the limitations in this review and the published literature, there
42 appears to be at least short-term benefit from RD of selected lumbosacral
43 anatomical targets for chronic back pain. However, the mean size of effect appears
44 to be small and, overall, clinical significance may be marginal. Hence, chronic back
45 pain remains a highly challenging condition to treat.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 **Acknowledgements** Thanks to Julie Aikens and Kerry Herbert at Hinchingsbrooke
4
5 Healthcare Library for their assistance in designing and running the search strategies
6
7 for the review.
8
9

10 **Contributors:** MC contributed to the planning of this work, selected articles for
11
12 inclusion, extracted data, quality assessed studies and drafted and re-drafted the
13
14 manuscript. RL contributed to the planning of this work, reviewed the manuscript and
15
16 approved the final version. PT extracted data from the trials, reviewed the
17
18 manuscript and approved the final version. MA contributed to the planning of this
19
20 work, reviewed the manuscript and approved the final version. ML contributed to the
21
22 planning of this work, reviewed the manuscript and approved the final version.
23
24
25

26
27 **Funding** This research received no specific grant from any funding agency in the
28
29 public, commercial or not-for-profit sectors. RL is supported by the Medical Research
30
31 Council (MC_UU_12015/2). MCL is supported by AABGI Foundation project grant
32
33 (RCZB/071).
34
35

36
37 **Competing interests** None declared.
38

39
40 **Patient consent for publication** Not required.
41

42
43 **Provenance and peer review** Not commissioned; externally peer reviewed.
44

45
46 **Data availability statement** All data relevant to the study are included in the article
47
48 or uploaded as supplementary information.
49

50
51 **Patient and Public Involvement** This research was done without patient
52
53 involvement.
54

55
56 **Open access** This is an open access article distributed in accordance with the
57
58 Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which
59
60 permits others to distribute, remix, adapt, build upon this work non-commercially, and

1
2
3 license their derivative works on different terms, provided the original work is
4 properly cited, appropriate credit is given, any changes made indicated, and the use
5 is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.
6
7
8
9

10 References

- 11
12
13 1 Hartvigsen J, Hancock MJ, Kongsted A, *et al*. What low back pain is and why
14 we need to pay attention. *Lancet* 2018;**391**:2356–67. doi:10.1016/S0140-
15 6736(18)30480-X
16
17
18
19
- 20
21 2 Hoy D, Bain C, Williams G, *et al*. A systematic review of the global prevalence
22 of low back pain. *Arthritis Rheum* 2012;**64**:2028–37. doi:10.1002/art.34347
23
24
25
- 26
27 3 Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain*
28 2000;**84**:95–103. doi:10.1016/S0304-3959(99)00187-6
29
30
- 31
32 4 Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of
33 illness studies in the United States and internationally. *Spine J* 2008;**8**:8–20.
34 doi:10.1016/j.spinee.2007.10.005
35
36
37
- 38
39 5 National Institute of Health and Care Excellence. Low back pain and sciatica in
40 over 16s: assessment and management. 2016.
41
42
- 43
44 6 Chou R, Baisden J, Carragee EJ, *et al*. Surgery for Low Back Pain: A Review
45 of the Evidence for an American Pain Society Clinical Practice Guideline.
46 *Spine (Phila Pa 1976)* 2009;**34**:1094–109.
47
48
- 49
50
51 7 Chou R, Loeser JD, Owens DK, *et al*. Interventional Therapies, Surgery, and
52 Interdisciplinary Rehabilitation for Low Back Pain: An Evidence-Based Clinical
53 Practice Guideline From the American Pain Society. *Spine (Phila Pa 1976)*
54 2009;**34**:1066–77. doi:10.1097/BRS.0b013e3181a1390d
55
56
57
58
59
60

- 1
2
3 8 Kline M. Radiofrequency techniques in clinical practice. In: *Waldman SD,*
4 *Winnie AP, eds. Interventional Pain Management. Philadelphia, PA: Saunders.*
5
6 *1996.*
7
8
9
10 9 Wray JK, Dixon B, Przkora R. *Radiofrequency Ablation.* 2019.
11
12
13 10 Manchikanti L, Hirsch J, Pampati V, *et al.* Utilization of Facet Joint and
14 Sacroiliac Joint Interventions in Medicare Population from 2000 to 2014:
15 Explosive Growth Continues! *Curr Pain Headache Rep* 2016;**20**:58.
16
17
18
19
20 11 Maas E, Ostelo R, Niemisto L, *et al.* Radiofrequency denervation for chronic
21 low back pain. *Cochrane Database Syst Rev* 2015;:Art. No.: CD008572.
22 doi:10.1001/jama.2017.16386
23
24
25
26
27 12 Brandon R, Cohen D, Edward T, *et al.* Pulsed Radiofrequency
28 Neuromodulation in Interventional Pain Management—A Growing Technology.
29 *J Radiol Nurs* 2018;**37**:181–7.
30
31
32
33 13 Schünemann H, Brożek J, Guyatt G, *et al.*, editors. *GRADE Handbook:*
34 *Handbook for grading the quality of evidence and the strength of*
35 *recommendations using the GRADE approach.*
36
37
38
39
40
41
42 14 Higgins JP, Savovic J, Page MJ, *et al.*, editors. *Revised Cochrane risk-of-bias*
43 *tool for randomized trials (RoB 2).* 2019.
44
45
46
47 15 Juch JNS, Maas ET, Ostelo RWJG, *et al.* Effect of Radiofrequency
48 Denervation on Pain Intensity Among Patients With Chronic Low Back Pain.
49 *JAMA* 2017;**318**:68–81.
50
51
52
53
54
55 16 Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen:
56 The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
57
58
59
60

- 1
2
3 17 Gallagher J, Petriccione di Vadi P, Wedley J, *et al.* Radiofrequency facet joint
4 denervation in the treatment of low back pain: a prospective controlled double-
5 blind study to assess its efficacy. *Pain Clin* 1994;**7**:193–8.
6
7
8
9
10 18 Leclaire R, Fortin L, Lambert R, *et al.* Radiofrequency Facet Joint Denervation
11 in the Treatment of Low Back Pain: A Placebo-Controlled Clinical Trial to
12 Assess Efficacy. *Spine (Phila Pa 1976)* 2001;**26**:1411–6.
13
14
15
16
17
18
19
20
21 19 Moussa WMM, Khedr W. Percutaneous radiofrequency facet capsule
22 denervation as an alternative target in lumbar facet syndrome. *Clin Neurol*
23
24
25
26
27
28 20 van Kleef M, Barendse GAM, Kessels A, *et al.* Randomised trial of
29 radiofrequency lumbar facet denervation for chronic low back pain. *Spine*
30
31
32
33
34
35 21 Van Tilburg CWJ, Schuurmans FA, Stronks DL, *et al.* Randomized sham-
36 controlled double-blind multicenter clinical trial to ascertain the effect of
37 percutaneous radiofrequency treatment for sacroiliac joint pain: Three-month
38 results. *Clin J Pain* 2016;**32**:921–6. doi:10.1097/AJP.0000000000000351
39
40
41
42
43
44
45 22 Van Wijk RMAW, Geurts JWM, Wynne HJ, *et al.* Radiofrequency denervation
46 of lumbar facet joints in the treatment of chronic low back pain: A randomized,
47 double-blind, sham lesion-controlled trial. *Clin J Pain* 2005;**21**:335–44.
48
49
50
51
52 23 Nath S, Nath CA, Pettersson K. Percutaneous Lumbar Zygapophysial (Facet)
53 Joint Neurotomy Using Radiofrequency Current, in the Management of
54 Chronic Low Back Pain. *Spine (Phila Pa 1976)* 2008;**33**:1291–1297.
55
56
57
58
59
60

- 1
2
3 24 Tekin I, Mirzai H, Ok G, *et al.* A comparison of conventional and pulsed
4 radiofrequency denervation in the treatment of chronic facet joint pain. *Clin J*
5 *Pain* 2007;**23**:524–9. doi:10.1097/AJP.0b013e318074c99c
6
7
8
9
10 25 Cohen SP, Hurley RW, Buckenmaier CC, *et al.* Randomized Placebo-
11 Controlled Study Evaluating Lateral Branch Radiofrequency Denervation for
12 Sacroiliac Joint Pain. *Anesthesiology* 2008;**109**:279–88.
13
14
15
16
17 doi:10.1038/mp.2011.182.doi
18
19
20 26 Patel N, Gross A, Brown L, *et al.* A Randomized, Placebo-Controlled Study to
21 Assess the Efficacy of Lateral Branch Neurotomy for Chronic Sacroiliac Joint
22 Pain. *Pain Med* 2012;**13**:383–98. doi:10.1111/j.1526-4637.2012.01328.x
23
24
25
26
27 27 Van Tilburg C, Stronks D, Groeneweg J, *et al.* Randomised sham-controlled
28 double-blind multicentre clinical trial to ascertain the effect of percutaneous
29 radiofrequency treatment for lumbar facet joint pain. *Spine (Phila Pa 1976)*
30 2016;**98-B**:1526–33.
31
32
33
34
35
36
37 28 Mehta V, Poply K, Husband M, *et al.* The Effects of Radiofrequency
38 Neurotomy Using a Strip-Lesioning Device on Patients with Sacroiliac Joint
39 Pain: Results from a Single-Center, Randomized, Sham-Controlled Trial. *Pain*
40 *Physician* 2018;**21**:607–18.
41
42
43
44
45
46
47 29 Barendse GAM, van den Berg SGM, Kessels AHF, *et al.* Randomized
48 Controlled Trial of Percutaneous Intradiscal Radiofrequency
49 Thermocoagulation for Chronic Discogenic Back Pain. Lack of Effect From a
50 90-Second 70 C Lesion. *Spine (Phila Pa 1976)* 2001;**26**:287–92.
51
52
53
54
55
56
57 doi:10.1097/00007632-200102010-00014
58
59 30 Kapural L, Vrooman B, Sarwar S, *et al.* A Randomized, Placebo-Controlled
60

- 1
2
3 Trial of Transdiscal Radiofrequency, Biacuplasty for Treatment of Discogenic
4 Lower Back Pain. *Pain Med* 2013;**14**:362–73. doi:10.1111/pme.12023
5
6
7
8
9 31 van Tilburg CWJ, Stronks DL, Groeneweg JG, *et al*. Randomized sham-
10 controlled, double-blind, multicenter clinical trial on the effect of percutaneous
11 radiofrequency at the ramus communicans for lumbar disc pain. *Eur J Pain*
12 2017;**21**:520–9. doi:10.1002/ejp.945
13
14
15
16
17 32 Desai MJ, Kapural L, Petersohn JD, *et al*. A prospective, randomized,
18 multicenter, open-label clinical trial comparing intradiscal biacuplasty to
19 conventional medical management for discogenic lumbar back pain. *Spine*
20 *(Phila Pa 1976)* 2016;**41**:1065–74. doi:10.1097/BRS.0000000000001412
21
22
23
24
25
26
27 33 Kvarstein G, Måwe L, Indahl A, *et al*. A randomized double-blind controlled trial
28 of intra-annular radiofrequency thermal disc therapy - A 12-month follow-up.
29
30
31
32
33
34
35
36 34 Fischgrund JS, Rhyne A, Franke J, *et al*. Intraosseous basivertebral nerve
37 ablation for the treatment of chronic low back pain: a prospective randomized
38 double-blind sham-controlled multi-center study. *Eur Spine J* 2018;**27**:1146–
39
40
41
42
43
44
45 35 The Cochrane Collaboration. Introduction to sources of bias in clinical trials. In:
46
47
48
49
50 36 Morley S, Williams A, Hussain S. Estimating the clinical effectiveness of
51 cognitive behavioural therapy in the clinic: Evaluation of a CBT informed pain
52 management programme. *Pain* 2008;**137**:670–80.
53
54
55
56
57 37 Dunn K, Croft P. Epidemiology and natural history of low back pain. *Eura*
58
59
60
Medicophys 2004;**40**:9–13.

- 1
2
3 38 Dunn K, Jordan K, Croft P. Characterizing the course of low back pain: a latent
4 class analysis. *Am J Epidemiol* 2006;**63**:754–61.
5
6
7
8 39 Dreyfuss P, Baker R. Comment on: Radiofrequency facet joint denervation in
9 the treatment of low back pain: a placebo-controlled clinical trial to assess
10 efficacy. *Spine (Phila Pa 1976)* 2002;**27**:556–7.
11
12
13
14
15 40 Kapural L, Provenzano D, Narouze S. RE: Juch JNS, et al. Effect of
16 Radiofrequency Denervation on Pain Intensity Among Patients With Chronic
17 Low Back Pain: The Mint Randomized Clinical Trials. *JAMA* 2017;**318**(1):68–
18 81. *Neuromodulation* 2017;**20**:844. doi:10.1111/ner.12729
19
20
21
22
23
24
25 41 Cohen SP, Julie JH, Brummett C. Facet joint pain-advances in patient
26 selection and treatment. *Nat Rev Rheumatol* 2013;**9**:101–16.
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1 Results of the meta-analyses of randomised controlled trials

	All trials					Sham controlled trials				
	k	N	MD (95% CI)	I ²	GRADE*	k	N	MD (95% CI)	I ²	GRADE*
RD of the facet joints										
1-3 months	7	599	-0.56 (-1.13, 0.01)	59%	Low	6	348	-0.63 (-1.39, 0.12)	66%	Low
6 months	4	361	-0.66 (-1.37, 0.05)	42%	Low	3	110	-1.05 (-2.21, 0.10)	32%	Low
1 year	2	291	-0.72 (-2.24, 0.80)	89%	Very low	1	40	-1.50 (-2.21, -0.79)	NA	Very low
RD of the sacroiliac joints										
1-3 months	5	384	-1.53 (-2.62, -0.45)	83%	Low	4	156	-1.89 (-3.45, -0.34)	87%	Very low
6 months	1	228	-0.28 (-1.00, 0.44)	NA	Low					
12 months	1	228	-0.19 (-0.92, 0.54)	NA	Low					
RD of the intervertebrae discs										
1-3 months	4	200	-0.98 (-1.84, -0.12)	40%	Low	3	144	-0.63 (-1.36, 0.10)	0%	Low
6 months	3	127	-1.74 (-2.58, -0.91)	0%	Low	2	75	-1.63 (-2.58, -0.68)	0%	Low
12 months	1	20	-1.70 (-3.63, 0.23)	NA	Very low	1	20	-1.70 (-3.63, 0.23)	NA	Very low
RD of the vertebrae body and endplate										
3 months	1	205	-0.34 (-1.09, 0.41)	NA	Moderate	1	205	-0.34 (-1.09, 0.41)	NA	Moderate
6 months	1	205	-0.67 (-1.44, 0.10)	NA	Moderate	1	205	-0.67 (-1.44, 0.10)	NA	Moderate
12 months	1	205	-0.50 (-1.29, 0.29)	NA	Moderate	1	205	-0.50 (-1.29, 0.29)	NA	Moderate

k, number of trials; N, number of participants; MD, Mean difference.

*GRADE assessment of the quality of the evidence

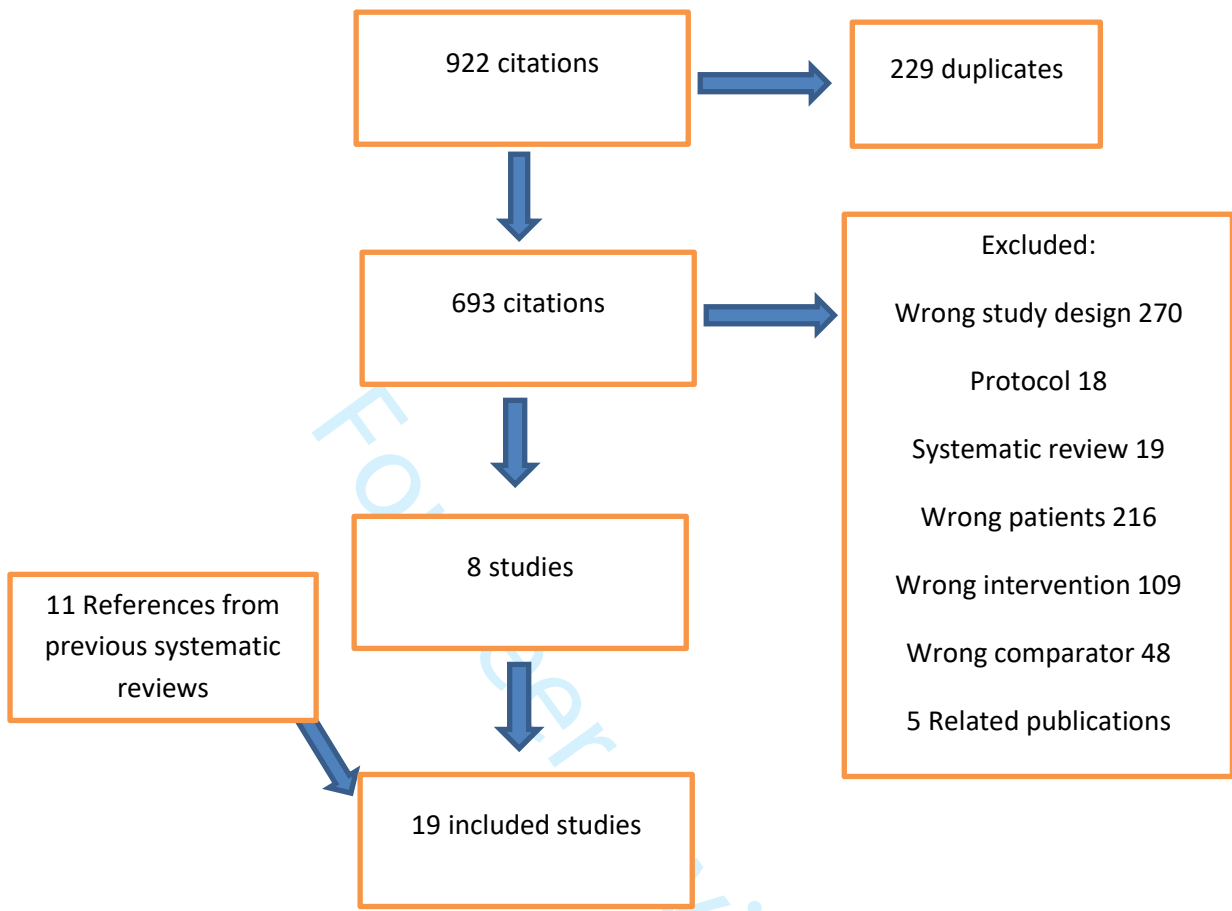
Figure 1 PRISMA flow diagram

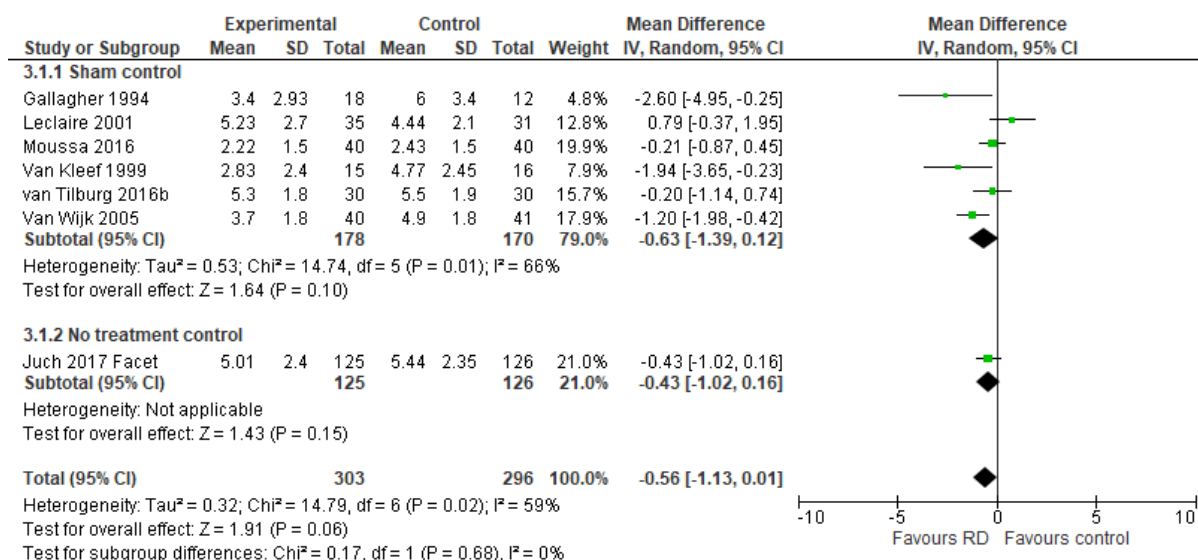
Figure 2 Post treatment pain score for radiofrequency denervation of the facet joints versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

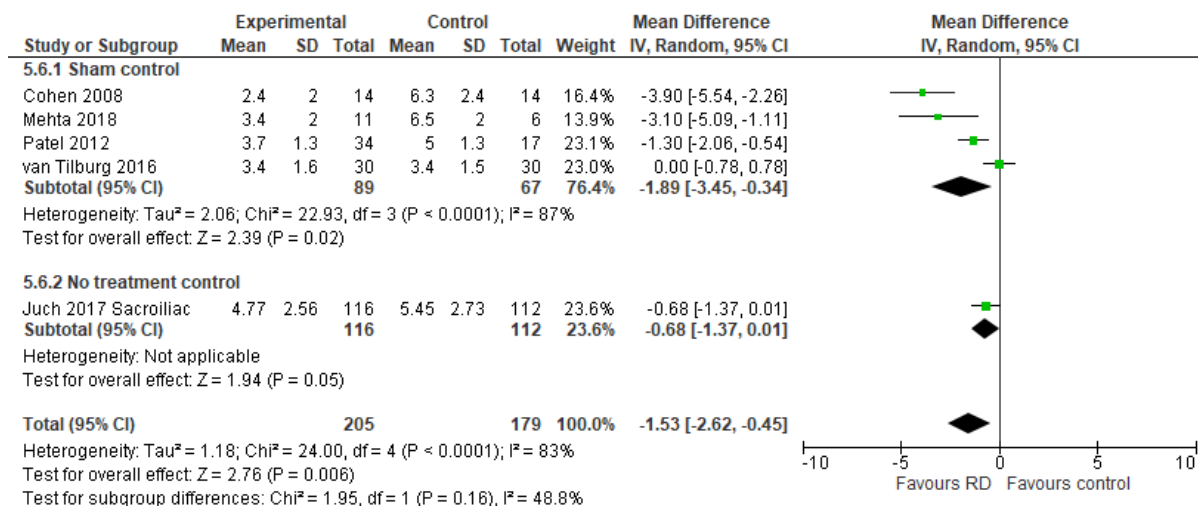
Figure 3 Post treatment pain score for radiofrequency denervation of the sacroiliac joints versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

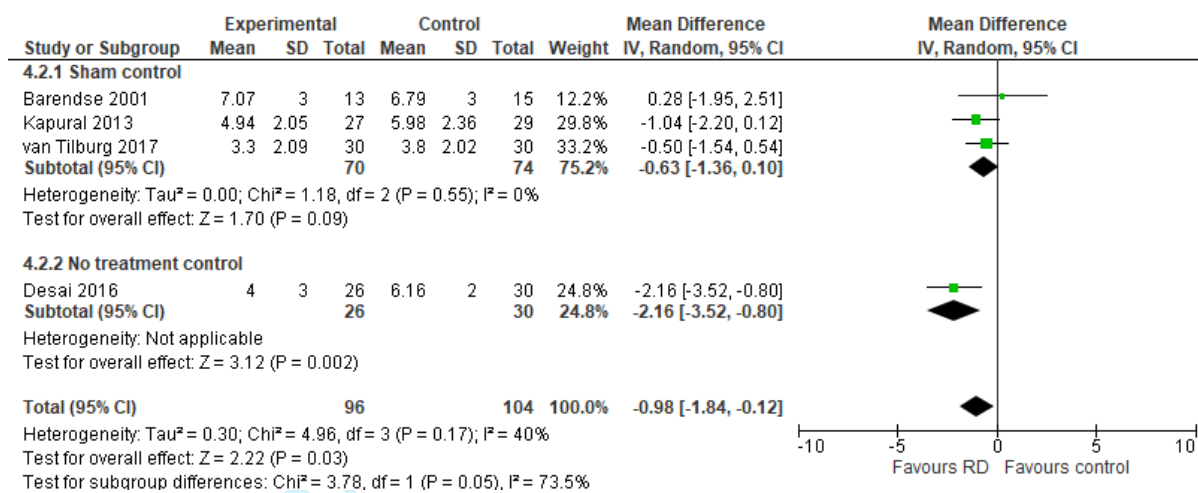
Figure 4 Post treatment pain score for radiofrequency denervation of the intervertebral discs versus control at 1-3 month follow-up (longest time point used for studies with multiple time points)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60









Appendix 1 Search strategies

Medline and Embase

#	Database	Search term
1	Medline	(randomized controlled trial).pt
2	Medline	(controlled clinical trial).pt
3	Medline	(randomi*ed).ab
4	Medline	(placebo).ti,ab
5	Medline	(drug therapy).fs
6	Medline	(randomly).ti,ab
7	Medline	(trial).ti,ab
8	Medline	(groups).ti,ab
9	Medline	(1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)
10	Medline	(animals NOT (humans AND animals)).su
11	Medline	9 not 10
12	Medline	(dorsalgia).ti,ab
13	Medline	exp "BACK PAIN"/
14	Medline	(backache).ti,ab
15	Medline	(lumbar ADJ pain).ti,ab
16	Medline	(coccyx).ti,ab
17	Medline	(coccydynia).ti,ab
18	Medline	(sciatica).ti,ab
19	Medline	"SCIATIC NEUROPATHY"/

- 1
2
3 20 Medline (spondylosis).ti,ab
4
5
6 21 Medline (lumbago).ti,ab
7
8 22 Medline (12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20
9 OR 21)
10
11
12 23 Medline exp SPINE/
13
14 24 Medline (discitis).ti,ab
15
16
17 25 Medline exp "SPINAL DISEASES"/
18
19 26 Medline (disc ADJ degeneration).ti,ab
20
21
22 27 Medline (disc ADJ prolapse).ti,ab
23
24
25 28 Medline (disc ADJ herniation).ti,ab
26
27 29 Medline (spinal fusion).su
28
29
30 30 Medline (facet ADJ joints).ti,ab
31
32
33 31 Medline (intervertebral disc).su
34
35 32 Medline (postlaminectomy).ti,ab
36
37
38 33 Medline (arachnoiditis).ti,ab
39
40
41 34 Medline (failed ADJ back).ti,ab
42
43 35 Medline (23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31
44 OR 32 OR 33 OR 34)
45
46 36 Medline (22 OR 35)
47
48
49 37 Medline exp "RADIO WAVES"/
50
51 38 Medline exp "PULSED RADIOFREQUENCY TREATMENT"/
52
53
54 39 Medline (radiofrequency).af
55
56
57 40 Medline (radio frequency).af
58
59
60

1		
2		
3	41	Medline exp ELECTROCOAGULATION/
4		
5	42	Medline (electrocoag*).af
6		
7		
8	43	Medline (thermocoag*).af
9		
10		
11	44	Medline neurotom* OR (neuroly*).af
12		
13	45	Medline (37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44)
14		
15		
16	46	Medline (11 AND 36 AND 45)
17		
18	47	EMBASE "CLINICAL TRIAL"/
19		
20		
21	48	EMBASE "CONTROLLED CLINICAL TRIAL"/
22		
23		
24	49	EMBASE "CONTROLLED STUDY"/
25		
26		
27	50	EMBASE "RANDOMIZED CONTROLLED TRIAL"/
28		
29		
30	51	EMBASE "DOUBLE BLIND PROCEDURE"/
31		
32	52	EMBASE "SINGLE BLIND PROCEDURE"/
33		
34		
35	53	EMBASE "CROSSOVER PROCEDURE"/
36		
37		
38	54	EMBASE PLACEBO/
39		
40	55	EMBASE (allocat*).ti,ab
41		
42	56	EMBASE (assign*).ti,ab
43		
44		
45	57	EMBASE (blind*).ti,ab
46		
47		
48	58	EMBASE (clinic* ADJ25 (study OR trial)).ti,ab
49		
50	59	EMBASE (crossover OR cross-over).ti,ab
51		
52		
53	60	EMBASE (factorial*).ti,ab
54		
55		
56	61	EMBASE (followup OR follow-up).ti,ab
57		
58	62	EMBASE (prospectiv*).ti,ab
59		
60		

- 1
2
3 63 EMBASE (placebo*).ti,ab
4
5
6 64 EMBASE (random*).ti,ab
7
8 65 EMBASE ((singl* OR doubl* OR trebl* OR trip*) ADJ25 (blind* OR
9 mask*)).ti,ab
10
11
12 66 EMBASE (volunteer*).ti,ab
13
14 67 EMBASE (47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55
15 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR
16 64 OR 65 OR 66)
17
18
19 68 EMBASE exp animals/ or exp invertebrate/ or animal experiment/ or
20 animal model/ or animal tissue/ or animal cell/ or nonhuman/
21
22 69 EMBASE exp ANIMALS/
23
24
25 70 EMBASE exp INVERTEBRATE/
26
27
28 71 EMBASE ANIMAL EXPERIMENT/
29
30
31 72 EMBASE ANIMAL MODEL/
32
33 73 EMBASE ANIMAL TISSUE/
34
35
36 74 EMBASE ANIMAL CELL/
37
38
39 75 EMBASE NONHUMAN/
40
41 76 EMBASE 71 or 72 or 73 or 74 or 75
42
43
44 77 EMBASE exp ANIMALS/
45
46
47 78 EMBASE exp INVERTEBRATE/
48
49 79 EMBASE (76 OR 77 OR 78)
50
51 80 EMBASE 77 or 78
52
53
54 81 EMBASE HUMAN/ OR NORMAL HUMAN/ OR HUMAN CELL/
55
56
57 82 EMBASE (76 AND 77 AND 78 AND 81)
58
59
60

- 1
2
3 83 EMBASE (dorsalgia).ti,ab
4
5
6 84 EMBASE (back pain).ti,ab
7
8 85 EMBASE exp BACKACHE/
9
10
11 86 EMBASE (lumbar ADJ pain).ti,ab
12
13
14 87 EMBASE (coccyx).ti,ab
15
16 88 EMBASE (coccydynia).ti,ab
17
18
19 89 EMBASE (sciatica).ti,ab
20
21 90 EMBASE ISCHIALGIA/
22
23
24 91 EMBASE (spondylosis).ti,ab
25
26 92 EMBASE (lumbago).ti,ab
27
28
29 93 EMBASE (back disorder*).ti,ab
30
31
32 94 EMBASE (83 OR 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90 OR 91
33 OR 92 OR 93)
34
35 95 EMBASE exp SPINE/
36
37
38 96 EMBASE (discitis OR diskitis).ti,ab
39
40
41 97 EMBASE exp "SPINE DISEASE"/
42
43 98 EMBASE (disc ADJ degeneration).ti,ab
44
45
46 99 EMBASE (disc ADJ prolapse).ti,ab
47
48
49 100 EMBASE (disc ADJ herniation).ti,ab
50
51 101 EMBASE (spinal fusion).ti,ab
52
53
54 102 EMBASE (facet ADJ joints).ti,ab
55
56 103 EMBASE (intervertebral disk OR Intervertebral disc).ti,ab
57
58
59 104 EMBASE (postlaminectomy).ti,ab
60

1		
2		
3	105	EMBASE (arachnoiditis).ti,ab
4		
5	106	EMBASE (failed ADJ back).ti,ab
6		
7		
8	107	EMBASE (95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102 OR
9		103 OR 104 OR 105 OR 106)
10		
11	108	EMBASE 94 or 107
12		
13		
14	109	EMBASE exp PULSED RADIOFREQUENCY TREATMENT/
15		
16		
17	110	EMBASE exp RADIOFREQUENCY/
18		
19	111	EMBASE exp RADIOFREQUENCY RADIATION/
20		
21		
22	112	EMBASE (radiofrequency OR radio-frequency).ti,ab
23		
24		
25	113	EMBASE exp THERMOCOAGULATION/ OR thermocoag*
26		
27	114	EMBASE exp ELECTROCOAGULATION/ OR electrocoag*
28		
29		
30	115	EMBASE (neurotom* OR neuroly*).ti,ab
31		
32	116	EMBASE (109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115)
33		
34		
35	117	EMBASE (108 AND 116)
36		
37		
38	118	Medline 46 [DT 2014-2019]
39		
40		
41		

Medline in process

#	Database	Search term
1	Medline	("randomi*ed controlled trial").ti,ab
2	Medline	("controlled clinical trial").ti,ab
3	Medline	("randomi*ed").ab
4	Medline	(placebo).ti,ab
5	Medline	("drug therapy").fs

- 1
- 2
- 3 6 Medline (randomly).ti,ab
- 4
- 5 7 Medline (trial).ti,ab
- 6
- 7
- 8 8 Medline (groups).ti,ab
- 9
- 10
- 11 9 Medline (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8)
- 12
- 13 10 Medline (dorsalgia).ti,ab
- 14
- 15
- 16 11 Medline ("back pain").ti,ab
- 17
- 18 12 Medline (backache).ti,ab
- 19
- 20 13 Medline ("lumber pain").ti,ab
- 21
- 22
- 23 14 Medline (coccyx).ti,ab
- 24
- 25 15 Medline (coccydynia).ti,ab
- 26
- 27
- 28 16 Medline (sciatica*).ti,ab
- 29
- 30
- 31 17 Medline (spondylosis).ti,ab
- 32
- 33
- 34 18 Medline (lumbago).ti,ab
- 35
- 36
- 37 19 Medline (10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
- 38 OR 18)
- 39
- 40 20 Medline (spine OR sacrum OR "lumber vertebrae" OR
- 41 "intervertebral disc*").ti,ab
- 42
- 43 21 Medline (discitis).ti,ab
- 44
- 45
- 46 22 Medline ("disc degeneration").ti,ab
- 47
- 48
- 49 23 Medline ("disc prolapse").ti,ab
- 50
- 51 24 Medline ("disc herniation").ti,ab
- 52
- 53
- 54 25 Medline ("spinal fusion").ti,ab
- 55
- 56
- 57 26 Medline ("facet joints").ti,ab
- 58
- 59
- 60

1		
2		
3	27	Medline (postlaminectomy).ti,ab
4		
5	28	Medline (arachnoiditis).ti,ab
6		
7		
8	29	Medline ("failed back").ti,ab
9		
10		
11	30	Medline (20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27
12		OR 28 OR 29)
13		
14	31	Medline (19 OR 30)
15		
16		
17	32	Medline (radiowave* OR "radio wave*").ti,ab
18		
19		
20	33	Medline (radiofrequency OR "radio frequency").ti,ab
21		
22	34	Medline (electrocoag*).ti,ab
23		
24		
25	35	Medline (thermocoag*).ti,ab
26		
27		
28	36	Medline (neurotom* OR neuroloy*).ti,ab
29		
30	37	Medline (32 OR 33 OR 34 OR 35 OR 36)
31		
32		
33	38	Medline (9 AND 31 AND 37)
34		
35	39	Medline 38 [Document status In Data Review OR In Process
36		OR PubMed not MEDLINE OR Publisher]
37		
38		
39		

Cinahl

#	Database	Search term
41		
42		
43		
44		
45	1	CINAHL exp "CLINICAL TRIALS"/
46		
47		
48	2	CINAHL ("randomi*ed controlled trial*").ti,ab
49		
50		
51	3	CINAHL (clinical ADJ3 trial).ti,ab
52		
53		
54	4	CINAHL (double-blind).ti,ab
55		
56	5	CINAHL (single-blind).ti,ab
57		
58		
59	6	CINAHL (triple-blind).ti,ab
60		

1			
2			
3	7	CINAHL	(1 OR 2 OR 3 OR 4 OR 5 OR 6)
4			
5	8	CINAHL	"PLACEBO EFFECT"/
6			
7			
8	9	CINAHL	PLACEBOS/
9			
10			
11	10	CINAHL	(placebo*).ti,ab
12			
13	11	CINAHL	(random*).ti,ab
14			
15			
16	12	CINAHL	(8 OR 9 OR 10 OR 11)
17			
18	13	CINAHL	"RANDOM SAMPLE"/
19			
20			
21	14	CINAHL	exp "STUDY DESIGN"/
22			
23			
24	15	CINAHL	(latin square).ti,ab
25			
26	16	CINAHL	exp "COMPARATIVE STUDIES"/
27			
28			
29	17	CINAHL	exp "EVALUATION RESEARCH"/
30			
31			
32	18	CINAHL	exp "PROSPECTIVE STUDIES"/
33			
34	19	CINAHL	(13 OR 14 OR 15 OR 16 OR 17 OR 18)
35			
36			
37	20	CINAHL	(follow-up stud*).ti,ab
38			
39			
40	21	CINAHL	(followup stud*).ti,ab
41			
42	22	CINAHL	(control*).ti,ab
43			
44			
45	23	CINAHL	(prospectiv*).ti,ab
46			
47	24	CINAHL	(volunteer*).ti,ab
48			
49			
50	25	CINAHL	(20 OR 21 OR 22 OR 23 OR 24)
51			
52	26	CINAHL	(7 OR 12 OR 19 OR 25)
53			
54			
55	27	CINAHL	ANIMALS/
56			
57			
58	28	CINAHL	26 not 27
59			
60			

- 1
2
3 29 CINAHL ("dorsalgia").ti,ab
4
5
6 30 CINAHL exp "BACK PAIN"/
7
8 31 CINAHL "LOW BACK PAIN"/
9
10
11 32 CINAHL ("backache").ti,ab
12
13
14 33 CINAHL (lumbar ADJ1 pain).ti,ab
15
16 34 CINAHL (lumbar ADJ5 pain).ti,ab
17
18
19 35 CINAHL (29 OR 30 OR 31 OR 32 OR 33 OR 34)
20
21 36 CINAHL COCCYX/
22
23
24 37 CINAHL SCIATICA/
25
26 38 CINAHL (sciatica).ti,ab
27
28
29 39 CINAHL (coccyx).ti,ab
30
31
32 40 CINAHL (coccydynia).ti,ab
33
34
35 41 CINAHL "LUMBAR VERTEBRAE"/
36
37 42 CINAHL (lumbar ADJ2 vertebra).ti,ab
38
39
40 43 CINAHL (36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42)
41
42 44 CINAHL "THORACIC VERTEBRAE"/
43
44
45 45 CINAHL exp SPONDYLOLYSIS/
46
47 46 CINAHL (lumbago).ti,ab
48
49
50 47 CINAHL (44 OR 45 OR 46)
51
52 48 CINAHL (35 OR 43 OR 47)
53
54
55 49 CINAHL (28 AND 48)
56
57
58 50 CINAHL (radiofrequency OR radio-frequency).ti,ab
59
60

1			
2			
3	51	CINAHL	(thermocoag*).ti,ab
4			
5	52	CINAHL	exp ELECTROCOAGULATION/ OR electrocoag*
6			
7			
8	53	CINAHL	(neurotom* OR neuroly*).ti,ab
9			
10			
11	54	CINAHL	"RADIO WAVES"/
12			
13	55	CINAHL	(50 OR 51 OR 52 OR 53 OR 54)
14			
15			
16	56	CINAHL	(49 AND 55)
17			
18			
19	57	CINAHL	56 [DT 2014-2019]
20			
21			
22			

Cochrane

#	Database	Search term	
23			
24			
25			
26			
27			
28	1	Cochrane	MeSH descriptor: [Back Pain] explode all trees
29			
30			
31	2	Cochrane	dorsalgia
32			
33	3	Cochrane	backache
34			
35			
36	4	Cochrane	MeSH descriptor: [Low Back Pain] explode all trees
37			
38			
39	5	Cochrane	lumbar next pain or coccyx or coccydynia or spondylosis
40			
41	6	Cochrane	MeSH descriptor: [Spine] explode all trees
42			
43			
44	7	Cochrane	MeSH descriptor: [Spinal Diseases] explode all trees
45			
46	8	Cochrane	lumbago OR discitis OR disc near degeneration OR disc near prolapse OR disc near herniation
47			
48			
49	9	Cochrane	spinal fusion
50			
51			
52	10	Cochrane	facet near joints
53			
54			
55	11	Cochrane	MeSH descriptor: [Intervertebral Disk] explode all trees
56			
57			
58	12	Cochrane	postlaminectomy
59			
60			

- 1
2
3 13 Cochrane arachnoiditis
4
5
6 14 Cochrane failed near back
7
8 15 Cochrane MeSH descriptor: [Cauda Equina] explode all trees
9
10
11 16 Cochrane lumbar near vertebra*
12
13
14 17 Cochrane spinal near stenosis
15
16 18 Cochrane slipped near (disc* or disk*)
17
18 19 Cochrane degenerat* near (disc* or disk*)
19
20
21 20 Cochrane stenosis near (spine or root or spinal)
22
23
24 21 Cochrane displace* near (disc* or disk*)
25
26 22 Cochrane prolap* near (disc* or disk*)
27
28
29 23 Cochrane MeSH descriptor: [Sciatic Neuropathy] explode all trees
30
31
32 24 Cochrane sciatic*
33
34 25 Cochrane back disorder*
35
36
37 26 Cochrane back near pain
38
39
40 27 Cochrane #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
41 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18
42 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
43
44 28 Cochrane MeSH descriptor: [Radio Waves] explode all trees
45
46
47 29 Cochrane MeSH descriptor: [Pulsed Radiofrequency Treatment]
48 explode all trees
49
50 30 Cochrane radiofrequency
51
52
53 31 Cochrane radio frequency or radio-frequency
54
55 32 Cochrane MeSH descriptor: [Electrocoagulation] explode all trees
56
57
58 33 Cochrane electrocoag*
59
60

- 1
- 2
- 3 34 Cochrane thermocoag*
- 4
- 5
- 6 35 Cochrane neurotom* or neuroly*
- 7
- 8 36 Cochrane #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35
- 9
- 10
- 11 37 Cochrane #27 and #36 in Trials
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47
- 48
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

For peer review only

Appendix 2 Study characteristics

Study	N	Inclusion criteria		Mean age (SD)	Mean pain score (SD)	Intervention	Control	Funding
RD of the facet joints								
Gallagher 1994	41	Low back pain >3 months duration with symptoms typical of facet joint pain	Improvement (n=30) or equivocal (n=11) response to anaesthetic block	NR	VAS RD 5.8 (1.78); Sham 7.2 (1.94)	Nerves above and below painful joint denervated at 80° for 90 seconds.	Nerves also identified with stimulation but no heat lesion made	NR
Juch 2017	251	Low back pain without response to conservative management and considered to be related to the facet joint	Positive response to anaesthetic block (reported 50% pain relief 30-90 minutes after block)	RD 53.0 (11.5); Control 52.6 (10.8)	NRS RD 7.14 (1.38) Control 7.19 (1.29)	Denervation at 90° for 90s of L3-4, L4-5 or L5-S1 with exercise program	Exercise program	The Netherlands Organization for Health Research and Development, by the Dutch Society for Anesthesiology, and the Dutch health insurance companies
Leclaire 2001	70	Low back pain for >3 months	“Significant” relief of back pain for >24h following facet injections	RD 46.7 (9.3); Sham 46.4 (9.8)	VAS RD 5.19 (2.67); Sham 5.15 (2.08)	RD with fluoroscopic guidance at 80°C for 90s of at least 2 levels	Nerves also identified with stimulation but electrode only heated to 37°C	Institut de recherche en sante´ and se´curite´ du travail du Que´bec
Moussa 2016	80	Low back pain for >1 year without response to conservative management	Complete or near complete reduction of CLBP on VAS 30 min after 2	RD capsule 58.1 (NR); RD conventional 56.5 (NR);	VAS RD 8.22 (NR); Sham 7.83 (NR)	RD of facet capsule on medial and lateral aspect or	Same procedure without elect current turned on	No funding received

			injections separated by >2 weeks	Sham 55.9 (NR)		conventional RD at 85°C for 90s		
Nath 2008	40	Low back pain for >2 years, not responded to previous treatment, pain attributable to lumbar facet joints	80% pain relief on 3 medial branch blocks	56 (range, 36–79)	VAS RD 5.98 (NR); Sham 4.38 (NR)	RD at 85°C for 60s with additional lesions just lateral and medial to the target nerve	Same procedure as RD but electrode tip remained at body temperature	No funding received
Tekin 2007	40	Back pain for >6 months with focal pain over the facet joints and unresponsive to conservative treatments	>50% reduction in VAS pain 30 minutes after diagnostic medial branch block	RD 60.5 (8.5); Sham 57.9 (9.3)	VAS RD 6.5 (1.5); Sham 6.8 (1.6)	RD at same levels as diagnostic blocks at 80°C for 90s.	Same procedure as RD but with current switched off	Not reported
Van Kleef 1999	32	Low back pain of >12 months duration, failure of conservative management	>50% reduction in pain following diagnostic nerve block of L3-L5 Baseline VAS score of >4	RD 46.6 (7.4); Sham 41.4 (7.5)	VAS RD 5.2 (1.7); Sham 5.2 (1.6)	RD at 80°C for 60s	Same procedure as RD but with current switched off	The Nederlandse organisatie voor wetenschappelijk
Van Tilburg 2016	60	Low back pain for >3 months and failure of conservative management	Decrease of >2 on medial branch block	RD 65 (12); Sham 58 (12)	NRS RD 7.2 (1.4); Sham 7.4 (0.8)	RD at 80°C for 60s per level for three steps with physiotherapy	Same procedure as RD but with current switched off with physiotherapy	No funding from a commercial party
Van Wijk 2005	81	Low back pain for >6 months	≥50% reduction on	RD 46.9 (11.5);	VAS RD 5.8 (1.8);	RD 80°C for 60 seconds	Same procedure as	Grant from the Dutch Health

			diagnostic block	Sham 48.1 (12.6)	Sham 6.5 (1.8)	at the levels concerned	RD but with current switched off	Insurance Council
RD of the sacroiliac joints								
Cohen 2008	28	Axial low back or buttock pain \geq 6 months, tenderness overlying the sacroiliac joint(s), failure to respond to conservative therapy	\geq 75% pain relief for \geq 3h following diagnostic sacroiliac joint injection, but back near baseline within 2 months	RD 51.9 (13.6); Sham 51.8 (13.1)	VAS RD 6.1 (1.8); Sham 6.5 (1.9)	RD 80°C for 90 seconds using cooling probe technology (Cooled RD)	Same procedure as RD but no current applied	John P. Murtha Neuroscience and Pain Institute, the Army Regional Anesthesia & Pain Medicine Initiative, and National Institutes of Health grant # MH075884
Juch 2017	228	Low back pain without response to conservative management, considered to be related to the sacroiliac joint.	Positive response to anaesthetic block (reported 50% pain relief 30-90 minutes after block)	RD 51.6 (10.9); Control 51.1 (12.2)	NRS RD 7.17 (1.65); Control 7.06 (1.43)	RD - 60° for 2.5 min per lesion of S1, S2 and S3 with exercise program	Exercise program	The Netherlands Organization for Health Research and Development, by the Dutch Society for Anesthesiology, and the Dutch health insurance companies
Mehta 2018	17	CLBP for >6 months. >5 on NRS	>80% pain reduction on 2 diagnostic blocks	RD 56.6 (NR); Sham 62.6 (NR)	VAS RD 8.1 (0.8); Sham 7.3 (0.8)	RD of the L5 medial branch of the primary dorsal root nerve and strip lesioning of the lateral branches	Identical to active RD treatment except that no RF energy was applied	None

						of the S1, 2, and 3 nerve roots		
Patel 2012	51	Pain for ≥6 months, 3-day average NRS between 4 and 8, failure of conservative management	≥75% pain reduction for 4h-7 days on two sets of anaesthetic blocks and back to baseline by start of the study	RD 56 (15); Sham 64 (14)	NRS RD 6.1 (1.3); Sham 5.8 (1.3)	RD at 60°C for 150s of L5 dorsal ramus and then acral lateral branches of S1, S2 and S3 (cooled RD)	Same procedure as RD but RF energy was not delivered.	Baylis Medical
Van Tilburg 2016	60	Sacroiliac joint pain for >3 months, failure of conservative management	Decrease of ≥2 on NRS following diagnostic block	RD 59.5 (27); Sham 62 (18)	NRS RD 7.2 (1.4); Sham 7.5 (1.2)	85°C each step for 90s, total of 5 steps	Same procedure as RD but no heat lesions made	Not reported
RD of the intervertebral discs								
Barendse 2001	28	Non-specific LBP for >1y, failure of conservative management	>50% pain relief 30 minutes after an analgesic discography at L4–L5 and L5–S1. Patients with multilevel pain excluded	RD 40.8 (7.5); Sham 45.2 (8.4)	VAS RD 6.5 (1.3); Sham 5.5 (1.1)	70°C for 90s without anaesthetic	Same procedure as RD but no current applied	Not reported
Desai 2016	63	Lumbar discogenic pain for ≥6 months, unresponsive to conservative management	Diagnosed via provocation discography - definite single-level concordant	Mean age 41 (11); Control 43 (11)	VAS RD 6.7 (NR); Sham 7 (NR)	RD at 50°C for 15 minutes and then 60°C for 2.5 min (bopolar cooled RD) with conventional	Conventional medical management	Halyard Health, Inc. (formerly Kimberly-Clark Health Care)

			pain on manometry			medical management		
Kapural 2013	55	CLBP unresponsive to conservative management for ≥6 months; no surgical interventions within previous 3 months	Single-level degenerative disc disease or two-level disease without evidence of additional degenerative changes in other disc spaces on MRI	RD 40.4 (10.3); Sham 38.4 (10.4)	VAS RD 7.13 (1.61); Sham 7.18 (1.98)	RD at 45°C bipolar for 15 minutes or 50°C bipolar for 15 minutes and monopolar at 60°C for 2.5 minutes	Mimicked active treatment, except that introducers and electrodes positioned just outside of the disc, and no RF energy delivered	Baylis Medical
Kvarstein 2009	20	Unremitting low back pain for more than 6 months; Pain intensity ≥5 /10 and low back pain greater than leg pain; Failure on conservative treatment	Positive one-level pain provocation discography	RD 44.7 (10.1); Sham 39.6 (8.9)	NRS RD 4.6 (1.8); Sham 5.5 (2.0)	RD increased by 5°C every second minute to 4-min interval at 65°C (from 50°C)	Exposed to a similar intervention, but the annulus was not exposed to RF heating	Radionics, TYCO Healthcare Group provided the discTRODE probes
Van Tilburg 2017	60	Low back pain >3 months and symptoms suggestive of lumbar disc problem	Reduction of ≥2 on a numerical rating scale (0–10) after a diagnostic ramus communicans test block	RD 50.5 (13.9); Sham 50.1 (12.3)	NRS 7.8 (1.05); Sham 7.8 (1.05)	RD treatment at 80 °C for 60s per level	Same procedure but without RF treatment	No support received that influenced submitted work
RD of the vertebrae body and endplate								

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

Fischgrund 2018	225	CLBP ≥6 months, not responded to conservative treatment, Type 1 or Type 2 Modic changes required at the proposed treatment levels	No diagnostic block for inclusion	RD 46.9 (range 26–69); Sham 47.1 (range 25–69)	VAS RD 6.73 (1.38); Sham 6.64 (1.34)	Thermal ablation at the terminus of the basivertebral nerve 85°C for 15 min	Same procedure as RD but only docking introducer cannula 1–2 mm into the pedicle and simulating RD	Not reported
------------------------	-----	---	-----------------------------------	--	--------------------------------------	---	--	--------------

CLBP, chronic low back pain; N, number of trials; NRS, numeric rating scale; RD, radiofrequency denervation; SD, standard deviation; VAS, visual analogue scale.

For peer review only