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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

**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.

Data synthesis: Three trials (N=283), none at low risk of bias for all domains, were included. 20 21 Low certainty evidence (1 trial, N=102) indicated improved function (20 points [95% CI 12 to 28 points] on 0-100 point scale) with higher load and volume exercise at three months, but 22 little or no clinically important between-group difference in activity or night pain (overall 23 pain not reported). Very low certainty evidence (1 trial, N=120) indicated higher load 24 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 function with higher versus lower volume exercise at three months and clinically important 27 benefit at >3 months (pain outcomes not reported). Risk of adverse events was uncertain. 28 29 Conclusions: There are few studies that investigate higher dose exercise for rotator cuff tendinopathy. There was low to very low certainty and conflicting evidence about the value 30 31 of higher exercise dose in people with rotator cuff tendinopathy.

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

33

## 34 Introduction

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

42

Clinical guidelines recommend clinician-prescribed exercise for rotator cuff tendinopathy[3, 43 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 patientreported benefits in pain and function outcomes over placebo at 22 weeks follow-up. 48 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 quality evidence from two trials (89 participants) that compared manual therapy and exercise 51 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 these treatment groups) that did progress load in the exercise group reported pain and 54 function outcome benefit favouring the exercise group for overall pain and function but not 55 56 activity pain or night pain [11].

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 considered whether exercise dose parameters such as load progression and repetitions 60 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 adaptation and muscular endurance could improve function and improve shoulder symptoms 63 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 trials where exercise was not progressively loaded [15]. However, it is unclear if these 67 improvements are clinically important or if these findings are robust in view of potential 68 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

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

75

### 76 Methods

### 77 Criteria for considering studies for this review

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

83

# 84 *Types of studies*

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

88

89 *Types of participants* 

We included trials that recruited participants aged 16 years and over with a primary 90 91 complaint (any duration) of shoulder pain (with or without referral into the arm) labelled and/or diagnosed as rotator cuff tendinopathy by any means. Rotator cuff tendinopathy has 92 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 using these synonyms were included as were trials where participants had unspecified 96 97 shoulder pain provided that the inclusion/exclusion criteria were compatible with a diagnosis of rotator cuff disease (i.e. anterolateral shoulder pain that is made worse by active and 98 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

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

pain condition, suspected cervical spine referred pain, or a systemic inflammatory condition(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 any active movement in any shoulder plane. Passive movements and pendular movements 112 113 (also classified as passive [e.g. [17]]) were excluded. Trials were included if they compared higher versus lower dose exercise as defined in the trials. Higher dose could include heavier 114 115 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 home-based exercise. There was no minimum dose (volume or load) because diverse exercise 117 118 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 primary variable being investigated. Trials that also progressed other exercise parameters 122 such as the range of motion or the type of exercise (static to dynamic) were included if these 123 were identical in both treatment groups. Co-interventions, including mobilisation, 124 125 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* 

For effectiveness we included patient-reported shoulder function, and the following pain
outcomes (as per the Page et al review [6]): overall shoulder pain, activity and night pain in
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		

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

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

167

## 168 Selection of studies

169 Two authors (PM, GS) independently screened titles and abstracts for potentially eligible

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

eligibility. Any discrepancies were resolved via discussion, or by consulting a third author

173 where necessary (CL).

174

## **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

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	٠	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	outcor	ne 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,		

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

208

The following domains were rated as high risk of bias if they were not performed adequately, unclear risk of bias if it was not clearly reported or low risk of bias if performed adequately: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, outcome reporting bias, and other sources of bias (i.e. baseline imbalance, unequal application of co-interventions across treatment groups). All domains had to achieve a low risk of bias rating for the study to be 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 scale, with a higher score indicating more pain. Mean function was also expressed as MD and 221 222 95% confidence intervals with a lower score indicating less disability or better function. So that zero was best function in all scales, we reversed scores for scales such as the Constant-223 224 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 to 0 to 100 scale [22]. We assumed a minimal clinically important difference of 10 on a 100-226 point scale for function and 15 points on a 100-point scale for pain [6]. A clinically important 227 difference was defined as a confidence interval where even the lower band (closest to null) 228 was greater than 10 (for function) or 15 points (for pain). 229

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 deviation (SD) from the standard errors (SE), 95% CIs or P values, or use median and the 233 234 Inter-quartile range (IQR) to approximate the mean and SD (SD=width of IQR/35), 235 respectively. 236 237 **Data synthesis** Meta-analysis was planned to pool results of trials with similar characteristics (e.g. 238 239 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 at the primary endpoint of >six weeks to three months. We rated the overall grading of the 244 245 certainty of the evidence based on the GRADE approach (Grades of Recommendation, Assessment, Development and Evaluation Working Group) [24]. From an initial starting 246 247 point of high certainty evidence, the level of evidence was downgraded (to moderate, low or very low) for each of the following: risk of bias, inconsistency of results, indirectness, 248 249 imprecision, and publication bias. 250 251 For dichotomous outcomes (e.g. adverse events), we planned to calculate absolute risk

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

was also calculated as the mean difference between groups at follow-up divided by the meanof 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

additional 915 records (730 unique studies) were identified from the updated search

conducted from 2015 to 9 March 2019. Of these, we assessed 12 in full text and identified

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 supervised exercise [34], one used the uninvolved asymptomatic shoulder as a control [35], 271 272 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

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

279

280 Trial, participant and intervention characteristics

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

287

One trial compared 12 weeks of either higher load and higher volume exercise or lower load 288 289 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 higher in the 'higher volume' (2160 to 3150) compared with the 'lower volume' comparators 296 297 (300 to 420) [14, 25].

298

One trial supervised all exercise sessions [25] while the other two trials included home exercise. Pain during exercise was permitted in all intervention and comparator groups, aside from the Holmgren et al. [14] trial where this detail was not described for the comparator group. All trials included active non-weightbearing exercises in anatomical planes (e.g. flexion, abduction, external rotation). All trial participants received a glucocorticoid injection at baseline in one trial [14]. This trial also provided manual therapy 'when necessary' to 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 [14]. One trial used the SPADI [26], one used the Constant-Murley Score [14] and one used 308 309 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 pain, and Heron et al. [26] did not report pain at all. One trial reported activity pain [14] and 311 312 one trial reported night pain [14]. Two trials also reported pain at rest (or inactivity) [14, 25] but as this was not a pre-specified outcome, we did not extract data for this outcome. Only 313 314 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 data were extracted at 15 months for the >three months endpoint. Although Holmgren et al. 316 317 [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 surgery. Therefore the 12-month data were not extracted for this review. One trial only 319 320 reported outcomes at 6 weeks [26]. 321

- 322 Table 1: Study, participant and exercise characteristics
- 323

## 324 Risk of bias in included trials

The risk of bias for each of the included trials is summarised in Figure 2. One trial was rated at low risk of bias for all domains other than performance bias, which was rated as uncertain [14]. Of note, this trial was rated at low risk of bias for all domains in the Page et al. Cochrane review [6]. While participants and the outcome assessor were blinded, the trial did not report whether the exercise explanations and verbal interaction (of potential effect and mechanisms) were identical between groups. Two of the remaining trials were susceptible to performance [25, 26] and one trial was at risk of detection biases [25] due to lack of blinding
of either participants or investigators; one trial was also at risk of attrition bias due to
differences in the proportion of drop outs between groups [26]; and two trials were at risk of
selective reporting [25, 26] because they reported one self-reported outcome measure and
there were no associated trial protocols so it is unclear whether all outcomes were reported.

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

339

# Comparison 1: higher load and higher volume versus lower load and lower volume 340 341 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. There was little or no clinically important benefit of higher dose exercise for pain outcomes 344 345 at > 6 weeks to three months. Activity pain was 41 points with low dose exercise and 16.0 (95% CI 5.4 to 26.6) points better with high dose. Similarly, night pain was 27 points with 346 low dose exercise and 12.0 points better (95% CI 2.1 to 21.9) with high dose. Overall pain 347 and adverse events were not reported. This evidence arose from a single trial (97 participants 348 349 for all reported outcomes) [14] and was low certainty (downgraded for bias and imprecision). 350 Figure 3: Effects of higher load and higher volume versus lower load and lower volume 351

352 exercise

353 Figure 4: Summary of findings for the comparison of higher load and higher volume

354 versus lower load and lower volume

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

357 Given outcomes were not reported at the primary endpoint for this comparison no summary of findings table was produced. There was no benefit with higher compared with lower load 358 359 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 worse). Overall, activity or night pain and adverse events outcomes were not reported. This 361 evidence was from a single trial (61 participants for function outcome) and was low certainty 362 363 (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 included in this review. 365

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 three months (Figures 6 & 7). Function was 45.4 points in the lower volume group and 12.9 371 points better (95% CI 7.6 to 18.1 points better) in the higher volume group. There was 372 373 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 adverse event rates. One participant in the higher volume group was reported to sustain a 376 neck injury (no adverse events reported for the lower volume group). This evidence arose 377 378 from one trial (56 participants for all reported outcomes) and was very low certainty 379 (downgraded for risk of bias and imprecision).

- **381** Figure 6: Effects of higher vs lower volume exercise
- Figure 7: Summary of findings for the comparison of higher volume versus lowervolume
- 384

### 385 Discussion

We found low to very low certainty and somewhat conflicting evidence about the value of 386 higher exercise dose in people with rotator cuff tendinopathy. There was low certainty 387 evidence from a single trial suggesting that higher load and higher volume exercise may 388 389 result in a clinically important benefit in function but not activity or night pain at >six weeks to three months. There was also very low certainty evidence from another small single trial 390 391 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 higher load exercise does not provide clinically important benefit over lower load exercise 394 395 with respect to function up to six weeks. We are uncertain if there is an increased risk of adverse events with higher dose exercise, given the incomplete reporting of events and the 396 397 low event rates. The evidence was downgraded for a variety of reasons including risk of performance and detection bias, imprecision and indirectness due to short follow-up times. 398 399

The exercise programs examined in the three included trials generally reflected the interventions that are delivered in practice and in the rotator cuff tendinopathy literature [6]. Load was progressed when the exercise could be performed easily or with a defined pain response. None of the studies reported the specific intensity (e.g. repetition maximum) or absolute load. In contrast, trials that evaluated the effect of volume utilised fixed rather than 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 exercise if one is present. Littlewood et al. [15] reported that maintenance of an exercise 413 414 program for at least 12 weeks may be needed to demonstrate improvements in function.

415

Adequate description of comparative load and volumes were part of our inclusion criteria. It 416 417 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 tempo (see Table 1). This limitation is important because clinicians are unable to implement 419 420 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 patient permission to perform progressively loaded exercise, or do more exercise, may reduce 423 424 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 (CERT) [38] to ensure findings are translatable to practice. 426

427

## 428 Comparison to the literature

429 Littlewood et al (2015) reported superior function outcomes with resisted and greater volume430 (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 review investigated the effect of higher exercise dose (load and/or volume) on function and 433 434 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 compared to their lower dose comparisons, we did not find that higher load exercise was 436 437 better than lower load exercise. However, if an exercise program needs to be maintained for at least 12 weeks before any benefit on function is evident as proposed by Littlewood et al. 438 439 [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 lower load but higher volume exercise for rotator cuff tendinopathy. This study was not 444 445 eligible for the current review but is worthy of discussion. The authors in this study equalized the work (volume multiplied by intensity) undertaken in each group. This is a worthwhile 446 447 approach because it is able to identify whether load or volume is beneficial when accounting for overall work. In contrast, in the current review we were interested in whether additional 448 449 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 groups at 12 weeks with no between groups differences for higher intensity or higher volume 451 exercise when work is equalized. This suggests that greater work may explain the between 452 453 groups differences observed in studies in this review with higher load and volume or higher volume interventions, but this requires investigation in future trials. 454

455

#### 456 Strengths of the systematic review

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

461

## 462 Limitations

The main limitation is that only three trials met our inclusion criteria. We performed a 463 464 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. Comparators in two of the three trials were unloaded and could be considered subtherapeutic 466 467 [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 specific levels of load (or intensity) or volume that may be beneficial for individuals. A 469 470 potential limitation among the included trials that may influence interpretation is 471 contamination (e.g. lower does groups receiving higher dose or vice versa) between exercise interventions. 472

473

### 474 Future research

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

interventions. These trials should adequately describe exercise interventions according to
published guidelines such as the CERT [38] Checklist [39]. Robust monitoring of exercise
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.

499

500

501

503	List of Figures and Tables
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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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