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# Clinical Rehabilitation

# Effectiveness of Progressive and Resisted and Non-Progressive or Non-Resisted Exercise in Rotator Cuff Related Shoulder Pain: A Systematic Review and Metaanalysis of Randomised Controlled Trials

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Keywords:	Rotator Cuff Related Pain, Tendinopathy, Sub-acromial impingement, Resistance Exercise, Shoulder pain

SCHOLARONE™ Manuscripts **Objective:** Synthesise 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:** Randomised 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.

# 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 Randomised Controlled Trials

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**Objective:** Synthesise 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:** Randomised 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.

**Key Words:** Rotator cuff related pain, rotator cuff tendinopathy, sub-acromial impingement, resistance exercise, progressive exercise, resistance training, shoulder pain

1 Shoulder pain affects 15-30% of the population and is the third most common

2 musculoskeletal condition presenting to primary care.<sup>1, 2</sup> Rotator cuff related pain is the most

common cause of shoulder pain, accounting for up to 80% of all cases.<sup>3</sup> Up to 50% of people

affected experience pain and disability beyond 12 months despite conservative treatment.<sup>3</sup>

5 Clinical guidelines recommend clinician-guided exercise for rotator cuff related pain.<sup>4,5</sup>

6 However, an updated Cochrane review found only one high quality randomised controlled

trial (120 participants) out of 60 (3,620 participants) that compared exercise and manual

therapy for rotator cuff related shoulder pain to placebo, with no difference in clinical

9 outcomes at 22 weeks.<sup>6, 7</sup> Two trials (89 participants) of very low quality found similar results

in comparison to no treatment.<sup>8,9</sup> 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, <sup>13</sup> back

pain<sup>14</sup> and is a widely used and recommended treatment modality. <sup>15, 16</sup> 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

19 placed under.

21 Prior reviews of rotator cuff related pain, including Page et al.<sup>7</sup> 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).<sup>7, 17-22</sup> Therefore, it remains unclear whether exercise that is resisted and

progressed is more beneficial than placebo or control in treating rotator cuff realated 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, shockwave therapy and therapeutic ultrasound.<sup>23</sup> 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.<sup>7</sup> This review was submitted May 30<sup>th</sup> 2019 to the International Prospective Register of Systematic Reviews (PROSPERO; reference CRD42019136513) and registered on August 2<sup>nd</sup> 2019.

Randomised 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).

Randomised 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

57 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. where all exercise was considered equal, we considered the type of exercise intervention. We included randomised 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 randomised trials that included cointerventions (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.<sup>24</sup> Composite pain and function based on standardised questionnaire was the primary outcome of interest. When multiple scales were reported, data were extracted according to the following hierarchy;<sup>7</sup> 1) Shoulder Pain and Disability Index (SPADI);<sup>25</sup> 2) Croft Shoulder Disability Questionnaire;<sup>26</sup> 3) Constant-Murley Score;<sup>27</sup> 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 6 weeks and up to 6 months given this is sufficient time for exercise interventions to have an effect. <sup>28</sup> The longest time point was extracted when multiple time points were reported within the above defined periods.

Randomised 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.<sup>7</sup> The search from the Page et al<sup>7</sup> 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/ictrp) 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.<sup>29</sup> For the primary outcome of function and pain we calculated the median of available SDs in three studies following the process described above.<sup>8, 30, 31</sup> For activity pain and rest pain we calculated SDs as above for two studies.<sup>30, 31</sup>. For Giombini et al,<sup>32</sup> 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	random	ised t	rial:	are s	hown 1	held	w.
I IIC data	CAHACICA	пош	Cacii	Tanaoni.	iscu i	ııaı (	$\mathbf{u} \mathbf{r} \mathbf{c}$	TIO WILL	-	JVV.

- 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
  minimise 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 cross-over trials.

The Cochrane Collaboration's tool was used to assess risk of bias.<sup>33</sup> The results of the risk of bias assessment for all included trials were extracted from Page et al<sup>7</sup> 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).<sup>34</sup> 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).<sup>34</sup> Minimal clinically important difference was assumed to be 10 on a 100-point scale for composite pain and function outcome,<sup>35-37</sup> and 15 points on a 100-point scale for pain outcome.<sup>38</sup>

Data were pooled in meta-analyses using Review Manager 5.3<sup>39</sup> 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<sup>2</sup> statistic.<sup>40</sup> For the I<sup>2</sup> statistic, we interpreted statistical heterogeneity as not important (<50%), moderate (50-75%) and high (>75%).<sup>40</sup>

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])<sup>41</sup>. 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 NNTH was calculated using the event rate in the control group and risk ratio. <sup>42</sup> 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<sup>7</sup> 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.<sup>9</sup> The other excluded trial included physiotherapy treatments as control (heat packs, transcutaneous electrical nerve stimulation and ultrasound).<sup>43</sup> No eligible trials were identified after the updated search (Figure 1), and screening reference lists of included studies, gray literature and clinical trials registries. We obtained data from the authors (July 2017) of two trials<sup>6,31</sup> that allowed us to confirm eligibility (Appendix 2). We acknowledge that within the trial protocol for the randomised trial by Bennell et al.<sup>44</sup> 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.

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 flow diagram for literature search results.

Trial characteristics

Trial and participant characteristics are shown in Table 1. Seven parallel group randomised trials (468 participants) were included. 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<sup>32</sup> (26 and 29 years). Men were more prevalent (54-100%) aside from Lombardi et al<sup>45</sup> (24% men). Baseline composite pain and function was comparable (33 to 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.<sup>8, 45, 46</sup> One trial compared progressive and resisted exercise with placebo (detuned laser).<sup>30</sup> All progressive and resisted exercise interventions included scapular and rotator cuff strengthening and progressed the load (intensity) with theraband or weights.<sup>8, 30, 45, 46</sup> Prescribed sets and repetitions varied, and only one study specified exercise intensity (50%-70% of the 6RM).<sup>45</sup> Three studies included cointerventions. Brox et al<sup>30</sup> included education about pathology, pain and ergonomics, Dickens et al<sup>8</sup> included manual therapy, postural advice, taping with or without electrotherapy and Ludwig et al<sup>46</sup> included shoulder stretching.

All three trials (four comparisons) of the non-progressive and non-resisted interventions were compared with placebo (two ultrasound<sup>6, 32</sup> and one brace<sup>31</sup>). One non-progressive and non-resisted exercise trial<sup>6</sup> targeted scapular and rotator cuff strengthening similar to progressive and resisted trials. Whereas, Walther et al<sup>31</sup> assessed static exercise and neck stretching (all other trials evaluate dynamic exercise) and Giombini et al<sup>32</sup> assessed pendular exercise and shoulder stretching. Load was applied without progression with theraband or 1kg weight in

two trials<sup>6, 31</sup> and no load applied in the remaining trial.<sup>32</sup> There were only co-interventions in Bennell et al<sup>6</sup> including manual therapy and behavioural strategies (e.g. goal setting, positive reinforcement).

# Table 1: Recruitment and retention, participant characteristics and eligibility criteria

## Table 2: Exercise characteristics and outcome

Risk of bias in included trials

Risk of bias assessment was extracted from Page et al<sup>7</sup> (summarised in Figure 2) 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.<sup>8, 30-32, 45, 46</sup> Further, two trials (29%) were at high risk of reporting bias<sup>31, 32</sup> (uncertain risk in a further four [57%]),<sup>8, 30, 45, 46</sup> one trial (14%) was at high risk of attrition bias,<sup>30</sup> and there was uncertain risk of selection bias in five (71%) trials.<sup>8, 30-32, 46</sup>

Figure 2: Risk of bias summary: judgements about each risk of bias item for each included study.

#### **Effects of interventions**

There were four trials with 271 participants that reported composite pain and function, 8, 30, 45,

46 three trials 30, 45, 46 (197 participants) reported overall pain and two trials 30, 45 (135

participants) reported activity pain and rest pain at >6 weeks to 6 months. No trials reported

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

adverse events. All outcomes were downgraded twice (low certainty) for risk of bias

(performance, detection, reporting and selection). 8, 30, 46 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 3, Table 3).8, 30, 45, 46 For overall pain there was a 10.7 point difference (95% CI 5.6 to 15.7; 3 trials, 197 participants, Figure 3, Table 3).<sup>30, 45, 46</sup> For pain with activity there was a 24.7 point difference (95% CI 13.9 to 35.5; 2 trials, 135 participants, Figure 3, Table 3).30,45 For pain at rest there was a 22.8 point difference (95% CI 14.0 to 31.6; 2 trials, 135 participants, Figure 3, Table 3).<sup>30, 45</sup> 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.<sup>6,31</sup> Two trials (83 participants) reported composite pain and 

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

function up to 6 weeks. One trial reported adverse events. Overall evidence was low

certainty for all outcomes (downgraded twice for risk of bias [performance, detection,

comparisons, 197 participants, Figure 4, Table 4).<sup>6, 31, 32</sup> For overall pain there was a 3.3 point difference (95% CI -1.5 to 8.1; 3 trials, 4 comparisons, 197 participants, Figure 4, Table 4).<sup>6, 31, 32</sup> 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 4, Table 4).<sup>6, 31, 32</sup> 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 4, Table 4).<sup>6, 31</sup>

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 4.02, 95% CI 1.56 to 10.37).

## Secondary analysis

Subgroup analsysis 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<sup>25,26</sup> and clinically important improvement for the two trials<sup>8,30</sup> that did. When subgrouping for supervised versus unsupervised exercise, comparison 1 pain and function outcome showed clinically important benefit in three trials<sup>10,28,42</sup> that utilised supervised exercise but uncertain clinical benefit in one trial<sup>46</sup> that utilised 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 randomised 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<sup>8, 30, 45, 46</sup> compared progressive and resisted exercise to no treatment or placebo (comparison 1) and three trials<sup>6, 31, 32</sup> compared non-progressive or non-resisted exercise to placebo (comparison 2). For progressive and resisted exercise, low certainty evidence indicates benefit of uncertain clinical importantance 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%)<sup>8, 30, 45</sup> of the progressive and resisted trials but only one (25%)<sup>31</sup> of the non-progressive and non-resisted trials utilised 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%)<sup>8, 45, 46</sup> comparing progressive and resisted exercise were compared to no treatment, whereas all non-progressive or non-resisted exercise 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.<sup>31, 32</sup> 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. <sup>7</sup>, <sup>10-12</sup>, <sup>47</sup> A recent Cochrane review concluded no benefit of exercise over placebo for rotator cuff related pain, <sup>7</sup> which contrasts with other systematic reviews. <sup>10</sup>, <sup>12</sup> 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 7 trials and 8 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.<sup>48</sup>

There are several limitations of the literature we included. There is low certainty evidence for both comparison one and two, only one trial<sup>6</sup> 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, indrectness [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)<sup>49</sup> 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 randomised 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



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Author, year, diagnostic label	Participants Number screened, number randomised total, per group, number available at follow-up	Mean age, function/pain, symptoms duration	Duration of pain	Pain on active movement	+ve resisted or orthopaedic tests	Dx imaging	Dx injection	Exclusion criteria	
D 1	105	Progressive and resis				27.	77 (T.A.)	D	
Brox et al. 1993, rotator cuff disease	195 screened, 125 randomised, 30 placebo laser, 50 supervised exercises, 45 arthroscopic surgery not included in this review, follow up 79	<b>Supervised exercise group:</b> 47 years, 44% men, 66 (10-100, 100 best), overall pain 15 (0-100, 0 best), 24 months <b>Placebo Laser group:</b> 48 years, 50% men, 65 (10-100, 100 best), overall pain 14.8 (0-100, 0 best), 20 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 randomised, 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	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 randomised, 30 no treatment (physiotherapy waiting list), 30 progressive resistance exercise, follow up 56	symptoms not reported  No treatment group: 55 years, 17% men, 47 (0-100, 0 best), overall pain 44 (0-100, 100 best), 14 months  Progressive resistance exercise group: 56 years, 30% men, 50 (0-100, 0 best), overall pain 43 (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 3 months; people undergoing any physical interventions for the shoulder	
Ludwig et al. 2003, shoulder impingement syndrome	randomised, 92 randomised, 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	Neer, Hawkins- Kennedy, Yocum, Jobe, and Speeds tests (≥2 positive). Resisted abduction, flexion, internal or external rotation.	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	

Tenderness on

		Non-progressive or non-	resisted exerc	cise versus pla	palpation of biceps or rotator cuff tendons cebo or no treatm	ent		
Bennell et al. 2010, rotator cuff disease	438 screened, 120 randomised, 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 xray), prior surgery or fracture, inflammatory arthritis, osteoarthritis or calcification on xray, neoplastic disorder, >50% reduction range of motion in 2 or more planes, pain referred from vertebral structures, complex regional pain syndrome, active interventions last 3 months (e.g. injection, physiotherapy), anti-inflammatories previous 2 weeks
Giombini et al. 2006, supraspinatus tendinopathy	159 screened, 37 randomised, 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), 5 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), 5 months (mean both groups)	3-6 months	Not reported	Hawkin's sign or impingement in 90 degrees forward flexion & +ve empty can test	Non-homogeneo us 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 intraarticular 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 randomised, 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

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
			Progressiv	e and resisted exercise ve	rsus placebo or	no treatmen	ıt	
Brox et al. 1993, RCT, Norway, Norwegian Research Council, no trial registration	Advice about pathology, pain, ergonomics, detuned laser  12 sessions in 6 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  Isometric, then inner range, 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
Lombardi et al. 2008, RCT, Brazil, no funding reported, no trial registration	Physiotherapy waitlist	Flexion, extension, medial and lateral rotation	Supervised, 4 sessions in 8 weeks (fortnightly)	2x8 (50% [1st set] to 70% [2nd set] of 6 repetition maximum load), twice weekly, 8 weeks, 4 sec, 2 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 SI 36 pain score for consistency with other studies.
Ludwig et al. 2003, RCT, USA, Centre to protect worker' rights, the	No treatment	Anterior and posterior shoulder stretches, abduction active movement, and	Home, 1 in person and 1 phone or in person (if required)	Stretches 30secx5/day & active movement 5x/day, progressive exercise 3x10 – 20 (by 3 <sup>rd</sup> week), 3x/week, 10	Theraband, based on ability to perform exercise	'No increased shoulder pain' (not clear if	Exercise log (27% completed 75% or more of	Outcomes: Composite pain and function with shoulder rating questionnaire (17-100, 100 is better), work related shoulder pain, work related disability
public health service and the University of		external rotation in neutral and in abduction	over 10 weeks Initial, at 1	weeks, ?, ?, 540/wk		increased their baseline	prescribed exercise	Outcomes extracted: composite pain and function, overall pain
Iowa, no trial registration		progressive resisted exercise	week, phone/option al at 4 weeks			or no pain)		Note: Overall pain assumed from work relate pain item. We reversed the direction of the function score and converted to a 0-100 scale for consistency with other studies. SE reporte and used to calculate SD.
			Non-progressiv	ve or non-resisted exercis	e versus placeb	o or no treat	ment	
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 stabiliser 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 (2x10 repetitions or 5 sec x 5 or 1-3 minute hold), twice daily for first week, daily after that to 10 weeks, ?, ?,	Theraband, not progressed	Not reported	Exercise log (participant s completed 82% of prescribed	Outcomes reported: Composite pain and function, and overall pain with SPADI (both 100, 0 is best), activity and rest pain with NR (0-10, 10 worse), quality of life using SF-36 Outcomes extracted: composite pain and function, overall, activity and rest pain
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, 4 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 i best),  Pain on active abduction 40-120 (4 point scale) is best)  Outcomes extracted: composite pain and

								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	Shoulder brace	Group a) Physiotherapy: Isometric shoulder	Group a supervised, 30 sessions in	Isometric 10x10sec, stretch 2x15sec, pendular 3-5 mins,	Theraband or 1kg weight, no	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 to 100 respiratory).
trial registration		retraction, abduction, external rotation, and rowing with elbow	12 weeks Group b home, 4 sessions in 12	adduction & distraction 3x15sec, group a 5x/wk; group b 2-3x/week, 12 weeks, ?,	progression			100, 100 maximum pain)  Outcomes extracted: composite pain and function, overall pain, activity and rest pain
		bent and straight, cervical lateral	weeks	?, incalculable				Note: Overall pain assumed from night pain.
		flexion stretch, pendular exercises, isometric		Group b 5xper week for 10-15 mins.				We reversed the direction of the function score for consistency with other studies. We estimated SD as a median of the available SDs.
		adduction with self protraction						
		mobilisation Group b) Self- training: as above	$O_{j}$	<b>^</b>				

Note: ?=data missing; rep=repetitions, repetitions/week is the average over intervention period if weekly repetitions vary erage over lines volume. Page 31 of 40 Clinical Rehabilitation

### Table 3. Summary of Findings: Progressive and resisted exercise compared to placebo for rotator cuff related pain

Patient or population: rotator cuff related pain

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44 45 Setting: Primary care patients (Norway), patients on surgery waiting list (UK), physiotherapy waiting list University hospital (Brazil), construction workers (USA)

**Intervention**: 8-26 weeks of progressive resisted exercise **Comparison**: placebo (detuned laser) or no treatment

Outcomes	Illustrative comparative ri	sks* (95% CI)	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Progressive and resisted exercise				
Function Assessed with Constant-Murley (0-100, 100 is best), Neer (10-100, 100 is best) or SRQ (17-100, 100 is best) or the DASH (0-100, 0 is best) Follow-up: 8 to 26 weeks	The mean function in the control group was 44.2 <sup>1</sup>	The mean function in the intervention group was <b>15.0 points better</b> (8.6 to 21.4 better)	-	271 (4 RCTs)	⊕⊕⊖⊖ LOW³	Statistically significant but uncertain clinical benefit <sup>2</sup> Absolute change 15% better (9% better to 21% better); relative change 32% better (18% better to 45% better) <sup>4</sup>
Overall pain Assessed with SF36 (0-100, 0 is best), Neer (10-100, 0 is best) or VAS (0-100, 0 is best) Follow-up: 8 to 26 weeks	The mean overall pain in the control group was 53.31	The mean overall pain in the intervention group was <b>10.7 points better</b> (5.6 to 15.7 better)	-	197 (3 RCTs)	⊕⊕⊖⊖ LOW³	Statistically significant but uncertain clinical benefit <sup>2</sup> Absolute change 11% better (6% better to 16% better); relative change 19% better (10% better to 28% better) <sup>4</sup>
Pain with activity Assessed with VAS (0-100; 0 is best) Follow-up: 8 to 26 weeks	The mean pain with activity in the control group was <b>71.0</b> <sup>1</sup>	The mean pain with activity in the intervention group was <b>24.7 points better</b> (13.9 to 35.5 better)	-	135 (2 RCTs)	⊕⊕⊖⊖ LOW³	Statistically significant but uncertain clinical benefit <sup>2</sup> Absolute change 25% better (14% better to 36% better); relative change 35% better (20% better to 50% better) <sup>4</sup>
Pain at rest Assessed with VAS (0-100; 0 is best) Follow-up: 8 to 26 weeks	The mean pain at rest in the control group was 43.01	The mean overall pain in the intervention group was <b>22.8 points better</b> (14.0 to 31.6 better)	ر ا	135 (2 RCTs)	⊕⊕⊖⊖ LOW³	Statistically significant but uncertain clinical benefit <sup>2</sup> Absolute change 23% better (14% better to 32% better); relative change 58% better (36% better to 81% better) <sup>4</sup>
Adverse events	-	-	- 11	9,	-	-

\*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI).

CI: Confidence interval; SRO: shoulder rating questionnaire; DASH: disability of the arm, shoulder and hand; VAS: visual analogue scale; NRS: numerical rating scale

#### **GRADE** Working Group grades of evidence

**High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

This table summarises data from the Brox 1993, Dickens 2005, Lombardi 2008, Ludwig 2003 trials.

<sup>1</sup>Lombardi was used as the control group risk

<sup>2</sup>We assumed a clinically important improvement in function of 10 points on a 100-point scale (or 10%) and a clinically important improvement in pain of 15 points on a 100-point scale (or 15%)

<sup>3</sup>Downgraded (-2) for risk of bias. Participants and outcome assessors were not blinded (risk of performance, detection and selection bias). Not all measured outcomes were reported

<sup>4</sup>Relative changes calculated as absolute change divided by mean at baseline in the control group from Lombardi: Mean SD values were 47.4 (24.7) for function on a 0-100 point DASH scale; 56.1 (19.2) for overall pain on 0-100 point SF36 scale; 7.1 (1.5) for activity pain on 0-10 point VAS; 3.9 (2.6) for rest pain on 0-10 point VAS

#### Table 4. Summary of Findings: Non-progressive and non-resisted exercise compared to placebo for rotator cuff related pain

Patient or population: rotator cuff related pain

 Setting: Primary care patients (Australia), University hospital (Germany) and athletes in University setting (Italy)

**Intervention**: 4 to 12 weeks of non-progressive and non-resisted exercise

Comparison: placebo (detuned laser, ultrasound, brace)

Outcomes	Illustrative comparative risks	s* (95% CI)	Relative effect	№ of participants	Certainty of the	Comments
	Assumed risk	Corresponding risk	(95% CI)	(studies)	evidence (GRADE)	
	Placebo	Non-progressive and non-resisted exercise			(378.15.2)	
Function Assessed with the Constant-Murley (0 to 100, 100 is best) or SPADI total score scales (0 to 100, 0 is best) Follow-up: 10 to 22 weeks	The mean function in the control group was 28.31	The mean function in the intervention group was <b>3.6 points better</b> (2.2 worse to 9.4 better)	-	197 (3 RCTs)	⊕⊕⊖⊖ LOW²	No significant benefit <sup>3</sup> Absolute risk difference 4% better (2% worse to 9% better); relative change 8% better (5% worse to 21% better) <sup>4</sup>
Overall pain Assessed with the SPADI pain (0-100, 0 is best), mean pain VAS (0-100, 0 is best), night pain (0-100, 0 is best) Follow-up: 10 to 22 weeks	The mean overall pain in the control group was 311	The mean overall pain in the intervention group was <b>3.3 points better</b> (1.5 worse to 8.1 better)	-	197 (3 RCTs)	⊕⊕⊖⊖ LOW²	No significant benefit <sup>3</sup> Absolute risk difference 3% better (1% worse to 8% better); relative change 7% better (3% worse to 17% better) <sup>4</sup>
Pain with activity Assessed with VAS (0-100, 0 is best) or NRS (0-100, 0 is best) Follow-up: 10 to 22 weeks	The mean pain with activity in the control group was $33^1$	The mean pain with activity in the intervention group was <b>3.4 points better</b> (5.0 worse to 11.8 better)	-	197 (3 RCTs)	⊕⊕⊖⊖ LOW <sup>2</sup>	No significant benefit <sup>3</sup> Absolute risk difference 3% better (5% worse to 12% better); relative change 7% better (10% worse to 24% better) <sup>4</sup>
Pain at rest Assessed with VAS (0-100, 0 is best) or NRS (0-100, 0 is best) Follow-up: 12 to 22 weeks	The mean pain at rest in the control group was 16 <sup>1</sup>	The mean pain at rest in the intervention group was <b>1.8 points better</b> (6.6 worse to 10.2 better)	D	174 (2 RCTs)	⊕⊕⊖⊖ LOW²	No significant benefit <sup>3</sup> Absolute risk difference 0.2% better (0.7% worse to 1% better); relative change 9% better (31% worse to 49% better) <sup>4</sup>
Adverse events Follow-up: 10-11 weeks	Study population 82 per 1000	<b>309 per 1000</b> (122 to 782)	<b>RR 3.77</b> (1.49 to 9.54)	116 (1 RCT)	⊕⊕⊕⊕ нібн	Absolute risk difference 23% (9% to 37% more); relative percentage change 277% (49% to 854% more) NNTH 5 (26 to 2). Adverse events were mild and included short-term pain after exercises

\*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI).

CI: Confidence interval; VAS: visual analogue scale; NRS; numerical rating scale; RR: Relative Risk; SPADI; Shoulder Pain and Disabilty Index

#### **GRADE** Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

This table summarises data from the Bennell 2010, Walther 2004 and Giombini 2006 trials.

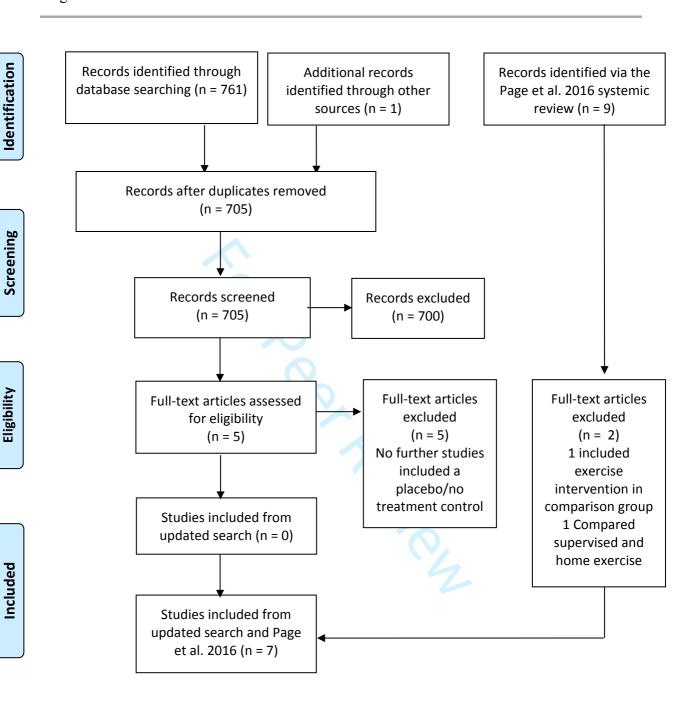
<sup>1</sup>Placebo group score in Bennell 2010 was used as assumed control group risk

<sup>2</sup>Downgraded (-2) for risk of bias. Participants and outcome assessors not blinded (risk of performance, detection and selection bias). Not all measured outcomes were reported in two studies with the lowest weighting

<sup>3</sup>We assumed a clinically important improvement in function of 10 points on a 100-point scale (or 10%) and a clinically important improvement in pain of 15 points on a 100-point scale (or 15%)

<sup>4</sup>Relative changes calculated as absolute change divided by mean at baseline in the control group from Bennell: Mean SD values were 43.9 (17.5) for function on a 0-100 point SPADI scale; 48.4 (17.5) for overall pain 0-100 point scale SPADI pain; 49 (18) for activity pain on 0-100 VAS, 21 (18) for rest pain on 0-100 point VAS

**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 flow diagram for literature search results.

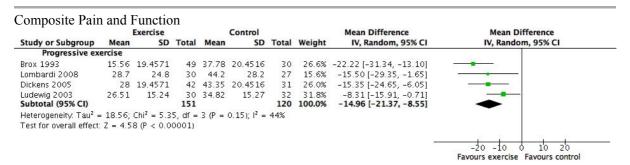


From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

**Figure 2.** Risk of bias summary: judgements about each risk of bias item for each included study (from Page et al).

	Random sequence generation (selection bias)	nt (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	data (attrition bias)	porting bias)	
	Random sequence ge	Allocation concealment (selection bias)	Blinding of participar	Blinding of outcome	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bennell 2010	•	•	•	•	•	•	•
Brox 1993	•	?	•	•	•	?	•
Dickens 2005	?	?	•	•	•	?	•
Giombini 2006	•	?	•	•	•	•	•
Lombardi 2008	•	•	•	•	•	?	•
Ludewig 2003	•	?	•	•	•	?	•
Walther 2004	?	?			•		•

**Figure 3.** 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

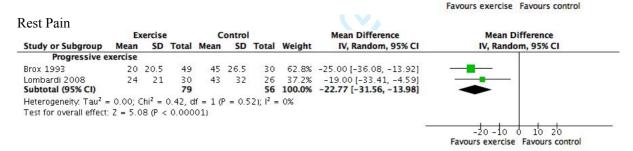


#### Overall Pain Experimental Mean Difference Mean Difference Control Mean Study or Subgroup SD Total Mean IV, Random, 95% CI IV, Random, 95% CI Progressive exercise 39.1% -13.00 [-21.04, -4.96] Ludewig 2003 41 16.405 Brox 1993 15.4 49 85 18.8 30 39.6% -10.00 [-17.99, -2.01] 26 21.3% -7.60 [-18.49, 3.29] 88 100.0% -10.66 [-15.69, -5.63] Lombardi 2008 16 30 53.3 24.1 Subtotal (95% CI) 109 Heterogeneity: $Tau^2 = 0.00$ ; $Chi^2 = 0.66$ , df = 2 (P = 0.72); $I^2 = 0\%$ Test for overall effect: Z = 4.16 (P < 0.0001)

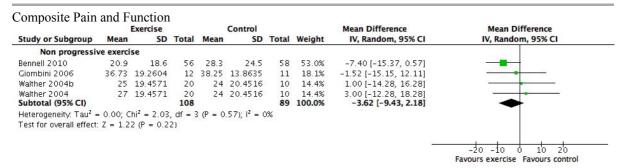
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Favours exercise Favours control

**Activity Pain** Mean Difference Mean Difference Exercise Control Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Progressive exercise Brox 1993 30 22 49 60 26 3.0 52.0% -30.00 [-41.16, -18.84] Lombardi 2008 26 48.0% -19.00 [-30.98, -7.02] 52 20 30 71 25 -24.73 [-35.50, -13.95] Subtotal (95% CI) 79 56 100.0% Heterogeneity.  $Tau^2 = 25.61$ ;  $Chi^2 = 1.73$ , df = 1 (P = 0.19);  $I^2 = 42\%$ Test for overall effect: Z = 4.50 (P < 0.00001) -20 -10 0 10 20



**Figure 4.** 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



#### Overall Pain

	Expe	riment	al	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Non progressi	ve exercis	e							
Bennell 2010	23	21	56	31	26	58	30.4%	-8.00 [-16.66, 0.66]	-
Giombini 2006	49	8.8	12	51.5	8.7	11	44.5%	-2.50 [-9.66, 4.66]	* <del></del>
Walther 2004b	28	15.4	20	30	18.8	10	12.6%	-2.00 [-15.47, 11.47]	-
Walther 2004	34	15.4	20	30	18.8	10	12.6%	4.00 [-9.47, 17.47]	(2 <u> </u>
Subtotal (95% CI)			108			89	100.0%	-3.29 [-8.06, 1.48]	•
Heterogeneity: Tau2 :	= 0.00; Ch	$10^2 = 2.3$	34, df =	= 3 (P =	0.50); I <sup>2</sup>	= 0%			10-00000
Test for overall effect	Z = 1.35	(P = 0)	18)						
								<u> </u>	-20 -10 0 10 20
									Favours exercise Favours control

#### Activity Pain

<del>-</del>	Ex	ercis	e	Co	ontro	d		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Non progress	ive exe	rcise							2
Bennell 2010	24	24	56	33	27	58	49.6%	-9.00 [-18.37, 0.37]	-
Giombini 2006	58	22	12	62	26	11	15.8%	-4.00 [-23.77, 15.77]	-
Walther 2004	32	22	20	21	26	10	17.3%	11.00 [-7.78, 29.78]	-
Walther 2004b	20	22	20	21	26	10	17.3%	-1.00 [-19.78, 17.78]	
Subtotal (95% CI)			108			89	100.0%	-3.37 [-11.75, 5.01]	•
Heterogeneity: Tau2 =	: 13.97;	Chi <sup>2</sup>	= 3.64	1, df =	3 (P	= 0.30	); $I^2 = 17\%$		NAME OF THE PARTY
Test for overall effect	Z = 0.7	79 (P	= 0.43	()					
								3/ <del></del>	-20 -10 0 10 20
									Favours exercise Favours control

#### Rest Pain

	E	xercise	1	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Non progress	sive exe	rcise							
Bennell 2010	10	20	56	16	21	58	65.1%	-6.00 [-13.53, 1.53]	
Walther 2004	26	20.5	20	18	26.5	10	17.4%	8.00 [-10.72, 26.72]	
Walther 2004b	22	20.5	20	18	26.5	10	17.4%	4.00 [-14.72, 22.72]	
Subtotal (95% CI)			96			78	100.0%	-1.82 [-10.18, 6.55]	•
Heterogeneity: Tau2 :	= 13.21;	Chi <sup>2</sup> =	2.47,	df = 2	(P = 0)	.29); l <sup>2</sup>	= 19%		
Test for overall effect	Z = 0.4	43 (P =	0.67)						
								S	-20 -10 0 10 20
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6	594	Search strategy for CENTRAL:
7	595	1. MeSH descriptor: [Shoulder Pain] explode all trees
8	596	2. MeSH descriptor: [Shoulder Impingement Syndrome] explode all trees
9	597	3. MeSH descriptor: [Rotator Cuff] explode all trees
10	598	4. MeSH descriptor: [Bursitis] explode all trees
11 12	599	5. ((shoulder* in AllText or rotator* in AllText) and (bursitis in AllText or impinge* in
13	600	AllText or tendonitis in All Text or tendonitis in All Text or tendinopathy in AllText or
14	601	pain* in All Text))
15	602	6. "rotator cuff" in AllText
16	603	7. #1 or #2 or #3 or #4 or #5 or #6
17	604	8. MeSH descriptor: [Rehabilitation] explode all trees
18	605	9. MeSH descriptor: [Physical Therapy Modalities] explode all trees
19	606	10. MeSH descriptor: [Exercise Movement Techniques] explode all trees
20 21	607	11. MeSH descriptor: [Ultrasonography, Interventional] explode all trees
22	608	12. rehabilitat* in All Text or physiotherapy* in AllText or "physical therap*" in AllText
23	609	or "manual therap*" in All Text or exercis* in All Text
24	610	13. (ultrasound in All Text or ultrasonograph* in All Text or this in AllText or tens in All
25	611	Text or shockwave in All Text or electrotherap*in All Text or mobili* in AllText)
26	612	14. #9 or #10 or #11 or #12 or #13
27	613	15. #8 and #15
28	614	Search strategy for MEDLINE (Ovid):
29 30	615	1. shoulder pain/
31	616	2. shoulder impingement syndrome/
32	617	3. rotator cuff/
33	618	4. exp bursitis/
34	619	5. ((shoulder\$ or rotator cuff) adj5 (bursitis or impinge\$ or tendinitis or tendonitis or
35	620	tendinopathy or pain\$)).mp.
36	621	6. rotator cuff.mp.
37 38	622	7. or/1-7
39	623	8. exp rehabilitation/
40	624	9. exp physical therapy techniques/
41	625	10. exp musculoskeletal manipulations/
42	626	11. exp exercise movement techniques/
43	627	12. exp ultrasonography, interventional/
44	628	13. (rehabilitat\$ or physiotherap\$ or physical therap\$ or manual therap\$ or exercis\$ or
45	629	ultrasound or ultrasonograph\$ or TNS or TENS or shockwave or electrotherap\$or
46 47	630	mobili\$). mp.
48	631	14. or/9-13
49	632	15. clinical trial.pt
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51	633	16. random\$.mp.
52	634	17. ((single or double) adj (blind\$ or mask\$)).mp.
53	635	18. placebo\$.mp.
54 	636	19. or/16-18
55 56	637	20. 7 and 14 and 19
50 57	638	Search strategy for EMBASE (Ovid):
58	639	1. 'shoulder pain'/exp
59	640	2. 'shoulder impingement syndrome'/exp
60	641	3. 'rotator cuff'/exp

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4. 'bursitis'/exp
  5. ((shoulder* OR rotator*) AND('bursitis'/de OR impinge* OR 'tendonitis'/de OR
  'tendinitis'/de OR 'tendinopathy'/ de OR pain*))
  6. 'rotator cuff'
  7. #1 OR #2 OR #3 OR #4 OR #5 OR #6
  8. 'rehabilitation'/exp
  9. 'physiotherapy'/exp
  10. 'kinesiotherapy'/exp
  11. 'endoscopic echography'/exp
  12. rehabilitat* OR physiotherapy* OR 'physical therapy'OR 'manual therapy'OR
  kinesiotherap* OR exercis*
  13. 'ultrasound'/de OR ultrasonograph* OR 'transcutaneous nerve stimulation' OR
  'transcutaneous electricalnerve stimulation' OR shockwave OR electrotherap*OR mobili*
   14. #9 OR #10 OR #11 OR #12 OR #13 OR #13
  15. 'randomized controlled trial'/exp
   16. #7 AND #14 AND #15
Search strategy for CINAHL Plus (EBSCO):
  • S1 MH "shoulder pain"
  • S2 MH "shoulder impingement syndrome"
  • S3 MH "rotator cuff"
  • S4 MH bursitis+
  • S5 TX (shoulder* N5 bursitis) or TX(shoulder* N5 impinge*) or TX(shoulder* N5
  tend?nitis) or TX(shoulder* N5 tendinopathy) or TX(shoulder* N5 pain*)
  • S6 TX (rotator cuff N5 bursitis) or TX(rotator cuff N5 impinge*) or TX(rotator cuff N5
  tend? nitis) or TX(rotator cuff N5 tendinopathy) or TX(rotator cuff N5 pain*)
  • S7 TX rotator cuff
  • S8 S1 or S2 or S3 or S4 or S5 or S6 or S7
  • S9 MH Rehabilitation+
  • S10 MH physical therapy+
  • S11 MH Manual Therapy+
  • S12 MH Therapeutic Exercise+
  • S13 MH Ultrasonography+
  • S14 TX rehabilitat* or physiotherapy* or physical therap* or manual therap* or exercise*
  or ultrasound or ultrasonograph* or TNS or TENS or shockwave or electrotherapy*or
  mobili*
  • S15 S10 or S11 or S12 or S13 or S14 or S15
  • S16 PT clinical trial

    S17 TX random*

  • S18 TX(single blind*) or TX(single mask*)
  • S19 TX(double blind*) or TX(double mask*)
  • S20 placebo*
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• S21 S17 or S18 or S19 or S20 or S21

• S22 S8 and S15 and S21

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Appendix 2

Email correspondence from Markus Walther clarifying if there was progression of resistance within each exercise.

688 Hi,

689 All did the same exercises.

690 The Theraband stayed the same - we did not change to a harder one.

691 Regards,

692 Markus Walther

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714715716

# Email correspondence from Kim Bennell clarifying if there was progression of resistance within each exercise.

697 Hi Peter,

698 Sounds like an interesting project.

No the resistance band wasn't changed in each exercise ... the program itself was progressive so the exercises were changed along the way to make them increasingly harder.

701 The exercises were checked by the physio for form particularly around correct posture.

However, if the physio felt that they weren't able to progress to the more difficult exercise or they were having pain etc, they could stay at the easier exercise level. I did manage to find

the therapist handbook

705 Hope that helps – it was a long time ago!

706 Regards,

707 Kim

Note: Our eligibility and exclusion criteria states progressive and resisted trials needed to state how load was applied (e.g. Theraband or weight) AND that there was progression of volume or load or both. Non-progressive or non-resisted trials could include progression of range or from static to through range. We specifically required that resistance or load was progressed within each exercise to be classified as progressive and resisted.

717 Appendix 3

#### **Included Studies**

- Brox JI, Staff PH, Ljunggren AE, et al. Arthroscopic surgery compared with
   supervised exercises in patients with rotator cuff disease (stage II impingement syndrome).
   BMJ (Clinical research ed) 1993; 307: 899-903.
  - 2. Bennell K, Wee E, Coburn S, et al. Efficacy of standardised manual therapy and home exercise programme for chronic rotator cuff disease: randomised placebo controlled trial. *BMJ (Clinical research ed)* 2010; 340. DOI: 10.1136/bmj.c2756.
  - 3. Dickens VA, Williams JL and Bhamra MS. Role of physiotherapy in the treatment of subacromial impingement syndrome: a prospective study. *Physiotherapy* 2005; 91: 159-164. DOI: https://doi.org/10.1016/j.physio.2004.10.008.
  - 4. Giombini A, Di Cesare A, Safran MR, et al. Short-term effectiveness of hyperthermia for supraspinatus tendinopathy in athletes: a short-term randomized controlled study. *Am J Sports Med* 2006; 34: 1247-1253. 2006/04/26. DOI: 10.1177/0363546506287827.
  - 5. Lombardi I, Jr., Magri AG, Fleury AM, et al. Progressive resistance training in patients with shoulder impingement syndrome: a randomized controlled trial. *Arthritis and rheumatism* 2008; 59: 615-622. 2008/04/29. DOI: 10.1002/art.23576.
  - 6. Ludewig PM and Borstad JD. Effects of a home exercise programme on shoulder pain and functional status in construction workers. *Occupational and environmental medicine* 2003; 60: 841-849. 2003/10/24.
  - 7. Walther M, Werner A, Stahlschmidt T, et al. The subacromial impingement syndrome of the shoulder treated by conventional physiotherapy, self-training, and a shoulder brace: results of a prospective, randomized study. *Journal of shoulder and elbow surgery / American Shoulder and Elbow Surgeons [et al]* 2004; 13: 417-423. 2004/06/29. DOI: 10.1016/s1058274604000485.