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Comparative effectiveness of treatment options for subacromial shoulder conditions: a systematic review and network meta-analysis

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Abstract

Background: There are currently many treatment options for patients with subacromial shoulder conditions (SSCs). Clinical decision-making regarding the best treatment option is often difficult. This study aims to evaluate the comparative effectiveness of treatment options for relieving pain and improving function in patients with SSCs.

Methods: Eight databases [including MEDLINE, Embase, CINAHL, AMED, PEDro, Cochrane Database of Systematic Reviews and World Health Organization (WHO) International Clinical Trials Registry] were searched from inception until April 2020. Randomised clinical/controlled trials of adult patients investigating the effects of nonsurgical (e.g. corticosteroid injections, therapeutic exercise, shockwave therapy) and surgical treatment for SSCs, compared with each other, placebo, usual care or no treatment, were retrieved. Pairs of reviewers screened studies independently, quality appraised eligible studies using the Cochrane risk of bias tool, extracted and checked data for accuracy. Primary outcomes were pain and disability in the short term (⩽3 months) and long term (⩾6 months). Direct and indirect evidence of treatment effectiveness was synthesised using random-effects network meta-analysis.

Results: The review identified 177 eligible trials. Summary estimates (based on 99 trials providing suitable data, 6764 patients, 20 treatment options) showed small to moderate effects for several treatments, but no significant differences on pain or function between many active treatment comparisons. The primary analysis indicated that exercise and laser therapy may provide comparative benefit in terms of both pain and function at different follow-up time-points, with larger effects found for laser in the short term at 2–6 weeks, although direct evidence was provided by one trial only, and for exercise in the longer term [standardised mean difference (SMD) 0.39, 95% confidence interval (CI) 0.18, 0.59 at 3–6 months] compared with control. Sensitivity analyses excluding studies at increased risk of bias confirmed only the comparative effects of exercise as being robust for both pain and function up until 3-month follow-up.

Conclusion: Current evidence shows small to moderate effect sizes for most treatment options for SSCs. Six treatments had a high probability of being most effective, in the short term, for pain and function [acupuncture, manual therapy, exercise, exercise plus manual therapy, laser therapy and Microcurrent (MENS) (TENS)], but with low certainty for most treatment options. After accounting for risk of bias, there is evidence of moderate certainty for

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the comparative effects of exercise on function in patients with SSCs. Future large, high-quality pragmatic randomised trials or meta-analyses are needed to better understand whether specific subgroups of patients respond better to some treatments than others.

Keywords: subacromial, shoulder impingement, rotator cuff, conservative treatments, systematic review, network meta-analysis

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Introduction

At any given time, up to 26% of the general adult population has shoulder pain.[1] Subacromial shoulder conditions (SSCs) including so-called subacromial impingement syndrome, rotator cuff disease and subacromial bursitis account for nearly 70% of all shoulder pain presentations.[1,2] The prevalence of shoulder pain in primary care has been estimated at 20 per 1000 registered patients per year,[3] amounting to more than one million consultations for shoulder pain in England each year. Several prospective cohort studies have indicated that 40% of patients still report pain or disability at 6–12 months after initial presentation in primary care.[4–8] Furthermore, the socioeconomic burden due to SSCs is substantial as ensuing pain and disability impair the ability to perform activities of daily living or work,[9,10] with economic losses as a result of work absence accounting for as much as 84% of total attributed cost of illness from SSCs.[11]

Currently, there many treatment options for patients with SSCs,[9–11] including nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroid injections, acupuncture, exercise therapy, mobilisation/manual therapy, ultrasound therapy, shockwave therapy, laser therapy and surgery. Previous guidelines and systematic reviews have summarised the available evidence about these treatments;[12–17] however, the clinical application of findings from these reviews is challenging, given that the reviews focus mostly on pairwise comparison of two or three treatment options only. For instance, NSAIDs might be prescribed in the acute phase of subacromial pain,[12,13] but the evidence of effectiveness for pain relief compared with placebo is limited.[12–15] Similarly, corticosteroid injections are widely used based on their perceived pain-relieving effects, but their effect on function is equivocal, and there is evidence that short-term pain relief is not sustained beyond 6–12 weeks and concerns about longer term harm.[18–20] Current evidence suggests that exercise is a promising intervention, but the evidence base for exercise, and exercise combined with manual therapy *versus* other treatments is limited.[12–16] Other treatments such as ultrasound therapy, laser therapy and acupuncture have been shown to be no more effective than placebo.[15,16]

Typically, as reflected by guidelines and treatment pathways,[15,16,21] management of patients with SSCs involves a stepped approach starting with advice and education, simple analgesics and progressing to other nonsurgical treatments or combination therapies where initial treatment has been unsuccessful. For persistent SSCs that have not responded to nonsurgical treatment, surgery may be considered. Two recent large, high-quality randomised trials have reported that surgical decompression for SSCs was not superior to sham surgery, and although both active and sham surgical interventions were superior to an active monitoring approach[22] or exercise therapy,[23] the differences did not exceed *a priori* defined levels of clinical importance. Previous guidelines, summaries of evidence and clinical pathways provide little or no guidance regarding the optimal sequence for these treatment options, based on evidence of their relative effectiveness. Neither is there robust evidence regarding the overall effectiveness of treatment options for SSCs in the short term ($\leqslant$3 months) or long term ($\geqslant$6 months). Hence, decision-making remains challenging for clinicians, patients and healthcare managers, given the lack of robust evidence regarding the comparative effectiveness of treatments for this common condition. The aim of this network meta-analysis (NMA) was to estimate the comparative effectiveness of current treatment options for relieving pain and improving function in patients with SSCs.

Specific objectives were to

1. Assess the effectiveness of currently available treatment options used in the management of SSCs compared with active, placebo, usual care or no treatment;
2. Determine the comparative effectiveness of the different treatment options for relieving pain and improving function in patients with SSCs;
3. Generate a clinically useful ranking of currently available treatment options in relation to short- and long-term effects on pain and function for patients with SSCs.

Methods

Patient and stakeholder involvement was important to the development of the research question. A group of five patient representatives with experience of living with shoulder pain and a stakeholder group involving clinicians (from general practice, physiotherapy and rheumatology) and musculoskeletal health researchers (e.g. systematic reviewers and clinical researchers within the musculoskeletal pain field) helped to define the review question, and informed the design, interpretation and dissemination of the study findings.

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension statement for systematic reviews incorporating NMAs for healthcare.[24] A protocol was developed and registered with the international prospective register of systematic reviews, PROSPERO ID CRD42014009788.

Information sources and literature search

A systematic search of databases, MEDLINE, Embase, PEDro, AMED, CINAHL, Web of Science and the Cochrane Central Register of Controlled Trials from their inceptions to November 2017, was conducted. This search was updated in April 2020 to include newly published, eligible studies (see Supplemental File 1 for the detailed MEDLINE and Embase search strategies). This was supplemented by searching clinical trial registries (e.g. the World Health Organization International Clinical Trials Registry), reference lists of included trials, relevant reviews and contact of expert authors/researchers in the field for unpublished and ongoing studies.

Study eligibility and selection

Titles of all citations retrieved from electronic database searches were screened by a systematic reviewer with subject knowledge expertise. Citations that were clearly not related to the subject of inquiry were removed. The abstract, and subsequently, full paper of each potentially eligible trial [randomised clinical/controlled trial (RCT)] was subsequently evaluated (independently by pairs of reviewers) for inclusion against the following predetermined selection criteria:

Trial population: Adults, 18 years and older with an SSC as diagnosed by clinical examination and/or diagnostic imaging, including non-tear populations with rotator cuff tendinitis/subacromial impingement/subacromial pain.
Intervention: All available treatment options (nonsurgical and surgical) for SSCs were sought excluding comparisons of different doses or procedural techniques of the same treatment options (e.g. arthroscopic *versus* open surgery for SSCs).
Comparator: All possible comparisons (direct and indirect) formed by the treatment options were considered, including comparisons between active treatments and comparisons with a control arm, regardless of mode of delivery or setting (community, primary healthcare or specialist healthcare). We classified placebo, usual care or no treatment controls as control arms.
Outcome measures: The primary outcomes for the review were shoulder pain and functional disability in the short term ($\leqslant$3 months) or long term ($\geqslant$6 months).

Conflicts were resolved through discussion and the opinion of a third reviewer, who undertook full-text analysis of article(s) when there was uncertainty regarding eligibility.

Data extraction and quality appraisal

Using a customised, pretested and piloted data extraction form, quality assessment and data extraction for each included trial were performed by one reviewer and independently checked for completion and accuracy by a second reviewer (all authors were involved in this process in pairs, JE the lead statistician also checked all data related to analysis for accuracy). The Cochrane Collaboration's risk of bias assessment tool was used to assess the quality of included trials.[25] Trials were graded (unclear, high or low risk of

bias) based on their risk of selection bias, performance bias, detection bias, attrition and reporting bias. For each included trial, details regarding trial design, sample characteristics (e.g. age, sex, duration of SSC), investigated treatments (e.g. type, professional delivering intervention, dose, duration, frequency of sessions) and outcome assessment (outcome domain, outcome measure, length of follow-up) were extracted. Discrepancies in data extraction or risk of bias assessment were resolved by discussion between pairs of reviewers or in review team meetings.

Evidence synthesis and data analyses

Initially all possible pairwise comparisons were analysed using a random-effects meta-analysis to obtain direct effect estimates, with results reported as standardised mean differences (SMDs), with 95% confidence intervals (CIs). Random-effects meta-analysis was used to account for expected between-study heterogeneity. The SMD enables comparison between treatment effects calculated on differing measurement scales by dividing the mean difference by the pooled standard deviation.[26] Further, where certain outcome measure scales favoured higher values, the scale was reversed so that for all trials and outcomes, a lower value represented improvement in outcome. All analyses were conducted using Stata version 15.1, based on the frequentist approach with parameter estimation using restricted maximum likelihood.[27]

Second, all evidence was combined in a random-effects NMA which combines both direct (within-trial) and indirect (across-trial) evidence on treatment effectiveness, to provide a pooled NMA treatment effect estimate, as well as providing a ranking treatment options for SSCs based on their relative effectiveness (SMD). One important assumption in NMA is that of consistency between direct and indirect evidence; that is, that for any closed loop, the evidence from direct and indirect comparisons agrees on average.[28] The consistency of direct and indirect evidence for treatment effects within the network was explored using Wald tests, with a global test across all direct evidence indicating inconsistency if the p value was <0.05.[29] Due to the low power associated with global tests, the node-splitting method of Dias and colleagues[30] was also used to test for inconsistency separately between each treatment comparison, again p values <0.05 indicated the presence of inconsistency.

The effectiveness of the different treatment options was summarised using pooled SMD estimates, 95% CIs and treatment rankings for pain and function outcomes at different follow-up points. Based on discussions with clinical advisors, information from the literature regarding the clinical course of SSCs and the distribution of available follow-up time-points in the included trials, follow-up time-point categories for the primary outcomes of pain and function was classified as short- (2–6 weeks, T1), medium- (6 weeks to 3 months, T2; 3–6 months, T3) and long-term (>6 months, T4) follow-up. This led to a maximum of eight networks for the primary analysis. Where multiple outcome measurements were reported within the same follow-up category for the same trial, the later follow-up data were used for synthesis. Network plots were used to visualise the amount of direct evidence available, with node size representing the number of participants receiving treatment and line size representing the number of trials providing direct evidence. Treatment effect estimates (SMDs) were considered statistically significant if the associated 95% CI did not include the null value of zero.

In terms of treatment option ranking, three measures were considered: (1) the probability of the treatment being in the top three ranked treatments, (2) the mean rank and (3) the surface under the cumulative ranking curve (SUCRA). Rankings were calculated by comparing relative treatment (SMD) estimates across 1000 simulations.[27]

Further, network meta-regression models were considered to investigate inconsistency with (1) trial sample size and (2) multimodal intervention (treatments offered in combination with advice, analgesics and home exercises rather than as a single treatment) included as potential effect modifiers in NMA models.

For the primary outcomes of pain and function, sensitivity analyses were conducted to assess the potential influence of small trials by excluding those with less than 60 participants at randomisation. Evidence from small trials is more likely to be affected by biases such as selection and publication bias, as well as potentially showing large effect sizes due to chance sampling variation.[31,32] For these reasons, we chose to primarily present the results of this sensitivity analysis, as discussed below in the network consistency section. We additionally conducted sensitivity NMAs removing trials that were not at low risk of bias in terms of random sequence

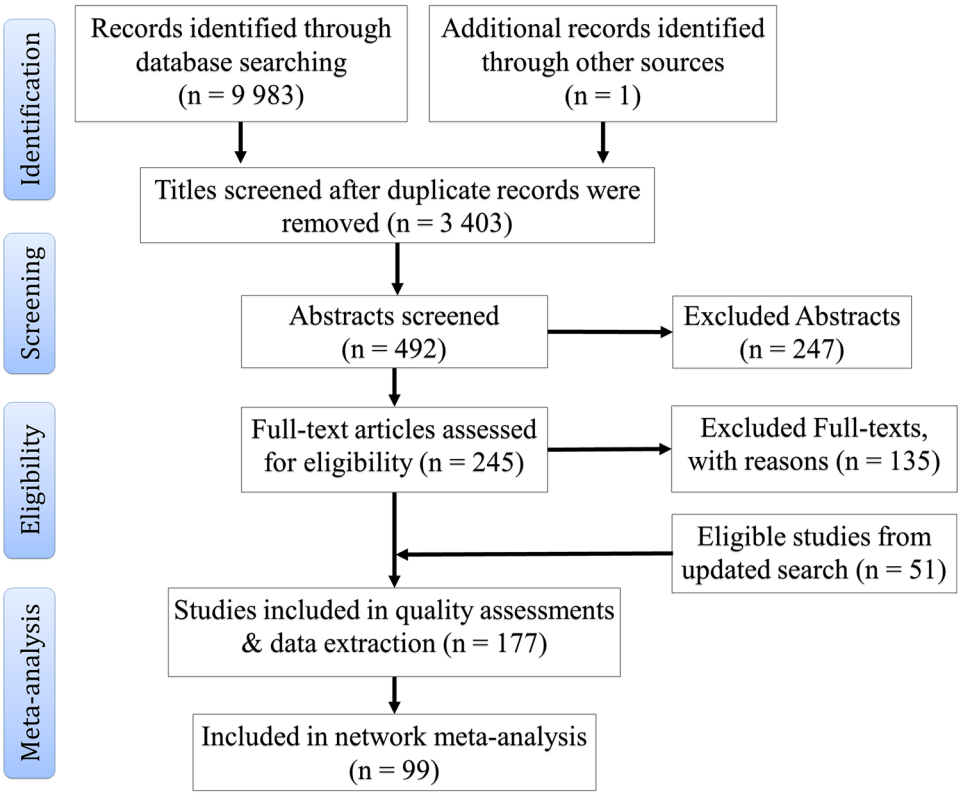


Figure 1. Study flow chart.

generation or poor presentation or analysis of data. These analyses could not be conducted for pain or function outcomes at T1 and T3, as data were too sparse due to the small number of trials considered to be at low risk of bias.

In assessing the quality of evidence (sensitivity and meta-regression analyses), we accounted for important domains of uncertainty of evidence, in terms of the grading of recommendations assessment, development and evaluation (GRADE) domains of study limitations (risk of bias), precision (small sample size), inconsistency, indirectness (where offering interventions as part of a combined, multimodal treatment was considered relevant for judging applicability of results) and reporting/publication bias (through risk of bias assessment and taking account of small study bias).

Based on our analyses, we briefly summarised and graded the certainty of evidence for comparative effectiveness (pain and function outcomes) based on our main NMA findings as high, moderate, low or very low. High certainty evidence would reflect results from NMAs including multiple studies considered at low risk of bias, limited evidence of small study bias and from networks demonstrating consistency between direct and indirect evidence and including direct evidence of comparisons from multiple trials. Certainty of evidence was downgraded for study limitations, imprecision, inconsistency and/or directness, if sensitivity or meta-regression analyses showed different outcomes when taking risk of bias, small sample size or differences between direct and indirect evidence (network inconsistency) into account, or when direct evidence for comparisons between active treatments was provided by one study only.

Results

Characteristics of included trials

In total, 177 trials of different treatment options for SSCs were eligible for inclusion in the review and were subjected to quality appraisal and data extraction (see Figure 1). Of these 177 trials, 99 trials ($n = 6764$ participants) provided sufficient data to be included in the NMA, covering 20 treatment options. Included trials were considered sufficiently similar with respect to basic

demographic characteristics of participants such as age, sex and baseline severity and duration of symptoms. A summary of characteristics of the trials included in the NMA are presented in Table 1. Supplemental File 1 presents a list of included trials as well as a list of eligible trials that could not be included in data analysis. A summary of all raw outcome data (means and standard deviations) used in the final analyses for all trials by treatment arm is available on request from the authors.

Risk of bias

The results of risk of bias assessment for 98 included trials are presented in Figure 2. One trial could not be double assessed for risk of bias due to the language of publication.[33] Only 63 RCTs clearly reported how randomisation was performed. Allocation of treatments was clearly reported as adequately concealed in only 48 trials, whereas papers for 44 trials contained insufficient information to judge whether trial procedures ensured adequate concealment. Nearly half of the included trials ($n=44$) were classified as at high risk of bias relating to blinding of participants and personnel. In most of these trials, blinding was difficult to achieve due to the nature of included treatment options (e.g. exercise, mobilisation or manual therapy). In relation to blinding of outcome assessment, 48 trials were classified as at low risk and 22 were considered to have high risk of bias. Items generating a large proportion of 'unclear' assessments (indicating a lack of clarity in reporting) often concerned other risks of bias, for example, adherence to treatment, or methods used to deal with missing data. A large proportion of trials were considered to have low risk of bias with respect to incomplete outcome data (77/98, 79%) and selective reporting of outcomes (84/98, 86%).

Network consistency

Six of a possible eight networks were connected, with the network for long-term pain and function disconnected. The consistency assumption was tested for all connected networks, with the assumption violated for five of the connected networks in the primary analysis (three for pain and two for function outcomes). For pain networks, global Wald test results at T1, T2 and T3 all gave values of $p<0.01$. Further investigation using node-splitting also indicated inconsistency between direct and indirect evidence for each of the treatment comparisons ($p<0.05$). Similar results were found for function networks at T1 and T2 (global Wald $p<0.01$). The consistency assumption only held for the network for function outcomes at T3, according to both the global Wald test ($p=0.186$) and node-splitting method (all $p>0.05$).

In the sensitivity analysis excluding 54 trials with less than 60 participants at randomisation, seven of the eight potential networks were connected, with the T4 network for pain outcomes being disconnected due to fewer trials with long-term follow-up. All but the T2 pain outcomes network ($p<0.001$) appeared to meet the consistency assumption with $p>0.05$ for both global tests and the node-splitting method. As NMA in the presence of inconsistency may potentially generate misleading results, we only present the results of the analysis excluding small trials in full here.

Evidence base

For pain outcomes, the largest network compared 16 treatment options for SSCs across 30 trials with short-term (T1) follow-up (see Figure 3). There was a maximum of six trials for a single direct comparison (corticosteroid injection *versus* control), with the number of participants receiving any one treatment in the network ranging from 30 to 523. For the pain outcome at T3, the network included 12 trials comparing eight treatment options (30–475 participants, Figure 3).

For function outcomes, all four networks were connected across all follow-up time-points; again, T1 was the largest network comparing 15 treatments across 25 trials, with participant numbers ranging from 30 to 442. Networks for T2, T3 and T4 included 13, 9 and 9 treatment options, across 20, 14 and 9 trials, respectively (see Figure 4).

For both pain and function outcomes, networks suffered from limited direct evidence for each comparison, with most only including one, two or three trials. As such, the included networks can be considered sparse, and so conclusions regarding comparative treatment effectiveness should be interpreted cautiously, also taking into account the uncertainty expressed by 95% CIs.[34]

Comparative effectiveness of treatments for SSCs: NMA

Estimates of the effectiveness of treatment options for SSCs are presented in Tables 2–7, with direct

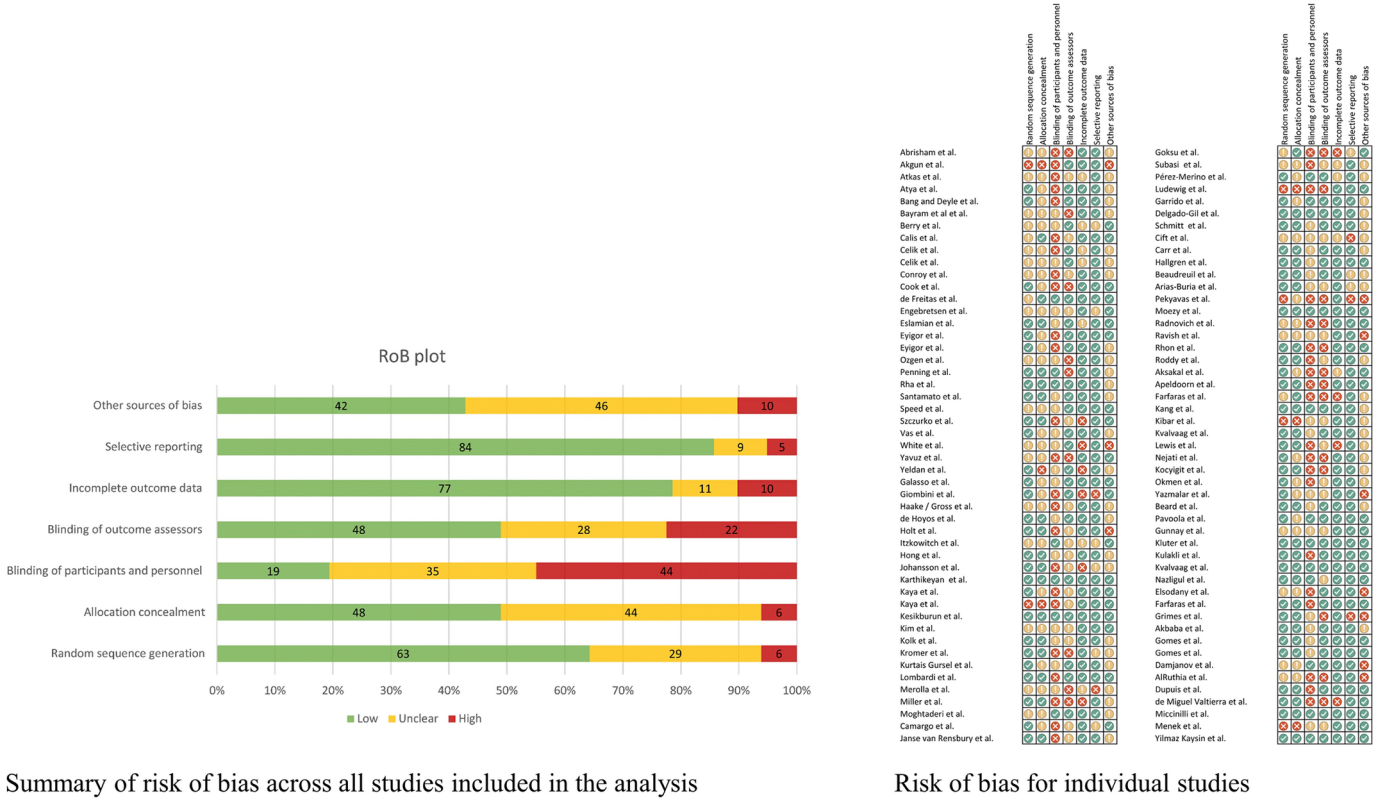
Table 1. Summary characteristics of included studies.

Summary characteristics	No. of studies	%
Continents		
Asia	42	42.4
Africa	1	1.0
North America	11	11.1
South America	5	5.1
Europe	39	39.4
Australia	1	1.0
Year of publication (>10 years old)	4	4.0
Study setting		
Community	2	2.0
Occupational healthcare	1	1.0
Primary care	3	3.0
Outpatient	27	27.3
Hospital/Rehabilitation	27	27.3
Secondary/Tertiary care	10	10.1
Unclear	29	29.3
Sample size at randomisation		
(>60)	45	45.5
(<60)	54	54.5
Diagnosis		
SIS	55	55.6
RC	21	21.2
SA	23	23.2
Baseline duration of symptoms		
⩾3 months	66	66.7
<3months	13	13.1
Not reported	20	20.2
Mean age		
⩾50 years	64	64.6
Not reported	4	4.0
Others (variable age range 18 years and above)	31	31.4
Proportion male[a]		
⩾50%	34	34.3
Not reported	6	6.1
Baseline pain reported[a]	85	85.9
Baseline function reported[a]	83	83.8
Baseline BMI reported[a]	20	20.2
Work status reported[a]	22	22.2
Outcome measures (pain)[b]		
VAS	73	79.3
Other	19	20.7
Outcome measures (function)[b]		
Constant/CMS	32	35.2
SPADI	26	28.6
DASH	13	14.3
Other	20	22.0
Multimodal interventions	52	52.5

BMI, body mass index; CMS, Constant–Murley score; DASH, Disabilities of the Arm, Shoulder and Hand; RC, rotator cuff; SA, subacromial syndrome; SIS, subacromial impingement syndrome; SPADI, Shoulder Pain and Disability Index; VAS, visual analogue scale.
[a]Others = not reported.
[b]Others = did not assesses pain/function.

evidence for pairwise comparisons listed in the upper left triangle of each table and NMA pooled treatment effect estimates listed in lower right triangle of each table.

Pain (T1: 2- to 6-week follow-up, Table 2). The NMA found 13 SMDs to be statistically significant; notably, the effect of taping was unfavourable compared with laser therapy (SMD of 1.12, 95% CI 0.40, 1.8) which was also reflected by the results of pairwise meta-analyses of the direct evidence. Comparisons of NSAIDs *versus* control, ultrasound therapy *versus* Microcurrent (MENS) (TENS) and NSAIDs *versus* corticosteroid injection were statistically significant for



Summary of risk of bias across all studies included in the analysis

Risk of bias for individual studies

Figure 2. Summary of risk of bias across all studies and risk of bias for all individual studies included in the analysis.
+ (green circle), low risk of bias; ? (amber circle), unclear risk of bias; - (red circle), high risk of bias.

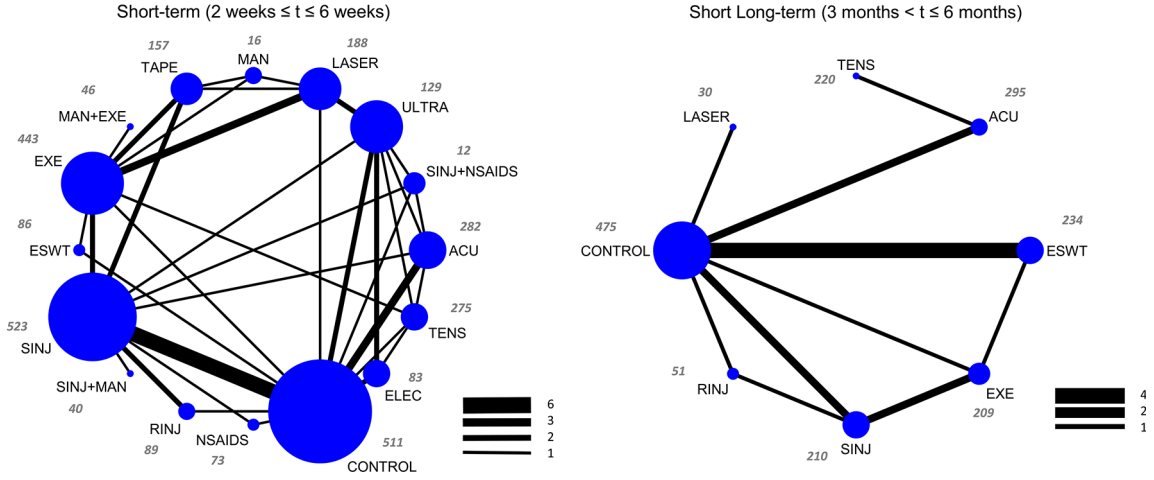


Figure 3. Network plot for pain outcomes in the short-term (T1) and short-long term (T3) follow-up categories.
Line width represents the number of trials providing direct evidence for the comparison. Node size and numbers represent the number of participants receiving the treatment.
ACU, acupuncture (inc. electro acupuncture); CONTROL, placebo/no intervention; ELEC, other electrotherapy (inc. PSWD, PEMF or PRF); ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; MAN, manual therapy; NSAIDS, nonsteroidal anti-inflammatory drugs; PEMF, pulsed electromagnetic field; PSWD, pulsed shortwave diathermy; PRF, pulsed radiofrequency; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; TAPE, taping; TENS, Microcurrent (MENS); ULTRA, ultrasound therapy.

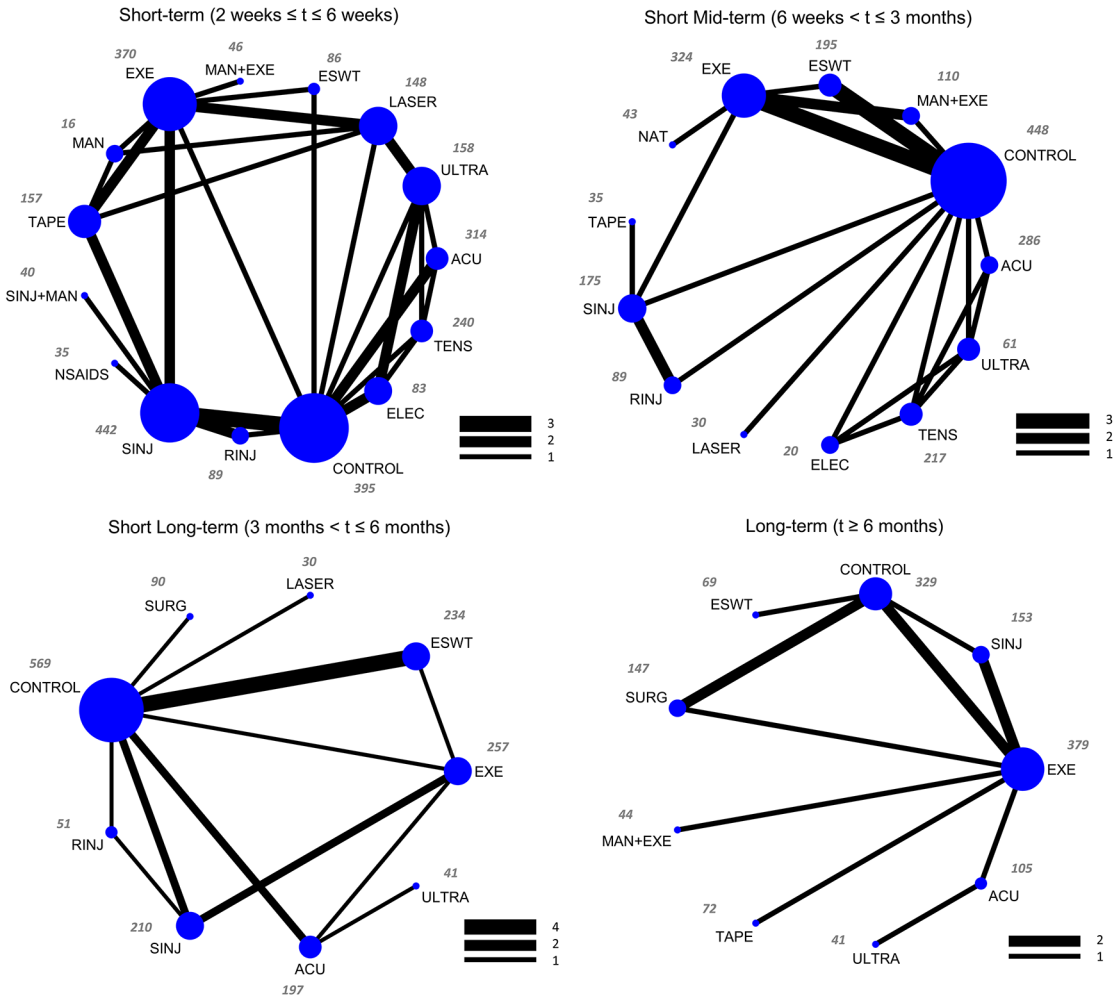


Figure 4. Network plot for function outcomes across all follow-up categories (T1–4).
Line width represents the number of trials providing direct evidence for the comparison. Node size and numbers represent the number of participants receiving the treatment.
ACU, acupuncture (inc. electro acupuncture); CONTROL, placebo/no intervention; ELEC, other electrotherapy (inc. PSWD, or PEMF or PRF); ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; MAN, manual therapy; NAT, naturopathic care; NSAIDS, nonsteroidal anti-inflammatory drugs; PEMF, pulsed electromagnetic field; PSWD, pulsed shortwave diathermy; PRF, pulsed radiofrequency; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; SURG, surgery (split into open surgery and arthroscopic surgery); TAPE, taping; TENS, Microcurrent (MENS); ULTRA, ultrasound therapy.

pairwise analyses (favouring NSAIDs, TENS and corticosteroid injection, respectively), but became nonsignificant after inclusion of indirect evidence in the NMA. While evidence of the benefits of laser therapy over ultrasound therapy remained statistically significant within the NMA (SMD 1.14, 95% CI 0.51, 1.76), laser therapy was also found to be favourable compared with corticosteroid injection, NSAIDS, electrotherapy and control arms. Other statistically significant pooled effects were identified in favour of acupuncture compared with taping (SMD 1.16, 95% CI 0.30, 2.01), NSAIDS (SMD 1.18, 95% CI 0.18, 2.19), ultrasound therapy (SMD 1.17, 95% CI 0.41, 1.94), corticosteroid injection (SMD 0.73, 95% CI 0.05, 1.41), electrotherapy (SMD 1.04, 95% CI 0.18, 1.90), and control arms (SMD 1.09, 95% CI 0.49, 1.70). Exercise was also found to be favourable compared with control arms (SMD 0.53, 95% CI 0.01, 1.04).

Table 2. Results of short-term (T1) pain outcomes.

CONTROL	−0.28 (−0.94, 0.37)	0.63 (−0.01, 1.27)		−0.25 (−1.05, 0.55)		0.27 (−0.06, 0.59)	−0.35 (−0.73, 0.03)	0.56 (0.1, 1.01)			0.7 (0.18, 1.22)	0.22 (−0.03, 0.48)	0.34 (−0.12, 0.8)	0.06 (−0.36, 0.49)	1.13 (−0.38, 2.64)
−0.08 (−0.68, 0.52)	ULTRA	0.63 (0, 1.25)		0.42 (−0.39, 1.22)		0.51 (−0.3, 1.32)					1.2 (0.78, 1.61)			0.15 (−0.23, 0.53)	0.25 (−0.55, 1.05)
0.46 (−0.23, 1.16)	0.54 (−0.24, 1.32)	TENS										0.18 (−0.3, 0.65)		−0.3 (−0.92, 0.32)	
−0.06 (−0.73, 0.61)	0.02 (−0.79, 0.82)	−0.53 (−1.41, 0.35)	TAPE			0.17 (−0.36, 0.69)				1.61 (0.9, 2.33)	1.66 (0.97, 2.35)	0.93 (−0.46, 2.32)			0.58 (0.39, 0.78)
0.40 (−0.66, 1.47)	0.48 (−0.64, 1.61)	−0.06 (−1.27, 1.15)	0.47 (−0.74, 1.68)	SINJ + NSAIDS		0.09 (−0.71, 0.89)									−0.17 (−0.97, 0.63)
0.40 (−0.79, 1.59)	0.48 (−0.82, 1.77)	−0.07 (−1.41, 1.28)	0.46 (−0.81, 1.74)	−0.01 (−1.57, 1.55)	SINJ + MAN	−0.04 (−0.47, 0.4)									
0.36 (−0.04, 0.77)	0.44 (−0.22, 1.10)	−0.10 (−0.85, 0.64)	0.42 (−0.19, 1.04)	−0.04 (−1.13, 1.04)	−0.04 (−1.15, 1.08)	SINJ	−0.09 (−1.42, 1.24)	−1.13 (−1.63,−0.62)				0.12 (−0.09, 0.33)			−0.26 (−1.06, 0.54)
0.18 (−0.60, 0.96)	0.26 (−0.69, 1.21)	−0.29 (−1.30, 0.73)	0.24 (−0.70, 1.19)	−0.23 (−1.51, 1.06)	−0.22 (−1.56, 1.12)	−0.18 (−0.92, 0.55)	RINJ								
−0.09 (−0.92, 0.73)	−0.01 (−1.01, 0.99)	−0.56 (−1.61, 0.50)	−0.03 (−1.04, 0.98)	−0.50 (−1.82, 0.83)	−0.49 (−1.88, 0.90)	−0.45 (−1.28, 0.38)	−0.27 (−1.36, 0.82)	NSAIDS							
0.61 (−0.61, 1.83)	0.69 (−0.61, 1.99)	0.15 (−1.18, 1.47)	0.67 (−0.60, 1.95)	0.21 (−1.38, 1.79)	0.21 (−1.44, 1.87)	0.25 (−0.97, 1.47)	0.43 (−0.98, 1.84)	0.70 (−0.75, 2.15)	MAN + EXE			−0.08 (−0.5, 0.33)			
1.00 (−0.11, 2.12)	1.08 (−0.09, 2.26)	0.54 (−0.70, 1.78)	1.07 (−0.03, 2.16)	0.60 (−0.91, 2.10)	0.61 (−0.97, 2.18)	0.64 (−0.47, 1.75)	0.82 (−0.49, 2.14)	1.09 (−0.26, 2.45)	0.39 (−1.14, 1.92)	MAN	0.05 (−0.61, 0.72)	0.06 (−0.64, 0.77)			
1.06 (0.47, 1.64)	1.14 (0.51, 1.76)	0.59 (−0.21, 1.39)	1.12 (0.40, 1.84)	0.65 (−0.51, 1.81)	0.66 (−0.62, 1.94)	0.69 (0.07, 1.32)	0.88 (−0.05, 1.81)	1.15 (0.16, 2.13)	0.44 (−0.79, 1.68)	0.05 (−1.02, 1.13)	LASER	−0.45 (−1.17, 0.28)			
0.53 (0.01, 1.04)	0.61 (−0.07, 1.28)	0.06 (−0.66, 0.79)	0.59 (−0.03, 1.21)	0.12 (−1.02, 1.26)	0.13 (−1.10, 1.36)	0.17 (−0.35, 0.68)	0.35 (−0.52, 1.22)	0.62 (−0.31, 1.55)	−0.08 (−1.19, 1.02)	−0.48 (−1.53, 0.58)	−0.53 (−1.07, 0.02)	EXE	−0.15 (−0.54, 0.24)		
0.36 (−0.47, 1.19)	0.44 (−0.54, 1.42)	−0.10 (−1.13, 0.93)	0.43 (−0.56, 1.41)	−0.04 (−1.37, 1.29)	−0.03 (−1.46, 1.39)	0.00 (−0.88, 0.88)	0.18 (−0.93, 1.30)	0.45 (−0.70, 1.61)	−0.25 (−1.63, 1.13)	−0.64 (−1.96, 0.68)	−0.69 (−1.63, 0.24)	−0.17 (−0.99, 0.66)	ESWT		
0.05 (−0.64, 0.75)	0.13 (−0.57, 0.84)	−0.41 (−1.26, 0.44)	0.12 (−0.80, 1.03)	−0.35 (−1.57, 0.87)	−0.34 (−1.70, 1.01)	−0.31 (−1.08, 0.46)	−0.13 (−1.15, 0.90)	0.15 (−0.92, 1.21)	−0.56 (−1.93, 0.81)	−0.95 (−2.22, 0.32)	−1.00 (−1.82,−0.19)	−0.47 (−1.27, 0.33)	−0.31 (−1.36, 0.75)	ELEC	
1.09 (0.49, 1.70)	1.17 (0.41, 1.94)	0.63 (−0.11, 1.36)	1.16 (0.30, 2.01)	0.69 (−0.44, 1.81)	0.70 (−0.61, 2.01)	0.73 (0.05, 1.41)	0.91 (−0.05, 1.88)	1.18 (0.18, 2.19)	0.48 (−0.85, 1.81)	0.09 (−1.14, 1.32)	0.04 (−0.75, 0.82)	0.57 (−0.17, 1.30)	0.73 (−0.27, 1.73)	1.04 (0.18, 1.90)	ACU

ACU, acupuncture (inc. electro acupuncture); CI, confidence interval; CONTROL, placebo/no intervention; ELEC, other electrotherapy (inc. PSWD, PEMF or PRF); ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; MAN, manual therapy; NSAIDS, nonsteroidal anti-inflammatory drugs; PEMF, pulsed electromagnetic field; PSWD, pulsed shortwave diathermy; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; SMD, standardised mean difference; TAPE, taping; TENS, Microcurrent (MENS); ULTRA, ultrasound therapy.
Lower left triangle presents the findings (SMD with 95% CI) of the network meta-analysis. Upper right triangle presents the findings (SMD with 95% CI) of pairwise meta-analyses. A positive SMD favours the lower right intervention; a negative SMD favours the upper left intervention. Statistically significant findings are shaded in green. Within the table, comparisons between treatments should be read from left to right (i.e. treatment 1 *versus* treatment 2). The estimate effect measure (SMD and their 95% CI) is in the cell in common between the row- and column-defining treatment.

Table 3. Results of short-long term (T3) pain outcomes.

CONTROL		0.09 (−0.12, 0.31)	−0.21 (−0.59, 0.17)	0.84 (0.31, 1.37)	0.42 (0.15, 0.68)	0.32 (0.09, 0.55)	0.81 (0.51, 1.12)
0.08 (−0.29, 0.44)	TENS						0.74 (0.54, 0.93)
0.10 (−0.10, 0.31)	0.03 (−0.39, 0.44)	SINJ	−0.18 (−0.56, 0.21)		0.25 (0.03, 0.48)		
−0.14 (−0.49, 0.20)	−0.22 (−0.72, 0.28)	−0.25 (−0.60, 0.10)	RINJ				
0.84 (0.31, 1.37)	0.76 (0.12, 1.40)	0.73 (0.17, 1.30)	0.98 (0.35, 1.61)	LASER			
0.39 (0.18, 0.59)	0.31 (−0.11, 0.73)	0.28 (0.07, 0.49)	0.53 (0.15, 0.91)	−0.45 (−1.02, 0.12)	EXE	−0.1 (−0.49, 0.28)	
0.31 (0.12, 0.49)	0.23 (−0.18, 0.64)	0.20 (−0.06, 0.46)	0.45 (0.06, 0.84)	−0.53 (−1.09, 0.03)	−0.08 (−0.32, 0.16)	ESWT	
0.81 (0.51, 1.12)	0.74 (0.54, 0.93)	0.71 (0.34, 1.08)	0.96 (0.49, 1.42)	−0.02 (−0.64, 0.59)	0.43 (0.06, 0.80)	0.51 (0.15, 0.87)	ACU

ACU, acupuncture (inc. electro acupuncture); CI, confidence interval; CONTROL, placebo/no intervention; ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; SMD, standardised mean difference; TENS, Microcurrent (MENS).
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Pain (T3: 3- to 6-month follow-up, Table 3): NMA results for the T3 pain network were consistent with pairwise comparisons. Fifteen of possible 28 comparisons yielded statistically significant pooled NMA SMDs, including treatment effects favouring laser therapy over all seven of the other treatment options included in the network. The effectiveness of laser therapy should be judged with caution; however, as only one trial ($n = 60$ participants) provided direct evidence regarding its effect.[35] Pooled results suggested that exercise remained favourable over both corticosteroid injection (SMD 0.28, 95% CI 0.07, 0.49) and control arms (SMD 0.39, 95% CI 0.18, 0.59), as seen in pairwise meta-analysis, as well as compared with regenerative injections (0.53, 95% CI 0.15, 0.91).

Function (T1:2- to 6-week follow-up, Table 4): Pooled NMA estimates at T1 showed 26 statistically significant results with laser therapy found to be significantly more effective than NSAIDS, regenerative or corticosteroid injection, taping and control arms, as well as acupuncture better than electrotherapy, extracorporeal shock wave therapy (ESWT), exercise, NSAIDS, regenerative or corticosteroid injection, corticosteroid injection in combination with mobilisation, taping, ultrasound therapy or control arms. It is important to note, however, that of these comparisons, direct evidence was only available for acupuncture *versus* control and ultrasound therapy and for laser therapy *versus* taping and control arms. This means that estimates for all other comparisons, although statistically significant, were based solely on indirect evidence, which is reflected in the large uncertainty surrounding the pooled SMD estimates. The direct evidence of the effects of laser and manual therapy *versus* taping was statistically significant at T1 follow-up, as seen for T1 pain outcomes.

Function (T2, T3 and T4: follow-up longer than 6 weeks, Tables 5–7): A total of 33 comparisons of 78 pooled results were statistically significant in the T2 function network (6-week to 3-month follow-up). Results of note included TENS performing worse than all other treatments in the network, whereas laser therapy performed better than all other treatments (Table 5). Exercise therapy and exercise in combination with manual therapy/mobilisations were significantly better

Table 4. Results of short-term (T1) function outcomes.

CONTROL	0.04 (−0.59, 0.67)	0.47 (−0.16, 1.1)			0.06 (−0.13, 0.26)	−0.25 (−0.63, 0.13)				1.54 (0.96, 2.12)	0.05 (−0.2, 0.31)	0.48 (0.01, 0.94)	−0.06 (−0.46, 0.34)	1.75 (0.23, 3.26)
0.57 (−0.01, 1.16)	ULTRA	0.43 (−0.19, 1.06)								0 (−1.05, 1.06)			0.24 (−0.15, 0.62)	0.3 (−0.13, 0.72)
0.78 (0.03, 1.53)	0.20 (−0.57, 0.98)	TENS											−0.28 (−0.9, 0.34)	0.52 (0.33, 0.72)
0.01 (−0.64, 0.66)	−0.56 (−1.36, 0.23)	−0.77 (−1.73, 0.20)	TAPE		0.14 (−0.35, 0.63)			1.03 (0.35, 1.71)	1.21 (0.55, 1.87)	0.33 (−0.83, 1.49)				
0.00 (−1.11, 1.12)	−0.57 (−1.80, 0.66)	−0.77 (−2.10, 0.56)	−0.01 (−1.15, 1.14)	SINJ + MAN	0.14 (−0.3, 0.57)									
0.14 (−0.35, 0.63)	−0.43 (−1.14, 0.27)	−0.64 (−1.51, 0.24)	0.13 (−0.43, 0.69)	0.14 (−0.86, 1.14)	SINJ	−0.28 (−0.82, 0.25)	−1.39 (−1.92, −0.87)			0.06 (−0.15, 0.27)				
−0.13 (−0.86, 0.60)	−0.71 (−1.61, 0.20)	−0.91 (−1.95, 0.13)	−0.14 (−0.99, 0.70)	−0.14 (−1.34, 1.06)	−0.27 (−0.93, 0.39)	RINJ								
−1.25 (−2.40, −0.10)	−1.83 (−3.09, −0.57)	−2.03 (−3.39, −0.67)	−1.26 (−2.45, −0.08)	−1.26 (−2.70, 0.19)	−1.39 (−2.43, −0.35)	−1.12 (−2.35, 0.11)	NSAIDS							
0.51 (−0.61, 1.64)	−0.06 (−1.28, 1.15)	−0.27 (−1.60, 1.06)	0.50 (−0.64, 1.64)	0.51 (−0.99, 2.00)	0.37 (−0.74, 1.48)	0.64 (−0.63, 1.91)	1.76 (0.24, 3.29)	MAN + EXE			−0.19 (−0.6, 0.23)			
0.69 (−0.35, 1.72)	0.11 (−0.99, 1.21)	−0.09 (−1.33, 1.15)	0.68 (−0.32, 1.67)	0.68 (−0.75, 2.12)	0.55 (−0.48, 1.57)	0.82 (−0.38, 2.02)	1.94 (0.48, 3.40)	0.18 (−1.21, 1.57)	MAN	0.18 (−0.48, 0.85)	−0.06 (−0.77, 0.64)			
0.81 (0.23, 1.38)	0.23 (−0.36, 0.82)	0.03 (−0.84, 0.89)	0.79 (0.10, 1.49)	0.80 (−0.39, 1.99)	0.67 (0.02, 1.31)	0.94 (0.07, 1.81)	2.06 (0.83, 3.28)	0.30 (−0.86, 1.45)	0.12 (−0.88, 1.12)	LASER	−0.18 (−0.58, 0.23)			
0.33 (−0.21, 0.86)	−0.25 (−0.95, 0.45)	−0.45 (−1.34, 0.44)	0.31 (−0.25, 0.88)	0.32 (−0.80, 1.44)	0.19 (−0.32, 0.69)	0.46 (−0.34, 1.25)	1.58 (0.42, 2.74)	−0.19 (−1.18, 0.80)	−0.36 (−1.34, 0.61)	−0.48 (−1.07, 0.11)	EXE	−0.34 (−0.73, 0.05)		
0.22 (−0.53, 0.98)	−0.35 (−1.27, 0.57)	−0.55 (−1.60, 0.50)	0.21 (−0.68, 1.10)	0.22 (−1.07, 1.51)	0.08 (−0.74, 0.90)	0.36 (−0.65, 1.36)	1.48 (0.15, 2.80)	−0.29 (−1.53, 0.95)	−0.46 (−1.66, 0.73)	−0.58 (−1.46, 0.29)	−0.10 (−0.85, 0.65)	ESWT		
0.38 (−0.26, 1.02)	−0.19 (−0.83, 0.45)	−0.39 (−1.22, 0.44)	0.37 (−0.50, 1.25)	0.38 (−0.89, 1.65)	0.24 (−0.54, 1.02)	0.52 (−0.44, 1.47)	1.64 (0.33, 2.94)	−0.13 (−1.40, 1.14)	−0.30 (−1.48, 0.87)	−0.42 (−1.18, 0.34)	0.06 (−0.74, 0.85)	0.16 (−0.81, 1.13)	ELEC	
1.37 (0.77, 1.96)	0.79 (0.14, 1.44)	0.59 (−0.12, 1.29)	1.35 (0.50, 2.21)	1.36 (0.11, 2.61)	1.23 (0.48, 1.97)	1.50 (0.56, 2.43)	2.62 (1.33, 3.90)	0.85 (−0.40, 2.11)	0.68 (−0.48, 1.84)	0.56 (−0.19, 1.31)	1.04 (0.27, 1.81)	1.14 (0.20, 2.09)	0.98 (0.21, 1.75)	ACU

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Table 5. Results of short mid-term (T2) function outcomes.

CONTROL	0.2 (−0.43, 0.83)	0.08 (−0.55, 0.7)		0.24 (−0.14, 0.62)	−0.22 (−0.6, 0.16)		0.52 (0.02, 1.03)	1.58 (0.99, 2.16)	0.69 (0.39, 0.99)	0.05 (−0.18, 0.28)	0.36 (−0.27, 0.99)	−0.42 (−0.8,−0.04)
−0.20 (−0.78, 0.38)	ULTRA	−0.12 (−0.74, 0.5)									0.16 (−0.46, 0.78)	0.24 (−0.19, 0.66)
−0.58 (−1.16,−0.01)	−0.38 (−0.94, 0.17)	TENS									0.29 (−0.34, 0.91)	0.82 (0.61, 1.03)
0.15 (−0.62, 0.93)	0.35 (−0.62, 1.32)	0.74 (−0.23, 1.70)	TAPE	0.06 (−0.41, 0.53)								
0.21 (−0.22, 0.64)	0.41 (−0.31, 1.13)	0.79 (0.08, 1.51)	0.06 (−0.59, 0.71)	SINJ	−0.17 (−0.77, 0.43)				0.19 (−0.22, 0.61)			
0.00 (−0.50, 0.50)	0.20 (−0.56, 0.96)	0.58 (−0.17, 1.34)	−0.15 (−0.92, 0.62)	−0.21 (−0.63, 0.21)	RINJ							
1.15 (0.46, 1.84)	1.35 (0.45, 2.25)	1.74 (0.84, 2.63)	1.00 (−0.00, 2.00)	0.94 (0.18, 1.71)	1.15 (0.33, 1.97)	NAT			−0.61 (−1.04,−0.17)			
0.61 (0.19, 1.04)	0.81 (0.09, 1.53)	1.20 (0.48, 1.91)	0.46 (−0.40, 1.32)	0.40 (−0.16, 0.96)	0.61 (−0.02, 1.24)	−0.54 (−1.28, 0.19)	MAN + EXE		−0.11 (−0.43, 0.2)			
1.58 (0.84, 2.31)	1.77 (0.84, 2.71)	2.16 (1.22, 3.09)	1.42 (0.35, 2.49)	1.36 (0.51, 2.22)	1.57 (0.68, 2.46)	0.42 (−0.59, 1.43)	0.96 (0.11, 1.81)	LASER				
0.55 (0.26, 0.84)	0.74 (0.10, 1.39)	1.13 (0.48, 1.77)	0.39 (−0.39, 1.18)	0.33 (−0.11, 0.77)	0.54 (0.01, 1.07)	−0.61 (−1.23, 0.02)	−0.07 (−0.45, 0.32)	−1.03 (−1.82,−0.24)	EXE	−0.34 (−0.73, 0.05)		
0.08 (−0.23, 0.39)	0.28 (−0.38, 0.94)	0.67 (0.01, 1.32)	−0.07 (−0.90, 0.76)	−0.13 (−0.64, 0.38)	0.08 (−0.50, 0.66)	−1.07 (−1.80,−0.34)	−0.53 (−1.03,−0.03)	−1.49 (−2.29, −0.69)	−0.46 (−0.83, −0.09)	ESWT		
0.01 (−0.71, 0.72)	0.20 (−0.50, 0.91)	0.59 (−0.12, 1.29)	−0.15 (−1.21, 0.91)	−0.21 (−1.04, 0.63)	0.00 (−0.87, 0.87)	−1.15 (−2.14, −0.16)	−0.61 (−1.44, 0.22)	−1.57 (−2.60, −0.54)	−0.54 (−1.31, 0.23)	−0.08 (−0.86, 0.70)	ELEC	
−0.01 (−0.49, 0.46)	0.18 (−0.30, 0.67)	0.57 (0.13, 1.01)	−0.17 (−1.08, 0.74)	−0.23 (−0.87, 0.41)	−0.02 (−0.70, 0.67)	−1.17 (−2.00, −0.33)	−0.63 (−1.26, 0.01)	−1.59 (−2.47, −0.71)	−0.56 (−1.11, −0.01)	−0.10 (−0.66, 0.47)	−0.02 (−0.73, 0.69)	ACU

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Table 6. Results of short-long term (T3) function outcomes.

CONTROL		−0.14 (−0.43, 0.15)	0.04 (−0.2, 0.29)	−0.4 (−0.79, −0.02)	1.73 (1.13, 2.32)	0.32 (0.06, 0.58)	0.32 (−0.17, 0.81)	0.08 (−1.17, 1.32)
0.09 (−0.94, 1.12)	ULTRA							0 (−0.43, 0.43)
−0.14 (−0.97, 0.68)	−0.23 (−1.55, 1.09)	SURG						
0.07 (−0.45, 0.60)	−0.01 (−1.13, 1.10)	0.22 (−0.76, 1.19)	SINJ	−0.28 (−0.67, 0.1)		0.14 (−0.08, 0.36)		
−0.31 (−1.10, 0.48)	−0.40 (−1.68, 0.89)	−0.16 (−1.31, 0.98)	−0.38 (−1.17, 0.41)	RINJ				
1.73 (0.75, 2.70)	1.64 (0.22, 3.06)	1.87 (0.59, 3.15)	1.65 (0.54, 2.76)	2.03 (0.78, 3.29)	LASER			
0.26 (−0.23, 0.76)	0.17 (−0.89, 1.24)	0.41 (−0.55, 1.37)	0.19 (−0.34, 0.71)	0.57 (−0.30, 1.44)	−1.46 (−2.56, −0.37)	EXE	−0.18 (−0.57, 0.21)	−0.1 (−0.47, 0.28)
0.27 (−0.14, 0.67)	0.18 (−0.91, 1.27)	0.41 (−0.51, 1.33)	0.19 (−0.43, 0.82)	0.57 (−0.30, 1.45)	−1.46 (−2.52, −0.40)	0.00 (−0.55, 0.56)	ESWT	
0.09 (−0.45, 0.62)	0.00 (−0.88, 0.88)	0.23 (−0.75, 1.21)	0.01 (−0.68, 0.70)	0.40 (−0.54, 1.33)	−1.64 (−2.75, −0.52)	−0.17 (−0.77, 0.43)	−0.18 (−0.82, 0.47)	ACU

ACU, acupuncture (inc. electro acupuncture); CI, confidence interval; CONTROL, placebo/no intervention; ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; SMD, standardised mean difference; SURG, surgery (split into open surgery and arthroscopic surgery); ULTRA, ultrasound therapy.
Lower left triangle presents the findings (SMD with 95% CI) of the network meta-analysis. Upper right triangle presents the findings (SMD with 95% CI) of pairwise meta-analyses. A positive SMD favours the lower right intervention; a negative SMD favours the upper left intervention. Statistically significant findings are shaded in green. Within the table, comparisons between treatments should be read from left to right (i.e. treatment 1 *versus* treatment 2). The estimate effect measure (SMD and their 95% CI) is in the cell in common between the row- and column-defining treatment.

than control, ultrasound therapy, TENS and regenerative injection with pooled SMDs between 0.54 and 1.20. By 3- to 6-month follow-up (T3), only the NMA estimates for laser therapy compared with all other treatments remained statistically significant (Table 6). This included decompression surgery, which only showed small and nonsignificant differences compared with other interventions, albeit based on one trial only,[22] at T3 and T4. Six of 36 comparisons were significant at the T4 (>6 months) follow-up, with taping outperforming all other treatment options in the network, although it should be noted that only one trial provided direct evidence about the effectiveness of taping (compared with exercise,[36] Table 7). Summary estimates for all other treatment options were small (summary SMD <0.3) and not statistically significant.

Treatment option rankings

The mean rank and SUCRA values for treatments included across the six connected networks are presented in Table 8. For pain outcomes at T1, acupuncture ranked highest, with laser therapy, mobilisations, exercise combined with mobilisations and exercise alone ranked second to fifth best; for the later follow-up at T3, the highest ranked treatments were acupuncture, laser therapy and exercise. Regarding function outcomes, the highest ranked treatments were acupuncture, exercise, laser therapy and taping at T1, T2, T3 and T4, respectively. It should be noted that treatment rankings are based on treatment effectiveness (SMDs) and as such can be susceptible to change if a treatment is added or removed from small networks. This is highlighted by significant changes in treatment rankings when looking at sensitivity analyses only including studies considered at low risk of bias (in both randomisation and analysis domains, see Supplemental File 2). Consequently, the rankings are subject to uncertainty, and it is therefore more informative to consider the ranking probabilities and the overall comparative effectiveness of treatments for both pain and function outcomes together.

Table 7. Results of long-term (T4) function outcomes.

CONTROL			0.09 (−0.17, 0.35)	0.18 (−0.09, 0.46)		0.05 (−0.3, 0.39)	0.05 (−0.27, 0.38)	
−0.27 (−0.88, 0.34)	ULTRA							0.22 (−0.21, 0.65)
0.52 (0.13, 0.91)	0.79 (0.13, 1.46)	TAPE				−0.48 (−0.82, −0.15)		
0.15 (−0.07, 0.37)	0.42 (−0.21, 1.06)	−0.37 (−0.80, 0.05)	SURG			−0.39 (−0.74, −0.04)		
0.06 (−0.18, 0.30)	0.34 (−0.28, 0.95)	−0.46 (−0.86, −0.06)	−0.09 (−0.39, 0.22)	SINJ		0.04 (−0.19, 0.26)		
−0.24 (−0.71, 0.22)	0.03 (−0.68, 0.74)	−0.77 (−1.31, −0.23)	−0.39 (−0.89, 0.10)	−0.31 (−0.78, 0.17)	MAN + EXE	0.28 (−0.14, 0.7)		
0.04 (−0.17, 0.24)	0.31 (−0.26, 0.89)	−0.48 (−0.82, −0.15)	−0.11 (−0.37, 0.15)	−0.03 (−0.24, 0.19)	0.28 (−0.14, 0.70)	EXE		−0.09 (−0.48, 0.3)
0.05 (−0.27, 0.38)	0.33 (−0.36, 1.02)	−0.47 (−0.98, 0.04)	−0.10 (−0.49, 0.30)	−0.01 (−0.42, 0.40)	0.30 (−0.27, 0.87)	0.02 (−0.37, 0.40)	ESWT	
−0.05 (−0.49, 0.38)	0.22 (−0.21, 0.65)	−0.57 (−1.09, −0.06)	−0.20 (−0.67, 0.26)	−0.12 (−0.56, 0.32)	0.19 (−0.38, 0.76)	−0.09 (−0.48, 0.30)	−0.11 (−0.65, 0.44)	ACU

ACU, acupuncture (inc. electro acupuncture); CI, confidence interval; CONTROL, placebo/no intervention; ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); MAN, manual therapy; SINJ, steroid injection; SMD, standardised mean difference; SURG, surgery (split into open surgery and arthroscopic surgery); TAPE, taping; ULTRA, ultrasound therapy.
Lower left triangle presents the findings (SMD with 95% CI) of the network meta-analysis. Upper right triangle presents the findings (SMD with 95% CI) of pairwise meta-analyses. A positive SMD favours the lower right intervention; a negative SMD favours the upper left intervention. Statistically significant findings are shaded in green. Within the table, comparisons between treatments should be read from left to right (i.e. treatment 1 *versus* treatment 2). The estimate effect measure (SMD and their 95% CI) is in the cell in common between the row- and column-defining treatment.

Figure 5 shows scatter plots of the SUCRA for each treatment option for pain and function outcomes, highlighting which treatments may be important for both pain and function. At the short-term T1 follow-up, six treatments (acupuncture, manual therapy, exercise, exercise plus manual therapy, laser therapy and TENS) had high probability (>50% SUCRA values) of being effective for both pain and function outcomes. At medium-term T3 follow-up ($3\,\text{months} < t \leqslant 6\,\text{months}$), laser therapy, exercise and ESWT appeared to have greater than 50% probability of effectiveness for both pain and function outcomes.

Meta-regression and sensitivity analyses

Meta-regression analyses were conducted to explore whether offering additional treatment, such as advice, analgesics and home exercises, to one or more arms of the trial (referred to as multimodal intervention) resulted in different (larger) summary effect estimates. Of the 99 trials included in the analysis, 52 were identified as implementing multimodal interventions. Results of the meta-regression analysis taking account of offering treatments as part of a multimodal intervention indicated only small changes in treatment rankings across all networks, and coefficients for the covariates had 95% CIs which included the null value, indicating no association with treatment effect.

Sensitivity analysis including all trials in the network, regardless of sample size, resulted in only one network with evidence of consistency, the function outcomes T3 network (see Supplemental File 2 for network plots of sensitivity analyses). Reestimating treatment rankings and treatment effect estimates indicated very different conclusions for all networks compared with those excluding smaller trials. For example, for the T3 function network, rankings altered dramatically, with platelet-rich plasma (PRP) injection ranked first when analyses included smaller trials but ranked last when excluding smaller trials. These differences are likely due to a high level of inconsistency and heterogeneity present in the networks containing all trial data, regardless of sample size, and hence, the NMA results based on the exclusion of smaller

Table 8. Treatment rankings for all networks.

Treatment	Pain short term			Pain short long			Function short term			Function short mid			Function short long			Function long		
	SUCRA	Rank	Prob	SUCRA	Rank	Prob	SUCRA	Rank	Prob	SUCRA	Rank	Prob	SUCRA	Rank	Prob	SUCRA	Rank	Prob
ACU	89.10	2.60	75.00	92.40	1.50	99.80	97.10	1.40	97.80	34.40	8.90	0.60	46.00	5.30	19.30	40.80	5.70	21.30
CONTROL	23.90	12.40	0.00	18.40	6.70	0.00	25.90	11.40	0.00	34.30	8.90	0.00	35.10	6.20	2.90	43.00	5.60	7.80
ELEC	29.70	11.50	0.50	–	–	–	53.40	7.50	8.10	37.20	8.50	5.40	–	–	–	–	–	–
ESWT	49.80	8.50	8.40	58.10	3.90	25.40	44.70	8.70	7.10	42.40	7.90	0.00	64.30	3.90	48.30	54.80	4.60	40.40
EXE	62.50	6.60	3.00	67.80	3.30	72.10	51.40	7.80	1.60	75.70	3.90	31.90	65.10	3.80	52.00	51.10	4.90	17.40
LASER	88.60	2.70	74.70	91.40	1.60	96.90	79.60	3.90	46.50	98.20	1.20	99.60	99.60	1.00	99.70	–	–	–
MAN	79.60	4.10	58.40	–	–	–	71.50	5.00	42.10	–	–	–	–	–	–	–	–	–
MAN + EXE	62.60	6.60	31.60	–	–	–	61.10	6.40	29.80	77.60	3.70	55.20	–	–	–	16.10	7.70	4.30
NAT	–	–	–	–	–	–	–	–	–	92.10	1.90	96.50	–	–	–	–	–	–
NSAIDS	22.00	12.70	0.70	–	–	–	1.10	14.80	0.00	–	–	–	–	–	–	–	–	–
RINJ	37.80	10.30	2.90	7.60	7.50	0.00	23.60	11.70	1.30	35.30	8.80	0.00	18.40	7.50	5.80	–	–	–
SINJ	51.20	8.30	0.70	33.60	5.60	0.10	38.00	9.70	0.20	53.60	6.60	1.70	46.90	5.30	20.90	56.20	4.50	33.10
SINJ + MAN	51.10	8.30	18.20	–	–	–	33.40	10.30	7.10	–	–	–	–	–	–	–	–	–
SINJ + NSAIDS	52.70	8.10	17.60	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
SURG	–	–	–	–	–	–	–	–	–	–	–	–	29.90	6.60	16.70	72.20	3.20	68.20
TAPE	21.30	12.80	0.00	–	–	–	29.00	10.90	0.20	44.90	7.60	8.70	–	–	–	98.20	1.10	98.90
TENS	56.90	7.50	8.30	30.60	5.90	5.70	74.70	4.50	45.00	2.90	12.70	0.10	–	–	–	–	–	–
ULTRA	21.30	12.80	0.00	–	–	–	65.50	5.80	13.20	21.50	10.40	0.30	44.70	5.40	34.40	17.60	7.60	8.60

ACU, acupuncture (inc. electro acupuncture); CONTROL, placebo/no intervention; ELEC, other electrotherapy (inc. PSWD, PEMF or PRF); ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; MAN, manual therapy; NAT, naturopathic care; NSAIDS, nonsteroidal anti-inflammatory drugs; PEMF, pulsed electromagnetic field; PSWD, pulsed shortwave diathermy; PRF, pulsed radiofrequency; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; SUCRA, surface under the cumulative ranking curve; SURG, surgery (split into open surgery and arthroscopic surgery); TAPE, taping; TENS, Microcurrent (MENS); ULTRA, ultrasound therapy.
SUCRA values (0–100) and mean ranks are presented, based on 1000 simulations. Higher SUCRAs and lower mean ranks indicate better performing treatments. Prob gives the probability of the specific treatment being ranked in the top three treatments, based on 1000 simulations.

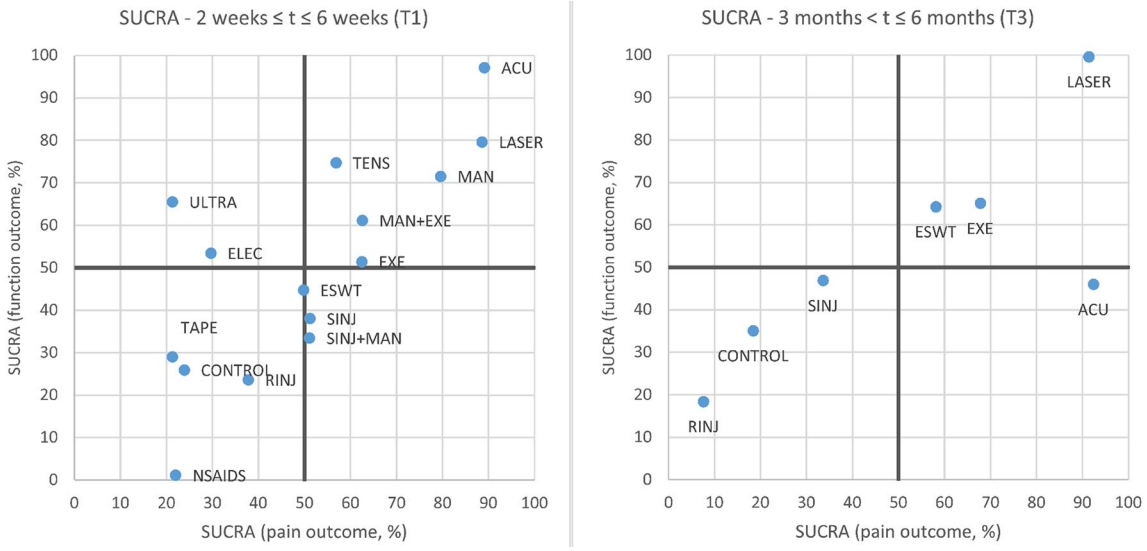

Figure 5. Scatter plot of the SUCRA for pain outcomes *versus* function outcomes at T1 and T3 follow-up.
ACU, acupuncture (inc. electro acupuncture); CONTROL, placebo/no intervention; ELEC, other electrotherapy (inc. PSWD, PEMF or PRF); ESWT, extracorporeal shock wave therapy; EXE, exercise (as part of multimodal physiotherapy); HILT, high-intensity laser therapy; LASER, laser therapy (inc. HILT or LLLT); LLLT, low-level laser therapy; MAN, manual therapy; NSAIDS, nonsteroidal anti-inflammatory drugs; PEMF, pulsed electromagnetic field; PSWD, pulsed shortwave diathermy; PRF, pulsed radiofrequency; RINJ, PRP injection (platelet-rich plasma/autologous blood) or hyaluronic injection; SINJ, steroid injection; SUCRA, surface under the cumulative ranking curve; TAPE, taping; TENS, Microcurrent (MENS); ULTRA, ultrasound therapy. In Figure 5, higher percentages indicate higher probability of being ranked highly compared with other treatments in the network in terms of effectiveness.

trials provide a better indication of comparative treatment effectiveness.

In the sensitivity analysis removing studies at increased risk of bias in both randomisation and analysis domains (see Online Supplemental File 2), the highest ranked treatments for pain T2 were naturopathic care, taping and exercise, with evidence for laser therapy and acupuncture coming from higher risk trials excluded from the analysis. Similarly for function outcomes at T2, high-ranking treatments included naturopathic care, exercise and exercise combined with mobilisations, with acupuncture and laser therapy trial evidence excluded. Function T4 identified surgery and taping as high-ranking treatments when excluding studies at increased risk of bias. These results add further weight to uncertainty of the evidence base, with studies classified as at unclear risk of bias remaining in this sensitivity analysis, and direct evidence from only a single study for some treatments (e.g. naturopathic care), results should be interpreted with great caution.

Summary of findings: certainty of evidence

Based on the analyses presented above, the certainty of evidence, taking into account risk of bias, consistency, precision and directness are summarised as follows (see also Summary of Findings Table 9).

The initial NMA showed inconsistency for nearly all the networks. Sensitivity analyses, removing trials with small sample sizes, showed deviating findings highlighting imprecision and risk of reporting bias for all networks. The primary analysis for this review was therefore based on larger studies only ($n \geqslant 60$). The networks for pain outcomes at T2 and T4 were still inconsistent or disconnected, reducing certainty in terms of consistency. The sensitivity analysis focusing on study limitations further reduced certainty of evidence, highlighting the small number of trials with low risk of bias, and affecting the results of comparative effectiveness of treatments. There was no high-quality evidence for the comparative effects of laser therapy or acupuncture (demonstrated in the primary analysis), with only the positive effects of exercise confirmed at T2 for both pain and function outcomes. Analyses for nearly all treatments, apart from exercise, were strongly affected by limited data from direct comparisons between active treatments, further downgrading certainty of the comparative effectiveness of laser therapy, taping and surgery. Meta-regression analysis did not demonstrate a

Table 9. Summary of main findings for each of the eight networks, including GRADE-informed approach to assess certainty of evidence.

Network	Findings of the primary analysis (excluding trials with $n < 60$), comparative benefit found for:	Findings following sensitivity analysis for risk of bias (excluding trials not at low risk of bias)	Risk of bias[a]	Precision[b]	Inconsistency[c]	Indirectness[d]	GRADE
Pain outcomes							
T1: 2–6 weeks	Exercise plus mobilisations, exercise alone, acupuncture, (laser[a])	All studies have significant limitations	⊗	⊗	✓	✓	Low
T2: 6–12 weeks	Inconsistent network	Exercise, (naturopathic care, taping[a])	✓	⊗	⊗	✓	Low
T3: 3–6 months	Exercise, acupuncture, (laser[a])	All studies have significant limitations	⊗	⊗	✓	✓	Low
T4: >6 months	Inconsistent network	(Surgery[a])	⊗	⊗	⊗	✓	Very low
Function outcomes							
T1: 2–6 weeks	Acupuncture, mobilisations, (laser[a])	All studies have significant limitations	⊗	⊗	✓	✓	Low
T2: 6–12 weeks	Exercise, exercise plus mobilisations, (laser[a])	Exercise, (naturopathic care[a])	✓	⊗	✓	✓	Moderate
T3: 3–6 months	(Laser[a]), decompression surgery	All studies have significant limitations	⊗	⊗	✓	✓	Low
T4: >6 months	(Taping[a])	(Taping[a], surgery[a])	⊗	⊗	✓	✓	Low

[a]Risk of bias: sensitivity analysis excluding studies not at low risk of bias showed deviating results for all networks, and for most treatments options. Only exercise was consistently more likely to be effective for relieving pain and improving function compared with other treatments up until 12-week follow-up. Direct evidence for the comparative effectiveness of laser, taping, surgery and naturopathic care compared with other active treatments was based on single trials only, and hence downgraded.
[b]Precision: the primary analysis was based on studies including at least 60 participants at randomisation, as sensitivity analysis showed high risk of small study bias across all networks, with results deviating when small trials were included in the network meta-analysis.
[c]Consistency: assessment of network consistency for the primary analysis (excluding trials with $n < 60$) showed all networks met the consistency assumption, apart from pain outcomes at T2 and T4.
[d]Directness: meta-regression analysis indicated similar findings for all networks when interventions were offered as part of a combined, multimodal treatment, compared with when offered as a single (stand-alone) treatment.
GRADE: The grading of recommendations assessment, development and evaluation.

large difference in results when offering additional treatments such as advice, analgesics and home exercises to an intervention, which strengthens certainty in terms of applicability of findings. Certainty of evidence for pain and function outcomes was therefore considered to be low for most networks and included treatment options (downgraded for imprecision, inconsistency and risk of bias), and moderate only for the comparative effects of exercise on function up until 3-month follow-up (downgraded for imprecision only).

Discussion

Main findings

This meta-analysis has brought together both direct and indirect evidence from a large number

of trials investigating the effectiveness of a wide range of treatment options for patients with SSCs. The results show small to moderate estimates of effect for most treatment options and no strong evidence for any one individual treatment being clearly superior to another. Nevertheless, the ranking probabilities, indicating the probability of each treatment option being in the top three treatments, offer some insight into which treatments may be best for both pain and function outcomes. At short-term (2–6 weeks) follow-up, five treatments (acupuncture, manual therapy, exercise, laser therapy and TENS) had high probability (>50% SUCRA values) of being effective for both pain and function outcomes. At 3- to 6-month follow-up, exercise, laser therapy and ESWT appeared to have greater than 50% probability of effectiveness for both pain and function outcomes.

However, there is considerable uncertainty regarding these comparative effectiveness results, mainly due to small study sizes, a very small number of studies directly comparing active interventions or with methodological concerns. For example, our results indicate that both laser therapy and exercise may provide benefits for patients for both pain and function outcomes across different follow-up time-points, with larger effects for exercise in the longer term. It must be noted, however, that only one relatively small trial[35] ($n = 60$) with large uncertainty around its estimate of effects and with considerable risk of bias provided direct evidence regarding the effect of laser therapy. A larger number of trials provided evidence for the benefits of exercise, and these results (up until 3-month follow-up) were considered robust in sensitivity analyses excluding trials at increased risk of bias related to randomisation and data presentation or analysis. However, our analyses do not offer guidance regarding the type of exercise programme that may be most effective for SSC. Previous systematic reviews focusing on exercise interventions using pairwise meta-analysis have been unable to identify optimal exercise programmes in terms of duration, dose, type or delivery of exercise.[14,37,38] Further NMA focusing specifically on exercise interventions may be conducted to determine the comparative effectiveness of different types of, or approaches to, exercise for patients with SSC.

Comparisons with previous research

A large number of systematic reviews and meta-analysis have reported on the effectiveness of treatments for SSCs, although most have used standard meta-analysis approaches where this was considered suitable. In their Cochrane review, Page and colleagues[17] included 60 trials investigating the effects of exercise and/or manual therapy in the treatment of rotator cuff disease. The authors conclude that the effects of manual therapy and exercise may be similar to those of corticosteroid injection and arthroscopic subacromial decompression. More recently, the Cochrane review by Karjalainen and colleagues[39] concluded that current data do not support the use of subacromial decompression in the treatment of rotator cuff disease presented as subacromial impingement, with high certainty evidence, subacromial decompression did not offer clinically important benefits over placebo for pain, function or health-related quality of life. Steuri and colleagues[12] conducted a systematic review and meta-analysis of 200 trials to investigate the effectiveness of several conservative interventions including exercise, manual therapy and medication. Their results indicate exercise should be considered for patients with shoulder impingement symptoms, and that tape, ESWT, laser or manual therapy might be added. They also conclude that NSAIDS and corticosteroids are superior to placebo, but that it is unclear how these treatments compare with exercise. Similar to our study, these systematic reviews[12,17,39] report small to moderate effect sizes for treatment options compared with control interventions and highlight the large number of small trials and low quality of the evidence base, and large number of small trials. Aiming to provide clear guidance for practice and patients by generating a clinically meaningful ranking of currently available treatment options for SSC, our study used evidence from both direct and indirect comparisons in 99 trials, but also could not provide strong evidence in favour of one particular treatment over other options, with low precision, risk of bias, inconsistency of networks and lack of direct evidence reducing confidence in the evidence for comparative effectiveness for most treatment options. Our primary analysis did indicate benefits from laser therapy, though evidence for this was largely driven by a single trial with large effect size and concerns in terms of study limitations. We urge readers to treat current results regarding the comparative effects of laser therapy with caution, as it does not feature in the sensitivity analysis, where trials considered at increased risk of bias were removed. More so, previous literature has suggested that ultrasound therapy, laser therapy and acupuncture are no

more effective than placebo.[15,16] Only for exercise interventions, the evidence appears to be slightly more robust, especially for function outcomes up until 3-month follow-up.

A few previous NMA studies have evaluated treatment options for SSCs, including Dong and colleagues[40] who investigated the comparative effectiveness of a range of treatments for shoulder impingement syndrome based on 33 trials, 2300 participants. In contrast to our NMA, their analysis included trials comparing different dosages or techniques of the same treatment option, resulting in the inclusion of a larger number of trials investigating surgical interventions in particular. Dong and colleagues conclude that exercise and other treatment options combined with exercise, such as acupuncture, are suitable treatments for patients at an early stage of shoulder impingement syndrome, but the authors presented no analysis based on duration of symptoms. Their analysis indicated operative interventions may be considered for patients with persistent symptoms, but the authors also caution that similar outcomes may be achieved from exercise therapy. Results of their sensitivity analyses and meta-regression supported the robustness and reliability of their NMA. Their study, however, which was published in 2015, includes a smaller sample of RCTs (only three studies with total sample size >50) compared with 99 in this study, and used different eligibility criteria, especially related to treatment options.

Two recent NMAs focused on the effects of treatment options for one specific subacromial condition, calcific rotator cuff tendinopathy.[41,42] Both NMAs showed that ultrasound-guided needling and ESWT reduce pain and the size of calcium deposits, but one of these (seven trials)[41] emphasises the lower risk of adverse effects of combined ultrasound-guided needling and subacromial corticosteroid injection compared with ESWT. They did not address heterogeneity or inconsistency of evidence making it difficult to interpret the findings from their analysis. The second NMA by Wu and colleagues[42] found no evidence of inconsistency between direct and indirect evidence but was unable to examine the effect of potential sources of heterogeneity because of the limited number of trials ($n = 14$) included in their NMA. More so, Lin and colleagues[43] focused their NMA on the comparative effectiveness of injection therapies only for rotator cuff tendinopathy (18 trials, 996 participants), and found corticosteroid injection to be effective for reducing pain and improving function in the short term (over 6 weeks) but not in the long term, while regenerative injection was reported to yield better outcomes in the long term (over 24 weeks). Similar to our NMA, the authors call for caution with the interpretation of results, given heterogeneity of trial findings, although no inconsistency of evidence was detected in their NMA, possibly because it addressed a more specific clinical diagnosis and treatment.

Overall, evidence from previous studies (systematic reviews with meta-analysis and NMA) is dissonant regarding the best treatment(s) for SSCs.[17,12,39–43] Our study, the largest shoulder NMA till date, including all available treatment options for SSCs, confirms small to moderate effect sizes for many treatments when compared head-to-head in an NMA. Our findings highlight the gaps in current research and indicate there is more to be done in uncovering what best treatment for SSCs should entail for subgroups of patients. However, given success of some treatments like injections in the short term and exercise for long-term symptoms relief, future research for ascertaining factors that predict treatment response in patients with SSCs will be valuable.

Strengths and limitations

We have reported the results of the largest NMA conducted so far evaluating the comparative effectiveness of a wide range of treatment options for patients with SSCs. Comprehensive searches were conducted to identify relevant trials, and careful attention was given to statistical inconsistency and heterogeneity of findings. We presented a number of sensitivity analyses to explore the influence of important limitations (small sample size, risk of bias, use of interventions as a single intervention rather than as a package of care). The ranking of treatments according to their relative effect sizes was highly sensitive to the lack of direct comparisons, risk of bias, inconsistency and imprecision, of the evidence base. Treatment rankings must therefore be interpreted with caution, as the difference in comparative effectiveness between treatments was often small and potentially not clinically important. Furthermore, there were high levels of heterogeneity across the trials in terms of population characteristics, the way treatments were delivered and the outcome measures used, which has likely contributed to the uncertainty of estimates.

Much time, effort and resources were put into data extraction and quality appraisal of 177 eligible trial reports; however, many did not provide sufficient data to be included in the NMA, despite available approaches being used to transform data where possible. A range of outcome measures were used to assess pain and function across trials and effect estimates were standardised to allow meta-analysis, but this may potentially explain some of the heterogeneity and inconsistency found in this analysis. Furthermore, there was wide variability in the content of similar treatment options, with exercise interventions, corticosteroid therapies or usual care control arms ranging widely in terms of content, dose or duration. Many treatments were offered in a wide range of combinations, and it was difficult to classify these consistently and fully take this into account within the NMA.

An important limitation of the NMA concerned the high level of inconsistency between effect estimates from direct (within-trial) comparisons compared with effect estimates derived from networks that also included indirect evidence. This was largely resolved by excluding small sample trials, although this further reduced the evidence base for our NMA. This also highlights the importance of designing trials of adequate sample size to ensure treatment effect estimates are sufficiently precise and reliable.

Implications for research and practice

This NMA has highlighted wide heterogeneity and clear gaps in the evidence underpinning treatment decisions for patients with SSCs. Despite availability of a large number of trials, they are often small and poorly reported in terms of randomisation, allocation concealment, blinding, handling of missing data, treatment adherence and outcome data. Our sensitivity analysis excluding studies that were not low risk of bias on random sequence generation (as a basic assumption of NMA) and others (where there had been poor presentation of data, unclear statistical analysis) resulted in networks which included data from a very small number of trials (Supplemental File 2). Particularly, the short-term network (T1) for both pain and function, including the largest number of trials in the primary analysis, was no longer viable (disconnected), showing most studies giving short-term outcomes are of poor quality. This highlights an important gap in current literature in this field. A lot of time, effort and resources were put into the review, data extraction and quality appraisal of 177 eligible trials; however, many studies ($n=78$) did not provide sufficient data to be included in the NMA, despite available approaches being used to transform data where possible. Furthermore, many of the trials are small with less than 60 participants at randomisation ($n=54$), and at high or unclear risk of bias across most of the Cochrane risk of bias domains. As many trials have evaluated treatments for this important condition (SSCs), current evidence from this study shows there is considerable research waste when considering questions of comparative effectiveness, related to poorly performed or presented studies, small trials and a lack of studies directly comparing active interventions, producing unreliable evidence that is potentially prone to bias, and limiting the opportunities to provide clear guidance regarding the most effective treatments in clinical practice.

NMA findings most helpful for clinical practice are possibly the scatter plots (Figure 5) which present the probability of treatment options being in the top three for pain and function outcomes and provide guidance as to which treatments are most likely to be best for pain, function or both. Future NMAs may usefully address more specific review questions and focus on specific treatment options, to investigate the comparative effectiveness of different approaches to delivering a certain treatment. This will be most valuable for exercise interventions, which were most often evaluated in trials and were found to show positive effects on both pain and function, but with persisting uncertainty as to the optimal exercise characteristics. For many treatment options, summary effect estimates were imprecise as a result of heterogeneity of effects between trials, but also reflecting individual variability in response to treatment. Future large trials or meta-analysis of individual participant data may explore which patient or disease characteristics (including age, characteristics of the shoulder pain condition, expectations and other psychological factors) may predict (or moderate) the effect of commonly used treatments for SSCs, which would generate evidence as to which subgroups of patients are most likely to benefit (or experience least harm) from specific types of treatment.

Conclusion

The results of this large NMA including 54 RCTs showed small to moderate effect sizes for most treatment options for SSCs. Six treatments had a high probability of being effective, in the short term, for pain and function (acupuncture, manual therapy, exercise, exercise plus manual therapy, laser therapy and TENS), but with very low certainty for most treatment options. After accounting for risk of bias, there is evidence of moderate certainty that exercise is an effective treatment option for both pain and function outcomes in patients with SSCs. Further NMA focusing specifically on exercise interventions may be conducted to determine the comparative effectiveness of different types of, or approaches to, exercise for patients with SSC. The review also highlights the need for large high-quality research to better understand whether specific subgroups of patients respond better to some treatments than others.

Author contributions

OOB, JE, CL, LC, JLJ, NC, GW-J, ER, NEF and DAvdW helped in investigation. JE and OOB helped in formal analysis and in writing the original draft. OOB, JE, CL, LC, JLJ, NC, GW-J, ER, NEF, and DAvdW helped in writing – review and editing. OOB and DAvdW helped in project administration.

Conflict of interest statement

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Ethical approval information

Ethical approval is not applicable for this project. This is a systematic review and network meta-analysis using aggregate data. No individual participant data are used.

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Data sharing statement

All data relevant to the study are included in the article or uploaded as supplemental information.

Supplemental material

Supplemental material for this article is available online.

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