

Effectiveness of progressive and resisted and non-progressive or non-resisted exercise in rotator cuff related shoulder pain: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Objective: Synthesize evidence regarding effectiveness of progressive and resisted or non-progressive and non-resisted exercise compared with placebo or no treatment, in rotator cuff related pain.

Data sources: English articles, searched in Cochrane CENTRAL, MEDLINE, EMBASE and CINAHL databases up until May 19, 2020.

Methods: Randomized controlled trials in people with rotator cuff related pain comparing either progressive and resisted exercise or non-progressive and non-resisted exercise, with placebo or no treatment were included. Data extracted independently by two authors. Risk of bias appraised with the Cochrane Collaboration tool.

Results: Seven trials (468 participants) were included, four trials (271 participants) included progressive and resisted exercise and three trials (197 participants) included non-progressive or non-resisted exercise. There was uncertain clinical benefit for composite pain and function (15 point difference, 95% CI 9 to 21, 100-point scale) and pain outcomes at >6 weeks to 6 months with progressive and resisted exercise compared to placebo or no treatment (comparison 1). For non-progressive or non-resisted exercise there was no significant benefit for composite pain and function (4 point difference, 95% CI -2 to 9, 100-point scale) and pain outcomes at >6 weeks to 6 months compared to placebo or no treatment (comparison 2). Adverse events were seldom reported and mild.

Conclusions: There is uncertain clinical benefit for all outcomes with progressive and resisted exercise and no significant benefit with non-progressive and non-resisted exercise, versus no treatment or placebo at >6 weeks to 6 months. Findings are low certainty and should be interpreted with caution.

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Shoulder pain affects 15–30% of the population and is the third most common musculoskeletal condition presenting to primary care.^{1,2} Rotator cuff related pain is the most common cause of shoulder pain, accounting for up to 80% of all cases.³ Up to 50% of people affected experience pain and disability beyond 12 months despite conservative treatment.³ Clinical guidelines recommend clinician-guided exercise for rotator cuff related pain.^{4,5} However, an updated Cochrane review found only one high quality randomized controlled trial (120 participants) out of 60 (3620 participants) that compared exercise and manual therapy for rotator cuff related shoulder pain to placebo, with no difference in clinical outcomes at 22 weeks.^{6,7} Two trials (89 participants) of very low quality found similar results in comparison to no treatment.^{8,9} Other systematic reviews that compare exercise with or without manual therapy to all no-exercise controls found very low quality evidence that exercise was beneficial for pain.^{10–12}

Resistance exercise has previously been shown to be of benefit for knee osteoarthritis,¹³ back pain¹⁴ and is a widely used and recommended treatment modality.^{15,16} Resistance exercise includes movement against body weight, gravity or by adding load with weight or elastic resistance band (Theraband). Exercise is considered progressive and resisted when the amount of load applied is increased over time as the body adapts to the demand that it is placed under.

Prior reviews of rotator cuff related pain, including Page et al.⁷ have considered all exercise interventions as equal, without consideration of how the exercise was prescribed (i.e. if there was added resistance that was progressed over time or if resistance was not applied or not progressed).^{7,17–22} Therefore, it remains unclear whether exercise that is resisted and progressed is more beneficial than placebo or control in treating rotator cuff related

pain. Likewise, it is not clear if exercise that is not resisted or not progressed is more effective than placebo or control in managing rotator cuff related pain. This remains an unanswered important clinical question in determining the most effective type of exercise intervention for rotator cuff related pain. In a previous narrative review, studies that included progressively loaded exercise and greater dose appeared to report superior outcomes compared to various interventions including no treatment, shock-wave therapy and therapeutic ultrasound.²³ No systematic reviews have distinguished between type of exercise for rotator cuff related pain.

This systematic review aims to investigate the effectiveness of progressive and resisted exercise and the effectiveness of non-progressive and non-resisted exercise; compared to placebo or no treatment in the management of rotator cuff related pain.

Methods

The methods in this review were similar to methods in the recently updated Cochrane review of manual therapy and exercise interventions for rotator cuff related pain.⁷ This review was submitted May 30th 2019 to the International Prospective Register of Systematic Reviews (PROSPERO; reference CRD42019136513) and registered on August 2nd 2019.

Randomized controlled trials written in any language were included regardless of type. Participants over 16 years old with a primary complaint of rotator cuff related pain of any duration were included. Diagnostic criteria included anterolateral shoulder pain (with or without referral into the arm), preserved passive range of shoulder movement, shoulder pain with movement or resisted shoulder muscle contraction (e.g. empty/full can tests). Randomized controlled trials using synonyms for rotator cuff

related pain (e.g. subacromial impingement syndrome, rotator cuff tendinopathy, rotator cuff tendinitis) were included.

Exclusion criteria included participants with a full thickness tear involving more than one rotator cuff tendon (based on clinical presentation or imaging findings, recognizing that some included participants may have undetected rotator cuff tears), gross shoulder instability, significant shoulder trauma, previous shoulder surgery, shoulder osteoarthritis, hemiplegic shoulders, a complex myofascial neck/shoulder/arm pain condition, suspected cervical spine referred pain, or a systemic inflammatory condition (e.g. rheumatoid arthritis), unless data were presented separately for our population of interest.

In contrast to the review by Page et al.⁷ where all exercise was considered equal, we considered the type of exercise intervention. We included randomized trials with the following comparisons: (1) Progressive and resisted exercise versus placebo or no treatment; (2) Non-progressive or non-resisted exercise versus placebo or no treatment. Trials using progressive and resisted exercise were eligible if they explicitly stated within the intervention description how resistance was applied (e.g. theraband, weight), and that there was progression of the volume or the load, or both, over time. Trials using non-progressive or non-resisted exercise were eligible if they explicitly stated that load was not applied or not progressed, or both. Non-progressive or non-resisted exercise could include active movement exercise against gravity or with gravity removed, and trials that progressed range of motion or the type of exercise (e.g. basic static to through range) were excluded if resistance within each exercise was progressed. The comparator group could include placebo interventions (e.g. detuned laser provided as an alternative to 'physical therapy') and no treatment. We did not exclude randomized trials that included co-interventions (e.g. manual therapy, advice) as part of the intervention or comparator group, but we planned secondary analyses to determine the effect of these interventions.

An a priori decision was made to include composite pain and function shoulder outcomes and/or

pain outcomes given these are patient-important and considered a core outcome domain by shoulder experts.²⁴ Composite pain and function based on standardized questionnaire was the primary outcome of interest. When multiple scales were reported, data were extracted according to the following hierarchy;⁷ (1) Shoulder Pain and Disability Index (SPADI);²⁵ (2) Croft Shoulder Disability Questionnaire;²⁶ (3) Constant-Murley Score;²⁷ (4) any other shoulder-specific function scale. Secondary outcomes of interest included overall pain, pain with activity, and pain at rest (measured on VAS, numerical or categorical rating scale). If overall pain was not reported, we substituted another pain measure for that analysis in the following hierarchy, unspecified, rest pain or other pain. Number of participants experiencing an adverse event (as defined by the authors) were also extracted.

All outcomes times were extracted and grouped to identify short (up to 6 weeks), medium (longer than 6 weeks and up to 6 months) and long-term (longer than 6 months) effects of the exercise interventions. The primary time range was longer than six weeks and up to six months given this is sufficient time for exercise interventions to have an effect.²⁸ The longest time point was extracted when multiple time points were reported within the above defined periods.

Randomized controlled trials published up to March 2015 were identified from the updated Cochrane review of manual therapy and exercise interventions for rotator cuff related pain.⁷ The search from the Page et al.⁷ 2016 review was repeated excluding search terms for adhesive capsulitis and manual therapy given these were not relevant for our review (Appendix 1).

The search included the following databases: Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* May 2020, Issue 5), Ovid MEDLINE (March 2015 to May 2020), Ovid EMBASE (March 2015 to May 2020), and CINAHL Plus (EBSCO, March 2015 to May 2020). Gray literature was searched via OpenGray and ongoing trials via the National Institute of Health (clinicaltrials.gov) and the World Health Organisation (<http://www.who.int/ictpr>) International Clinical Trials Registries.

Titles and abstracts were screened independently by two authors (PM, GS), and the full text was reviewed by the same author independently if required to determine eligibility. Consensus on discrepancies was reached via discussion, otherwise a third author (CL or JN) was available to assist if consensus was not reached.

Data were extracted independently by two authors (PM, GS) to a standard data extraction form, and discrepancies were resolved via discussion, or a third author (CL) was consulted to adjudicate when required. Authors were emailed twice over four weeks to retrieve missing data. All data extraction was checked by a third author (JN). Missing SDs were calculated from standard errors (SEs), 95% CIs or P values, otherwise we planned to impute SDs from other trials in the meta-analyses (median of available SDs) if no measures of variation were reported.²⁹ For the primary outcome of function and pain we calculated the median of available SDs in three studies following the process described above.^{8,30,31} For activity pain and rest pain we calculated SDs as above for two studies.^{30,31} For Giombini et al.,³² the reported measure of variability was much lower (by a factor of 4) than all other studies and we assumed it was a standard error (this could not be confirmed by the authors at the time of publication).

The data extracted from each randomized trial are shown below:

- Trial characteristics (author name, year published, trial type [e.g. parallel, crossover], country, funding source, trial registration [with number]).
- Participant characteristics (age, gender, duration of symptoms, inclusion/exclusion criteria).
- Exercise intervention characteristics (exercises, sets, repetitions, frequency, duration, how exercises was loaded and progressed, co-interventions, adherence measures, advice about pain).
- Comparator intervention characteristics (details of placebo or no treatment).
- Outcome instrument used and timing.
- Outcome data were extracted according to the following a priori decision rules to minimize

bias: (1) preference to data that was adjusted for baseline values (e.g. ANCOVA) and intention-to-treat; (2) follow up rather than change scores extracted where possible; (3) and data extracted for only the first period of crossover trials.

The Cochrane Collaboration's tool was used to assess risk of bias.³³ The results of the risk of bias assessment for all included trials were extracted from Page et al.⁷ as no new studies were identified in our updated search.

Dichotomous (relative risk [RR] and 95% confidence intervals [CI]) and continuous measures (mean difference [MD] and 95% CI) of treatment effect were calculated using Review Manager 5.3 (RevMan). For continuous outcomes, MD was used after scores for the Shoulder Rating Questionnaire (17–100) and the Neer Shoulder Score (10–100) were transformed to a 0–100 scale (0 is best).³⁴ We reversed the direction of the Constant-Murley, Neer and Shoulder Rating Questionnaire scores so that zero was best in all scales (to match the SPADI, the highest outcome in our hierarchy).³⁴ Minimal clinically important difference was assumed to be 10 on a 100-point scale for composite pain and function outcome,^{35–37} and 15 points on a 100-point scale for pain outcome.³⁸

Data were pooled in meta-analyses using Review Manager 5.3³⁹ if participants, interventions and outcome measures were similar. A random effects models was chosen a priori given heterogeneity is likely. Where data could not be pooled, we summarized findings descriptively and reported effect estimates and 95% confidence intervals.

Assessment of statistical heterogeneity was based on Chi-square statistic and the I^2 statistic.⁴⁰ For the I^2 statistic, we interpreted statistical heterogeneity as not important (<50%), moderate (50–75%) and high (>75%).⁴⁰

A sensitivity analysis was planned to investigate the influence of high risk of bias studies on treatment outcomes. Subgroup analysis was planned a priori to investigate (1) the effect of exercise interventions alone versus exercise interventions including co-interventions, and (2) the effects of exercise setting (e.g. clinician-supervised or home exercise).

We prepared summary of findings tables for both comparisons and graded the certainty of evidence using a GRADE approach [Grades of Recommendation, Assessment, Development and Evaluation Working Group].⁴¹ Level of evidence was downgraded (to moderate, low or very low) for each of the following: risk of bias, inconsistency of results, indirectness, imprecision, and publication bias.

For dichotomous outcomes (e.g. adverse events), absolute risk difference was expressed as a percentage and relative percent change was the risk ratio – 1 expressed as a percentage. The NNT_H was calculated using the event rate in the control group and risk ratio.⁴² For continuous outcomes (e.g. composite pain and function), absolute risk difference was the mean difference in outcome between the intervention and comparator group expressed as a percentage. The relative percent change was the mean intervention group difference (absolute change) divided by the mean at baseline in the control group, expressed as a percentage.

Results

Study selection

Nine eligible trials were identified from the Page et al.⁷ 2016 systematic review. One trial was excluded because the control group received a standard exercise instruction pamphlet in addition to education and therefore is not a true comparison to no treatment or placebo.⁹ The other excluded trial included physiotherapy treatments as control (heat packs, transcutaneous electrical nerve stimulation and ultrasound).⁴³ No eligible trials were identified after the updated search (Figure 1), and screening reference lists of included studies, gray literature and clinical trials registries. Full text of five articles were screened from the updated search, all were excluded as an exercise program was used in both the intervention and comparator groups.^{44–48} We obtained data from the authors (July 2017) of two trials^{6,31} that allowed us to confirm eligibility. We acknowledge that within the trial protocol for the randomized trial by Bennell et al.⁴⁹ there was progression of exercise through range (e.g. external rotation in side lying, to

standing in neutral, to elbow supported at 90° abduction, to unsupported elbow at 45° abduction). However, there was not progression of load or volume as specified in our eligibility criteria.

Trial characteristics

Trial and participant characteristics are shown in Table 1. Seven parallel group randomized trials (468 participants) were included (see Online Appendix 2). Multiple diagnostic labels were used for rotator cuff related pain but there was overlapping and consistent diagnostic criteria between trials (Table 1). Mean age was between 47 and 61 years, but lower in Giombini et al.³² (26 and 29 years). Men were more prevalent (54–100%) aside from Lombardi et al.⁵⁰ (24% men). Baseline composite pain and function was comparable (33–50, 0–100-point scale where 0 is best).

Description of the interventions and comparators are shown in Table 2. Three trials compared progressive and resisted exercise with no treatment.^{8,50,51} One trial compared progressive and resisted exercise with placebo (detuned laser).³⁰ All progressive and resisted exercise interventions included scapular and rotator cuff strengthening and progressed the load (intensity) with theraband or weights.^{8,30,50,51} Prescribed sets and repetitions varied, and only one study specified exercise intensity (50–70% of the 6RM).⁵⁰ Three studies included co-interventions. Brox et al.³⁰ included education about pathology, pain and ergonomics, Dickens et al.⁸ included manual therapy, postural advice, taping with or without electrotherapy and Ludwig et al.⁵¹ included shoulder stretching.

All three trials (four comparisons) of the non-progressive and non-resisted interventions were compared with placebo (two ultrasound^{6,32} and one brace³¹). One non-progressive and non-resisted exercise trial⁶ targeted scapular and rotator cuff strengthening similar to progressive and resisted trials. Whereas, Walther et al.³¹ assessed static exercise and neck stretching (all other trials evaluate dynamic exercise) and Giombini et al.³² assessed pendular exercise and shoulder stretching. Load was applied without progression with theraband or 1kg weight in two trials^{6,31} and no load applied in the remaining trial.³² There were

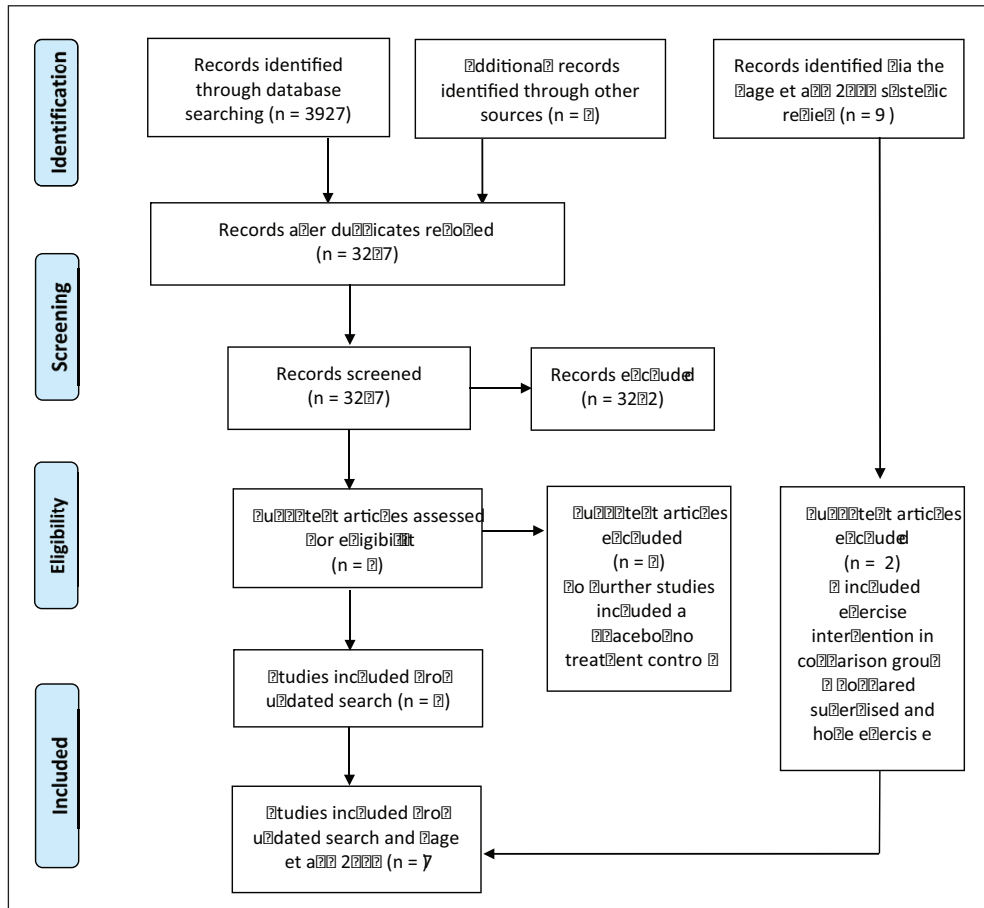


Figure 1. Preferred reporting items for systematic reviews and meta-analyses 2009 flow diagram for literature search results.

only co-interventions in Bennell et al.⁶ including manual therapy and behavioral strategies (e.g. goal setting, positive reinforcement).

Risk of bias in included trials

Risk of bias assessment was extracted from Page et al.⁷ (summarized in Supplemental Figure S1) as all our studies were also in this Cochrane review from 2016. Among trials comparing progressive and resisted exercise or non-progressive and non resisted exercise to placebo or no treatment, six (86%) were rated high risk of performance and detection bias.^{8,30–32,50,51} Further, two trials (29%) were at high risk of reporting bias^{31,32} (uncertain risk in a further four [57%]),^{8,30,50,51} one trial (14%)

was at high risk of attrition bias,³⁰ and there was uncertain risk of selection bias in five (71%) trials.^{8,30–32,51}

Effects of interventions

Comparison 1: Progressive and resisted exercise versus placebo or no treatment

There were four trials with 271 participants that reported composite pain and function,^{8,30,50,51} three trials^{30,50,51} (197 participants) reported overall pain and two trials^{30,50} (135 participants) reported activity pain and rest pain at >6 weeks to 6 months. No trials reported adverse events. All outcomes were downgraded twice (low certainty)

Table 1. Recruitment and retention, participant characteristics and eligibility criteria.

Author, year, diagnostic label	Participants number screened, number randomized total, per group, number available at follow up	Mean age, function/pain, symptoms duration	Duration of pain	Pain on active movement	+ve resisted or orthopedic tests	Dx imaging	Dx injection	Exclusion criteria
Progressive and resisted exercise versus placebo or no treatment								
Brox et al. 1993, rotator cuff disease	195 screened, 125 randomized, 30 placebo laser, 50 supervised exercises, 45 arthroscopic surgery not included in this review, follow up 79	47 years, 44% men, 66 (10–100, 100 best), overall pain 15 (0–100, 0 best), 24 months	>3 months	Abduction	Abduction (0, 30 degrees), external rotation, positive impingement test	Not reported	Yes (LA)	Restricted passive range of motion, arthritis acromioclavicular joint, cervical syndrome, rotator cuff rupture, glenohumeral instability, bilateral pain and tenderness/decreased ability to relax shoulder, neck and temporomandibular joints
Dickens et al. 2005, subacromial impingement syndrome	Number screened not reported, 85 randomized, 40 no treatment, 45 non-progressive physiotherapy exercises, follow up 73	No treatment group: 54 years, 55% men, 56 (0–100, 100 best), overall pain not reported, duration of symptoms not reported Non-progressive physiotherapy exercise group: 55 years, 58% men, 52 (0–100, 100 best), overall pain not reported, duration of symptoms not reported	Not reported	Dx based on clinical exam (not described)	Dx based on clinical exam (not described)	Not reported	Yes (3 steroid in 6 weeks)	Cervical radiculopathy, adhesive capsulitis, 'clinically obvious' rotator cuff tear, grade III subacromial spur on x-ray, previous physiotherapy treatment
Lombardi et al. 2008, shoulder impingement syndrome	Number screened not reported, 60 randomized, 30 no treatment (physiotherapy waiting list), 30 progressive resistance exercise, follow up 56	55 years, 17% men, 47 (0–100, 0 best), overall pain 44 (0–100, 100 best), 14 months	>2 months	Arc of movement that produces the greatest shoulder pain	Neer, Hawkins-Kennedy	Not reported	Not reported	Shoulder fractures or dislocation history; cervical radiculopathy; degenerative glenohumeral joint disease; shoulder, back, or thorax surgery; inflammatory arthropathy; shoulder injection in previous three months; people undergoing any physical interventions for the shoulder

(Continued)

Table 1. (Continued)

Author, year, diagnostic label	Participants number screened, number randomized total, per group, number available at follow up	Mean age, function/pain, symptoms duration	Duration of pain	Pain on active movement	+ve resisted or orthopedic tests	Dx imaging	Dx injection	Exclusion criteria
Ludwig et al. 2003, shoulder impingement syndrome	110 screened, 92 randomized, 33 no treatment, 34 progressive resistance exercise, 25 asymptomatic subjects not included in this review, follow up 62	No treatment group: 49 years, 100% male, 73 (17–100, 100 best), overall pain 5 (0–10, 0 best), duration of symptoms not reported Progressive resistance exercise group: 48 years, 100% male, 66 (17–100, 100 best), overall pain 5 (0–10, 0 best), duration of symptoms not reported	Not reported	Abduction painful arc	Near, Hawkins-Kennedy, Yocum, Jobe, and Speeds tests (≥ 2 positive). Resisted abduction, flexion, internal or external rotation. Tenderness on palpation of biceps or rotator cuff tendons	Not reported	Not reported	Less than 130 degrees shoulder elevation; cervical spine or periscapular pain; shoulder symptoms reproduced by cervical spine assessment; previous rotator cuff surgery or glenohumeral dislocation or other traumatic injury
Non-progressive or non-resisted exercise versus placebo or no treatment								
Bennell et al. 2010, rotator cuff disease	438 screened, 120 randomized, 59 active intervention non-progressive exercise group, 61 placebo sham ultrasound group, follow up 114	Active intervention non-progressive exercise group: 59 years, 58% men, 43 (0–100, 0 best), overall pain 48 (0–100, 0 best), 24 months Placebo sham ultrasound group: 61 years, 49% men, 44 (0–100, 0 best), overall pain 48 (0–100, 0 best), 14 months	>3 months	Abduction or external rotation >3/10 pain	Quick test for shoulder impingement	Not reported	Not reported	Shoulder pain severity >7/10 at rest, suspected complete rotator cuff tear (+ve drop arm test, substantial shoulder weakness, high riding humeral head on x-ray), prior surgery or fracture, inflammatory arthritis, osteoarthritis or calcification on x-ray, neoplastic disorder, >50% reduction range of motion in 2 or more planes, pain referred from vertebral structures, complex regional pain syndrome, active interventions last three months (e.g. injection, physiotherapy), anti-inflammatories previous two weeks

(Continued)

Table 1. (Continued)

Author, year, diagnostic label	Participants number screened, number randomized total, per group, number available at follow up	Mean age, function/pain, symptoms duration	Duration of pain	Pain on active movement	+ve resisted or orthopedic tests	Dx imaging	Dx injection	Exclusion criteria
Giombini et al. 2006, supraspinatus tendinopathy	159 screened, 37 randomized, 12 ultrasound control group, 11 non-progressive exercise, 14 hyperthermia group not included in this review, follow up 23	Ultrasound control group: 29 years, 67% men, 59 (0–100, 100 best), overall pain 6.3 (0–10, 0 best), five months (mean both groups) Non-progressive exercise group: 26 years, 82% male, 59 (0–100, 100 best), overall pain 6.1 (0–10, 0 best), five months (mean both groups)	3–6 months	Not reported	Hawkin's sign or impingement in 90 degrees forward flexion & +ve empty can test	Non-homogeneous signal intensity without a tear	Not reported	Restricted passive range of motion, traumatic onset, severe neck pain, frozen shoulder, calcific tendinopathy, degenerative joint disease of the acromioclavicular or glenohumeral joint; prior intra-articular or subacromial injection of corticosteroids; clinical or ultrasonographic diagnosis of a rotator cuff tear; previous shoulder surgery on the affected or contralateral shoulder
Walther et al. 2004, subacromial impingement syndrome	Number screened not reported, 60 randomized, 20 functional brace (placebo), 20 self-training non-progressive exercise group, 20 physiotherapy non-progressive exercise group, follow up	Functional brace (placebo) group: 49 years, 70% men, 63 (0–100, 100 best), overall pain 50 (0–100, 0 best), 27 months Self-training non-progressive exercise group: 52 years, 45% male, 58 (0–100, 100 best), overall pain 47 (0–100, 0 best), 23 months Physio non-progressive exercise grouping: 52 years, 55% male, 60 (0–100, 100 best), overall pain 54 (0–100, 0 best), 32 months	Not reported	Dx based on clinical exam (not described)	Neer test	X-ray and ultrasound (measures not described)	Yes (LA)	Cervical radiculopathy, frozen shoulder; full thickness tear of the rotator cuff; acromioclavicular pathology; glenohumeral joint arthritis; calcifying tendinitis, shoulder instability, posttraumatic disorders, pending workers' compensation claim

Table 2. Exercise characteristics and outcomes.

Author, year, trial type, country, funding, trial registration	No treatment or placebo group description, frequency, duration	Exercise group intervention description, exercise type, additional interventions	Home or supervised exercise, follow up sessions	Sets x repetitions or time, frequency, duration, total sessions, time under tension, rest time, repetitions per week	How load was applied, progression criteria	Advice about pain during exercise	Adherence	Outcomes, extracted outcomes
Progressive and resisted exercise versus placebo or no treatment								
Brox et al. 1993, RCT, Norway, Norwegian Research Council, no trial registration	Advice about pathology, pain, ergonomics, detuned laser 12 sessions in six weeks	Advice about pathology, pain, ergonomics, shoulder rotation, then flexion-extension, then abduction-adduction	Supervised twice weekly and daily home exercise on other days, 12–26 weeks	?, daily for one hour, 12–26 weeks, ?, ?, ?, incalculable	Load 'added gradually', did not specify how, did not specify criteria	Not reported	Not reported	Outcomes: Composite pain and function with Neer shoulder score (10–100, 100 is best), activity, rest and night pain with NRS (1–9, 9 worst possible pain) Outcomes extracted: composite pain and function, overall pain, activity pain, rest pain Note: Overall pain assumed from Neer pain item. We reversed the direction of the function score and converted to a 0–100 scale for consistency with other studies. We estimated SD as a median of the available SDs
Dickens et al. 2005, RCT, UK, Physiotherapy Research Council, no trial registration	Surgical waiting list, maintain normal ADLs	Manual therapy, postural advice, strapping +/- electrotherapy and exercises (not specified) for scapularthoracic muscles including trapezius and serratus anterior and rotator cuff muscles	Supervised 1–2 x per week and home, progressed 'regularly'	Sets/ reps not specified, twice daily, 26 weeks, ?, ?, ?, incalculable inner range, then through range, outer range, functional positions. Resistance and speed of exercises progressed	Range, load (theraband), and speed were progressed 'regularly' based on ability to perform exercise	Not reported	Not reported	Outcomes: Composite pain and function with Constant score (0–100, 100 is best) Outcomes extracted: composite pain and function Note: We reversed the direction of the function score for consistency with other studies. We estimated SD as a median of the available SDs

(Continued)

Table 2. (Continued)

Author, year, trial type, country, funding, trial registration	No treatment or placebo group description, frequency, duration	Exercise group intervention description, exercise type, additional interventions	Home or supervised exercise, follow up sessions	Sets x repetitions or time, frequency, duration, total sessions, time under tension, rest time, repetitions per week	How load was applied, progression criteria	Advice about pain during exercise	Adherence	Outcomes, extracted outcomes
Lombardi et al. 2008, RCT, Brazil, no funding reported, no trial registration	Physiotherapy waitlist	Flexion, extension, medial and lateral rotation	Supervised, 4 sessions in eight weeks (fortnightly)	2 × 8 (50% [1st set] to 70% [2nd set] of 6 repetition maximum load), twice weekly, eight weeks, four seconds, two minutes, 128/wk	Pulley system progressed, based on 6 repetition maximum reassessment	Painfree	Not reported	Outcomes: Composite pain and function with disability of arm and shoulder score (laborious function component and activities of daily living component) (0–100, 0 better), quality of life short form SF-36, activity and rest pain with VAS (0–10, 10 worse pain) Outcomes extracted: composite pain and function (laborious function), overall, activity and rest pain Note: Overall pain assumed from the SF-36 pain item. We reversed the direction of the SF-36 pain score for consistency with other studies.
Ludwig et al. 2003, RCT, USA, Center to protect worker' rights, the public health service and the University of Iowa, no trial registration	No treatment	Anterior and posterior shoulder stretches, abduction active movement, and external rotation in neutral and in abduction progressive resisted exercise	Home, 1 in person and 1 phone or in person (if required) over 10 weeks Initial, at one week, phone/optional at four weeks	Stretches 30 seconds × 5/day & active movement 5 × /day, progressive exercise 3 × 10 – 20 (by 3rd week), 3 × /week, 10 weeks, ?, ?, 540/wk	Theraband, based on ability to perform exercise	'No increased shoulder pain', (not clear if increased their baseline or no pain)	Exercise log (27% completed 75% or more of prescribed exercise)	Outcomes: Composite pain and function with shoulder rating questionnaire (17–100, 100 is better), work related shoulder pain, work related disability Outcomes extracted: composite pain and function, overall pain Note: Overall pain assumed from work related pain item. We reversed the direction of the function score and converted to a 0–100 scale for consistency with other studies. SE reported and used to calculate SD.
Non-progressive or non-resisted exercise versus placebo or no treatment								
Bennell et al. 2010, RCT, Australia, National Health and Medical Research Council, no NCT00415441	Sham ultrasound, no instruction to do any home exercises, no instruction in exercise technique 10 sessions in 10 weeks	Education, goal setting, manual therapy and home exercise program including dynamic scapular control, strengthening scapular stabilizer and rotator cuff muscles, improving shoulder and thoracic posture and increasing range of motion of thoracic extension	Home, 10 sessions over 10 weeks. Then instructed to continue daily exercises for further 12 weeks.	Variable sets/reps (2 × 10 repetitions or 5 seconds × 5 or 1–3 minute hold), twice daily for first week, daily after that to 10 weeks, ?, ?, incalculable	Theraband, not progressed	Not reported	Exercise log (participants completed 82% of prescribed exercise at 11 weeks, 70% at 22 weeks)	Outcomes reported: Composite pain and function, and overall pain with SPADI (both 0–100, 0 is best), activity and rest pain with NRS (0–10, 10 worse), quality of life using SF-36 Outcomes extracted: composite pain and function, overall, activity and rest pain

(Continued)

Table 2. (Continued)

Author, year, trial type, country, funding, trial registration	No treatment or placebo group description, frequency, duration	Exercise group intervention description, exercise type, additional interventions	Home or supervised exercise, follow up sessions	Sets x repetitions or time, frequency, duration, total sessions, time under tension, rest time, repetitions per week	How load was applied, progression criteria	Advice about pain during exercise	Adherence	Outcomes, extracted outcomes
Giombini et al. 2006, RCT, Italy, no funding reported, no trial registration	Therapeutic ultrasound	Pendular flexion and extension in prone and passive glenohumeral stretching	Home, weekly, four weeks	Sets/reps not specified (5 minutes), twice daily, 4 weeks, ?, ?, incalculable	No load applied	To tolerance'	Not reported	Outcomes reported: Composite pain and function with Constant-Murley score (0–100, 100 is best), mean pain using a 10cm VAS, pain on resisted movement (4 point scale, 0 is best), Pain on active abduction 40–120 (4 point scale, 0 is best) Outcomes extracted: composite pain and function, overall pain, pain during movement Note: Overall pain assumed from mean pain. Reversed the direction of the function score for consistency with other studies.
Walther et al. 2004, RCT, Germany, ?, no trial registration	Shoulder brace	Group a) Physiotherapy: Isometric shoulder retraction, abduction, external rotation, and rowing with elbow bent and straight, cervical lateral flexion stretch, pendular exercises, isometric adduction with self protraction mobilization Group b) Self-training: as above	Group a supervised, 30 sessions in 12 weeks Group b home, 4 sessions in 12 weeks	Isometric 10 × 10 seconds, stretch 2 × 15 seconds, pendular 3–5 minutes, adduction & distraction 3 × 15 seconds, group a 5 ×/wk; group b 2–3 ×/week, 12 weeks, ?, ?, incalculable Group b 5 × per week for 10–15 minutes.	Theraband or 1kg weight, no progression	Not reported	Not reported	Outcomes reported; Composite pain and function and with Constant-Murley (0–100, 100 is best), activity, night and rest pain (0–100, 100 maximum pain) Outcomes extracted: composite pain and function, overall pain, activity and rest pain Note: Overall pain assumed from night pain. We reversed the direction of the function score for consistency with other studies. We estimated SD as a median of the available SDs.

Note: ? : data missing; rep: repetitions, repetitions/week is the average over intervention period if weekly repetitions vary.

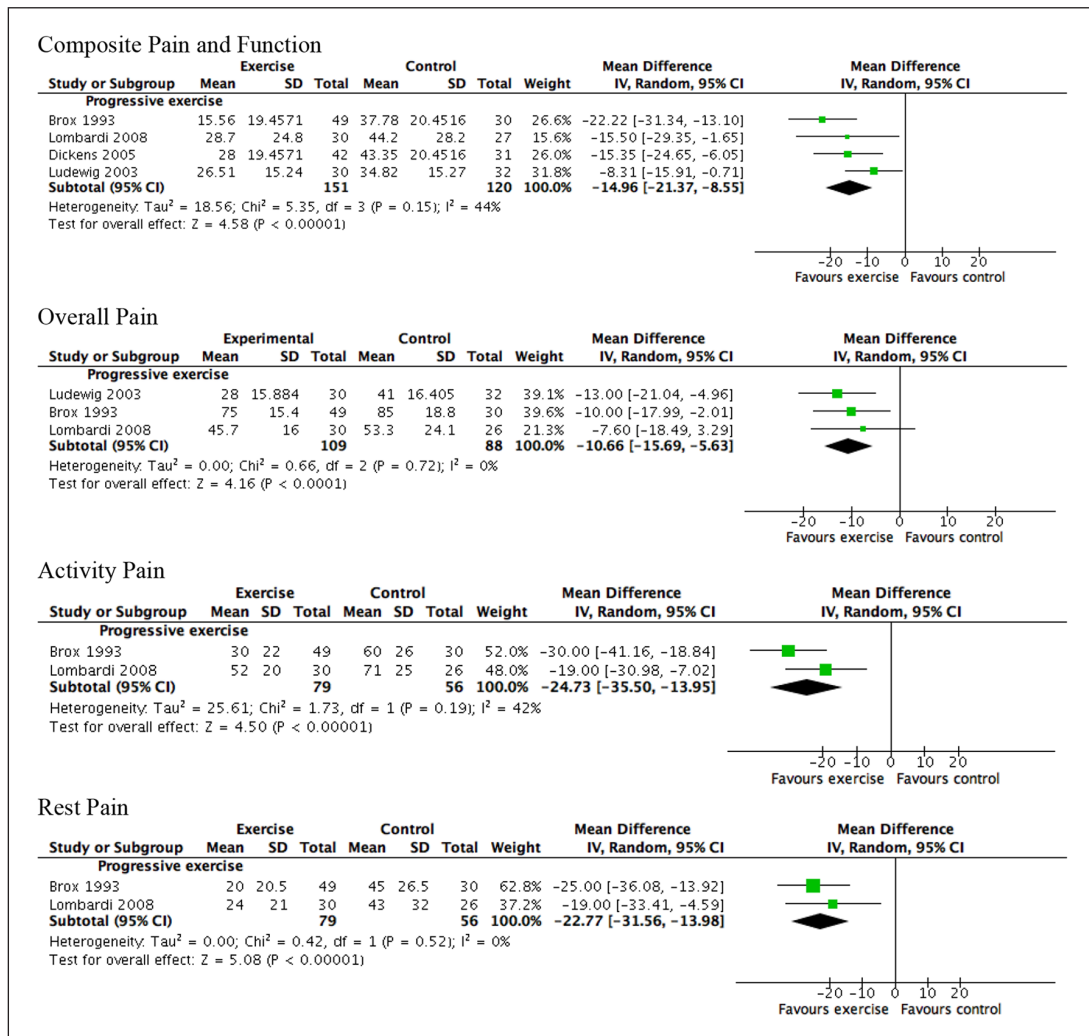


Figure 2. Comparison One – Effects of progressive and resisted exercise versus placebo or no treatment on composite pain and function, overall pain, activity pain and rest pain.

for risk of bias (performance, detection, reporting and selection).^{8,30,51}

There was uncertain clinical benefit (low certainty evidence) in all outcomes with progressive and resisted exercise. For composite pain and function there was a 15.0 point difference (95% CI 8.6 to 21.4; 4 trials, 271 participants, Figure 2, Supplemental Table S1).^{8,30,50,51} For overall pain there was a 10.7 point difference (95% CI 5.6 to 15.7; 3 trials, 197 participants, Figure 2, Supplemental Table S1).^{30,50,51}

For pain with activity there was a 24.7 point difference (95% CI 13.9 to 35.5; 2 trials, 135 participants, Figure 2, Supplemental Table S1).^{30,50} For pain at rest there was a 22.8 point difference (95% CI 14.0 to 31.6; 2 trials, 135 participants, Figure 2, Supplemental Table S1).^{30,50}

Adverse events. Unclear as no trials of progressive and resisted exercise reported whether adverse events occurred.

Comparison 2: Non-progressive or non-resisted exercise versus placebo and no treatment

Three trials (197 participants) reported composite pain and function, overall pain and pain with activity at >6 weeks to 6 months.^{6,31,32} Two trials (174 participants) reported pain at rest at >6 weeks to 6 months.^{6,31} Two trials (83 participants) reported composite pain and function up to 6 weeks. One trial reported adverse events.⁶ Overall evidence was low certainty for all outcomes (downgraded twice for risk of bias [performance, detection, reporting and selection]).

There was low certainty evidence of no benefit in all outcomes with non-progressive or non-resisted exercise. For function there was a 3.6 point difference (95% CI -2.2 to 9.4; 3 trials, 4 comparisons, 197 participants, Figure 3, Supplemental Table S2).^{6,31,32} For overall pain there was a 3.3 point difference (95% CI -1.5 to 8.1; 3 trials, 4 comparisons, 197 participants, Figure 3, Supplemental Table S2).^{6,31,32} For pain with activity there was a 3.4 point difference (95% CI -5.0 to 11.8; 3 trials, 4 comparisons, 197 participants, Figure 3, Supplemental Table S2).^{6,31,32} For pain at rest there was a 1.8 point difference (95% CI -6.6 to 10.2; 2 trials, 3 comparisons, 174 participants, Figure 3, Supplemental Table S2).^{6,31}

Adverse events. One trial reported a short term increase in pain that was greater following exercise intervention (17/55) compared with placebo (5/61) (RR 3.77, 95% CI 1.49 to 9.54).⁶

Secondary analysis

Subgroup analysis for co-interventions were similar to the overall effect for all outcomes (composite pain and function, overall pain, activity pain and rest pain) in both comparisons. One exception was composite pain and function in comparison 1, where there was benefit of uncertain clinical importance among the two trials that did not include co-interventions^{25,26} and clinically important improvement for the two trials^{8,30} that did. When subgrouping for supervised versus unsupervised exercise, comparison 1 pain and function

outcome showed clinically important benefit in three trials^{10,28,42} that utilized supervised exercise but uncertain clinical benefit in one trial⁵¹ that utilized unsupervised exercise. All other findings were identical to the overall effect for all outcomes (composite pain and function and overall pain). There was insufficient data to perform other planned secondary analyses.

Discussion

This review identified seven randomized trials (eight comparisons, 468 participants) that compared exercise (progressive and resisted or not) to placebo or no treatment among people with rotator cuff related shoulder pain. Four trials^{8,30,50,51} compared progressive and resisted exercise to no treatment or placebo (comparison 1) and three trials^{6,31,32} compared non-progressive or non-resisted exercise to placebo (comparison 2). For progressive and resisted exercise, low certainty evidence indicates benefit of uncertain clinical importance in composite pain and function, overall pain outcomes, pain with activity and pain at rest at >6 weeks to 6 months compared to placebo or no treatment. For non-progressive or non-resisted exercise, low certainty evidence indicates no benefit for composite pain and function, overall pain, pain with activity and pain at rest at >6 weeks to 6 months compared to placebo or no treatment (comparison 2). Adverse events were reported in only one study and included only mild differences in short term pain after exercise. The trials were heterogenous (e.g. whether exercise was supervised, co-interventions used, comparators) so these findings should be viewed as preliminary and hypothesis generating.

Three (75%)^{8,30,50} of the progressive and resisted trials but only one (25%)³¹ of the non-progressive and non-resisted trials utilized supervised exercise interventions. Three out of four (75%) progressive and resisted interventions included co-interventions in the exercise arm (e.g. manual therapy, advice) whereas only one non-progressive and non-resisted intervention (25%) utilized co-interventions. Further, three trials (75%)^{8,50,51} comparing progressive and resisted exercise were compared to no treatment, whereas all non-progressive or non-resisted exercise

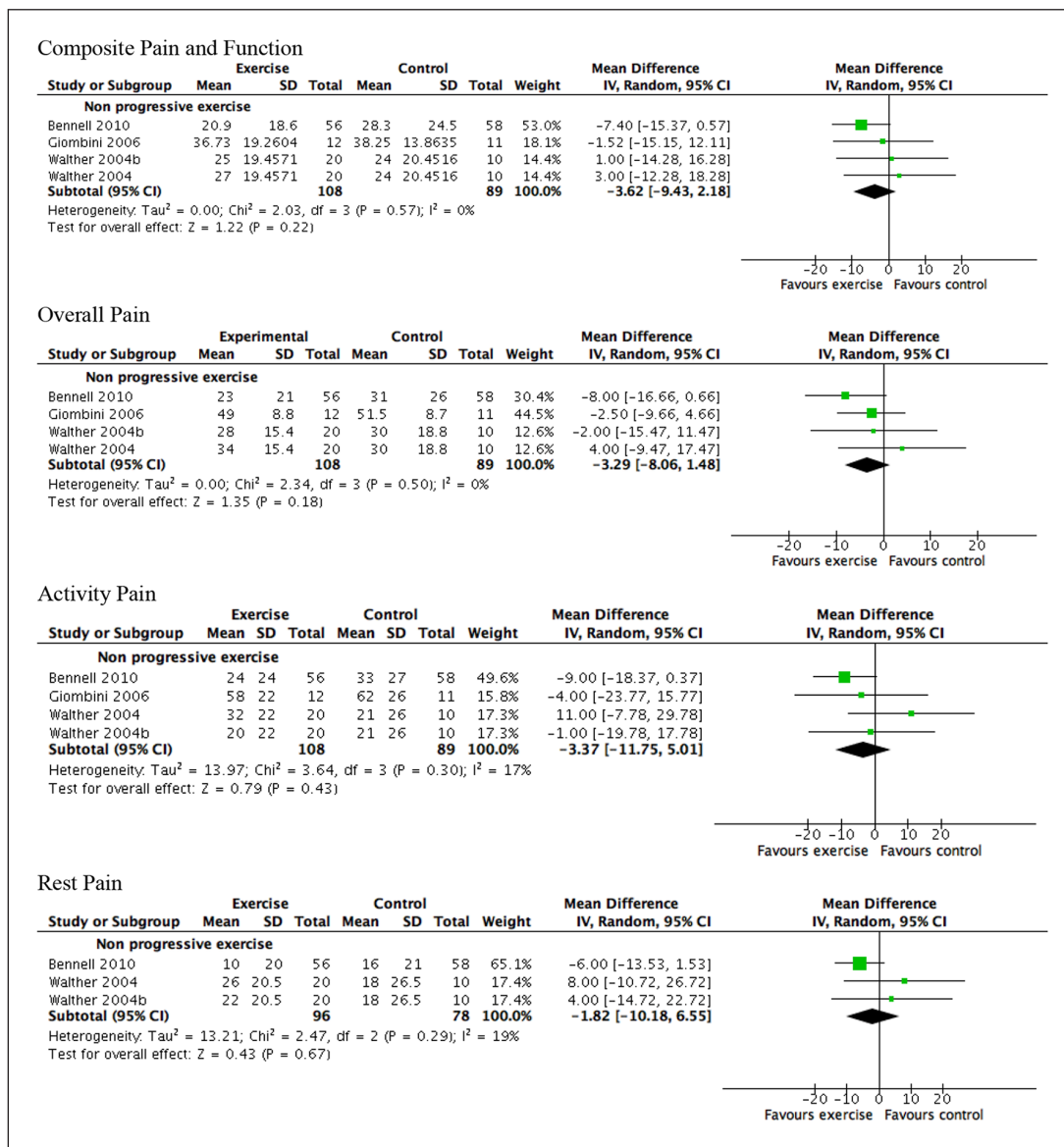


Figure 3. Comparison Two – Effects of non-progressive or non-resisted exercise versus placebo or no treatment on composite pain and function, overall pain, activity pain and rest pain.

trials were compared with placebo. Therefore, we can only conclude that progressive and resisted studies, most of which are supervised, may offer benefit of uncertain clinical importance compared with primarily no treatment comparators.

All progressive and resisted exercise programs increased load (intensity), only two progressed

range of motion, volume or speed. Load progression was based on either achieving a pain response within defined limits (e.g. pain of no more than 4/10 on a 0–10 scale) or based on ability (e.g. when the prescribed sets were no longer achieving muscle fatigue). There were important differences in the exercise approaches between the progressive

and resisted and non-progressive and non-resisted trials that may have influenced our findings. Two trials that utilized non-progressive and non-resisted exercise prescribed either pendular exercises or isometric (static hold) exercises.^{31,32} This is in contrast to the dynamic scapular and rotator cuff exercises prescribed in the progressive and resisted trials.

It is possible that mechanisms other than the exercise undertaken explain the findings. For example, giving a patient permission to perform progressive exercise, or do more exercise, may reduce fear of movement and lead to greater general shoulder use in some patients. Adherence and exercise dose parameters were also poorly reported, so we are unable to determine the dose response and actual volume of exercise completed for each intervention. We urge caution in interpreting these findings given the certainty of evidence supporting the findings are generally low using a GRADE approach.

There have been multiple systematic reviews of exercise interventions for rotator cuff related pain.^{7,10–12,52} A recent Cochrane review concluded no benefit of exercise over placebo for rotator cuff related pain,⁷ which contrasts with other systematic reviews.^{10,12} The difference is the Cochrane review was based on a single (judged by the authors of this review) low risk of bias study. Our findings are broadly consistent with this Cochrane review as most studies using a placebo comparison did not find benefit for exercise (albeit 75% utilized non-progressive and non-resisted exercise). Future high quality studies investigating whether progressive and resisted exercise is more beneficial than placebo are warranted.

This is the first systematic review with meta-analysis to focus on progressive and resisted exercise or not versus no treatment or placebo. Further, in this review we followed as closely as possible best practice guidelines as outlined by the Cochrane Collaboration and PRISMA to minimize potential sources of bias in this review. Inclusion and exclusion criteria were carefully decided a priori and were clearly defined to minimize selection bias.

The main limitation of our review is that there were only seven trials and eight comparisons that met our inclusion and exclusion criteria. Potential bias and the limited number of trials identified

reduced confidence in our findings, however the findings are consistent with evidence in other tendinopathies around the body and worthy of further investigation.⁵³

There are several limitations of the literature we included. There is low certainty evidence for both comparison one and two, only one trial⁶ in this review has a low risk of bias (86% had a high risk of bias, therefore certainty was downgraded two levels, we did not downgrade for inconsistency, indirectness [all interventions reflected clinical practice] or imprecision). This precluded sensitivity analysis including only low risk of bias trials. Further, as discussed, there were more progressive and resisted trials that utilized supervised exercise and co-interventions, and used non-placebo controls, so these factors may have influenced the positive findings reported for this exercise type.

Exercise programs were not described fully. This included characteristics such as pain during loading, exercise adherence, rest between exercise sets and exercise tempo. This limitation is important because exercise dose may contribute to the positive findings and clinicians are unable to implement an exercise program if exercise characteristics are incompletely reported. Limited reporting on exercise programs may also have influenced our decision to classify studies as progressive and resisted or non-progressive and non-resisted. Future trials should consider reporting guidelines (e.g. Consensus on Exercise Reporting Template)⁵⁴ to ensure findings are translatable to practice.

Implications for practice

Progressive resistance exercise may improve function and pain outcomes in rotator cuff related cuff related pain in comparison to placebo or no treatment comparators. The benefit was of uncertain clinical importance and placebo effects were not controlled in 75% of studies. Three quarters of progressive and resisted exercise interventions were supervised and included co-interventions such as manual therapy or advice or shoulder stretching. Clinicians can consider adopting similar progressive and resisted exercise interventions for rotator cuff related pain but the low certainty findings in this review indicate that our findings may change in the future (if there are larger and adequately powered

studies addressing the same question). Non-progressive and non-resisted exercise did not demonstrate benefit over primary (75%) placebo comparisons. Our results question the use of non-resisted or non-progressive exercise for rotator cuff related pain.

Future high quality, adequately powered randomized trials should consider the type of exercise prescribed for the intervention, specifically how resistance is added and if it is progressed appropriately throughout the treatment (increasing the intensity of the resistance and also increasing the range at which the exercise is performed).

Clinical messages

- Progressive and resisted exercise may provide uncertain clinical benefit in pain and function compared with primarily no treatment comparators at >6 weeks to 6 months among people with rotator cuff related pain
- Non-progressive and non-resisted exercise did not demonstrate benefit over placebo at >6 weeks to 6 months among people with rotator cuff related pain

Author's Note

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Data curation: PM, GS, CL, JN

Formal analysis: JN, PM

Methodology: PM, GS

Writing - original draft preparation: JN

Writing - reviewing and editing: JN, GS, CL, PM

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Supplemental Material

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