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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 Meta-analysis of Randomised Controlled Trials

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

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3 **Objective:** Synthesise evidence regarding effectiveness of progressive and resisted or non-
4 progressive and non-resisted exercise compared with placebo or no treatment, in rotator cuff
5 related pain.
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9
10 **Data sources:** English articles, searched in Cochrane CENTRAL, MEDLINE, EMBASE and
11 CINAHL databases up until May 19, 2020.
12
13

14 **Methods:** Randomised controlled trials in people with rotator cuff related pain comparing
15 either progressive and resisted exercise or non-progressive and non-resisted exercise, with
16 placebo or no treatment were included. Data extracted independently by two authors. Risk of
17 bias appraised with the Cochrane Collaboration tool.
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23 **Results:** Seven trials (468 participants) were included, four trials (271 participants) included
24 progressive and resisted exercise and three trials (197 participants) included non-progressive
25 or non-resisted exercise. There was uncertain clinical benefit for composite pain and function
26 (15 point difference, 95% CI 9 to 21, 100 point scale) and pain outcomes at >6 weeks to 6
27 months with progressive and resisted exercise compared to placebo or no treatment
28 (comparison 1). For non-progressive or non-resisted exercise there was no significant benefit
29 for composite pain and function (4 point difference, 95% CI -2 to 9, 100 point scale) and pain
30 outcomes at >6 weeks to 6 months compared to placebo or no treatment (comparison 2).
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42 Adverse events were seldom reported and mild.
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44 **Conclusions:** There is uncertain clinical benefit for all outcomes with progressive and
45 resisted exercise and no significant benefit with non-progressive and non-resisted exercise,
46 versus no treatment or placebo at >6 weeks to 6 months. Findings are low certainty and
47 should be interpreted with caution.
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3 **Effectiveness of Progressive and Resisted and Non-Progressive or Non-Resisted**
4 **Exercise in Rotator Cuff Related Shoulder Pain: A Systematic Review and Meta-**
5 **analysis of Randomised Controlled Trials**
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34 The study protocol was approved by: NA
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3 **Objective:** Synthesise evidence regarding effectiveness of progressive and resisted or non-
4 progressive and non-resisted exercise compared with placebo or no treatment, in rotator cuff
5 related pain.
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11 CINAHL databases up until May 19, 2020.
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14 **Methods:** Randomised controlled trials in people with rotator cuff related pain comparing
15 either progressive and resisted exercise or non-progressive and non-resisted exercise, with
16 placebo or no treatment were included. Data extracted independently by two authors. Risk of
17 bias appraised with the Cochrane Collaboration tool.
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21

22 **Results:** Seven trials (468 participants) were included, four trials (271 participants) included
23 progressive and resisted exercise and three trials (197 participants) included non-progressive
24 or non-resisted exercise. There was uncertain clinical benefit for composite pain and function
25 (15 point difference, 95% CI 9 to 21, 100 point scale) and pain outcomes at >6 weeks to 6
26 months with progressive and resisted exercise compared to placebo or no treatment
27 (comparison 1). For non-progressive or non-resisted exercise there was no significant benefit
28 for composite pain and function (4 point difference, 95% CI -2 to 9, 100 point scale) and pain
29 outcomes at >6 weeks to 6 months compared to placebo or no treatment (comparison 2).
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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*

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3 1 Shoulder pain affects 15-30% of the population and is the third most common
4
5 2 musculoskeletal condition presenting to primary care.^{1, 2} Rotator cuff related pain is the most
6
7 3 common cause of shoulder pain, accounting for up to 80% of all cases.³ Up to 50% of people
8
9 4 affected experience pain and disability beyond 12 months despite conservative treatment.³
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11 5 Clinical guidelines recommend clinician-guided exercise for rotator cuff related pain.^{4, 5}
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13 6 However, an updated Cochrane review found only one high quality randomised controlled
14
15 7 trial (120 participants) out of 60 (3,620 participants) that compared exercise and manual
16
17 8 therapy for rotator cuff related shoulder pain to placebo, with no difference in clinical
18
19 9 outcomes at 22 weeks.^{6, 7} Two trials (89 participants) of very low quality found similar results
20
21 10 in comparison to no treatment.^{8, 9} Other systematic reviews that compare exercise with or
22
23 11 without manual therapy to all no-exercise controls found very low quality evidence that
24
25 12 exercise was beneficial for pain.¹⁰⁻¹²
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33 14 Resistance exercise has previously been shown to be of benefit for knee osteoarthritis,¹³ back
34
35 15 pain¹⁴ and is a widely used and recommended treatment modality.^{15, 16} Resistance exercise
36
37 16 includes movement against body weight, gravity or by adding load with weight or elastic
38
39 17 resistance band (Theraband). Exercise is considered progressive and resisted when the
40
41 18 amount of load applied is increased over time as the body adapts to the demand that it is
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43 19 placed under.
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49 21 Prior reviews of rotator cuff related pain, including Page et al.⁷ have considered all exercise
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51 22 interventions as equal, without consideration of how the exercise was prescribed (i.e. if there
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53 23 was added resistance that was progressed over time or if resistance was not applied or not
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55 24 progressed).^{7, 17-22} Therefore, it remains unclear whether exercise that is resisted and
56
57 25 progressed is more beneficial than placebo or control in treating rotator cuff related pain.
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3 26 Likewise, it is not clear if exercise that is not resisted or not progressed is more effective than
4
5 27 placebo or control in managing rotator cuff related pain. This remains an unanswered
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8 28 important clinical question in determining the most effective type of exercise intervention for
9
10 29 rotator cuff related pain. In a previous narrative review, studies that included progressively
11
12 30 loaded exercise and greater dose appeared to report superior outcomes compared to various
13
14 31 interventions including no treatment, shockwave therapy and therapeutic ultrasound.²³ No
15
16 32 systematic reviews have distinguished between type of exercise for rotator cuff related pain.
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21 34 This systematic review aims to investigate the effectiveness of progressive and resisted
22
23 35 exercise and the effectiveness of non-progressive and non-resisted exercise; compared to
24
25 36 placebo or no treatment in the management of rotator cuff related pain.
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30 38 **Methods**

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33 39 The methods in this review were similar to methods in the recently updated Cochrane review
34
35 40 of manual therapy and exercise interventions for rotator cuff related pain.⁷ This review was
36
37 41 submitted May 30th 2019 to the International Prospective Register of Systematic Reviews
38
39 42 (PROSPERO; reference CRD42019136513) and registered on August 2nd 2019.
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44 44 Randomised controlled trials written in any language were included regardless of type.

45
46 45 Participants over 16 years old with a primary complaint of rotator cuff related pain of any
47
48 46 duration were included. Diagnostic criteria included anterolateral shoulder pain (with or
49
50 47 without referral into the arm), preserved passive range of shoulder movement, shoulder pain
51
52 48 with movement or resisted shoulder muscle contraction (e.g. empty/full can tests).
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56 49 Randomised controlled trials using synonyms for rotator cuff related pain (e.g. subacromial
57
58 50 impingement syndrome, rotator cuff tendinopathy, rotator cuff tendinitis) were included.
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5 52 Exclusion criteria included participants with a full thickness tear involving more than one
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8 53 rotator cuff tendon (based on clinical presentation or imaging findings, recognizing that some
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10 54 included participants may have undetected rotator cuff tears), gross shoulder instability,
11
12 55 significant shoulder trauma, previous shoulder surgery, shoulder osteoarthritis, hemiplegic
13
14 56 shoulders, a complex myofascial neck/shoulder/arm pain condition, suspected cervical spine
15
16
17 57 referred pain, or a systemic inflammatory condition (e.g. rheumatoid arthritis), unless data
18
19 58 were presented separately for our population of interest.
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23
24 60 In contrast to the review by Page et al. where all exercise was considered equal,⁷ we
25
26 61 considered the type of exercise intervention. We included randomised trials with the
27
28 62 following comparisons: 1) Progressive and resisted exercise versus placebo or no treatment;
29
30 63 2) Non-progressive or non-resisted exercise versus placebo or no treatment. Trials using
31
32 64 progressive and resisted exercise were eligible if they explicitly stated within the intervention
33
34 65 description how resistance was applied (e.g. theraband, weight), and that there was
35
36 66 progression of the volume or the load, or both, over time. Trials using non-progressive or
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38 67 non-resisted exercise were eligible if they explicitly stated that load was not applied or not
39
40 68 progressed, or both. Non-progressive or non-resisted exercise could include active movement
41
42 69 exercise against gravity or with gravity removed, and trials that progressed range of motion
43
44 70 or the type of exercise (e.g. basic static to through range) were excluded if resistance within
45
46 71 each exercise was progressed. The comparator group could include placebo interventions
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48 72 (e.g. detuned laser provided as an alternative to ‘physical therapy’) and no treatment. We did
49
50 73 not exclude randomised trials that included cointerventions (e.g. manual therapy, advice) as
51
52 74 part of the intervention or comparator group, but we planned secondary analyses to determine
53
54 75 the effect of these interventions.
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77 An a priori decision was made to include composite pain and function shoulder outcomes
78 and/or pain outcomes given these are patient-important and considered a core outcome domain
79 by shoulder experts.²⁴ Composite pain and function based on standardised questionnaire was
80 the primary outcome of interest. When multiple scales were reported, data were extracted
81 according to the following hierarchy;⁷ 1) Shoulder Pain and Disability Index (SPADI);²⁵ 2)
82 Croft Shoulder Disability Questionnaire;²⁶ 3) Constant-Murley Score;²⁷ 4) any other shoulder-
83 specific function scale. Secondary outcomes of interest included overall pain, pain with
84 activity, and pain at rest (measured on VAS, numerical or categorical rating scale). If overall
85 pain was not reported, we substituted another pain measure for that analysis in the following
86 hierarchy, unspecified, rest pain or other pain. Number of participants experiencing an adverse
87 event (as defined by the authors) were also extracted.

88

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

95

96 Randomised controlled trials published up to March 2015 were identified from the updated
97 Cochrane review of manual therapy and exercise interventions for rotator cuff related pain.⁷
98 The search from the Page et al⁷ 2016 review was repeated excluding search terms for
99 adhesive capsulitis and manual therapy given these were not relevant for our review
100 (Appendix 1).

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5 102 The search included the following databases: Cochrane Central Register of Controlled Trials
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7 103 (CENTRAL; *The Cochrane Library* May 2020, Issue 5), Ovid MEDLINE (March 2015 to
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9 104 May 2020), Ovid EMBASE (March 2015 to May 2020), and CINAHL Plus (EBSCO, March
10
11 105 2015 to May 2020). Gray literature was searched via OpenGray and ongoing trials via the
12
13 106 National Institute of Health (clinicaltrials.gov) and the World Health Organisation
14
15 107 (<http://www.who.int/ictrp>) International Clinical Trials Registries.
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21 109 Titles and abstracts were screened independently by two authors (PM, GS), and the full text
22
23 110 was reviewed by the same author independently if required to determine eligibility.
24

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26 111 Consensus on discrepancies was reached via discussion, otherwise a third author (CL or JN)
27
28 112 was available to assist if consensus was not reached.
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33 114 Data were extracted independently by two authors (PM, GS) to a standard data extraction
34
35 115 form, and discrepancies were resolved via discussion, or a third author (CL) was consulted to
36
37 116 adjudicate when required. Authors were emailed twice over four weeks to retrieve missing
38
39 117 data. All data extraction was checked by a third author (JN). Missing SDs were calculated
40
41 118 from standard errors (SEs), 95% CIs or P values, otherwise we planned to impute SDs from
42
43 119 other trials in the meta-analyses (median of available SDs) if no measures of variation were
44
45 120 reported.²⁹ For the primary outcome of function and pain we calculated the median of
46
47 121 available SDs in three studies following the process described above.^{8, 30, 31} For activity pain
48
49 122 and rest pain we calculated SDs as above for two studies.^{30, 31} For Giombini et al,³² the
50
51 123 reported measure of variability was much lower (by a factor of 4) than all other studies and
52
53 124 we assumed it was a standard error (this could not be confirmed by the authors at the time of
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55 125 publication).
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127 The data extracted from each randomised trial are shown below:

- 128 • Trial characteristics (author name, year published, trial type [e.g. parallel, crossover],
129 country, funding source, trial registration [with number]).
- 130 • Participant characteristics (age, gender, duration of symptoms, inclusion/exclusion
131 criteria).
- 132 • Exercise intervention characteristics (exercises, sets, repetitions, frequency, duration,
133 how exercises was loaded and progressed, co-interventions, adherence measures,
134 advice about pain).
- 135 • Comparator intervention characteristics (details of placebo or no treatment).
- 136 • Outcome instrument used and timing.
- 137 • Outcome data were extracted according to the following a priori decision rules to
138 minimise bias: 1) preference to data that was adjusted for baseline values (e.g.
139 ANCOVA) and intention-to-treat; 2) follow-up rather than change scores extracted
140 where possible; 3) and data extracted for only the first period of cross-over trials.

141

142 The Cochrane Collaboration's tool was used to assess risk of bias.³³ The results of the risk of
143 bias assessment for all included trials were extracted from Page et al⁷ as no new studies were
144 identified in our updated search.

145

146 Dichotomous (relative risk [RR] and 95% confidence intervals [CI]) and continuous
147 measures (mean difference [MD] and 95% CI) of treatment effect were calculated using
148 Review Manager 5.3 (RevMan). For continuous outcomes, MD was used after scores for the
149 Shoulder Rating Questionnaire (17-100) and the Neer Shoulder Score (10-100) were
150 transformed to a 0-100 scale (0 is best).³⁴ We reversed the direction of the Constant-Murley,

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3 151 Neer and Shoulder Rating Questionnaire scores so that zero was best in all scales (to match
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5 152 the SPADI, the highest outcome in our hierarchy).³⁴ Minimal clinically important difference
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7 153 was assumed to be 10 on a 100-point scale for composite pain and function outcome,³⁵⁻³⁷ and
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9 154 15 points on a 100-point scale for pain outcome.³⁸

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14 156 Data were pooled in meta-analyses using Review Manager 5.3³⁹ if participants, interventions
15
16 157 and outcome measures were similar. A random effects models was chosen a priori given
17
18 158 heterogeneity is likely. Where data could not be pooled, we summarized findings
19
20 159 descriptively and reported effect estimates and 95% confidence intervals.
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26 162 Assessment of statistical heterogeneity was based on Chi-square statistic and the I^2 statistic.⁴⁰
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28 163 For the I^2 statistic, we interpreted statistical heterogeneity as not important (<50%), moderate
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30 164 (50-75%) and high (>75%).⁴⁰
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36 166 A sensitivity analysis was planned to investigate the influence of high risk of bias studies on
37
38 167 treatment outcomes. Subgroup analysis was planned a priori to investigate 1) the effect of
39
40 168 exercise interventions alone versus exercise interventions including co-interventions, and 2)
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42 169 the effects of exercise setting (e.g. clinician-supervised or home exercise).
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48 171 We prepared summary of findings tables for both comparisons and graded the certainty of
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50 172 evidence using a GRADE approach [Grades of Recommendation, Assessment, Development
51
52 173 and Evaluation Working Group]⁴¹. Level of evidence was downgraded (to moderate, low or
53
54 174 very low) for each of the following: risk of bias, inconsistency of results, indirectness,
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56 175 imprecision, and publication bias.
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3 176 For dichotomous outcomes (e.g. adverse events), absolute risk difference was expressed as a
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5 177 percentage and relative percent change was the risk ratio – 1 expressed as a percentage. The
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7 178 NNT_H was calculated using the event rate in the control group and risk ratio.⁴² For
9
10 179 continuous outcomes (e.g. composite pain and function), absolute risk difference was the
11
12 180 mean difference in outcome between the intervention and comparator group expressed as a
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14 181 percentage. The relative percent change was the mean intervention group difference (absolute
15
16 182 change) divided by the mean at baseline in the control group, expressed as a percentage.
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21 184 **Results**

23 185 *Study selection*

26 186 Nine eligible trials were identified from the Page et al⁷ 2016 systematic review. One trial was
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28 187 excluded because the control group received a standard exercise instruction pamphlet in
29
30 188 addition to education and therefore is not a true comparison to no treatment or placebo.⁹ The
31
32 189 other excluded trial included physiotherapy treatments as control (heat packs, transcutaneous
33
34 190 electrical nerve stimulation and ultrasound).⁴³ No eligible trials were identified after the
35
36 191 updated search (Figure 1), and screening reference lists of included studies, gray literature
37
38 192 and clinical trials registries. We obtained data from the authors (July 2017) of two trials^{6, 31}
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40 193 that allowed us to confirm eligibility (Appendix 2). We acknowledge that within the trial
41
42 194 protocol for the randomised trial by Bennell et al.⁴⁴ there was progression of exercise through
43
44 195 range (e.g. external rotation in side lying, to standing in neutral, to elbow supported at 90°
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46 196 abduction, to unsupported elbow at 45° abduction). However, there was not progression of
47
48 197 load or volume as specified in our eligibility criteria.
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56 199 **Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009**
57
58 200 **flow diagram for literature search results.**
59
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201

202 *Trial characteristics*

203 Trial and participant characteristics are shown in Table 1. Seven parallel group randomised
204 trials (468 participants) were included. Multiple diagnostic labels were used for rotator cuff
205 related pain but there was overlapping and consistent diagnostic criteria between trials (Table
206 1). Mean age was between 47 and 61 years, but lower in Giombini et al³² (26 and 29 years).
207 Men were more prevalent (54-100%) aside from Lombardi et al⁴⁵ (24% men). Baseline
208 composite pain and function was comparable (33 to 50, 0-100 point scale where 0 is best).

209

210 Description of the interventions and comparators are shown in Table 2. Three trials compared
211 progressive and resisted exercise with no treatment.^{8, 45, 46} One trial compared progressive and
212 resisted exercise with placebo (detuned laser).³⁰ All progressive and resisted exercise
213 interventions included scapular and rotator cuff strengthening and progressed the load
214 (intensity) with theraband or weights.^{8, 30, 45, 46} Prescribed sets and repetitions varied, and only
215 one study specified exercise intensity (50%-70% of the 6RM).⁴⁵ Three studies included co-
216 interventions. Brox et al³⁰ included education about pathology, pain and ergonomics, Dickens
217 et al⁸ included manual therapy, postural advice, taping with or without electrotherapy and
218 Ludwig et al⁴⁶ included shoulder stretching.

219

220 All three trials (four comparisons) of the non-progressive and non-resisted interventions were
221 compared with placebo (two ultrasound^{6, 32} and one brace³¹). One non-progressive and non-
222 resisted exercise trial⁶ targeted scapular and rotator cuff strengthening similar to progressive
223 and resisted trials. Whereas, Walther et al³¹ assessed static exercise and neck stretching (all
224 other trials evaluate dynamic exercise) and Giombini et al³² assessed pendular exercise and
225 shoulder stretching. Load was applied without progression with theraband or 1kg weight in

226 two trials^{6, 31} and no load applied in the remaining trial.³² There were only co-interventions in
227 Bennell et al⁶ including manual therapy and behavioural strategies (e.g. goal setting, positive
228 reinforcement).

229

230 **Table 1: Recruitment and retention, participant characteristics and eligibility criteria**

231 **Table 2: Exercise characteristics and outcome**

232

233 *Risk of bias in included trials*

234 Risk of bias assessment was extracted from Page et al⁷ (summarised in Figure 2) as all our
235 studies were also in this Cochrane review from 2016. Among trials comparing progressive
236 and resisted exercise or non-progressive and non resisted exercise to placebo or no treatment,
237 six (86%) were rated high risk of performance and detection bias.^{8, 30-32, 45, 46} Further, two
238 trials (29%) were at high risk of reporting bias^{31, 32} (uncertain risk in a further four [57%]),^{8,}
239 ^{30, 45, 46} one trial (14%) was at high risk of attrition bias,³⁰ and there was uncertain risk of
240 selection bias in five (71%) trials.^{8, 30-32, 46}

241

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

244

245 **Effects of interventions**

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

247 There were four trials with 271 participants that reported composite pain and function,^{8, 30, 45,}
248 ⁴⁶ three trials^{30, 45, 46} (197 participants) reported overall pain and two trials^{30, 45} (135
249 participants) reported activity pain and rest pain at >6 weeks to 6 months. No trials reported
250 adverse events. All outcomes were downgraded twice (low certainty) for risk of bias

251 (performance, detection, reporting and selection).^{8, 30, 46}

252

253 There was uncertain clinical benefit (low certainty evidence) in all outcomes with progressive

254 and resisted exercise. For composite pain and function there was a 15.0 point difference (95%

255 CI 8.6 to 21.4; 4 trials, 271 participants, Figure 3, Table 3).^{8, 30, 45, 46} For overall pain there

256 was a 10.7 point difference (95% CI 5.6 to 15.7; 3 trials, 197 participants, Figure 3, Table

257 3).^{30, 45, 46} For pain with activity there was a 24.7 point difference (95% CI 13.9 to 35.5; 2

258 trials, 135 participants, Figure 3, Table 3).^{30, 45} For pain at rest there was a 22.8 point

259 difference (95% CI 14.0 to 31.6; 2 trials, 135 participants, Figure 3, Table 3).^{30, 45}

260

261 *Adverse events*

262 Unclear as no trials of progressive and resisted exercise reported whether adverse events

263 occurred.

264

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

266 **treatment**

267 Three trials (197 participants) reported composite pain and function, overall pain and pain

268 with activity at >6 weeks to 6 months.^{6, 31, 32} Two trials (174 participants) reported pain at rest

269 at >6 weeks to 6 months.^{6, 31} Two trials (83 participants) reported composite pain and

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

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

272 reporting and selection]).

273

274 There was low certainty evidence of no benefit in all outcomes with non-progressive or non-

275 resisted exercise. For function there was a 3.6 point difference (95% CI -2.2 to 9.4; 3 trials, 4

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3 276 comparisons, 197 participants, Figure 4, Table 4).^{6, 31, 32} For overall pain there was a 3.3 point
4
5 277 difference (95% CI -1.5 to 8.1; 3 trials, 4 comparisons, 197 participants, Figure 4, Table 4).^{6,}
6
7 278 ^{31, 32} For pain with activity there was a 3.4 point difference (95% CI -5.0 to 11.8; 3 trials, 4
8
9 279 comparisons, 197 participants, Figure 4, Table 4). ^{6, 31, 32} For pain at rest there was a 1.8 point
10
11 280 difference (95% CI -6.6 to 10.2; 2 trials, 3 comparisons, 174 participants, Figure 4, Table 4).^{6,}
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15 281 ³¹

16
17 282

18 19 283 *Adverse events*

20
21 284 One trial reported a short term increase in pain that was greater following exercise
22
23 285 intervention (17/55) compared with placebo (5/61) (RR 4.02, 95% CI 1.56 to 10.37).⁶
24
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26 286

27 28 287 **Secondary analysis**

29
30 288 Subgroup analysis for co-interventions were similar to the overall effect for all outcomes
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32 289 (composite pain and function, overall pain, activity pain and rest pain) in both comparisons.
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34 290 One exception was composite pain and function in comparison 1, where there was benefit of
35
36 291 uncertain clinical importance among the two trials that did not include co-interventions^{25,26}
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38 292 and clinically important improvement for the two trials^{8, 30} that did. When subgrouping for
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40 293 supervised versus unsupervised exercise, comparison 1 pain and function outcome showed
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42 294 clinically important benefit in three trials^{10,28,42} that utilised supervised exercise but uncertain
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44 295 clinical benefit in one trial⁴⁶ that utilised unsupervised exercise. All other findings were
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46 296 identical to the overall effect for all outcomes (composite pain and function and overall pain).
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48 297 There was insufficient data to perform other planned secondary analyses.
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53 54 299 **Discussion**

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3 300 This review identified seven randomised trials (eight comparisons, 468 participants) that
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5 301 compared exercise (progressive and resisted or not) to placebo or no treatment among people
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7 302 with rotator cuff related shoulder pain. Four trials^{8, 30, 45, 46} compared progressive and resisted
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9 303 exercise to no treatment or placebo (comparison 1) and three trials^{6, 31, 32} compared non-
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11 304 progressive or non-resisted exercise to placebo (comparison 2). For progressive and resisted
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13 305 exercise, low certainty evidence indicates benefit of uncertain clinical importance in
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15 306 composite pain and function, overall pain outcomes, pain with activity and pain at rest at >6
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17 307 weeks to 6 months compared to placebo or no treatment. For non-progressive or non-resisted
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19 308 exercise, low certainty evidence indicates no benefit for composite pain and function, overall
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21 309 pain, pain with activity and pain at rest at >6 weeks to 6 months compared to placebo or no
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23 310 treatment (comparison 2). Adverse events were reported in only one study and included only
24
25 311 mild differences in short term pain after exercise. The trials were heterogeneous (e.g. whether
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27 312 exercise was supervised, co-interventions used, comparators) so these findings should be
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29 313 viewed as preliminary and hypothesis generating.
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38 315 Three (75%)^{8, 30, 45} of the progressive and resisted trials but only one (25%)³¹ of the non-
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40 316 progressive and non-resisted trials utilised supervised exercise interventions. Three out of
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42 317 four (75%) progressive and resisted interventions included co-interventions in the exercise
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44 318 arm (e.g. manual therapy, advice) whereas only one non-progressive and non-resisted
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46 319 intervention (25%) utilized co-interventions. Further, three trials (75%)^{8, 45, 46} comparing
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48 320 progressive and resisted exercise were compared to no treatment, whereas all non-progressive
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50 321 or non-resisted exercise trials were compared with placebo. Therefore, we can only conclude
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52 322 that progressive and resisted studies, most of which are supervised, may offer benefit of
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54 323 uncertain clinical importance compared with primarily no treatment comparators.
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5 326 All progressive and resisted exercise programs increased load (intensity), only two
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7 327 progressed range of motion, volume or speed. Load progression was based on either
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9 328 achieving a pain response within defined limits (e.g. pain of no more than 4/10 on a 0-10
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11 329 scale) or based on ability (e.g. when the prescribed sets were no longer achieving muscle
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13 330 fatigue). There were important differences in the exercise approaches between the
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15 331 progressive and resisted and non-progressive and non-resisted trials that may have influenced
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17 332 our findings. Two trials that utilized non-progressive and non-resisted exercise prescribed
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19 333 either pendular exercises or isometric (static hold) exercises.^{31, 32} This is in contrast to the
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21 334 dynamic scapular and rotator cuff exercises prescribed in the progressive and resisted trials.
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28 336 It is possible that mechanisms other than the exercise undertaken explain the findings. For
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30 337 example, giving a patient permission to perform progressive exercise, or do more exercise,
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32 338 may reduce fear of movement and lead to greater general shoulder use in some patients.

33 339 Adherence and exercise dose parameters were also poorly reported, so we are unable to
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35 340 determine the dose response and actual volume of exercise completed for each intervention.
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37 341 We urge caution in interpreting these findings given the certainty of evidence supporting the
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39 342 findings are generally low using a GRADE approach.
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47 344 There have been multiple systematic reviews of exercise interventions for rotator cuff related
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49 345 pain.^{7, 10-12, 47} A recent Cochrane review concluded no benefit of exercise over placebo for
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51 346 rotator cuff related pain,⁷ which contrasts with other systematic reviews.^{10, 12} The difference
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53 347 is the Cochrane review was based on a single (judged by the authors of this review) low risk
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55 348 of bias study. Our findings are broadly consistent with this Cochrane review as most studies
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57 349 using a placebo comparison did not find benefit for exercise (albeit 75% utilized non-
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3 350 progressive and non-resisted exercise). Future high quality studies investigating whether
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5 351 progressive and resisted exercise is more beneficial than placebo are warranted.
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10 353 This is the first systematic review with meta-analysis to focus on progressive and resisted
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12 354 exercise or not versus no treatment or placebo. Further, in this review we followed as closely
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14 355 as possible best practice guidelines as outlined by the Cochrane collaboration and PRISMA
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16 356 to minimize potential sources of bias in this review. Inclusion and exclusion criteria were
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19 357 carefully decided a priori and were clearly defined to minimize selection bias.
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24 359 The main limitation of our review is that there were only 7 trials and 8 comparisons that met
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26 360 our inclusion and exclusion criteria. Potential bias and the limited number of trials identified
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28 361 reduced confidence in our findings, however the findings are consistent with evidence in
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30 362 other tendinopathies around the body and worthy of further investigation.⁴⁸
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35 364 There are several limitations of the literature we included. There is low certainty evidence for
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37 365 both comparison one and two, only one trial⁶ in this review has a low risk of bias (86% had a
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39 366 high risk of bias, therefore certainty was downgraded two levels, we did not downgrade for
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41 367 inconsistency, indirectness [all interventions reflected clinical practice] or imprecision). This
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43 368 precluded sensitivity analysis including only low risk of bias trials. Further, as discussed,
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45 369 there were more progressive and resisted trials that utilized supervised exercise and co-
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47 370 interventions, and used non-placebo controls, so these factors may have influenced the
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49 371 positive findings reported for this exercise type.
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55 373 Exercise programs were not described fully. This included characteristics such as pain during
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57 374 loading, exercise adherence, rest between exercise sets and exercise tempo. This limitation is
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3 375 important because exercise dose may contribute to the positive findings and clinicians are
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5 376 unable to implement an exercise program if exercise characteristics are incompletely
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8 377 reported. Limited reporting on exercise programs may also have influenced our decision to
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10 378 classify studies as progressive and resisted or non-progressive and non-resisted. Future trials
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12 379 should consider reporting guidelines (e.g. Consensus on Exercise Reporting Template)⁴⁹ to
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14 380 ensure findings are translatable to practice.
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19 382 **Implications for practice**

21 383 Progressive resistance exercise may improve function and pain outcomes in rotator cuff
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23 384 related cuff related pain in comparison to placebo or no treatment comparators. The benefit
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25 385 was of uncertain clinical importance and placebo effects were not controlled in 75% of
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28 386 studies. Three quarters of progressive and resisted exercise interventions were supervised and
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30 387 included co-interventions such as manual therapy or advice or shoulder stretching. Clinicians
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32 388 can consider adopting similar progressive and resisted exercise interventions for rotator cuff
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34 389 related pain but the low certainty findings in this review indicate that our findings may
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37 390 change in the future (if there are larger and adequately powered studies addressing the same
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39 391 question). Non-progressive and non-resisted exercise did not demonstrate benefit over
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41 392 primary (75%) placebo comparisons. Our results question the use of non-resisted or non-
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43 393 progressive exercise for rotator cuff related pain.
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47 394 Future high quality, adequately powered randomised trials should consider the type of
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49 395 exercise prescribed for the intervention, specifically how resistance is added and if it is
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51 396 progressed appropriately throughout the treatment (increasing the intensity of the resistance
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53 397 and also increasing the range at which the exercise is performed).
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3 398 **Clinical Messages**

4 399 • Progressive and resisted exercise may provide uncertain clinical benefit in pain and
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7 400 function compared with primarily no treatment comparators at >6 weeks to 6 months
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9 401 among people with rotator cuff related pain

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11 402 • Non-progressive and non-resisted exercise did not demonstrate benefit over placebo
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13 403 at >6 weeks to 6 months among people with rotator cuff related pain

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Formal analysis: JN, PM

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

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

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
Progressive and resisted exercise versus placebo or no treatment								
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	Supervised exercise group: 47 years, 44% men, 66 (10-100, 100 best), overall pain 15 (0-100, 0 best), 24 months Placebo Laser group: 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 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 randomised, 30 no treatment (physiotherapy waiting list), 30 progressive resistance exercise, follow up 56	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	110 screened, 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 palpation of biceps or rotator cuff tendons
Non-progressive or non-resisted exercise versus placebo or no treatment								
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	<p>Active intervention non-progressive exercise group: 59 years, 58% men, 43 (0-100, 0 best), overall pain 48 (0-100, 0 best), 24 months</p> <p>Placebo sham ultrasound group: 61 years, 49% men, 44 (0-100, 0 best), overall pain 48 (0-100, 0 best), 14 months</p>	>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	<p>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)</p> <p>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)</p>	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 randomised, 20 functional brace (placebo), 20 self-training non-progressive exercise group, 20 physiotherapy non-progressive exercise group, follow up	<p>Functional brace (placebo) group: 49 years, 70% men, 63 (0-100, 100 best), overall pain 50 (0-100, 0 best), 27 months</p> <p>Self training non-progressive exercise group: 52 years, 45% male, 58 (0-100, 100 best), overall pain 47 (0-100, 0 best), 23 months</p> <p>Physio non-progressive exercise grouping: 52 years, 55% male, 60 (0-100, 100 best), overall pain 54 (0-100, 0 best), 32 months</p>	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 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% [1 st set] to 70% [2 nd 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 SF-36 pain score for consistency with other studies.

1									
2									
3	Ludwig et al.	No treatment	Anterior and	Home, 1 in	Stretches 30secx5/day	Theraband,	'No	Exercise	Outcomes: Composite pain and function with
4	2003, RCT,		posterior shoulder	person and 1	& active movement	based on	increased	log (27%	shoulder rating questionnaire (17-100, 100 is
5	USA, Centre to		stretches,	phone or in	5x/day, progressive	ability to	shoulder	completed	better), work related shoulder pain, work
6	protect worker'		abduction active	person (if	exercise 3x10 – 20 (by	perform	pain' (not	75% or	related disability
7	rights, the		movement, and	required)	3 rd week), 3x/week, 10	exercise	clear if	more of	
8	public health		external rotation in	over 10	weeks, ?, ?, 540/wk		increased	prescribed	Outcomes extracted: composite pain and
9	service and the		neutral and in	weeks			their	exercise	function, overall pain
10	University of		abduction	Initial, at 1			baseline		
11	Iowa, no trial		progressive	week,			or no		Note: Overall pain assumed from work related
12	registration		resisted exercise	phone/option			pain)		pain item. We reversed the direction of the
13				al at 4 weeks					function score and converted to a 0-100 scale
14									for consistency with other studies. SE reported
15									and used to calculate SD.
16	Non-progressive or non-resisted exercise versus placebo or no treatment								
17	Bennell et al.	Sham	Education, goal	Home, 10	Variable sets/reps	Theraband,	Not	Exercise	Outcomes reported: Composite pain and
18	2010, RCT,	ultrasound, no	setting, manual	sessions over	(2x10 repetitions or 5	not	reported	log	function, and overall pain with SPADI (both 0-
19	Australia,	instruction to	therapy and home	10 weeks.	sec x 5 or 1-3 minute	progressed		(participant	100, 0 is best), activity and rest pain with NRS
20	National	do any home	exercise program	Then	hold), twice daily for			s completed	(0-10, 10 worse), quality of life using SF-36
21	Health and	exercises, no	including dynamic	instructed to	first week, daily after			82% of	
22	Medical	instruction in	scapular control,	continue	that to 10 weeks, ?, ?,			prescribed	Outcomes extracted: composite pain and
23	Research	exercise	strengthening	daily	incalculable			exercise at	function, overall, activity and rest pain
24	Council, no	technique	scapular stabiliser	exercises for				11 weeks,	
25	NCT00415441		and rotator cuff	further 12				70% at 22	
26		10 sessions in	muscles,	weeks.				weeks)	
27		10 weeks	improving						
28			shoulder and						
29			thoracic posture						
30			and increasing						
31			range of motion of						
32			thoracic extension						
33	Giombini et al.	Therapeutic	Pendular flexion	Home,	Sets/reps not specified	No load	'To	Not	Outcomes reported: Composite pain and
34	2006, RCT,	ultrasound	and extension in	weekly, 4	(5 minutes), twice	applied	tolerance'	reported	function with Constant-Murley score (0-100,
35	Italy, no		prone and passive	weeks	daily, 4 weeks, ?, ?,				100 is best), mean pain using a 10cm VAS,
36	funding		glenohumeral		incalculable				pain on resisted movement (4 point scale, 0 is
37	reported, no		stretching						best),
38	trial								Pain on active abduction 40-120 (4 point scale,
39	registration								0 is best)
40									
41									Outcomes extracted: composite pain and
42									function, overall pain, pain during movement
43									
44									
45									
46									

1									Note: Overall pain assumed from mean pain. Reversed the direction of the function score for consistency with other studies.
2	Walther et al.	Shoulder brace	Group a)	Group a	Isometric 10x10sec,	Theraband	Not	Not	Outcomes reported; Composite pain and
3	2004, RCT,		Physiotherapy:	supervised,	stretch 2x15sec,	or 1kg	reported	reported	function and with Constant-Murley (0-100,
4	Germany, ?, no		Isometric shoulder	30 sessions in	pendular 3-5 mins,	weight, no			100 is best), activity, night and rest pain (0-
5	trial		retraction,	12 weeks	adduction & distraction	progression			100, 100 maximum pain)
6	registration		abduction, external	Group b	3x15sec, group a				Outcomes extracted: composite pain and
7			rotation, and	home, 4	5x/wk; group b 2-				function, overall pain, activity and rest pain
8			rowing with elbow	sessions in 12	3x/week, 12 weeks, ?,				
9			bent and straight,	weeks	?, in calculable				
10			cervical lateral						Note: Overall pain assumed from night pain.
11			flexion stretch,		Group b 5xper week				We reversed the direction of the function score
12			pendular exercises,		for 10-15 mins.				for consistency with other studies. We
13			isometric						estimated SD as a median of the available SDs.
14			adduction with self						
15			protraction						
16			mobilisation						
17			Group b) Self-						
18			training: as above						

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

Table 3. Summary of Findings: Progressive and resisted exercise compared to placebo for rotator cuff related pain**Patient or population:** rotator cuff related pain**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 risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk Placebo	Corresponding risk 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 ¹	The mean function in the intervention group was 15.0 points better (8.6 to 21.4 better)	-	271 (4 RCTs)	⊕⊕○○ LOW ³	Statistically significant but uncertain clinical benefit ² Absolute change 15% better (9% better to 21% better); relative change 32% better (18% better to 45% better) ⁴
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 53.3 ¹	The mean overall pain in the intervention group was 10.7 points better (5.6 to 15.7 better)	-	197 (3 RCTs)	⊕⊕○○ LOW ³	Statistically significant but uncertain clinical benefit ² Absolute change 11% better (6% better to 16% better); relative change 19% better (10% better to 28% better) ⁴
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 71.0 ¹	The mean pain with activity in the intervention group was 24.7 points better (13.9 to 35.5 better)	-	135 (2 RCTs)	⊕⊕○○ LOW ³	Statistically significant but uncertain clinical benefit ² Absolute change 25% better (14% better to 36% better); relative change 35% better (20% better to 50% better) ⁴
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 43.0 ¹	The mean overall pain in the intervention group was 22.8 points better (14.0 to 31.6 better)	-	135 (2 RCTs)	⊕⊕○○ LOW ³	Statistically significant but uncertain clinical benefit ² Absolute change 23% better (14% better to 32% better); relative change 58% better (36% better to 81% better) ⁴
Adverse events	-	-	-	-	-	-

*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; SRQ: 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.

¹Lombardi was used as the control group risk

²We 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%)

³Downgraded (-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

⁴Relative 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* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Non-progressive and non-resisted exercise				
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 28.3 ¹	The mean function in the intervention group was 3.6 points better (2.2 worse to 9.4 better)	-	197 (3 RCTs)	⊕⊕○○ LOW ²	No significant benefit ³ Absolute risk difference 4% better (2% worse to 9% better); relative change 8% better (5% worse to 21% better) ⁴
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 31 ¹	The mean overall pain in the intervention group was 3.3 points better (1.5 worse to 8.1 better)	-	197 (3 RCTs)	⊕⊕○○ LOW ²	No significant benefit ³ Absolute risk difference 3% better (1% worse to 8% better); relative change 7% better (3% worse to 17% better) ⁴
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 3.4 points better (5.0 worse to 11.8 better)	-	197 (3 RCTs)	⊕⊕○○ LOW ²	No significant benefit ³ Absolute risk difference 3% better (5% worse to 12% better); relative change 7% better (10% worse to 24% better) ⁴
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 ¹	The mean pain at rest in the intervention group was 1.8 points better (6.6 worse to 10.2 better)	-	174 (2 RCTs)	⊕⊕○○ LOW ²	No significant benefit ³ Absolute risk difference 0.2% better (0.7% worse to 1% better); relative change 9% better (31% worse to 49% better) ⁴
Adverse events Follow-up: 10-11 weeks	Study population 82 per 1000	309 per 1000 (122 to 782)	RR 3.77 (1.49 to 9.54)	116 (1 RCT)	⊕⊕⊕⊕ HIGH	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 Disability 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, Walthers 2004 and Giombini 2006 trials.

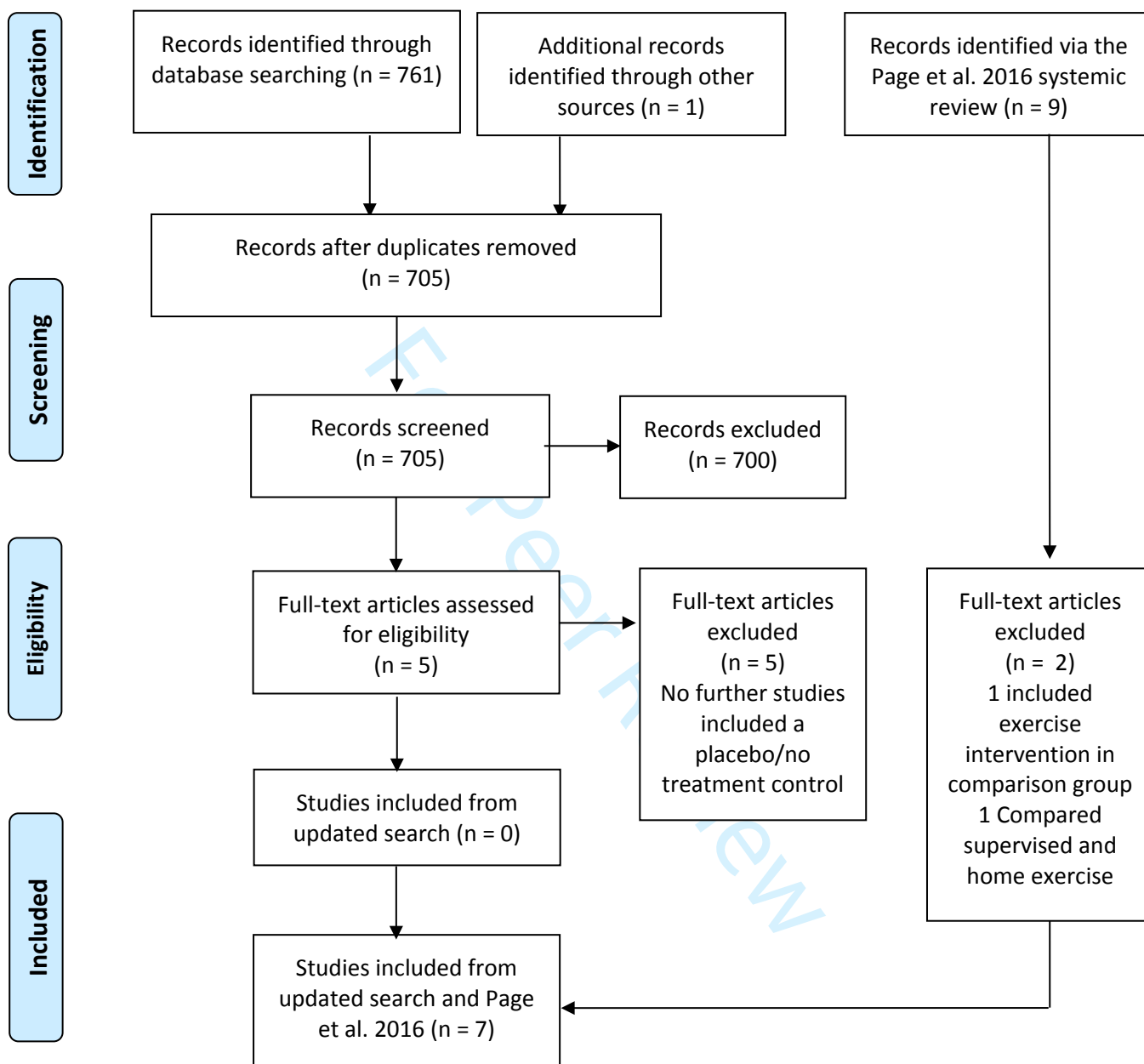
¹Placebo group score in Bennell 2010 was used as assumed control group risk

²Downgraded (-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

³We 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%)

⁴Relative 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

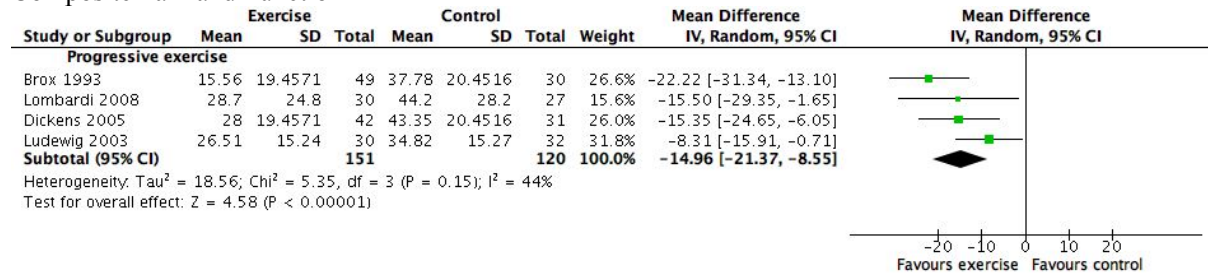
For more information, visit www.prisma-statement.org.

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

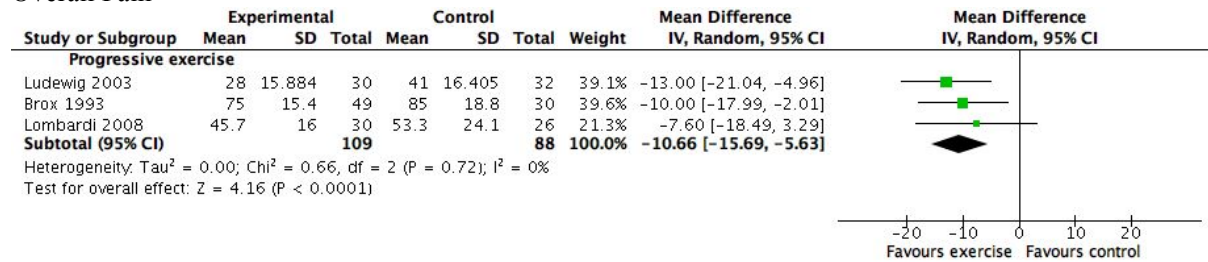
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bennell 2010	+	+	+	+	+	+	+
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

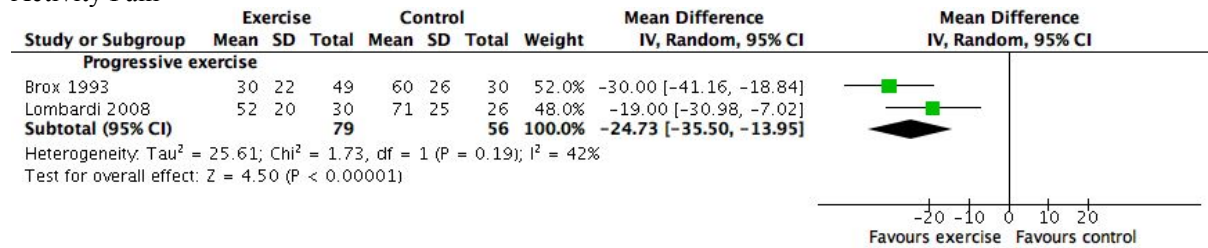
Composite Pain and Function



Overall Pain



Activity Pain



Rest Pain

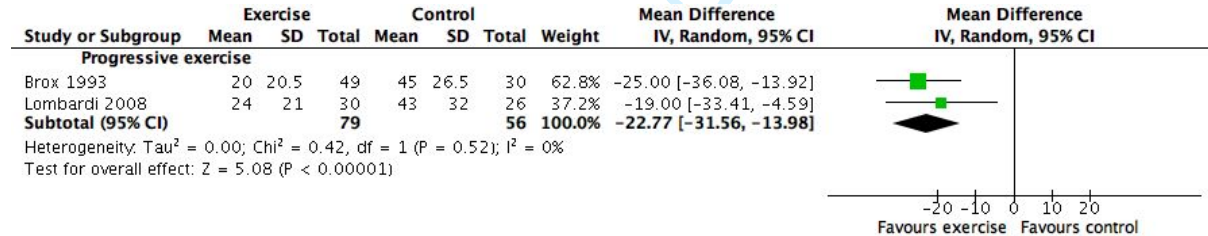
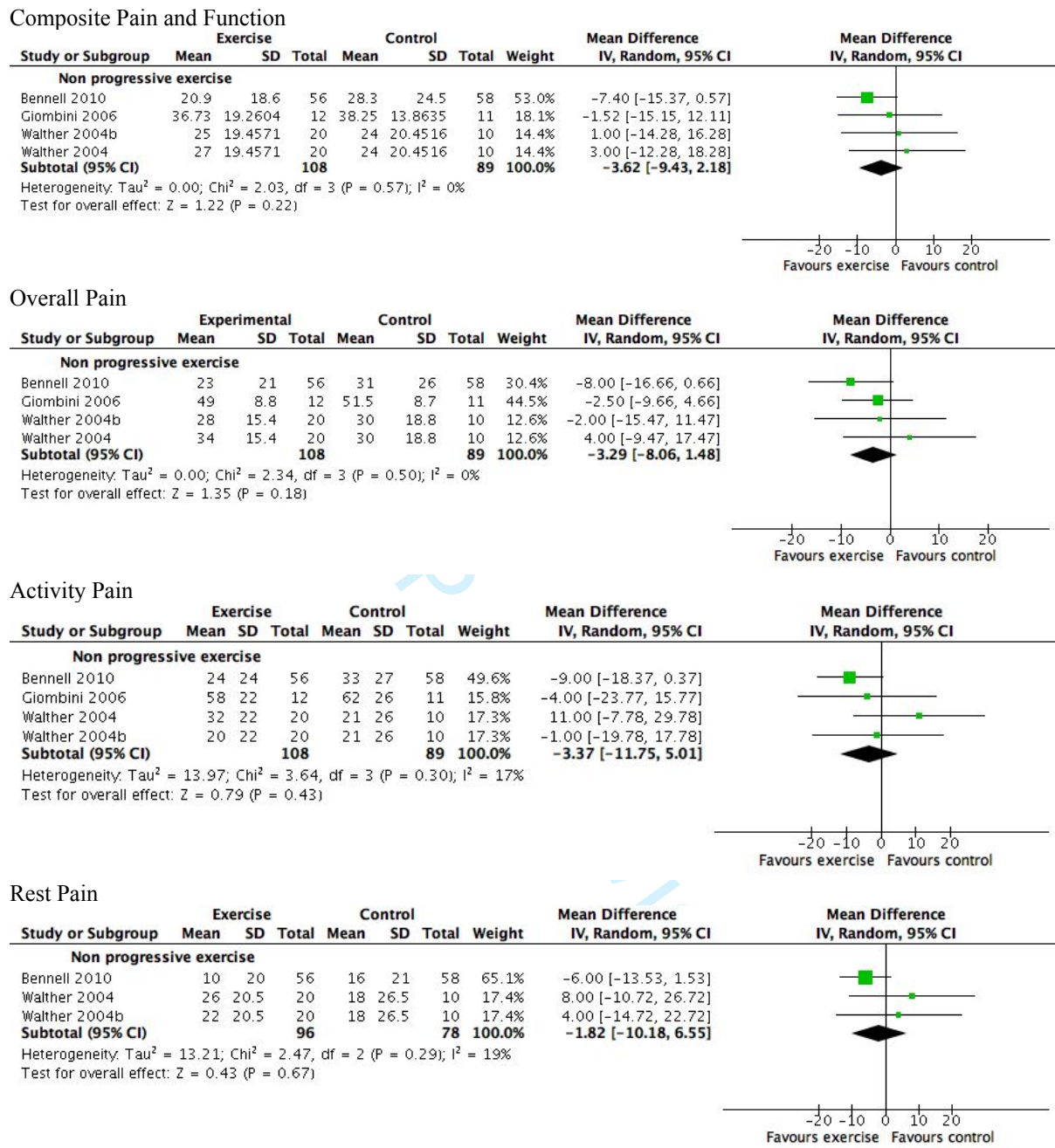


Figure 4. Comparison Two - Effects of non-progressive or non-resisted exercise versus placebo or no treatment on composite pain and function, overall pain, activity pain and rest pain



593

Appendix 1**594 Search strategy for CENTRAL:**

- 595 1. MeSH descriptor: [Shoulder Pain] explode all trees
- 596 2. MeSH descriptor: [Shoulder Impingement Syndrome] explode all trees
- 597 3. MeSH descriptor: [Rotator Cuff] explode all trees
- 598 4. MeSH descriptor: [Bursitis] explode all trees
- 599 5. ((shoulder* in AllText or rotator* in AllText) and (bursitis in AllText or impinge* in
600 AllText or tendonitis in All Text or tendonitis in All Text or tendinopathy in AllText or
601 pain* in All Text))
- 602 6. "rotator cuff" in AllText
- 603 7. #1 or #2 or #3 or #4 or #5 or #6
- 604 8. MeSH descriptor: [Rehabilitation] explode all trees
- 605 9. MeSH descriptor: [Physical Therapy Modalities] explode all trees
- 606 10. MeSH descriptor: [Exercise Movement Techniques] explode all trees
- 607 11. MeSH descriptor: [Ultrasonography, Interventional] explode all trees
- 608 12. rehabilitat* in All Text or physiotherapy* in AllText or "physical therap*" in AllText
609 or "manual therap*" in All Text or exercis* in All Text
- 610 13. (ultrasound in All Text or ultrasonograph* in All Text or tns in AllText or tens in All
611 Text or shockwave in All Text or electrotherap*in All Text or mobili* in AllText)
- 612 14. #9 or #10 or #11 or #12 or #13
- 613 15. #8 and #15

614 Search strategy for MEDLINE (Ovid):

- 615 1. shoulder pain/
- 616 2. shoulder impingement syndrome/
- 617 3. rotator cuff/
- 618 4. exp bursitis/
- 619 5. ((shoulder\$ or rotator cuff) adj5 (bursitis or impinge\$ or tendinitis or tendonitis or
620 tendinopathy or pain\$)).mp.
- 621 6. rotator cuff.mp.
- 622 7. or/1-7
- 623 8. exp rehabilitation/
- 624 9. exp physical therapy techniques/
- 625 10. exp musculoskeletal manipulations/
- 626 11. exp exercise movement techniques/
- 627 12. exp ultrasonography, interventional/
- 628 13. (rehabilitat\$ or physiotherap\$ or physical therap\$ or manual therap\$ or exercis\$ or
629 ultrasound or ultrasonograph\$ or TNS or TENS or shockwave or electrotherap\$ or
630 mobili\$). mp.
- 631 14. or/9-13
- 632 15. clinical trial.pt
- 633 16. random\$.mp.
- 634 17. ((single or double) adj (blind\$ or mask\$)).mp.
- 635 18. placebo\$.mp.
- 636 19. or/16-18
- 637 20. 7 and 14 and 19

638 Search strategy for EMBASE (Ovid):

- 639 1. 'shoulder pain'/exp
- 640 2. 'shoulder impingement syndrome'/exp
- 641 3. 'rotator cuff'/exp

- 1
2
3 642 4. 'bursitis'/exp
4 643 5. ((shoulder* OR rotator*) AND('bursitis'/de OR impinge* OR 'tendonitis'/de OR
5 644 'tendinitis'/de OR 'tendinopathy'/ de OR pain*))
6 645 6. 'rotator cuff'
7 646 7. #1 OR #2 OR #3 OR #4 OR #5 OR #6
8 647 8. 'rehabilitation'/exp
9 648 9. 'physiotherapy'/exp
10 649 10. 'kinesiotherapy'/exp
11 650 11. 'endoscopic echography'/exp
12 651 12. rehabilitat* OR physiotherapy* OR 'physical therapy'OR 'manual therapy'OR
13 652 kinesiotherap* OR exercis*
14 653 13. 'ultrasound'/de OR ultrasonograph* OR 'transcutaneous nerve stimulation' OR
15 654 'transcutaneous electricalnerve stimulation' OR shockwave OR electrotherap*OR mobili*
16 655 14. #9 OR #10 OR #11 OR #12 OR #13 OR #13
17 656 15. 'randomized controlled trial'/exp
18 657 16. #7 AND #14 AND #15

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22 **Search strategy for CINAHL Plus (EBSCO):**

- 23 659 • S1 MH "shoulder pain"
24 660 • S2 MH "shoulder impingement syndrome"
25 661 • S3 MH "rotator cuff"
26 662 • S4 MH bursitis+
27 663 • S5 TX (shoulder* N5 bursitis) or TX(shoulder* N5 impinge*) or TX(shoulder* N5
28 664 tend?nitis) or TX(shoulder* N5 tendinopathy) or TX(shoulder* N5 pain*)
29 665 • S6 TX (rotator cuff N5 bursitis) or TX(rotator cuff N5 impinge*) or TX(rotator cuff N5
30 666 tend? nitis) or TX(rotator cuff N5 tendinopathy) or TX(rotator cuff N5 pain*)
31 667 • S7 TX rotator cuff
32 668 • S8 S1 or S2 or S3 or S4 or S5 or S6 or S7
33 669 • S9 MH Rehabilitation+
34 670 • S10 MH physical therapy+
35 671 • S11 MH Manual Therapy+
36 672 • S12 MH Therapeutic Exercise+
37 673 • S13 MH Ultrasonography+
38 674 • S14 TX rehabilitat* or physiotherapy* or physical therap*or manual therap* or exercise*
39 675 or ultrasound or ultrasonograph* or TNS or TENS or shockwave or electrotherapy*or
40 676 mobili*
41 677 • S15 S10 or S11 or S12 or S13 or S14 or S15
42 678 • S16 PT clinical trial
43 679 • S17 TX random*
44 680 • S18 TX(single blind*) or TX(single mask*)
45 681 • S19 TX(double blind*) or TX(double mask*)
46 682 • S20 placebo*
47 683 • S21 S17 or S18 or S19 or S20 or S21
48 684 • S22 S8 and S15 and S21
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Appendix 2

686 **Email correspondence from Markus Walther clarifying if there was progression of**
687 **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

693

694

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

697 Hi Peter,

698 Sounds like an interesting project.

699 No the resistance band wasn't changed in each exercise ... the program itself was progressive
700 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.

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

704 the therapist handbook

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

706 Regards,

707 Kim

708

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

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3 717**Appendix 3**4
5 718 **Included Studies**

- 6
7 719 1. Brox JI, Staff PH, Ljunggren AE, et al. Arthroscopic surgery compared with
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