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1      **The efficacy of higher versus lower dose exercise in rotator cuff tendinopathy: A**  
2                            **systematic review of randomised controlled trials**

3

4                            Running head: Exercise dose and rotator cuff tendinopathy

5

6

7 **Abstract**

8 **Objective:** to compare the effectiveness and harms of higher exercise dose, including higher  
9 exercise load and/or higher volume, with lower exercise dose (lower load and/or lower  
10 volume) in people with rotator cuff tendinopathy

11 **Design:** Systematic review (PROSPERO: CRD42017077478)

12 **Data sources:** CENTRAL, MEDLINE, EMBASE, CINAHL from inception to March 2019.

13 **Study selection:** Randomised controlled trials comparing higher versus lower dose exercise  
14 that investigated function and pain (overall, activity, night) and adverse event outcomes were  
15 independently determined by two reviewers.

16 **Data extraction and risk of bias:** Two authors independently extracted data and assessed  
17 risk of bias using the Cochrane tool. The primary endpoint was >six weeks to three months  
18 (other endpoints included up to six weeks & beyond three months) and GRADE was used to  
19 assess evidence certainty.

20 **Data synthesis:** Three trials (N=283), none at low risk of bias for all domains, were included.  
21 Low certainty evidence (1 trial, N=102) indicated improved function (20 points [95% CI 12  
22 to 28 points] on 0-100 point scale) with higher load and volume exercise at three months, but  
23 little or no clinically important between-group difference in activity or night pain (overall  
24 pain not reported). Very low certainty evidence (1 trial, N=120) indicated higher load  
25 exercise conferred no function benefits over lower load exercise at six weeks. Very low  
26 certainty evidence (1 trial, N=61) indicated benefit of uncertain clinical importance in  
27 function with higher versus lower volume exercise at three months and clinically important  
28 benefit at >3 months (pain outcomes not reported). Risk of adverse events was uncertain.

29 **Conclusions:** There are few studies that investigate higher dose exercise for rotator cuff  
30 tendinopathy. There was low to very low certainty and conflicting evidence about the value  
31 of higher exercise dose in people with rotator cuff tendinopathy.

32 **Key Words:** Rotator cuff tendinopathy, dose-response, exercise

33

### 34 **Introduction**

35 Shoulder pain is estimated to have a prevalence between 15 to 30% in the general population,  
36 with prevalence increasing with age [1]. Rotator cuff tendinopathy is the most common  
37 cause, accounting for up to 80% of all cases of shoulder pain in primary care [2]. While often  
38 self-limiting, up to 50% of patients who present for care may continue to experience ongoing  
39 pain and disability beyond 12 months [2]. This results in significant morbidity and health  
40 resource utilisation given shoulder function is essential to personal hygiene, dressing and  
41 work [2].

42

43 Clinical guidelines recommend clinician-prescribed exercise for rotator cuff tendinopathy[3,  
44 4]. However, there are conflicting data about its benefits [5-7]. An updated Cochrane review  
45 synthesised exercise and manual therapy evidence for rotator cuff tendinopathy from 60 trials  
46 (3,620 participants) up until 2015. The authors reported high quality evidence from a single  
47 trial (120 participants) [8] indicating that manual therapy and exercise provided no patient-  
48 reported benefits in pain and function outcomes over placebo at 22 weeks follow-up.

49 However, the exercise component was not loaded progressively so could be defined as lower  
50 load [6]. This lack of benefit in pain and function outcomes was supported by very low

51 quality evidence from two trials (89 participants) that compared manual therapy and exercise  
52 to no treatment although only one trial progressed exercise load in the active group [9, 10].

53 By contrast low quality evidence from one trial of exercise versus placebo (80 participants in  
54 these treatment groups) that did progress load in the exercise group reported pain and  
55 function outcome benefit favouring the exercise group for overall pain and function but not  
56 activity pain or night pain [11].

57

58 While the overall body of evidence indicates a lack of consensus regarding the benefit of  
59 exercise for rotator cuff tendinopathy, previous systematic reviews have not generally  
60 considered whether exercise dose parameters such as load progression and repetitions  
61 influence outcomes. Higher load may be more beneficial for neuromuscular adaptation and  
62 higher volume might develop greater muscular endurance [12, 13]. Greater neuromuscular  
63 adaptation and muscular endurance could improve function and improve shoulder symptoms  
64 [14]. In a systematic review of prescription parameters reported in randomised controlled  
65 trials (RCTs) of exercise interventions for rotator cuff tendinopathy, trials that progressively  
66 loaded exercise were more likely to report improvements in shoulder function compared with  
67 trials where exercise was not progressively loaded [15]. However, it is unclear if these  
68 improvements are clinically important or if these findings are robust in view of potential  
69 biases in the included studies. Further exploration of the relationship between exercise dose  
70 and outcomes in rotator cuff tendinopathy therefore appears warranted.

71

72 The aim of this systematic review was to compare the effectiveness and harms of higher  
73 exercise dose, including higher exercise load and/or higher volume, with lower exercise dose  
74 (lower load and/or lower volume) in people with rotator cuff tendinopathy.

75

## 76 **Methods**

### 77 **Criteria for considering studies for this review**

78 We adopted similar methods to the updated Cochrane review of manual therapy and exercise  
79 interventions for rotator cuff tendinopathy [6]. Our review was conducted in accordance with  
80 the PRISMA statement guidelines (Preferred Reporting Items for Systematic reviews and  
81 Meta-Analyses) [16] and was registered with the International Prospective Register of  
82 Systematic Reviews (PROSPERO; reference CRD42017077478).

83

84 *Types of studies*

85 We included RCTs of any design (e.g. parallel, factorial, cross-over) and controlled trials  
86 using a quasi-randomised method of allocation. There were no restrictions based on  
87 language.

88

89 *Types of participants*

90 We included trials that recruited participants aged 16 years and over with a primary  
91 complaint (any duration) of shoulder pain (with or without referral into the arm) labelled  
92 and/or diagnosed as rotator cuff tendinopathy by any means. Rotator cuff tendinopathy has  
93 many synonyms in the literature including rotator cuff disease, rotator cuff related pain,  
94 subacromial impingement syndrome, rotator cuff tendinitis, supraspinatus, infraspinatus or  
95 subscapularis tendonitis or tendinopathy, subacromial bursitis and rotator cuff tears. Trials  
96 using these synonyms were included as were trials where participants had unspecified  
97 shoulder pain provided that the inclusion/exclusion criteria were compatible with a diagnosis  
98 of rotator cuff disease (i.e. anterolateral shoulder pain that is made worse by active and  
99 resisted shoulder elevation and associated with preserved passive range of motion [4]). We  
100 included trials with participants with multiple shoulder disorders, if data were presented  
101 separately for our population of interest.

102

103 Trials were excluded if they included participants with a full thickness tear involving more  
104 than one rotator cuff tendon (based on presentation or imaging findings), gross shoulder  
105 instability, significant shoulder trauma, previous shoulder surgery, shoulder osteoarthritis,  
106 patients with hemiplegia affecting the shoulder, a complex myofascial neck/shoulder/arm

107 pain condition, suspected cervical spine referred pain, or a systemic inflammatory condition  
108 (e.g. rheumatoid arthritis).

109

### 110 *Types of interventions*

111 We included trials that utilised exercise designed to load the shoulder joint, this could include  
112 any active movement in any shoulder plane. Passive movements and pendular movements  
113 (also classified as passive [e.g. [17]]) were excluded. Trials were included if they compared  
114 higher versus lower dose exercise as defined in the trials. Higher dose could include heavier  
115 load (using external weight or resistance) or greater volume (repetitions x sets x frequency).  
116 The volume was defined as a total of all sessions they performed, including supervised and/or  
117 home-based exercise. There was no minimum dose (volume or load) because diverse exercise  
118 interventions can lead to neuromuscular adaptations [12, 13]. Trials needed to explicitly state  
119 the load or volume, or both, in each group so there was certainty that these dose parameters  
120 varied. The comparator group needed to be the same setting (e.g. home-based, supervised, or  
121 a combination) and type of exercise (e.g. isometric, isotonic, eccentric) so dose was the  
122 primary variable being investigated. Trials that also progressed other exercise parameters  
123 such as the range of motion or the type of exercise (static to dynamic) were included if these  
124 were identical in both treatment groups. Co-interventions, including mobilisation,  
125 manipulation and massage modalities, glucocorticoid injections and analgesia were allowed  
126 even if they were not applied equally to groups.

127

### 128 *Types of outcome measures*

129 For effectiveness we included patient-reported shoulder function, and the following pain  
130 outcomes (as per the Page et al review [6]): overall shoulder pain, activity and night pain in  
131 the shoulder. When data for more than one function scale was reported within a trial, we

132 extracted data from the function scale highest on the shoulder function scale hierarchy  
133 reported by Page et al [6]:

- 134 • Shoulder Pain and Disability Index (SPADI) [18]. Scored on a 0 to 100-point scale,  
135 where 0 best;
- 136 • Croft Shoulder Disability Questionnaire [19] Scored on a 0 to 22-point scale, where 0  
137 is best;
- 138 • Constant-Murley Score [20] Scored on a 0 to 100-point scale, where 100 is best;
- 139 • any other shoulder-specific function scale.

140

141 Overall pain, pain with activity and night pain could be measured on a visual analogue scale  
142 (VAS), numerical or categorical rating scale. For harms we included the proportion of  
143 participants experiencing adverse events.

144

145 Outcome times were selected to identify short (up to 6 weeks), medium (>six and up to three  
146 months) and longer-term (>three months) effects of the exercise interventions. The longest  
147 timepoint was extracted where multiple timepoints were reported within a given range. We  
148 chose >six weeks and up to three months as the primary endpoint given this is enough time  
149 for exercise to lead to greater muscle volume and strength, and potentially, better function  
150 [12].

151

## 152 **Data sources and search**

153 Relevant trials published up to March 2015 were identified from the updated Cochrane  
154 review of manual therapy exercise interventions for rotator cuff tendinopathy [6]. Given we  
155 focused on exercise for rotator cuff tendinopathy, the search strategy from the Page et al. [6]  
156 was modified to exclude terms related to adhesive capsulitis as well as non-exercise



157 interventions. For more recent papers we repeated the search in the Cochrane Central  
158 Register of Controlled Trials (CENTRAL; *The Cochrane Library March 2019*, Issue 3), Ovid  
159 MEDLINE (March 2015 to March 2019), Ovid EMBASE (March 2015 to March 2019), and  
160 CINAHL Plus (EBSCO, March 2015 to March 2019).

161

162 The updated search strategies for all databases are shown in Supplementary appendix 1. We  
163 also searched gray literature via OpenGray and ongoing trials via the National Institute of  
164 Health (clinicaltrials.gov) and the World Health Organisation (<http://www.who.int/ictrp>)  
165 International Clinical Trials Registries, using the terms ‘rotator cuff disease’ [condition] and  
166 ‘exercise’ [intervention] up to March 2019.

167

#### 168 **Selection of studies**

169 Two authors (PM, GS) independently screened titles and abstracts for potentially eligible  
170 trials, based on a predetermined checklist of inclusion criteria. The full text of potentially  
171 eligible trials was retrieved and independently assessed by the same two authors to determine  
172 eligibility. Any discrepancies were resolved via discussion, or by consulting a third author  
173 where necessary (CL).

174

#### 175 **Data extraction**

176 Two authors (PM, GS) independently extracted data onto a standard data extraction form.  
177 Discrepancies were resolved through discussion until consensus was reached, otherwise a  
178 third author (RB) was consulted to adjudicate.

179

180 The following data were extracted from each study:

- 181 • Trial characteristics (sample size, first author name, year of publication, type of trial  
182 [e.g. parallel, crossover], country, source of funding, trial registration status  
183 [registration number if reported]).
- 184 • Participant characteristics (inclusion and exclusion criteria, age, gender, duration of  
185 symptoms,).
- 186 • Intervention including exercise characteristics (exercises performed, sets, repetitions,  
187 frequency, duration, how exercise was loaded, how exercise was progressed and how  
188 often, adherence measures, advice about pain during exercise)
- 189 • Comparator intervention exercise characteristics
- 190 • Co-interventions in each group, if any
- 191 • Outcomes reported, including the measurement instrument used and timing of  
192 outcome assessment.

193

194 To minimise potential bias, we used the following a priori decision rules for selecting  
195 outcome data:

- 196 • Preference was given to data that were adjusted for baseline values (e.g. ANCOVA) if  
197 available and intention-to-treat.
- 198 • Where follow-up and change scores were reported for the same outcome, we planned  
199 to extract follow up scores.
- 200 • For cross-over RCTs, we planned to only extract data for the first period.

201

## 202 **Risk of bias assessment**

203 Risk of bias for each study was performed using the Cochrane Collaboration's tool for  
204 assessing risk of bias, described fully in the Cochrane Handbook for Systematic Reviews of  
205 Interventions [21]. Risk of bias was performed independently by two of three authors (PM,

206 GS or RJ) and discrepancies were resolved through discussion until consensus was reached,  
207 otherwise a third author (RB) was consulted to adjudicate.

208

209 The following domains were rated as high risk of bias if they were not performed adequately,  
210 unclear risk of bias if it was not clearly reported or low risk of bias if performed adequately:  
211 random sequence generation, allocation concealment, blinding of participants and personnel,  
212 blinding of outcome assessment, incomplete outcome data, outcome reporting bias, and other  
213 sources of bias (i.e. baseline imbalance, unequal application of co-interventions across  
214 treatment groups). All domains had to achieve a low risk of bias rating for the study to be  
215 classified as being at low overall risk of bias.

216

#### 217 **Measures of treatment effect**

218 Review Manager (RevMan) 5.3 was used to calculate measures of treatment effect. Adverse  
219 events were expressed as relative risk (RR) and 95% confidence intervals. Mean pain was  
220 expressed as mean difference (MD) and 95% confidence intervals on a 0 to 100-point VAS  
221 scale, with a higher score indicating more pain. Mean function was also expressed as MD and  
222 95% confidence intervals with a lower score indicating less disability or better function. So  
223 that zero was best function in all scales, we reversed scores for scales such as the Constant-  
224 Murley score and Shoulder Rating Questionnaire (SRQ) where a higher score indicates less  
225 disability or better function. For the SRQ we also transformed scores from a scale of 17 to 90  
226 to 0 to 100 scale [22]. We assumed a minimal clinically important difference of 10 on a 100-  
227 point scale for function and 15 points on a 100-point scale for pain [6]. A clinically important  
228 difference was defined as a confidence interval where even the lower band (closest to null)  
229 was greater than 10 (for function) or 15 points (for pain).

230

231 Study authors were contacted (twice over four weeks) via email in any instances of missing  
232 data. If the data were not retrieved from the study authors, we planned to calculate standard  
233 deviation (SD) from the standard errors (SE), 95% CIs or P values, or use median and the  
234 Inter-quartile range (IQR) to approximate the mean and SD (SD=width of IQR/35),  
235 respectively.

236

### 237 **Data synthesis**

238 Meta-analysis was planned to pool results of trials with similar characteristics (e.g.  
239 participants, interventions, outcomes), however there was insufficient data to undertake data  
240 pooling.

241

### 242 **Summary of findings**

243 We created summary of findings tables [23] for a priori comparisons that included outcomes  
244 at the primary endpoint of >six weeks to three months. We rated the overall grading of the  
245 certainty of the evidence based on the GRADE approach (Grades of Recommendation,  
246 Assessment, Development and Evaluation Working Group) [24]. From an initial starting  
247 point of high certainty evidence, the level of evidence was downgraded (to moderate, low or  
248 very low) for each of the following: risk of bias, inconsistency of results, indirectness,  
249 imprecision, and publication bias.

250

251 For dichotomous outcomes (e.g. adverse events), we planned to calculate absolute risk  
252 difference expressed as a percentage and relative percent change (the risk ratio – 1) expressed  
253 as a percentage. For continuous outcomes (e.g. function), we planned to calculate absolute  
254 change which is the difference in mean of higher and lower load groups at follow-up  
255 standardised to the original units and expressed as a percentage. The relative percent change

256 was also calculated as the mean difference between groups at follow-up divided by the mean  
257 of the lower load group at baseline, expressed as a percentage.

258

## 259 **Results**

### 260 **Study selection**

261 Two eligible trials were identified from the Page et al. [6] systematic review [14, 25]. An  
262 additional 915 records (730 unique studies) were identified from the updated search  
263 conducted from 2015 to 9 March 2019. Of these, we assessed 12 in full text and identified  
264 one additional trial for inclusion [26] (Figure 1). Two trials were registered in trial registries  
265 [14, 26], (Table 1) but none published their protocol.

266

267 We excluded eleven trials after full text assessment for the following reasons: four compared  
268 different types of exercise as opposed to dose [27-30], one compared home versus group  
269 supervised group exercise [31], one compared pendular exercise with and without load [32],  
270 one compared painful vs painfree exercise [33], one compared home versus individual  
271 supervised exercise [34], one used the uninvolved asymptomatic shoulder as a control [35],  
272 one study compared the effect of the sequence in which exercises were performed [36] and  
273 one study included high dose exercise in both treatment arms (higher load and lower volume  
274 exercise versus lower load and higher volume exercise) [37], meaning it could not contribute  
275 to an understanding of the role of high versus low dose of exercise.

276

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

279

280 **Trial, participant and intervention characteristics**

281 The three included trials were all parallel group RCTs and included 283 participants [14, 25,  
282 26]. All trials had similar inclusion criteria (see Supplementary appendix 2). The trial,  
283 participant and intervention characteristics of the included trials are shown in table 1. Mean  
284 age varied between 46 and 55 years (slight male dominance) and symptom duration between  
285 three months and four years. Mean baseline function scores varied between 49 to 63 out of  
286 100 (lower score indicates better function).

287

288 One trial compared 12 weeks of either higher load and higher volume exercise or lower load  
289 and lower volume exercise [14]; one trial compared higher versus lower load exercise over  
290 six weeks [26]; and one trial compared 12 weeks of either higher or lower volume exercise  
291 [25]. With regards to the comparators, two trials simply utilised active shoulder movements  
292 without additional load that can be considered subtherapeutic [14, 26]. In contrast, the  
293 comparator in Osteras et al [25] still contained progressive load exercise but of lower volume.  
294 No trials reported the actual load during exercise or exercise intensity. Exercise intensity (e.g.  
295 >70% 1 repetition maximum) was not reported in any trial [12]. Repetitions per week were  
296 higher in the 'higher volume' (2160 to 3150) compared with the 'lower volume' comparators  
297 (300 to 420) [14, 25].

298

299 One trial supervised all exercise sessions [25] while the other two trials included home  
300 exercise. Pain during exercise was permitted in all intervention and comparator groups, aside  
301 from the Holmgren et al. [14] trial where this detail was not described for the comparator  
302 group. All trials included active non-weightbearing exercises in anatomical planes (e.g.  
303 flexion, abduction, external rotation). All trial participants received a glucocorticoid injection  
304 at baseline in one trial [14]. This trial also provided manual therapy 'when necessary' to  
305 participants in only the higher load and volume exercise group.

306

307 All three trials assessed function with one trial measuring function using two instruments  
308 [14]. One trial used the SPADI [26], one used the Constant-Murley Score [14] and one used  
309 the SRQ [25]. Holmgren et al. [14] also used the Disability of the Arm and Shoulder Score  
310 (DASH) but we extracted data from the Constant-Murley Score. No trial reported overall  
311 pain, and Heron et al. [26] did not report pain at all. One trial reported activity pain [14] and  
312 one trial reported night pain [14]. Two trials also reported pain at rest (or inactivity) [14, 25]  
313 but as this was not a pre-specified outcome, we did not extract data for this outcome. Only  
314 two trials reported outcomes at our primary endpoint of >6 weeks to three months (both at  
315 three months) [14, 25]. Østeras et al. [25] also reported outcomes at nine and 15 months and  
316 data were extracted at 15 months for the >three months endpoint. Although Holmgren et al.  
317 [14] reported results at 12 months participants were offered surgery after the three-month  
318 assessment and data were reported sub-grouped by whether or not participants underwent  
319 surgery. Therefore the 12-month data were not extracted for this review. One trial only  
320 reported outcomes at 6 weeks [26].

321

## 322 **Table 1: Study, participant and exercise characteristics**

323

### 324 **Risk of bias in included trials**

325 The risk of bias for each of the included trials is summarised in Figure 2. One trial was rated  
326 at low risk of bias for all domains other than performance bias, which was rated as uncertain  
327 [14]. Of note, this trial was rated at low risk of bias for all domains in the Page et al.  
328 Cochrane review [6]. While participants and the outcome assessor were blinded, the trial did  
329 not report whether the exercise explanations and verbal interaction (of potential effect and  
330 mechanisms) were identical between groups. Two of the remaining trials were susceptible to

331 performance [25, 26] and one trial was at risk of detection biases [25] due to lack of blinding  
332 of either participants or investigators; one trial was also at risk of attrition bias due to  
333 differences in the proportion of drop outs between groups [26]; and two trials were at risk of  
334 selective reporting [25, 26] because they reported one self-reported outcome measure and  
335 there were no associated trial protocols so it is unclear whether all outcomes were reported.

336

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

339

340 **Comparison 1: higher load and higher volume versus lower load and lower volume**

341 There may be clinically important improvement in function with higher load and higher  
342 volume exercise at three months (Figures 3 & 4). Function was 47.5 points in the lower dose  
343 group and this improvement was 20 points better (95% CI 12 to 28) in the high dose group.  
344 There was little or no clinically important benefit of higher dose exercise for pain outcomes  
345 at > 6 weeks to three months. Activity pain was 41 points with low dose exercise and 16.0  
346 (95% CI 5.4 to 26.6) points better with high dose. Similarly, night pain was 27 points with  
347 low dose exercise and 12.0 points better (95% CI 2.1 to 21.9) with high dose. Overall pain  
348 and adverse events were not reported. This evidence arose from a single trial (97 participants  
349 for all reported outcomes) [14] and was low certainty (downgraded for bias and imprecision).

350

351 **Figure 3: Effects of higher load and higher volume versus lower load and lower volume**  
352 **exercise**

353 **Figure 4: Summary of findings for the comparison of higher load and higher volume**  
354 **versus lower load and lower volume**

355



356 **Comparison 2: higher load versus lower load**

357 Given outcomes were not reported at the primary endpoint for this comparison no summary  
358 of findings table was produced. There was no benefit with higher compared with lower load  
359 exercise for function at six weeks (Figure 5). Function was 42 points in the lower load group  
360 and this improvement was 5 points better in the higher load group (95% CI 15.9 better to 5.9  
361 worse). Overall, activity or night pain and adverse events outcomes were not reported. This  
362 evidence was from a single trial (61 participants for function outcome) and was low certainty  
363 (downgraded for risk of bias and imprecision due to the very short follow-up time). Note that  
364 only two ('open chain' and 'range of movement') of the three trial arms were eligible and  
365 included in this review.

366

367 **Figure 5: Effects of higher vs lower load exercise**

368

369 **Comparison 3: higher volume versus lower volume**

370 There was benefit of uncertain clinical importance with higher volume exercise in function at  
371 three months (Figures 6 & 7). Function was 45.4 points in the lower volume group and 12.9  
372 points better (95% CI 7.6 to 18.1 points better) in the higher volume group. There was  
373 clinically important benefit at >three months; function was 43.1 points in the lower volume  
374 group and 17.8 points better in the higher volume group (95% CI 11.8 to 23.8 points better).  
375 Overall, activity or night pain were not reported. There was no reliable estimate of the  
376 adverse event rates. One participant in the higher volume group was reported to sustain a  
377 neck injury (no adverse events reported for the lower volume group). This evidence arose  
378 from one trial (56 participants for all reported outcomes) and was very low certainty  
379 (downgraded for risk of bias and imprecision).

380

381 **Figure 6: Effects of higher vs lower volume exercise**

382 **Figure 7: Summary of findings for the comparison of higher volume versus lower**  
383 **volume**

384

## 385 **Discussion**

386 We found low to very low certainty and somewhat conflicting evidence about the value of  
387 higher exercise dose in people with rotator cuff tendinopathy. There was low certainty  
388 evidence from a single trial suggesting that higher load and higher volume exercise may  
389 result in a clinically important benefit in function but not activity or night pain at >six weeks  
390 to three months. There was also very low certainty evidence from another small single trial  
391 indicating that higher volume exercise might provide benefit of uncertain clinical importance  
392 for function at >six weeks to three months compared with lower volume exercise, although  
393 no data for pain were collected. Very low certainty evidence from one trial indicated that  
394 higher load exercise does not provide clinically important benefit over lower load exercise  
395 with respect to function up to six weeks. We are uncertain if there is an increased risk of  
396 adverse events with higher dose exercise, given the incomplete reporting of events and the  
397 low event rates. The evidence was downgraded for a variety of reasons including risk of  
398 performance and detection bias, imprecision and indirectness due to short follow-up times.

399

400 The exercise programs examined in the three included trials generally reflected the  
401 interventions that are delivered in practice and in the rotator cuff tendinopathy literature [6].  
402 Load was progressed when the exercise could be performed easily or with a defined pain  
403 response. None of the studies reported the specific intensity (e.g. repetition maximum) or  
404 absolute load. In contrast, trials that evaluated the effect of volume utilised fixed rather than  
405 progressive volumes and these were at least five times greater in the high volume (2160 to

406 3150 repetitions per week) versus the lower volume (300 to 420 repetitions per week) trial  
407 arms. Importantly, comparisons were unloaded active movements in two studies [14, 26] but  
408 still contained progressive load with lower volume [25] in one study. Given the poorly  
409 reported and heterogeneous interventions we cannot make any specific comments about the  
410 level of load (or intensity) and volume that may confer greater benefit. Final follow-up for  
411 the trial included in the higher load versus lower load exercise comparison was between four  
412 to six weeks which may not be enough time to demonstrate a beneficial effect of higher load  
413 exercise if one is present. Littlewood et al. [15] reported that maintenance of an exercise  
414 program for at least 12 weeks may be needed to demonstrate improvements in function.

415

416 Adequate description of comparative load and volumes were part of our inclusion criteria. It  
417 was common across studies for other exercise parameters to be incompletely described,  
418 including pain during loading, exercise adherence, rest between exercise sets and exercise  
419 tempo (see Table 1). This limitation is important because clinicians are unable to implement  
420 incompletely described exercise interventions. Further, given adherence was poorly  
421 described, it is impossible to be certain of the dose in each comparator group, and therefore  
422 whether exercise dose or other mechanisms influenced outcome. For example, giving a  
423 patient permission to perform progressively loaded exercise, or do more exercise, may reduce  
424 fear, increase general shoulder use, and thereby improve outcome. Future exercise trials  
425 should consider reporting guidelines such as the Consensus on Exercise Reporting Template  
426 (CERT) [38] to ensure findings are translatable to practice.

427

### 428 **Comparison to the literature**

429 Littlewood et al (2015) reported superior function outcomes with resisted and greater volume  
430 (repetitions and sets) [15], but this was based on a narrative synthesis. Fourteen studies were

431 included in the Littlewood review, and only one of these studies specifically examined the  
432 effect of exercise dose and was also included in the current review [25]. Our systematic  
433 review investigated the effect of higher exercise dose (load and/or volume) on function and  
434 pain outcomes in rotator cuff tendinopathy. While our review suggested that higher load and  
435 higher volume exercise or higher volume exercise might confer superior functional outcomes  
436 compared to their lower dose comparisons, we did not find that higher load exercise was  
437 better than lower load exercise. However, if an exercise program needs to be maintained for  
438 at least 12 weeks before any benefit on function is evident as proposed by Littlewood et al.  
439 [15], this may explain the lack of observed benefit in the higher load versus lower load  
440 exercise comparison as exercise intervention and outcome reported extended only four to six  
441 weeks.

442

443 A randomized trial by Ingwersen et al. [37] compared higher load but lower volume with  
444 lower load but higher volume exercise for rotator cuff tendinopathy. This study was not  
445 eligible for the current review but is worthy of discussion. The authors in this study equalized  
446 the work (volume multiplied by intensity) undertaken in each group. This is a worthwhile  
447 approach because it is able to identify whether load or volume is beneficial when accounting  
448 for overall work. In contrast, in the current review we were interested in whether additional  
449 load (and work) or additional volume (and work) or a combination of both were beneficial.  
450 The Ingwersen et al. [37] trial reported meaningful benefit in pain and function in both  
451 groups at 12 weeks with no between groups differences for higher intensity or higher volume  
452 exercise when work is equalized. This suggests that greater work may explain the between  
453 groups differences observed in studies in this review with higher load and volume or higher  
454 volume interventions, but this requires investigation in future trials.

455

456 **Strengths of the systematic review**

457 Our methods were based on a prior Cochrane review of exercise interventions for rotator cuff  
458 tendinopathy and adhered to best practice guidelines as outlined by the Cochrane  
459 collaboration and PRISMA to minimise potential sources of bias. Inclusion and exclusion  
460 criteria were determined a priori and were clearly defined to minimise selection bias.

461

462 **Limitations**

463 The main limitation is that only three trials met our inclusion criteria. We performed a  
464 comprehensive search and did not find any ongoing trials in trial registries, so publication  
465 bias is not likely. A further substantial limitation is diversity between exercise interventions.  
466 Comparators in two of the three trials were unloaded and could be considered subtherapeutic  
467 [14, 26], while the third trial included substantial progressive load in the higher load arm  
468 [25]. This, coupled with the sparse literature, makes it impossible to provide guidance about  
469 specific levels of load (or intensity) or volume that may be beneficial for individuals. A  
470 potential limitation among the included trials that may influence interpretation is  
471 contamination (e.g. lower dose groups receiving higher dose or vice versa) between exercise  
472 interventions.

473

474 **Future research**

475 Only three studies that meet our selection criteria were identified. High quality adequately  
476 powered randomised trials are needed to investigate the value of exercise for rotator cuff  
477 tendinopathy. Future research should seek to determine optimal dose parameters for  
478 improvement in pain and function outcomes among people with rotator cuff tendinopathy.  
479 Future trialists should consider using function as the primary outcome given that the higher  
480 dose interventions in this review seemed to confer less differential benefit between exercise

481 interventions. These trials should adequately describe exercise interventions according to  
482 published guidelines such as the CERT [38] Checklist [39]. Robust monitoring of exercise  
483 fidelity (e.g. appropriately implementing progressive load) and adherence is also required in  
484 order to draw valid conclusions about the effect of dose on outcomes.

485

#### 486 **Implications for practice**

487 Despite conflicting data, clinical guidelines continue to recommend clinician-prescribed  
488 exercise for rotator cuff tendinopathy. Based upon the currently available low to very low  
489 certainty evidence, exercise that progressively increases load and utilises greater volume may  
490 confer superior function outcomes compared with lower dose exercise regimens, although the  
491 certainty of these findings need to be confirmed in high quality trials. Clinicians should  
492 explain to patients that it is unclear whether exercise improves pain, while exercise may need  
493 to be maintained for at least 12 weeks before benefits in function become evident.

494

#### 495 **Conclusions:**

496 There are few studies that investigate higher dose exercise for rotator cuff tendinopathy.  
497 There was low to very low certainty and conflicting evidence about the value of higher  
498 exercise dose in people with rotator cuff tendinopathy.

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503 List of Figures and Tables

504

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

507

508 Figure 2: Risk of bias summary: judgements about each risk of bias item for each included  
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510

511 Figure 3: Effects of higher load and higher volume versus lower load and lower volume

512

513 Figure 4: Summary of findings for the comparison of higher load and higher volume versus  
514 lower load and lower volume

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520 Table 7: Summary of findings for the comparison of higher volume versus lower volume

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522 Table 1: Study, participant and intervention characteristics

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