Interventional procedure overview of radiofrequency denervation for osteoarthritic knee pain

Contents

Table 1 Abbreviations

Abbreviation	Definition
ADL	Activities of daily living
CI	Confidence interval
EQ-5D	Euroqol 5-Dimensions
MCID	Minimum clinically important difference
NR	Not reported
NRS	Numeric rating scale
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
RCT	Randomised controlled trial
RD	Risk difference
RF	Radiofrequency
ROM	Range of motion
SD	Standard deviation
SMD	Standardised mean difference
SUCRA	Surface under the cumulative ranking curve
TUG	Timed Up and Go
US	United States
VAS	Visual analogue scale
WMD	Weighted mean difference
WOMAC	Western Ontario and McMaster Universities Arthritis Index

Indications and current treatment

Osteoarthritis is characterised by localised loss of cartilage, remodelling of adjacent bone and associated inflammation. Knees are one of the most affected joints, with pain being a significant symptom.

Various treatments are available for pain due to knee osteoarthritis, including nonpharmacological (such as physiotherapy), pharmacological (such as analgesics and intra-articular corticosteroids) and surgical approaches (such as knee arthroplasty). When nonpharmacological and pharmacological interventions do not work or symptoms are severe, surgery may be needed.

What the procedure involves

This procedure is often performed in 2 stages. Both stages are performed under fluoroscopic or ultrasound guidance. First, to assess suitability for RF denervation, patients are given a diagnostic block by injection of a local anaesthetic to the target nerves. If the diagnostic block provides pain relief, the patient is a candidate for RF denervation.

A probe is introduced to the treatment site. Several targets have been described, including the genicular nerves, the saphenous nerve, and the articular cavity. RF energy is used to denervate the target nerves. The RF energy can be delivered as conventional RF, cooled RF, or pulsed RF. The aim is to reduce pain and delay the need for knee arthroplasty.

Outcome measures

The main outcomes included VAS, NRS, and WOMAC. The measures used are detailed in the following paragraphs.

- The **Kellgren-Lawrence** system is used for classifying the severity of osteoarthritis by radiological findings. It ranges from 0 (no osteoarthritis) to 4 (severe osteoarthritis).

- The **VAS** and **NRS** are similar instruments used to assess pain. The simplest VAS is a straight line of fixed length. The scale ranges from least pain to most pain and the participant marks the line corresponding to the level of pain they feel. A ruler is used to measure the distance from the end of the line to the participant's mark. Higher scores indicate worse pain. An NRS is a segmented, numeric VAS, in which participants rate their pain on an 11-point scale (0 to 10). NRS scores may be converted into VAS scores. MCID estimates vary, but an MCID of 1.99 cm (or 19.9 mm) has been reported for VAS and an MCID of 1 point or 15% has been reported for NRS.

- The **Global Perceived Effect** scale is a scale used to assess the participant's perception of how their pain has changed after they have an intervention. It is typically a 7-point scale ranging from 1 – very much deteriorated, to 7 – very much improved.

- The **WOMAC** is a self-administered, 24-item instrument. The WOMAC is subdivided into 3 components: pain, stiffness, and physical function.

Higher scores indicate worse osteoarthritis-related health. MCID estimates vary, but an MCID of 11 points has been reported for people with knee osteoarthritis.

- The **Timed Up and Go** test measures the time taken to rise from sitting on a standard chair, walk 3 metres in a straight line, turn around, walk back, and sit again.
- The **EQ-5D** is an instrument used to assess health-related quality of life across 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The instrument also contains a VAS on general health.

Evidence summary

Population and studies description

This interventional procedures overview is based on approximately 2,896 patients from 1 systematic review and network meta-analysis, 2 systematic reviews and meta-analyses, 1 RCT, 1 long-term cohort study that was a single-arm extension of an RCT, 1 cohort study, 1 narrative review and 2 case reports. There was some overlap in studies included in the systematic reviews. Of these patients, approximately 2,047 had the procedure. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 9 studies as the key evidence in table 2 and table 3, and lists 48 other relevant studies in table 5.

Of the 9 key evidence studies, 3 were systematic reviews and meta-analyses. Wu (2022) is a comprehensive network meta-analysis of RCTs that compares the efficacy of all modalities of RF denervation with each other, non-RF comparators, and placebo. Chou (2021) is a meta-analysis of RCTs and observational studies of the treatment effect of RF denervation (before versus after treatment). Liu (2022) is a meta-analysis of RF denervation versus several comparators pooled into a single group.

One further comparative study was an RCT of conventional RF versus sham versus control (best supportive care only; Kumaran, 2019). This study was also included in the Liu (2022) meta-analysis.

Long-term data is reported in a long-term cohort study which was a long-term extension of an RCT (Lyman, 2022). This study reported 2-year outcomes of cooled RF denervation. An observational study (Chen, 2021) provides real-world outcomes of RF denervation and reports prognostic factors. A narrative review and 2 case reports are included to report unique safety events (McCormick, 2021; Mateev, 2021; Jorge 2019).

In the Liu (2022) systematic review, there were 7 studies from China, 2 from the US, and 1 each from the UK, Italy, Korea, Iran, Turkey, and Egypt. The locations of studies were not well reported in the other systematic reviews; of the other studies, Chen (2021) and Lyman (2022) were conducted in the US; Kumaran (2019) was conducted in the UK. Follow-up periods were typically 6 to 12 months.

Table 2 presents study details.

Figure 1 Flow chart of study selection

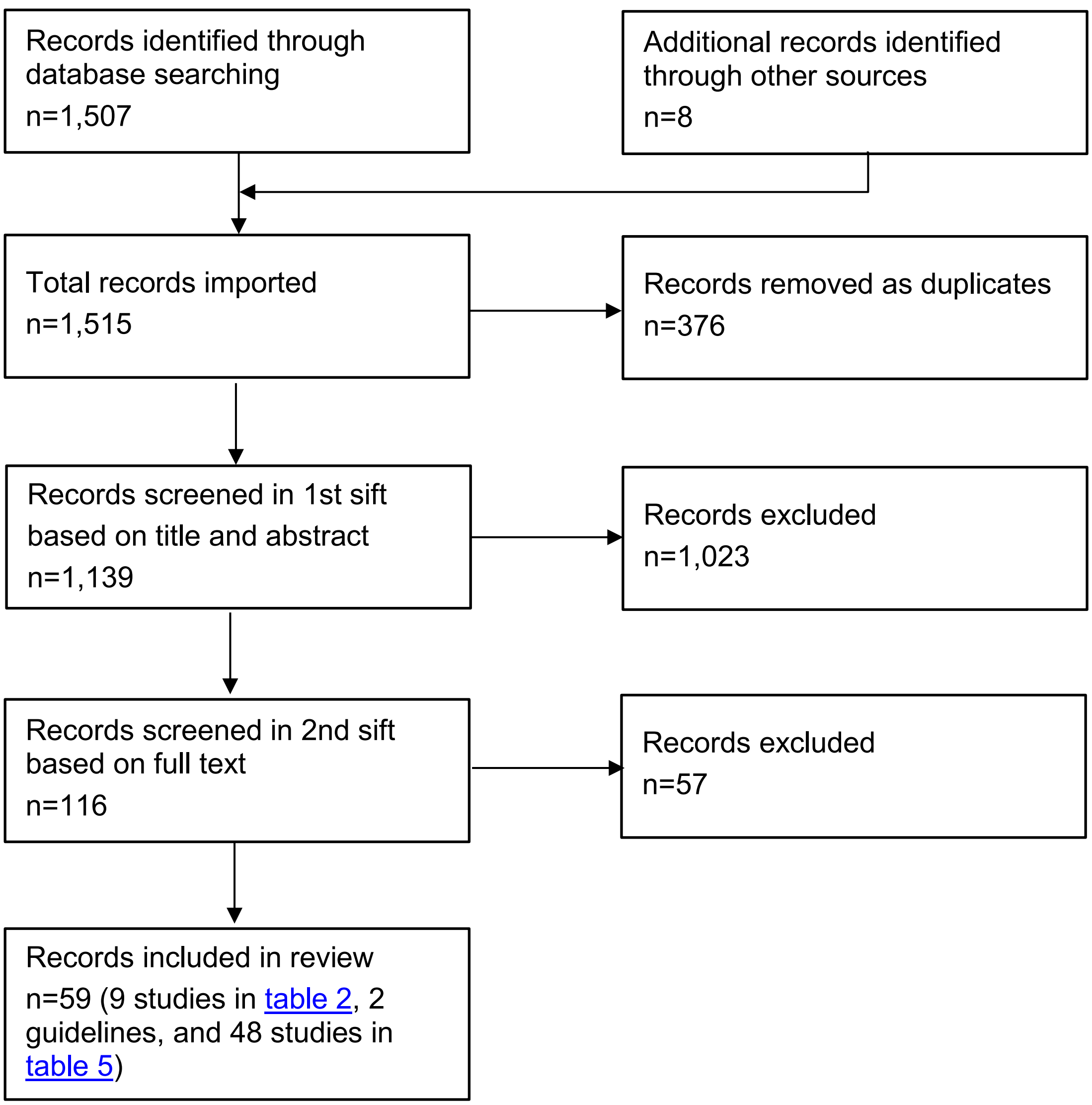

Table 2 Study details

No.	Author, date Location	Patients (m:f) Studies	Age	Study design	Inclusion criteria	Intervention	Follow up
1	Wu, 2022 Various	21 studies n=1,818 (657 non-RF comparator)	NR	Systematic review and network meta-analysis of RCTs	RCTs with at least 1 treatment arm using a RF denervation treatment and a comparator arm using placebo or other active treatment; Studies including patients with knee osteoarthritis; Studies containing pain or functional outcome scores; Studies fully reporting the numbers of patients and involved knees and the time of follow up; Studies completely reporting the RF denervation methodology, target, and number of electrodes; Studies diagnosing OA clinically and radiographically.	Conventional RF: 10 studies Pulsed RF: 11 studies Cooled RF: 2 studies (some studies used multiple types) Network meta-analysis consisted of all treatments vs. all comparators	Various; only 3 and 6 month results included in network meta-analysis.
2	Chou, 2021 Various	20 studies n=605	Means ranged from	Systematic review and meta-analysis of RCTs and	Articles investigating the efficacy of pulsed, conventional,	Conventional RF: 11 studies	Up to 12 months

No.	Author, date Location	Patients (m:f) Studies	Age	Study design	Inclusion criteria	Intervention	Follow up
		148 male; 343 female	53.3 to 77.2	observational studies	or cooled RF denervation techniques; Patients with knee osteoarthritis; VAS or NRS used to evaluate pain; Articles written in English or Chinese.	Pulsed RF: 8 studies Cooled RF: 2 studies Meta-analysis was conducted on before vs. after treatment	
3	Liu, 2022 Various	15 studies n=1,009 (506 non-RF comparator) 309 male; 594 female	Means ranged from 47.8 to 70.9	Systematic review and meta-analysis of RCTs	Patients were diagnosed with knee osteoarthritis; Patients in the experimental group received RF therapy; The trial had a control group; Included the following outcome measurements: VAS or NRS, WOMAC, Oxford Knee Score, Global Perceived Effect scale, and adverse effects at different time points after treatment; Studies were RCTs.	Conventional RF: 9 studies Pulsed RF: 4 studies Cooled RF: 2 studies Meta-analysis was conducted on RF denervation vs. comparator	Up to 24 weeks
4	Kumaran, 2019 UK	n=45 (15 conventional RF; 15 sham; 15 control)	Mean RF 63; mean sham 63; mean	RCT	Symptomatic for a minimum of 6 months; A prior clinical and/or radiological diagnosis of osteoarthritis knee meeting the	Conventional RF	3 months

No.	Author, date Location	Patients (m:f) Studies	Age	Study design	Inclusion criteria	Intervention	Follow up
		18 male;27 female	control 60		American College of Rheumatology criteria.		
5	Lyman, 2022 US	n=32 Male:female breakdown NR	NR	Prospective cohort study (Single arm, multicentre, long-term extension of an RCT [Chen, 2020 in the appendix])	Baseline NRS score of 6 or more (usual daily pain) for the index knee was required for enrolment in the RCT Baseline of score of 2 or 3 on WOMAC question A1 (pain while walking on flat surface) and a baseline mean score of 1.5 to 3.5 on all five questions of the WOMAC subscale A (pain) Only people initially randomised to cooled RF denervation were eligible for the extension.	Cooled RF	Up to 24 months
6	Chen, 2021 US	n=265 96 male;169 female	Mean 64.3	Retrospective, multicentre, cohort study	Patients with a primary complaint of knee pain treated with a radiofrequency procedure(s).	Conventional RF: n=103 Pulsed RF: n=7 Cooled RF: n=151	3 months or more
Safety studies – the following studies were included to show unique safety events							
7	McCormick, 2021	5 studies n=8	NR	Narrative review	NR	Conventional RF: 2 study	NR

No.	Author, date Location	Patients (m:f) Studies	Age	Study design	Inclusion criteria	Intervention	Follow up
		Male:female breakdown NR				Cooled RF: 3 studies	
8	Matveev, 2021 US	n=1 Male	49	Case report	NR	Conventional RF	NR
9	Jorge, 2019 US	n=1 Male	76	Case report	NR	Conventional RF	NR

Table 3 Study outcomes

Author, date	Efficacy outcomes	Safety outcomes
Wu, 2022 Network meta-analysis	**VAS pain** *3 months* • Network comprised of 16 studies and 1,401 patients • All treatments except for exercise had statistically significantly decreased VAS compared to placebo at 3 months. • Top 5 treatment rankings were (MD of treatment vs. placebo [95% CI] shown): 1. Cooled monopolar genicular nerve RF, -4.0 (-4.6 to -3.4) 2. Pulsed bipolar articular cavity RF, -3.8 (-4.8 to -2.8) 3. Conventional monopolar genicular nerve RF, -3.5 (-3.8 to -3.2) 4. Pulsed monopolar articular cavity RF combined with intra-articular platelet-rich plasma injection, -3.5 (-4.3 to -2.6) 5. Intra-articular erythropoietin injection, -3.1 (-4.5 to -1.7) *6 months* • Network comprised of 10 studies and 1,021 patients • All treatments except for NSAIDs had statistically significantly improved VAS compared to exercise at 6 months (placebo was not included in the network). • Top 5 treatment rankings were (MD of placebo vs. treatment [95% CI] shown): 1. Conventional bipolar genicular nerve RF, 5.5 (4.3 to 6.7) 2. Cooled monopolar genicular nerve RF, 4.7 (3.8 to 5.6) 3. Conventional monopolar genicular nerve RF, 3.5 (3.1 to 3.9) 4. Pulsed monopolar articular cavity RF combined with intra-articular protein-rich plasma, 3.3 (2.6 to 3.9) 5. Pulsed monopolar genicular nerve RF, 2.5 (2.2 to 2.8)	Adverse events were reported in 6 studies, comprising 836 patients. 51 adverse events were reported as probably related to treatment, including: • RF: 43 adverse events in 513 patients (8.4%) • Comparators: 8 adverse events in 323 patients (2.5%) 20 (3.9%) major adverse events were possibly related to RF denervation: • Pain, n=5 • Postprocedural pain, n=7 • Falls, n=5 • Stiffness, n=1 • Swelling, n=2

<table>
<tr><th>Author, date</th><th>Efficacy outcomes</th><th>Safety outcomes</th></tr>
<tr><td></td><td>WOMAC
3 months
Network comprised of 14 studies and 1,091 patients
All treatments except for exercise, NSAIDs, and pulsed monopolar saphenous nerve RF, had statistically significantly decreased WOMAC compared to placebo at 3 months.
Top 5 treatment rankings were (MD of treatment vs. placebo [95% CI] shown):
Cooled monopolar genicular nerve RF, -32 (-41 to -22)
Pulsed bipolar articular cavity RF, -26 (-37 to -14)
Conventional bipolar genicular nerve RF, -25 (-34 to -16)
Pulsed monopolar articular cavity RF, -22 (-34 to -10)
Conventional monopolar genicular nerve RF, -20 (-29 to -12)
6 months
Network comprised of 9 studies and 821 patients
All treatments had statistically significantly decreased WOMAC compared to exercise at 6 months (placebo was not included in the network).
Top 5 treatment rankings were (MD of exercise vs. treatment [95% CI] shown):
Cooled monopolar genicular nerve RF, 33 (29 to 37)
Pulsed monopolar articular cavity RF combined with intra-articular platelet-rich plasma injection, 30 (27 to 33)
Conventional bipolar genicular nerve RF, 24 (20 to 28)
Conventional monopolar genicular nerve RF, 20 (18 to 22)
Pulsed monopolar articular cavity RF, not reported</td><td></td></tr>
<tr><td>Chou, 2021
Meta-analysis</td><td>Pain (VAS or NRS)
1 month</td><td>Adverse events were reported in 14 studies.</td></tr>
</table>

Author, date	Efficacy outcomes	Safety outcomes
	- Overall effect (all 3 modalities; 17 studies): statistically significant decrease in pain after treatment compared to baseline, SMD 3.25 (95% CI 2.56 to 3.93; I^2=93%; p<0.00001) - There was no statistically significant difference in pain relief observed between the treatments (p=0.25) *3 months* - Overall effect (all 3 modalities; 14 studies): statistically significant decrease in pain after treatment compared to baseline, SMD 3.39 (95% CI 2.47 to 4.31; I^2=96%; p<0.00001) - There was no statistically significant difference in pain relief observed between the treatments (p=0.95) *6 months* - Overall effect (all 3 modalities; 12 studies): statistically significant decrease in pain after treatment compared to baseline, SMD 4.84 (95% CI 3.62 to 6.03; I^2=95%; p<0.00001) - There was no statistically significant difference in pain relief observed between the treatments (p=0.14) *12 months* - Overall effect (conventional and cooled RF; 4 studies): statistically significant decrease in pain after treatment compared to baseline, SMD 2.71 (95% CI 1.23 to 4.18; I^2=94%; p=0.00003) - There was no statistically significant difference in pain relief observed between the treatments (p=0.58)	No serious or adverse events or complications related to RF were reported.
Liu, 2022 Meta-analysis	**Pain (VAS or NRS)** *1 to 2 weeks*	**Adverse events** Overall risk (all 3 modalities; 13 studies): No statistically

Author, date	Efficacy outcomes	Safety outcomes
	• Overall effect (conventional and pulsed RF; 10 studies): statistically significant decrease in pain after RF denervation compared to control, WMD -1.72 (95% CI -2.17 to -1.30; I^2=78%; p<0.00001) *4 weeks* • Overall effect (all 3 modalities; 9 studies): statistically significant decrease in pain after RF denervation compared to control, WMD 1.49 (95% CI -1.76 to -1.21; I^2=66%; p<0.00001) *12 weeks* • Overall effect (all 3 modalities; 11 studies): statistically significant decrease in pain after RF denervation compared to control, WMD 1.83 (95% CI -2.39 to -1.26; I^2=88%; p<0.00001) *24 weeks* • Overall effect (all 3 modalities; 6 studies): statistically significant decrease in pain after RF denervation compared to control, WMD 1.96 (95% CI -2.89 to -1.04; I^2=97%; p<0.0001) **WOMAC** *4 weeks* • Overall effect (all 3 modalities; 4 studies): statistically significant decrease in WOMAC score after RF denervation compared to control, WMD -10.64 (95% CI -13.11 to -8.17; I^2=1%; p<0.00001) *12 weeks* • Overall effect (all 3 modalities; 4 studies): statistically significant decrease in WOMAC score after RF denervation	significant difference in the occurrence of adverse events between the RF denervation and control groups, RD 0.03 (95% CI -0.01 to 0.06; I^2=7%; p=0.14)

Author, date	Efficacy outcomes	Safety outcomes
	compared to control, WMD -6.12 (95% CI -7.67 to -4.57; I^2=0%; p<0.00001) *24 weeks* • Overall effect (all 3 modalities; 4 studies): statistically significant decrease in WOMAC score after RF denervation compared to control, WMD -10.89 (95% CI -12.28 to -9.51; I^2=57%; p<0.00001) **Global Perceived Effect** *4 weeks* • Overall effect (conventional and cooled RF; 3 studies): no statistically significant difference in Global Perceived Effect scores between RF denervation and comparator, WMD 0.63 (95% CI –0.15 to 1.42; I^2=93%; p=0.12) *12 weeks* • Overall effect (conventional and cooled RF; 3 studies): statistically significant difference in Global Perceived Effect scores in favour of control, WMD 1.12 (95% CI 0.61 to 1.63; I^2=78%; p<0.0001) • Note that this analysis appears to have been conducted incorrectly – the 3 studies cited all report that Global Perceived Effect improvement was statistically significantly greater in the RF denervation arm.	
Kumaran, 2019 RCT	**Pain (VAS)** • There was a statistically significant main effect for time (within group change) (F [2.1, 88]=16, p<0.001) and a significant interaction between group and time (F[4.2]=5.2, p=0.001).	No adverse events were reported.

Author, date	Efficacy outcomes	Safety outcomes
	• This infers that the type of intervention made a statistically significant difference to pain, and that there was a statistically significant overall difference between pre, post, 1 month, and 3 months. *Post-treatment* • RF group: MD of 1.2 (95% CI 0.81 to 1.5) vs. baseline. • Sham group: MD of 0.25 (95% CI -0.10 to 0.61) vs. baseline. • Control group: MD of 0.11 (95% CI -0.25 to 0.47) vs. baseline. • Note all MDs are of the transformed square root data; the non-transformed data show a clinically significant improvement in the RF group. *3 months* • RF group: MD of 0.76 (95% CI 0.18 to 1.3) vs. baseline. • Sham group: MD of 0.43 (95% CI -0.15 to 1.0) vs. baseline. • Control group: MD of 0.30 (95% CI -0.28 to 0.88) vs. baseline. • Note all MDs are of the transformed square root data; the non-transformed data show a clinically significant improvement in the RF group. **WOMAC** • There was a statistically significant main effect for time (within group change) (F [2.2, 91]=18, p<0.001) and a significant interaction between group and time (F[4.3]=2.7, p=0.031). • This infers that the type of intervention made a statistically significant difference to WOMAC score, and that there was a statistically significant overall difference between pre, post, 1 month, and 3 months. *Post-treatment*	

Author, date	Efficacy outcomes	Safety outcomes
	• RF group: MD of 1.9 (95% CI 1.1 to 2.8) vs. baseline. • Sham group: MD of 0.98 (95% CI 0.16 to 1.8) vs. baseline. • Control group: MD of 0.09 (95% CI -0.73 to 0.92) vs. baseline. • Note all MDs are of the transformed square root data; the non-transformed data show a clinically significant improvement in the RF group. *3 months* • RF group: MD of 1.7 (95% CI 0.41 to 2.9) vs. baseline. • Sham group: MD of 1.4 (95% CI 0.15 to 2.7) vs. baseline. • Control group: MD of 1.1 (95% CI -0.20 to 2.3) vs. baseline. • Note all MDs are of the transformed square root data; the non-transformed data show a clinically significant improvement in the RF group. **Walking ability** • There was a statistically significant main effect for time (F [2, 85]=15, p<0.001); however, there was no significant interaction between group and time. • This infers that the type of intervention did not make a statistically significant difference to walking ability. **Knee ROM** • There was a statistically significant main effect for time (within group change) (F [3, 126)=9.1, p<0.001) and a significant interaction between group and time (F(6)=2.6, p=0.023). • This infers that the type of intervention made a statistically significant difference to knee ROM, and that there was a statistically significant overall difference between pre, post, 1 month, and 3 months.	

<table>
<tr><th>Author, date</th><th>Efficacy outcomes</th><th>Safety outcomes</th></tr>
<tr><td></td><td>Post-treatment
RF group: MD of 0.48 (95% CI 0.16 to 7.9) vs. baseline.
Sham group: MD of 0.06 (95% CI -0.26 to 0.37) vs. baseline.
Control group: MD of 0.02 (95% CI -0.30 to 0.34) vs. baseline.
Note all MDs are of the transformed square root data.
3 months
RF group: MD of 0.29 (95% CI -0.06 to 0.64) vs. baseline.
Sham group: MD of 0.22 (95% CI -0.14 to 0.57) vs. baseline.
Control group: MD of 0.26 (95% CI -0.09 to 0.61) vs. baseline.
Note all MDs are of the transformed square root data.</td><td></td></tr>
<tr><td>Lyman, 2022
Cohort study (single arm, long-term extension of an RCT)</td><td>NRS
18 and 24 months
The NRS pain score for people treated with cooled RF denervation statistically significantly decreased from 6.8 (SD 0.8; n=32) at baseline to 2.4 (SD 2.5; n=32) at 18 months and 3.4 (SD 3.2; n=27) at 24 months after treatment (p<0.0001).
The NRS score at 1 month after treatment was 2.8 (SD 2.6; n=32) and at 12 months was 1.9 (SD 1.9; n=32).
Kaplan-Meier analysis suggested that patients had approximately a 50% chance of maintaining 50% or greater pain relief through 700 days after treatment.
WOMAC
18 and 24 months
The WOMAC total score for people treated with cooled RF denervation statistically significantly decreased from 64.4 (SD 14.7; n=32) at baseline to 29.3 (SD 25.3; n=32) at 18 months</td><td>There were no adverse events related to cooled RF denervation reported at 18- and 24-months following treatment.</td></tr>
</table>

<table>
<tr><th>Author, date</th><th>Efficacy outcomes</th><th>Safety outcomes</th></tr>
<tr><td></td><td>(p<0.0001) and 41.3 (SD 29.9; n=27) at 24 months after treatment (p=0.0007).
The WOMAC total score at 1 month after treatment was 34.1 (SD 23.8; n=32) and at 12 months was 27.4 (SD 23.2; n=32).
Global Perceived Effect
18 and 24 months
At 18 months, 75% (24/32) of patients reported a perceived improvement in pain. At 24 months, 63% (17/27) of patients reported a perceived improvement in pain.
At 1 month, 78.1% (25/32) of patients reported a perceived improvement in pain. At 12 months, 78.1% (25/32) of patients reported a perceived improvement in pain.
Radiographic changes
24 months
At 24 months, 68.2% (15/22) of patients had no change in Kellgren-Lawrence grade, 22.7% (5/22) showed worsening of 1 grade, and 9.1% of subjects (2/22) showed worsening by 2 grades.
EQ-5D
18 and 24 months
The total EQ-5D-5L score statistically significantly increased from baseline by 0.15 points at 18 months (p<0.0001) and 0.07 points at 24 months (p=0.0146).</td><td></td></tr>
<tr><td>Chen, 2021
Cohort study</td><td>Patients were categorised as having either a positive or negative outcome:</td><td>Not reported.</td></tr>
</table>

<table>
<tr><th>Author, date</th><th>Efficacy outcomes</th><th>Safety outcomes</th></tr>
<tr><td></td><td>Positive: at least 30% pain relief lasting at least 3 months after RF denervation
Negative: less than 30% pain relief or not relief not lasting for 3 months after RF denervation
Factors associated with positive outcome
In total, 162/265 patients had a positive outcome (61.1%).
In multivariate analysis, the following factors were associated with positive outcome:
Being obese, OR 3.68 (95% CI 1.66 to 8.19, p=0.001)
Not using opioids, OR 0.35 (95% CI 0.16 to 0.77, p=0.009)
Not being depressed, OR 0.29 (95% CI 0.10 to 0.82, p=0.02)
Use of cooled RF, OR 3.88 (95% CI 1.63 to 9.23, p=0.002)
Performing multiple lesions at each neural target, OR 15.88 (95% CI 4.24 to 59.50, p<0.001)</td><td></td></tr>
<tr><td colspan="3">Safety studies – the following studies were included to show unique safety events</td></tr>
<tr><td>McCormick, 2021
Narrative review</td><td>Not reported.</td><td>Adverse events:
Septic arthritis, n=1
Pes anserine tendon injury, n=1
Skin burn, n=1
Periarticular hematoma and/or hemarthrosis, n=5</td></tr>
<tr><td>Matveev, 2021
Case report</td><td>Not reported.</td><td>Adverse event:
Foot drop, n=1</td></tr>
<tr><td>Jorge, 2019</td><td>Not reported.</td><td>Adverse event:</td></tr>
</table>

Author, date	Efficacy outcomes	Safety outcomes
Case report		• Vascular injury, n=1

Procedure technique

All 3 modalities of RF denervation were included in the overview. In addition, the Wu (2022) network meta-analysis included comparisons between polarity of RF treatment (bipolar vs. monopolar) and target of RF (genicular nerve vs. saphenous nerve vs. articular cartilage). The Chen (2021) cohort study also identified treatment characteristics associated with a positive outcome.

Efficacy

Pain relief

Six studies reported on pain relief.

In the Wu (2022) network meta-analysis, pain relief (as measured by VAS) was assessed at 3 and 6 months. At 3 months, the network was comprised of 16 RCTs (16 interventions) of 1,401 patients, for a total of 120 paired estimates (17 direct and indirect evidence; 103 indirect evidence only). All treatments except for exercise had statistically significantly decreased VAS compared to placebo at 3 months. According to the surface under the cumulative ranking curve (SUCRA), the treatment rankings were as follows (best to worst; MD of treatment vs. placebo [95% CI] shown):

1. Cooled monopolar genicular nerve RF, -4.0 (-4.6 to -3.4)
2. Pulsed bipolar articular cavity RF, -3.8 (-4.8 to -2.8)
3. Conventional monopolar genicular nerve RF, -3.5 (-3.8 to -3.2)
4. Pulsed monopolar articular cavity RF combined with intra-articular platelet-rich plasma injection, -3.5 (-4.3 to -2.6)
5. Intra-articular erythropoietin injection, -3.1 (-4.5 to -1.7)
6. Intra-articular platelet-rich plasma injection, -2.8 (-3.7 to -1.9)
7. Pulsed monopolar genicular nerve RF, -2.8 (-3.2 to -2.5)
8. Pulsed monopolar articular cavity RF, -2.8 (-3.8 to -1.8)
9. Intra-articular anaesthesia, -2.0 (-2.5 to -1.5)
10. Intra-articular dextrose injection, -2.0 (-3.4 to -0.6)
11. Intra-articular sodium hyaluronate injection, -1.8 (-2.3 to -1.3)
12. Pulsed monopolar saphenous nerve RF, -1.6 (-2.1 to -1.1)
13. Intra-articular corticosteroid injection, -1.6 (-2.5 to -0.7)
14. NSAIDs, -1.4 (-1.7 to -1.0)
15. Exercise, -0.2 (-0.7 to 0.3)
16. Placebo, reference

At 6 months, the network was comprised of 10 RCTs (10 interventions) of 1,021 patients, for a total of 45 paired estimates (10 direct and indirect evidence; 35 indirect evidence only). All treatments except for NSAIDs had statistically significantly improved VAS compared to exercise at 6 months (placebo was not included in the network). According to the SUCRA, the treatment rankings were as follows (best to worst; MD of exercise vs. treatment [95% CI] shown):

1. Conventional bipolar genicular nerve RF, 5.5 (4.3 to 6.7)
2. Cooled monopolar genicular nerve RF, 4.7 (3.8 to 5.6)
3. Conventional monopolar genicular nerve RF, 3.5 (3.1 to 3.9)
4. Pulsed monopolar articular cavity RF combined with intra-articular protein-rich plasma, 3.3 (2.6 to 3.9)
5. Pulsed monopolar genicular nerve RF, 2.5 (2.2 to 2.8)
6. Intra-articular corticosteroid injection, 1.9 (1.1 to 2.7)
7. Intra-articular sodium hyaluronate injection, 1.9 (1.0 to 2.7)
8. Intra-articular platelet-rich plasma injection, 1.5 (0.4 to 2.6)
9. NSAIDs, 0.06 (-0.7 to 0.9)
10. Exercise, reference

In the Chou (2021) meta-analysis, there was a statistically significant decrease in pain from before treatment to 1, 3, 6, and 12 months after treatment. There was no statistically significant difference in pain relief between the RF modalities at any time point.

- 1 month (17 studies): SMD 3.25 (95% CI 2.56 to 3.93; I^2=93%; p<0.00001)
- 3 months (14 studies): SMD 3.39 (95% CI 2.47 to 4.31; I^2=96%; p<0.00001)
- 6 months (12 studies): SMD 4.84 (95% CI 3.62 to 6.03; I^2=95%; p<0.00001)
- 12 months (4 studies): SMD 2.71 (95% CI 1.23 to 4.18; I^2=94%; p=0.00003)

In the Liu (2022) meta-analysis, there was a statistically significant decrease in pain compared to control (either sham, intra-articular injection, or oral NSAIDs) at 1 to 2, 4, 12, and 24 weeks after treatment.

- 1 to 2 weeks (10 studies): WMD -1.72 (95% CI -2.17 to -1.30; I^2=78%; p<0.00001)
- 4 weeks (9 studies): WMD 1.49 (95% CI -1.76 to -1.21; I^2=66%; p<0.00001)
- 12 weeks (6 studies): WMD 1.83 (95% CI -2.39 to -1.26; I^2=88%; p<0.00001)
- 24 weeks (studies): WMD 1.96 (95% CI -2.89 to -1.04; I^2=97%; p<0.0001)

In the Kumaran (2019) RCT of conventional RF vs. sham vs. control, there was a statistically significant main effect for time (within group change) (F [2.1, 88]=16, p<0.001) and a significant interaction between group and time (F[4.2]=5.2, p=0.001). This infers that the type of intervention made a statistically significant difference to VAS pain, and that there was a statistically significant overall difference between pre, post, 1-month, and 3 months. The decrease in VAS score in the RF group was greater than published MCID estimates.

In the long-term cohort study, patients treated with cooled RF denervation had statistically significantly lower scores on the pain NRS at 18 and 24 months than at baseline (all p<0.0001). In Kaplan-Meier analysis, there was approximately a 50% chance that patients maintained a 50% or greater pain relief through 700 days after treatment (Lyman, 2022). Per the Global Perceived Effect questionnaire, 63% reported a perceived improvement in pain at 24 months (Lyman, 2022).

In the Chen (2021) cohort study, 162/265 (61.1%) patients had a positive outcome, defined as at least 30% pain relief lasting at least 3 months after RF denervation. In multivariate analysis, the following factors were associated with positive outcome:

- Being obese, OR 3.68 (95% CI 1.66 to 8.19, p=0.001)
- Not using opioids, OR 0.35 (95% CI 0.16 to 0.77, p=0.009)
- Not being depressed, OR 0.29 (95% CI 0.10 to 0.82, p=0.02)
- Use of cooled RF, OR 3.88 (95% CI 1.63 to 9.23, p=0.002)
- Performing multiple lesions at each neural target, OR 15.88 (95% CI 4.24 to 59.50, p<0.001)

Composite knee function and pain measures

WOMAC

Four studies reported WOMAC outcomes.

In the Wu (2022) network meta-analysis, WOMAC score was assessed at 3 and 6 months. At 3 months, the network was comprised of 14 RCTs (14 interventions) of 1,091 patients, for a total of 91 paired estimates (14 direct and indirect evidence; 77 indirect evidence only). All treatments except for exercise, NSAIDs, and pulsed monopolar saphenous nerve RF, had statistically significantly decreased WOMAC compared to placebo at 3 months. According to the SUCRA, the treatment rankings were as follows (best to worst; MD of treatment vs. placebo [95% CI] shown):

1. Cooled monopolar genicular nerve RF, -32 (-41 to -22)
2. Pulsed bipolar articular cavity RF, -26 (-37 to -14)
3. Conventional bipolar genicular nerve RF, -25 (-34 to -16)
4. Pulsed monopolar articular cavity RF, -22 (-34 to -10)
5. Conventional monopolar genicular nerve RF, -20 (-29 to -12)
6. Pulsed monopolar articular cavity RF combined with intra-articular platelet-rich plasma injection, -18 (-27 to -9)

7. Intra-articular anaesthesia, -18 (-27 to -8.2)
8. Pulsed monopolar genicular nerve RF, -16 (-24 to -6.9)
9. Pulsed monopolar saphenous nerve RF, -12 (-30 to 5.1)
10. Intra-articular corticosteroid injection, -14 (-24 to -5.5)
11. Intra-articular sodium hyaluronate injection, -13 (-22 to -4.4)
12. NSAIDs, -7.5 (-16 to 1.2)
13. Exercise, -0.5 (-8.3, 9.4)
14. Placebo, reference

At 6 months, the network was comprised of 9 RCTs (9 interventions) of 821 patients, for a total of 36 paired estimates (10 direct and indirect evidence; 26 indirect evidence only). All treatments had statistically significantly decreased WOMAC compared to exercise at 6 months (placebo was not included in the network). According to the SUCRA, the treatment rankings were as follows (best to worst; MD of exercise vs. treatment [95% CI] shown):

1. Cooled monopolar genicular nerve RF, 33 (29 to 37)
2. Pulsed monopolar articular cavity RF combined with intra-articular platelet-rich plasma injection, 30 (27 to 33)
3. Conventional bipolar genicular nerve RF, 24 (20 to 28)
4. Conventional monopolar genicular nerve RF, 20 (18 to 22)
5. Pulsed monopolar articular cavity RF, not reported
6. Intra-articular corticosteroid injection, 13 (10 to 17)
7. Intra-articular sodium hyaluronate injection, 9.1 (6.1 to 12)
8. NSAIDs, 9.7 (7.2 to 12)
9. Exercise, reference

In the Liu (2022) meta-analysis, there was a statistically significant decrease in WOMAC compared to control (either sham, intra-articular injection, or oral NSAIDs) at 4, 12, and 24 weeks after treatment.

- 4 weeks (4 studies): WMD -10.64 (95% CI -13.11 to -8.17; I^2=1%; p<0.00001)
- 12 weeks (4 studies): WMD -6.12 (95% CI -7.67 to -4.57; I^2=0%; p<0.00001)
- 24 weeks (4 studies): WMD -10.89 (95% CI -12.28 to -9.51; I^2=57%; p<0.00001)

In the Kumaran (2019) RCT of conventional RF vs. sham vs. control, there was a statistically significant main effect for time (within group change) (F [2.2, 91]=18, p<0.001) and a significant interaction between group and time (F[4.3]=2.7, p=0.031). This infers that the type of intervention made a statistically significant difference to WOMAC score, and that there was a statistically significant overall difference between pre, post, 1 month, and 3 months. The decrease in WOMAC score in the RF group was greater than published MCID estimates.

In the Lyman (2022) long-term cohort study, the WOMAC total score for people treated with cooled RF denervation statistically significantly decreased from 64.4 (SD 14.7; n=32) at baseline to 29.3 (SD 25.3; n=32) at 18 months ($p<0.0001$) and 41.3 (SD 29.9; n=27) at 24 months after treatment ($p=0.0007$).

Other functional outcomes

Walking ability

One study reported walking ability outcomes.

In the Kumaran (2019) RCT of conventional RF vs. sham vs. control, there was a statistically significant main effect for time ($F [2, 85]=15$, $p<0.001$); however, there was no significant interaction between group and time for walking ability as measured by the TUG test. This infers that the type of intervention did not make a statistically significant difference to walking ability.

Knee ROM

One study reported walking ability outcomes.

In the Kumaran (2019) RCT of conventional RF vs. sham vs. control, There was a statistically significant main effect for time (within group change) ($F [3, 126)=9.1$, $p<0.001$) and a significant interaction between group and time ($F(6)=2.6$, $p=0.023$). This infers that the type of intervention made a statistically significant difference to knee ROM, and that there was a statistically significant overall difference between pre, post, 1 month, and 3 months.

Radiographic outcomes

One study reported radiographic outcomes.

In the Lyman (2022) long-term cohort study, at 24 months, 68.2% (15/22) of patients had no change in Kellgren-Lawrence grade, 22.7% (5/22) showed worsening of 1 grade, and 9.1% of patients (2/22) showed worsening by 2 grades.

Generic Quality of Life measures

EQ-5D

One study reported EQ-5D outcomes.

In the Lyman (2022) long-term cohort study, the total EQ-5D-5L score statistically significantly increased from baseline by 0.15 points at 18 months ($p<0.0001$) and 0.07 points at 24 months ($p=0.0146$).

Safety

Rates of complications and major complications

In the Wu (2022) network meta-analysis, adverse events were reported in 6 studies. There were 43 (8.4%) adverse events in 513 patients treated with RF that were probably related to treatment; 20 (3.9%) major adverse events were possibly related to RF.

In the Liu (2022) meta-analysis, there was no statistically significant difference in the risk of adverse events between patients treated with RF denervation and patients treated with control, RD 0.03 (95% CI -0.01 to 0.06; $I^2=7\%$; $p=0.14$; all 3 modalities, 13 studies).

Specific complications

Pain

In the Wu (2022) network meta-analysis, 5 people had pain and 7 people had postprocedural pain. These were major adverse events that were deemed possibly related to RF denervation.

Falls

In the Wu (2022) network meta-analysis, 5 people experienced falls. These were major adverse events that were deemed possibly related to RF denervation.

Stiffness

In the Wu (2022) network meta-analysis, 1 person had stiffness. This was a major adverse event that was deemed possibly related to RF denervation.

Swelling

In the Wu (2022) network meta-analysis, 2 people had swelling. These were major adverse events that were deemed possibly related to RF denervation.

Septic arthritis

In the McCormick (2021) narrative review, there was a report of 1 person who had septic arthritis after treatment with RF.

Pes anserine tendon injury

In the McCormick (2021) narrative review, there was a report of 1 person who had a pes anserine tendon injury after treatment with RF.

Skin burn

In the McCormick (2021) narrative review, there was a report of 1 person who had a skin burn after treatment with RF.

Foot drop

In the Matveev (2021) case report, there was a report of 1 person who had foot drop after treatment with RF.

Vascular injury

In the Jorge (2019) case report, there was a report of 1 person who had a vascular injury after treatment with RF.

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they have never happened (theoretical).

They listed the following anecdotal adverse events:

- Numbness

They listed the following theoretical adverse events:

- Osteomyelitis
- Injuries to motor nerves
- Post ablation neuritis
- Charcot neuropathy

Three professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Nine studies were included in the key evidence summary, including 1 systematic review and network meta-analysis, 2 systematic reviews and meta-analyses, 1 RCT, 1 long-term cohort study that was an extension of an RCT, 1 cohort study, and 3 case series/reports.
- All 3 modalities of RF denervation were captured in the key evidence studies.
- Important efficacy data came from the systematic reviews and meta-analyses:
    - The Wu (2022), Chou (2021), and Li (2021) systematic reviews included a large number of RCTs. Chou (2021) additionally included observational studies.
    - Chou (2021) found that RF denervation has a statistically significant beneficial effect on osteoarthritic knee pain compared to baseline, at a magnitude greater than published MCID estimates. Furthermore, there was no statistically significant difference in pain relief between the modalities.
    - Wu (2022) found that whilst all modalities of RF denervation were typically more effective than placebo or exercise, patients responded better to the cooled modality than the conventional and pulsed modalities, and bipolar is more effective than monopolar for pain and function in conventional and pulsed modalities. Several RF modalities saw improvements in pain and WOMAC score greater than published MCID estimates when compared to placebo or exercise.
        - However, the authors caution that the number of studies, including for the cooled modality, is insufficient.
    - Liu (2022) found that RF denervation was statistically significantly better than control in several measures of knee pain and function. Interpretation of whether these statistical differences were clinically important was complicated due to the comparator arm consisting of sham and active comparators.
        - The authors conclude that thought the meta-analysis shows that RF denervation is efficacious, the clinical utility of RF denervation is currently poorly defined and that further studies are required.

- Further efficacy evidence came from the Kumaran (2019) RCT. This UK-based study demonstrated statistical and clinical significance over sham and control in improving pain and function. However, this study was limited by small sample size and short follow-up.
- The Lyman (2022) cohort study showed that the treatment effect of RF denervation can last up to 2 years. Some attenuation of treatment effect is expected due to nerve regrowth. This study had high attrition rates.
- Long-term evidence was generally limited.
- The Chen (2021) cohort study gave real-world evidence on the effectiveness of RF denervation, with 61.1% of patients having a positive outcome. Significant prognostic factors for a positive outcome included use of cooled RF and performing multiple lesions at each target.
- In the Wu (2022) network meta-analysis, 5 and 4 out of 21 studies were judged to have ‘some concerns’ or to be at ‘high risk’ of bias, respectively. The main reason for having some concern of bias was a lack of description of the randomisation process and the selection of the reported result; the main reason for having a high risk of bias was the selection of the reported result.
- The studies list various sources of funding, including from companies involved in the manufacture of RF devices. The sources of funding and conflicts of interest were not well described in the systematic reviews.
- The following ongoing studies were identified:
    - Coolief Cooled Radiofrequency vs. Conventional Radiofrequency to Manage OA Knee Pain. Prospective, multicentre, single-blind RCT of cooled RF versus conventional RF. Enrolment: 153 patients. Estimated study completion: August 2022. NCT04145011
    - Radiofrequency Ablation in the Pain Management of Knee Osteoarthritis. Double-blind RCT of conventional RF versus pulsed RF versus intra-articular steroids. Estimated enrolment: 150 patients. Estimated completion: March 2023. NCT05303766
    - Ultrasound-Guided Pulsed Radiofrequency In The Treatment Of Patients With Osteoarthritis Knee (USPRFGENOAK). Triple-blind RCT of pulsed RF versus sham. Estimated enrolment: 142 patients. Estimated completion: December 2022. NCT02915120.

- Comparison of Conventional and Cooled Radiofrequency of the Genicular Nerves in Patients With Chronic Knee Pain (COGENIUS). Prospective, multicentre, double-blind RCT of conventional RF versus cooled RF versus sham. Estimated enrolment: 400 patients. Estimated completion September 2026. NCT05407610

- Innovations in Genicular Outcomes Registry (iGOR). Prospective registry of patients undergoing several pain therapies including RF denervation. Estimated enrolment: 2,000 patients. Estimated completion: March 2025. NCT05495334

Existing assessments of this procedure

In 2022, the American Society of Pain and Neuroscience published the Consensus Guidelines on Interventional Therapies for Knee Pain (STEP Guidelines; Hunter, 2022). A literature search was performed to identify relevant studies, and consensus statements were formulated by a panel of specialists. There were 4 consensus statements relevant to RF treatment:

- RF denervation of the SM, SL and IM genicular nerves is a safe and effective therapeutic option for treating knee pain secondary to osteoarthritis as well as pain refractory to total knee arthroplasty; Level 1, Grade A, Consensus Strong.

- RF denervation of the SM, SL and IM genicular nerves can significantly reduce knee pain and improve function in patients with knee osteoarthritis and pain refractory to total knee arthroplasty; Level 1, Grade A, Consensus Strong.

- Thermal or cooled RF denervation should be utilized when performing genicular nerve ablation; Level 1, Grade A, Consensus Strong.

- In patients with persistent knee pain after genicular nerve ablation targeting the SM, SL and LM genicular nerves, one may consider targeting inferior lateral, medial retinacular nerve and/or infrapatellar branch of the saphenous nerve for supplemental treatment; Level III, Grade B, Consensus Moderate.

In 2019, the American College of Rheumatology/Arthritis Foundation published the Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee (Kolasinski, 2020). A literature search was performed to identify relevant studies, and recommendations were voted upon by an interprofessional voting panel. The recommendation relevant to RF denervation was:

- Radiofrequency ablation is conditionally recommended for patients with knee osteoarthritis.
    - A number of studies have demonstrated potential analgesic benefits with various ablation techniques but, because of the heterogeneity of techniques and controls used and lack of long-term safety data, this recommendation is conditional.

Related NICE guidance

Interventional procedures

- Magnetic resonance therapy for knee osteoarthritis Interventional procedures guidance [IPG702] Published: 25 August 2021
- Platelet-rich plasma injections for knee osteoarthritis Interventional procedures guidance [IPG637] Published: 23 January 2019
- Genicular artery embolisation for pain from knee osteoarthritis interventional procedures guidance [IPG708] Published: 27 October 2021
- Joint distraction for knee osteoarthritis without alignment correction Interventional procedures guidance [IPG529] Published: 23 July 2015
- Implantation of a shock or load absorber for mild to moderate symptomatic medial knee osteoarthritis Interventional procedures guidance [IPG512] Published: 23 January 2015

NICE guidelines

- Osteoarthritis: care and management Clinical guideline [CG177] Published: 12 February 2014 Last updated: 11 December 2020
- Joint replacement (primary): hip, knee and shoulder NICE guideline [NG157] Published: 04 June 2020

Professional societies

- British Orthopaedic Association
- British Association for Surgery of the Knee (BASK).

- British Society of Rheumatology
- Chartered Society of Physiotherapists (CSP)
- Royal College of Anaesthetists: Faculty of Pain Medicine
- British Pain Society

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Wu L, Li Y, Si H, et al. (2022) Radiofrequency Ablation in Cooled Monopolar or Conventional Bipolar Modality Yields More Beneficial Short-Term Clinical Outcomes Versus Other Treatments for Knee Osteoarthritis: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. Arthroscopy: the journal of arthroscopic & related surgery: official publication of the Arthroscopy Association of North America and the International Arthroscopy Association 38(7):2287-2302.
2. Chou SH, Shen PC, Lu CC, et al. (2021) Comparison of Efficacy among Three Radiofrequency Ablation Techniques for Treating Knee Osteoarthritis: A Systematic Review and Meta-Analysis. International journal of environmental research and public health 18(14).
3. Liu J, Wang T, Zhu ZH. (2022) Efficacy and safety of radiofrequency treatment for improving knee pain and function in knee osteoarthritis: a meta-analysis of randomized controlled trials. Journal of orthopaedic surgery and research 17(1).
4. Kumaran B and Watson T. (2019) Treatment using 448kHz capacitive resistive monopolar radiofrequency improves pain and function in patients with osteoarthritis of the knee joint: a randomised controlled trial. Physiotherapy 105(1):98-107.
5. Lyman J, Khalouf F, Zora K, et al. (2022) Cooled radiofrequency ablation of genicular nerves provides 24-Month durability in the management of osteoarthritic knee pain: Outcomes from a prospective, multicenter, randomized trial. Pain practice: the official journal of World Institute of Pain 22(6):571-581.

6. Chen Y, Vu TNH, Chinchilli VM, et al. (2021) Clinical and technical factors associated with knee radiofrequency ablation outcomes: a multicenter analysis. Regional anesthesia and pain medicine 46(4):298-304.
7. McCormick ZL, Patel J, Conger A, Smith CC, Spine Intervention Society's Patient Safety Committee. (2021) The Safety of Genicular Nerve Radiofrequency Ablation. Pain medicine (Malden, Mass) 22(2):518-519.
8. Matveev A, Kiymaz TC, Medina T, Maitin I. (2021) Acute foot drop following genicular nerve radiofrequency ablation: A case report. PM and R 13:73.
9. Jorge PG, Strand N. (2019) Vascular injury following genicular nerve radiofrequency ablation: A case report. Pain Medicine (United States) 20(3):619-620.
10. Hunter CW, Deer TR, Jones MR, et al. (2022) Consensus Guidelines on Interventional Therapies for Knee Pain (STEP Guidelines) from the American Society of Pain and Neuroscience. Journal of pain research 15:2683-2745.
11. Kolasinski SL, Neogi T, Hochberg MC, et al. (2020) 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis care & research 72(2):149-162.

Methods

NICE identified studies and reviews relevant to radiofrequency denervation for osteoarthritic knee pain from the medical literature. The following databases were searched between the date they started to 1st August 2022: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with osteoarthritic knee pain.

- Intervention or test: radiofrequency denervation.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Databases	**Date searched**	**Version/files**
MEDLINE (Ovid)	01/08/2022	1946 to July 29, 2022
MEDLINE In-Process (Ovid)	01/08/2022	1946 to July 29, 2022
MEDLINE Epubs ahead of print (Ovid)	01/08/2022	July 29, 2022
EMBASE (Ovid)	01/08/2022	1974 to 2022 July 29
EMBASE Conference (Ovid)	01/08/2022	1974 to 2022 July 29
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	01/08/2022	Issue 8 of 12, August 2022
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	01/08/2022	Issue 7 of 12, July 2022
International HTA database (INAHTA)	01/08/2022	-

Trial sources searched February 2022

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

Strategy used.
1 Radiofrequency Ablation/
2 ((radiofrequen* or radio-frequen* or radio frequen* or rf) adj4 ablat*).tw.
3 (Radio* adj4 frequen* adj4 ablat*).tw.
4 ((catheter* or needle* or electrode* or heat* or (transvenous adj1 electric*)) adj4 ablat*).tw.
5 RFA.tw.
6 Catheter Ablation/
7 ((radiofrequen* or radio-frequen* or radio frequen* or rf) adj4 (ablat* or leson* or neurotom* or rhizomot*)).tw.
8 Pulsed Radiofrequency Treatment/
9 ((Conventio* or pulse* or cool*) adj4 Radiofrequen*).tw.
10 (CRF or PRF).tw.
11 Denervation/
12 denervat*.tw.
13 or/1-12
14 Osteoarthritis, Knee/
15 exp Knee Joint/
16 OA.ti,ab.
17 ((knee* or patella* or meniscal* or articular* or patellofem*) adj4 (OA or osteoarthrit* or cartilag* or degenerat* or diseas* or deteriorat* or injur* or defect*)).ti,ab.
18 ((knee* or patella* or meniscal* or articula* or patellofem*) adj4 (cartilage* or joint* or cap*) adj4 (degenerat* or diseas* or deteriorat* or injur* or defect*)).ti,ab.
19 Gonarthrosis*.ti,ab.
20 (degenerativ* adj4 arthriti*).ti,ab.
21 Genicul* neuroto*.tw.
22 or/14-21
23 13 and 22
24 COOLIEF.tw.
25 CRFA.tw.
26 24 or 25
27 23 or 26
28 Animals/ not Humans/
29 27 not 28
30 limit 29 to english language

Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5. Observational studies with fewer than 50 patients were not included in the table.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Ajrawat P, Radomski L, Bhatia A et al. (2020) Radiofrequency Procedures for the Treatment of Symptomatic Knee Osteoarthritis: A Systematic Review. Pain medicine (Malden, Mass.) 21(2):333-48	Systematic review n=33 studies	Current evidence substantiates that RF modalities for knee OA potentially improve pain, functionality, and disease-specific QOL for up to three to 12 months with minimal localized complications. This suggests that RF modalities are perhaps an effective adjunct therapy for patients with knee OA who are unresponsive to conservative therapies. Further RCTs with larger sample sizes and long-term follow-up that directly compare the three primary RF modalities are warranted to confirm the clinical efficaciousness and superiority of these RF modalities for knee OA.	More recent systematic reviews included.
Akbas M, Luleci N, Dere K et al. (2011) Efficacy of pulsed radiofrequency treatment on the saphenous nerve in patients with chronic knee pain. Journal of	Case series n=115 FU=22 months	PRF application to the saphenous nerve for eight minutes showed remarkable amount of patient satisfaction. Application of PRF for the second time could	Studies with more patients or longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
back and musculoskeletal rehabilitation 24(2):77-82		be recommended if it shows some benefit after the sixth month. But none of our patients needed a second application of PRF after six months period.	
Burgos LA, Greenwood AJ, Tarima SS, et al. (2021) Pain relief following genicular nerve radiofrequency ablation: does knee compartment matter?. Pain management 11(6):705-714.	Case series n=62 FU=6 months	Compartmental location of knee OA impacts pain relief following genicular radiofrequency ablation. Future protocols could target nerves based on which compartments are more affected on imaging.	Studies with more patients or longer follow up included.
Carlone AG, Grothaus O, Jacobs C, and Duncan ST. (2021) Is Cooled Radiofrequency Genicular Nerve Block and Ablation a Viable Option for the Treatment of Knee Osteoarthritis? Arthroplasty Today 7:220-224	Case series n=176 FU=6 weeks	Cooled RFA may be an effective adjunct therapy as part of a multimodal pain regimen; however, individual patient characteristics must be considered.	Studies with more patients or longer follow up included.
Carpenedo R, Al-Wardat M, Vizzolo L, et al. (2022) Ultrasound-guided pulsed radiofrequency of the saphenous nerve for knee osteoarthritis pain: a pilot randomized trial. Pain management 12(2):181-193.	Pilot RCT n=20 (10 PRF; 10 sham) FU=6 months	PRF of the saphenous nerve is an alternative to relieve pain in gonarthritis. Our results provide data to support a sample size calculation for future trials.	RCTs with more patients included in systematic reviews.
Chen AF, Mullen K, Casambre F et al. (2021) Thermal Nerve Radiofrequency Ablation for the Nonsurgical Treatment of Knee	Systematic review n=7 studies	These results demonstrate geniculate nerve thermal RFA to be a superior nonsurgical treatment of knee OA compared	More recent meta-analyses included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Osteoarthritis: A Systematic Literature Review. The Journal of the American Academy of Orthopaedic Surgeons 29(9):387-96		with NSAIDs and IA corticosteroid injections. None of the RCTs reported any serious AEs with geniculate nerve thermal RFA, as opposed to known cardiovascular, gastrointestinal, and renal AEs for NSAIDs and accelerated cartilage loss and periprosthetic infection risk for IA corticosteroid injections.	
Chen AF, Khalouf F, Zora K et al. (2020) Cooled radiofrequency ablation provides extended clinical utility in the management of knee osteoarthritis: 12-month results from a prospective, multi-center, randomized, cross-over trial comparing cooled radiofrequency ablation to a single hyaluronic acid injection. BMC musculoskeletal disorders 21(1):363	RCT n=175 (88 Cooled RF; 87 control) FU=12 months	A majority of subjects treated with CRFA demonstrated sustained knee pain relief for at least 12-months. Additionally, CRFA provided significant pain relief for HA subjects who crossed over 6 months after treatment.	Captured in the Wu, 2022 network meta-analysis.
Chen AF, Khalouf F, Zora K, et al. (2020) Cooled Radiofrequency Ablation Compared with a Single Injection of Hyaluronic Acid for Chronic Knee Pain: A Multicenter, Randomized Clinical Trial Demonstrating	RCT n=175 (88 Cooled RF; 87 control) FU=6 months	CRFA-treated subjects demonstrated a significant improvement in pain relief and overall function compared with subjects treated with a single injection of HA. No serious adverse events related to either procedure were noted,	Captured in the Wu, 2022 network meta-analysis.

Article	**Number of patients and follow up**	**Direction of conclusions**	**Reason study was not included in main evidence summary**
Greater Efficacy and Equivalent Safety for Cooled Radiofrequency Ablation. The Journal of bone and joint surgery American volume 102(17):1501-1510.		and the overall adverse-event profiles were similar.	
Choi WJ, Hwang SJ, Song JG, et al. (2011) Radiofrequency treatment relieves chronic knee osteoarthritis pain: a double-blind randomized controlled trial. Pain 152(3):481-487.	RCT n=38 (19 RF; 19 sham) FU=12 weeks	RF neurotomy of genicular nerves leads to significant pain reduction and functional improvement in a subset of elderly chronic knee OA pain, and thus may be an effective treatment in such cases. Further trials with larger sample size and longer follow-up are warranted.	Captured in the Wu, 2022 network meta-analysis.
Davis T, Loudermilk E, Depalma M et al. (2019) Twelve-month analgesia and rescue, by cooled radiofrequency ablation treatment of osteoarthritic knee pain: Results from a prospective, multicenter, randomized, cross-over trial. Regional Anesthesia and Pain Medicine 44(4):499-506	RCT n=151 (76 cooled RF; 75 sham) FU=12 months	This study demonstrates that analgesia following cooled RFA for OA knee pain could last for at least 12 months and could rescue patients who continue to experience intolerable discomfort following IAS.	Captured in the Wu, 2022 network meta-analysis.
Davis T, Loudermilk E, DePalma M et al. (2018) Prospective, Multicenter, Randomized, Crossover Clinical Trial Comparing the Safety and Effectiveness of Cooled Radiofrequency Ablation With Corticosteroid Injection in the	RCT n=151 (76 cooled RF; 75 sham) FU=6 months	This study demonstrates that cooled RFA is an effective long-term therapeutic option for managing pain and improving physical function and quality of life for patients with painful knee OA when	Captured in the Wu, 2022 network meta-analysis.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Management of Knee Pain From Osteoarthritis. Regional anesthesia and pain medicine 43(1):84-91		compared with IAS injection	
El-Hakeim EH, Elawamy A, Kamel EZ, et al. (2018) Fluoroscopic Guided Radiofrequency of Genicular Nerves for Pain Alleviation in Chronic Knee Osteoarthritis: A Single-Blind Randomized Controlled Trial. Pain physician 21(2):169-177.	RCT n=60 (30 RF; 30 control) FU=6 months	RF can ameliorate pain and disability in chronic knee osteoarthritis in a safe and effective manner.	Captured in the Chou, 2021 meta-analysis.
El-Tamboly S, Medhat M, Khattab R, et al. (2021). Pulsed radiofrequency ablation of genicular nerve versus intra-articular radiofrequency ablation combined with platelets rich plasma for chronic kneeosteoarthritis. Egyptian Journal of Anaesthesia 37(1):317-325.	RCT n=60 FU=12 months	The use of ultrasonography intra-articular-platelet-rich plasma injection combined to pulsed radiofrequency ablation of articular surface show significant improvement in pain compared to the genicular nerve.	RCTs with more patients or longer follow up included.
Elemam EM, Abdel Dayem OT, Mousa SA, Mohammed HM. (2022) Ultrasound-guided monopolar versus bipolar radiofrequency ablation for genicular nerves in chronic knee osteoarthritis pain: A randomized controlled study. Annals of Medicine and Surgery 77:103680.	RCT n=50 (25 monopolar; 25 bipolar) FU=24 weeks	Ultrasound guided bipolar RF ablation is more effective than monopolar RF ablation in controlling knee osteoarthritis pain as for the duration and severity of pain without fluoroscopic confirmation.	RCTs with more patients or longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Elawamy A, Kamel EZ, Mahran SA et al. (2021) Efficacy of Genicular Nerve Radiofrequency Ablation Versus Intra-Articular Platelet Rich Plasma in Chronic Knee Osteoarthritis: A Single-Blind Randomized Clinical Trial. Pain physician 24(2):127-34	RCT n=200 (110 pulsed RF; 100 platelet rich plasma injection) FU=12 months	Pulsed radiofrequency of the genicular nerves can be considered superior to knee intra-articular platelet-rich plasma injection for sustained pain relief and the lower severity index in patients with chronic knee osteoarthritis.	Captured in the Wu, 2022 network meta-analysis.
Gulec E, Ozbek H, Pektas S, Isik G. (2017) Bipolar Versus Unipolar Intra-articular Pulsed Radiofrequency Thermocoagulation in Chronic Knee Pain Treatment: A Prospective Randomized Trial. Pain physician 20(3):197-206.	RCT n=100 (50 monopolar; 50 bipolar) FU=3 months	Bipolar IAPRF is more advantageous in reducing chronic knee pain and functional recovery compared with unipolar IAPRF. Further studies with longer follow-up times, laboratory-based tests, and different generator settings are required to establish the clinical importance and well-defined mechanism of action of PRF.	Captured in the Wu, 2022 network meta-analysis.
Gupta A, Huettner DP, Dukewich M. (2017) Comparative Effectiveness Review of Cooled Versus Pulsed Radiofrequency Ablation for the Treatment of Knee Osteoarthritis: A Systematic Review. Pain physician 20(3):155-171.	Systematic review n=17 studies	Overall, the studies showed promising results for the treatment of severe chronic knee pain by radiofrequency ablation at up to one year with minimal complications. Numerous studies, however, yielded concerns about procedural protocols, study quality, and patient follow-up. Radiofrequency ablation can offer	More recent systematic reviews included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
		substantial clinical and functional benefit to patients with chronic knee pain due to osteoarthritis or post total knee arthroplasty.	
Han Q, Ma Y, Jia P, et al. (2021) A Randomized Controlled Pilot Study Comparing the Efficacy of Pulsed Radiofrequency Combined With Exercise Versus Exercise Alone in Pain Relief and Functional Improvement for Chronic Knee Osteoarthritis. Pain practice: the official journal of World Institute of Pain 21(2):160-170.	RCT n=62 (32 pulsed RF; 32 exercise)	The improvement in pain relief and knee function might be associated with restoration of muscle strength after PRF-PS exercise by overcoming muscle inhibition.	RCTs with more patients or longer follow up included.
Hong T, Wang H, Li G, et al. (2019) Systematic Review and Meta-Analysis of 12 Randomized Controlled Trials Evaluating the Efficacy of Invasive Radiofrequency Treatment for Knee Pain and Function. BioMed research international 9037510.	Systematic review and meta-analysis n=12 studies	RF treatment significantly reduces the knee pain, but rarely improves the knee joint function. Radiofrequency ablation has better efficacy than pulsed radiofrequency ablation in reducing pain. Furthermore, subgroup analysis and meta-regression suggested that women are more sensitive to RF treatment than men.	More recent systematic reviews included.
Hong T, Wang S, Ding Y, et al. (2020) High-Voltage Intra-articular Pulsed Radiofrequency for Chronic Knee Pain Treatment: A Single-	Cohort study n=57 FU=6 months	CT-guided high-voltage intra-articular PRF is more beneficial in reducing knee pain and improving knee function compared with low-	Experimental studies with more patients, or studies with longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Center Retrospective Study. Pain physician 23(5):e549-e558.		voltage intra-articular PRF. In addition, patients who received high-voltage intra-articular PRF were more satisfied with their treatment.	
Hong T, Li G, Han Z et al. (2020) Comparing the safety and effectiveness of radiofrequency thermocoagulation on genicular nerve, intra-articular pulsed radiofrequency with steroid injection in the pain management of knee osteoarthritis. Pain Physician 23(4specialissue):295-s303	Cohort study n=97 (32 RF; 34 pulsed RF; 31 control) FU=6 months	Both RF of the genicular nerve and intra-articular pulsed RF could alleviate the knee joint pain and improve the knee joint dysfunction; however, the treatment efficacy of RF of the genicular nerve was better than that of intra-articular pulsed RF.	Studies with more patients or longer follow up included.
Huang Y, Deng Q, Liuqing Y, et al. (2020) Efficacy and Safety of Ultrasound-Guided Radiofrequency Treatment for Chronic Pain in Patients with Knee Osteoarthritis: A Systematic Review and Meta-Analysis. Pain Res Manag. 19(19).	Systematic review and meta-analysis n=8 studies	Ultrasonography is an effective, safe, nonradiative, and easily applicable guidance method for RF in pain relief and functional improvement in KOA patients.	More recent meta-analyses included.
Hunter C, Davis T, Loudermilk E, et al. (2020) Cooled Radiofrequency Ablation Treatment of the Genicular Nerves in the Treatment of Osteoarthritic Knee Pain: 18- and 24-Month Results. Pain practice:	Cohort study n=33 FU=24 months	In this subset of subjects from a randomised controlled trial, CRFA provided sustained pain relief, improved function, and perceived positive effect through 24 months for subjects with osteoarthritis knee	Similar outcomes as Lyman (2022).

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
the official journal of World Institute of Pain 20(3):238-246		pain with no safety concerns identified.	
Ikeuchi M, Ushida T, Izumi M, Tani T. (2011) Percutaneous Radiofrequency Treatment for Refractory Anteromedial Pain of Osteoarthritic Knees. Pain Medicine 12(4):546-551.	Non-randomised, open-label study n=35 (18 RFA; 17 nerve block) FU=6 months	Some patients were able to benefit substantially from radiofrequency treatment. Even if its effective period is limited, radiofrequency application is a promising treatment to alleviate refractory anteromedial knee pain with osteoarthritis. Further experience and technical improvements are needed to establish its role in the management of knee osteoarthritis.	Studies with more patients or longer follow up included.
Jadon A, Jain P, Motaka M, et al. (2018) Comparative evaluation of monopolar and bipolar radiofrequency ablation of genicular nerves in chronic knee pain due to osteoarthritis. Indian Journal of Anaesthesia 62(11):876-880.	RCT n=30 (15 monopolar; 15 bipolar) FU=6 months	Bipolar RFA is an effective alternative for ablation of genicular nerves in patients with knee pain due to OA. It causes less procedural pain compared with monopolar RFA.	Captured in the Wu, 2022 systematic review and network meta-analysis.
Kapural L, Lee N, Neal K, Burchell M. (2019) Long-Term Retrospective Assessment of Clinical Efficacy of Radiofrequency Ablation of the Knee Using a Cooled Radiofrequency System. Pain physician 22(5):489-494.	Case series n=205	This study demonstrates the clinical effectiveness of cooled RFA in the treatment of chronic knee pain from osteoarthritis, and even in those patients who maintained chronic knee pain after TKA. Our real-life data	Studies with more patients or longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
		seems to agree with data previously published in a randomised controlled trial, despite the fact that this was quite a heterogenous patient population with various sources of chronic pain.,	
Kocayigit H, Beyaz SG. (2021) Comparison of cooled and conventional radiofrequency applications for the treatment of osteoarthritic knee pain. Journal of Anaesthesiology Clinical Pharmacology 37(3):464-468.	Cohort study n=63 (34 conRF; 29 cooled RF) FU=6 months	We found that both cooled and conventional RF techniques in genicular nerve ablation are similarly effective in reducing pain in patients with osteoarthritis-induced knee pain and improving patients' physical functions. The complication rates are very low and there was no superiority to each other.	Studies with more patients or longer follow up included.
Leoni MLG, Schatman ME, Demartini L et al. (2020) Genicular nerve pulsed dose radiofrequency (PDRF) compared to intra-articular and genicular nerve PDRF in knee osteoarthritis pain: A propensity score-matched analysis. Journal of Pain Research 13:1315-1321.	Cohort study n=78 FU=6 months	This is the first study that compared two different RF techniques. Pulsed RF of the genicular nerve and pulsed RF intra-articular + genicular nerve were both effective in reducing pain at 3- and 6-months follow-up. However, only PDRF intra-articular + genicular nerve was able to improve WOMAC scores at 3 months after the treatment with	Studies with more patients or longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
		a longer period of efficacy compared to pulsed RF genicular nerve alone.	
Li G, Zhang Y, Tian L, Pan J. (2021) Radiofrequency ablation reduces pain for knee osteoarthritis: A meta-analysis of randomized controlled trials. International journal of surgery 91:105951	Systematic review and meta-analysis n=8 studies	RF ablation showed better effectiveness in relieving pain and promoting function recovery in patients with knee osteoarthritis. Considering the small sample size of the included studies, the results should be treated with caution.	More recent meta-analyses included.
McCormick ZL, Reddy R, Korn M, et al. (2018) A Prospective Randomized Trial of Prognostic Genicular Nerve Blocks to Determine the Predictive Value for the Outcome of Cooled Radiofrequency Ablation for Chronic Knee Pain Due to Osteoarthritis. Pain medicine (Malden, Mass) 19(8):1628-1638.	RCT n=54 (29 cooled RF with block; 25 cooled RF without block) FU=6 months	Clinically meaningful improvements in pain and function were observed at 6 months in over 60% of participants who underwent genicular nerve cooled RFA. However, genicular nerve block using the common protocol of 1mL local anaesthetic volume at each injection site and a threshold of >50% pain relief for subsequent cooled RFA eligibility did not improve the rate of treatment success.	Study focus is prognostic value of nerve block.
Mohamed OS, Omar SM, Gaber AF et al. (2021) Three Needles Approach-A New Technique of Genicular Nerves Radiofrequency Ablation for Pain Relief in Advanced Chronic Knee Osteoarthritis: A	RCT n=50 (25 single needle; 25 three needle) FU=6 months	Compared to the conventional single-needle genicular nerve ablation technique, the 3-needle approach appears to be a promising, safe, and more effective ablation	Studies with more patients or longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Randomized Trial. Pain physician 24(7):e1067-e1074.		technique for patients with chronic knee OA.	
Monerris Tabasco MM, Roca Amatria G, Rios Marquez N, et al. (2019) Assessment of the effectiveness and safety of two radiofrequency techniques for the treatment of knee pain secondary to gonarthrosis. Prospective randomized double blind study. Revista espanola de anestesiologia y reanimacion. 66(7):362-369.	RCT n=28 (12 pulsed and conventional RF; 16 placebo) FU=6 months	The combination of two radiofrequency techniques, does not cause a reduction in the intensity of the knee pain, at month, three, or at six months after its completion. It is necessary to change the radiofrequency technique and include more variables to continue with the efficacy study.	Captured in the Wu, 2022 systematic review and network meta-analysis.
Orhurhu V, Urits I, Grandhi R, Abd-Elsayed A. (2019) Systematic Review of Radiofrequency Ablation for Management of Knee Pain. Current pain and headache reports 23(8):55.	Systematic review n=19 studies	In summary, the data available suggests radiofrequency ablation as a promising and efficacious with all 19 studies revealing significant short- and long-term pain reductions in patients with knee pain.	More recent systematic reviews included.
Philip A, Williams M, Davis J, et al. (2021) Evaluating predictors of pain reduction after genicular nerve radiofrequency ablation for chronic knee pain. Pain management 11(6):669-677.	Case series n=124	Identifying patients who may benefit the most from genicular RFA is still not clear. Pain reduction differences between patients with and without depression and RFA type deserves further exploration.	Studies with more patients or longer follow up included.
Ray D, Goswami S, Dasgupta S, Ray S, Basu S. (2018) Intra-Articular hyaluronic acid injection versus RF	RCT n=24 (12 RF; 12 control)	As compared to intra-articular hyaluronic acid injection, RF neurotomy of genicular nerves appears to be a	Captured in the Wu, 2022 systematic review and

Article	**Number of patients and follow up**	**Direction of conclusions**	**Reason study was not included in main evidence summary**
ablation of genicular nerve for knee osteoarthritis pain: A randomized, open-label, clinical study. Indian Journal of Pain 32(1):36-39.		promising and more effective therapeutic procedure for patients with chronic knee OA.	network meta-analysis.
Sajan A, Mehta T, Griepp DW, et al. (2022) Comparison of Minimally Invasive Procedures to Treat Knee Pain Secondary to Osteoarthritis: A Systematic Review and Meta-Analysis. Journal of vascular and interventional radiology : JVIR. 33(3):238-248e4.	Systematic review and meta-analysis n=11 studies	The current evidence does not suggest a significant difference in outcomes among IA injection, RF ablation, and genicular artery embolisation for knee pain secondary to OA.	More comprehensive network meta-analysis included.
Santana-Pineda MM, Vanlinthout LE, Santana-Ramirez S et al. (2021) A Randomized Controlled Trial to Compare Analgesia and Functional Improvement After Continuous Neuroablative and Pulsed Neuromodulative Radiofrequency Treatment of the Genicular Nerves in Patients with Knee Osteoarthritis up to One Year After the Intervention. Pain medicine (Malden, Mass.) 22(3):637-52	RCT n=216 (108 pulsed RF; 108 conventional RF) FU=12 months	Therapeutic efficacy and reduction in analgesic consumption were superior after conventional RF. Treatment success at 6 months after radiofrequency intervention decreased with more severe gonarthritis; higher pre-interventional pain intensity; and concomitant depression, anxiety disorder, and diabetes mellitus.	Captured in the Wu, 2022 network meta-analysis.
Sari S, Aydin ON, Turan Y et al. (2018) Which one is more effective for the clinical treatment of	RCT n=73 (37 RF; 36 intra-	This study is the first controlled study in the literature which compares RF genicular	Captured in the Wu, 2022 systematic review and

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
chronic pain in knee osteoarthritis: radiofrequency neurotomy of the genicular nerves or intra-articular injection?. International journal of rheumatic diseases 21(10):1772-1778.	articular injection) FU=3 months	nerve to intra-articular injections. This study demonstrated that genicular nerve RF neurotomy is a safe and efficient treatment modality and provides functional improvement along with an analgesia in patients with chronic knee OA.	network meta-analysis.
Shen WS, Xu XQ, Zhai NN, et al. (2017) Radiofrequency Thermocoagulation in Relieving Refractory Pain of Knee Osteoarthritis. American journal of therapeutics 24(6):e693-e700.	RCT n=54 (27 RF; 27 control) FU=3 months	RFA may have better efficacy in relieving refractory pain and promoting function recovery in patients with knee OA than regular treatment.	Studies with more patients or longer follow up included.
Takahashi K, Hashimoto S, Kurosaki H et al. (2016) A pilot study comparing the efficacy of radiofrequency and microwave diathermy in combination with intra-articular injection of hyaluronic acid in knee osteoarthritis. Journal of physical therapy science 28(2)	RCT n=17 (9 RF; 9 control) FU=3 weeks	This study revealed that symptom relief in patients with knee OA was greater with radiofrequency diathermy than with microwave diathermy with concurrent use of hyaluronic acid injection, presumably due to the different heating characteristics of the two methods.	Studies with more patients or longer follow up included.
Uematsu H, Osako S, Hakata S, et al. A Double-Blind, Placebo-Controlled Study of Ultrasound-Guided Pulsed Radiofrequency Treatment of the Saphenous Nerve for Refractory Osteoarthritis-	RCT n=70 (37 pulsed RF;33 sham) FU=12 weeks	Ultrasound-guided saphenous nerve PRF proved to be effective for at least 12 weeks in patients with knee OA and showed no adverse events.	Studies with more patients or longer follow up included.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Associated Knee Pain. Pain physician 24(6):e761-e769.			
Wang R, Ma C, Han Y, Tan M, Lu L. (2019) Effectiveness of Denervation Therapy on Pain and Joint Function for Patients with Refractory Knee Osteoarthritis: A Systematic Review and Meta-Analysis. Pain physician 22(4):341-352.	Systematic review and meta-analysis n=6 studies	Denervation of the knee joint may become a promising therapy for patients with knee OA who are refractory to conservative treatment. This therapy can provide short-term therapeutic effect in pain alleviation for 6 months and joint function recovery for 3 months. The therapeutic effect in joint function may decrease 6 months after operation. The long-term efficacy in pain remission and function improvement is still elusive and controversial; therefore, further research with larger sample sizes are needed in the future.	More recent meta-analyses included.
Wong PKW, Kokabi N, Guo Y, et al. (2021) Safety and efficacy comparison of three- vs four-needle technique in the management of moderate to severe osteoarthritis of the knee using cooled radiofrequency ablation. Skeletal radiology 50(4):739-750.	Cohort study n=50 FU=6 months	The four-needle treatment approach offers an advantage in the overall efficacy in treating stiffness and pain in patients with moderate-to-severe OA refractory to conservative treatments leading to decreased opiate usage without complications.	Studies with more patients or longer follow up included.
Wu BP, Grits D, Foorsov V et al. (2022) Cooled and traditional thermal	Cohort study (retrospective)	Both thermal RF ablation and cooled RF ablation effectively	Studies with better designs

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
radiofrequency ablation of genicular nerves in patients with chronic knee pain: a comparative outcomes analysis. Reg Anesth Pain Med 0: 1-6	n=208 FU=1 year	reduced NRS pain scores in most patients with chronic knee pain within the 1-year follow-up period. Genicular nerve thermal RF ablation was associated with a higher probability of treatment success and a greater degree of pain relief at 1 month after the procedure when compared with cooled RF ablation in propensity score matched patients with chronic knee pain.	or more patients included.
Xiao L, Shu F, Xu C, et al. (2018) Highly selective peripheral nerve radio frequency ablation for the treatment of severe knee osteoarthritis. Experimental and Therapeutic Medicine 16(5):3973-3977.	RCT n=96 (49 RF; 47 control) FU=12 months	Compared with sodium hyaluronate injection, highly selective peripheral nerve RF ablation of the knee was more effective, easy to operate and had no significant adverse effects for the treatment of knee OA.	Captured in the Wu, 2022 systematic review and network meta-analysis.
Yuan Y, Shen W, Han Q, et al. (2016) Clinical observation of pulsed radiofrequency in treatment of knee osteoarthritis. International Journal of Clinical and Experimental Medicine 9(10):20050-20055.	RCT n=42 (22 pulsed RF; 20 control) FU=24 weeks	The effect of intra-articular pulsed RF treatment is obviously superior to the traditional compound betamethasone injection group in the treatment for refractory knee osteoarthritis; pulsed RF could obviously alleviate the clinical symptoms and decrease the content of TNF-alpha, MMP-3 and IL-1 in the synovial, in addition, it is safe and	Captured in the Wu, 2022 systematic review and network meta-analysis.

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
		reliable, all of these make it an effective method for senile refractory knee osteoarthritis	
Zeitlinger L, Kopinski J, Dipasquale T (2019). Genicular nerve ablation: A systematic review of procedure outcomes for chronic knee pain. Current Orthopaedic Practice 30(5):477-483.	Systematic review n=11 studies	Genicular nerve ablation with radiofrequency has demonstrated favourable outcomes with low complication rates.	More recent systematic reviews included.
Zhang H, Wang B, He J, and Du Z. (2021) Efficacy and safety of radiofrequency ablation for treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. The Journal of international medical research 49(4): 3000605211006647	Systematic review and meta-analysis n=9 studies	Radiofrequency ablation is efficacious and safe for reducing pain and improving knee function in patients with knee osteoarthritis, without increasing the risk of adverse effects.	Same studies and outcomes as Li (2021).