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1 **Title: Running Head:** Mental practice for the upper-limb

2 **Title:** A systematic review and meta-analysis of the effectiveness of mental practice
3 for the upper-limb after stroke: Imagined or real benefit?

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25 reference number CRD42019126044).

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34 Word count: 4769

35

36 **A systematic review and meta-analysis of the effectiveness of mental practice**
37 **for the upper-limb after stroke: Imagined or real benefit?**

38

39 **Abstract**

40 **Objective:** This systematic review sought to determine the effectiveness of mental
41 practice (MP) upon the activity limitations of the upper-limb in people after stroke,
42 and when, in whom and how it should be delivered.

43 **Data sources:** Ten electronic databases were searched from November 2009 to
44 May 2020. Search terms included: Arm; Practice; Stroke Rehabilitation; Imagination;
45 Paresis; Recovery of Function; Stroke

46 Studies from a Cochrane review of MP (up to November 2009) were automatically
47 included. The review was registered with Prospero database of systematic reviews
48 (Reference number: CRD42019126044).

49 **Study selection:** Randomised controlled trials of adults after stroke using MP for the
50 upper-limb were included if they compared to usual care, conventional therapy or no
51 treatment and reported activity limitations of the upper-limb as outcomes.
52 Independent screening was carried out by two reviewers.

53 **Data extraction:** One reviewer extracted data using a tool based upon the Template
54 for Intervention Description and Replication. Data extraction was independently
55 verified by a second reviewer. Quality was assessed using the PEDro tool.

56 **Data Synthesis:** Fifteen studies (n=486) were included and 12 (n=328) underwent
57 meta-analysis. MP demonstrated significant benefit upon upper-limb activities
58 compared to usual treatment (standardised mean difference, SMD: 0.6, 95%

59 confidence intervals, CI: 0.32 to 0.88). Sub-group analyses demonstrated that MP
60 appeared most effective in the first 3 months after stroke (SMD: 1.01, 95% CI: 0.53
61 to1.50) and in people with the most severe upper-limb deficits (weighted mean
62 difference, WMD: 7.33; 95% CI:0.94 to 13.72).

63 **Conclusions:** This review demonstrates that MP appears effective in reducing
64 activity limitations of the upper-limb after stroke particularly in people in the first three
65 months after stroke and in those with the most severe upper-limb dysfunction. There
66 was no clear pattern of the ideal dosage of MP.

67 **Word count: Abstract: 286; Manuscript: 4769**

68 **Keywords:** mental practice; imagery; stroke; systematic review; upper limb

69 **List of abbreviations:**

70 Confidence interval, CI

71 Mental Practice, MP

72 Standardised mean difference, SMD

73 Weighted mean difference, WMD

74

75 **A systematic review and meta-analysis of the effectiveness of mental practice**
76 **for the upper-limb after stroke: Imagined or real benefit?**

77

78 Stroke is the single main cause of acquired disability in high income countries.¹
79 Difficulties in using the arm, wrist and hand (the upper-limb) is the most common
80 deficit after stroke, being reported by at least 70% of stroke survivors.² This has a
81 significant impact on daily activities, and has been shown to reduce independence,
82 the likelihood of returning to employment and hobbies, and poorer mental health and
83 quality of life.^{3,4}

84 Mental practice (MP) is one of only a handful of interventions included in evidence
85 based guidelines for the rehabilitation of the upper-limb after stroke.^{5,6} It comprises
86 the repeated practice of motor (or kinaesthetic) imagery.⁷ During MP participants are
87 typically guided to cognitively rehearse, but not physically perform, movements of the
88 upper-limb often to complete a functional task^{8,9} or to consider how one might
89 perform a task (e.g. grip a cup).¹⁰ This can be from a first person perspective
90 (egocentric, through one's own eyes) or a third person perspective (as an observer
91 watching from a distance).¹¹ Mental practice was initially developed in sports
92 psychology to improve performance, and has been used in both cognitive and
93 physical therapies.^{12,13} Whilst the precise mechanisms by which MP may work have
94 not been fully elucidated, it is agreed that mental imagery utilises stored multimodal
95 (motor and sensory) representational formats and/or previous experiences of
96 movements.¹⁴ It has been shown that MP activates many of the same areas of the
97 brain that are stimulated when physically executing a movement.^{15,16} These include
98 the premotor cortex, basal ganglia and cerebellum and associative parietal cortex.

99 7,¹⁵ Consequently MP may provide a 'back door' to the motor cortex as it facilitates
100 motor cortex activity and neuroplasticity without physical movement.^{15,17-19}

101 Studies indicate that the majority of people can undertake MP within the first six
102 weeks after stroke. This does vary depending upon the test used to assess MP
103 ability,^{16,20,21} but the ability to undertake MP after stroke does not appear to be
104 significantly influenced by age.²² It is also one of very few treatments that can be
105 used by those who have no voluntary movement of their upper-limb. This enables
106 participation in an upper-limb rehabilitative intervention for those who could not
107 undertake exercise based interventions for the upper-limb, such as constraint
108 induced movement therapy or repetitive task practice.^{23,24} Conversely, its use in high
109 performance sport indicates that it is suitable to be used by people with good upper-
110 limb function to refine high-level skills after stroke.⁷ Crucially, as MP does not require
111 any actual physical movement, it is safe for people after stroke to undertake with
112 only minimal or no supervision. This means that if MP can be shown to be effective,
113 it could provide multiple practice opportunities and be a useful method to supplement
114 the amount of therapist-provided rehabilitation for the upper-limb after stroke and
115 improve outcomes.

116 Several trials of mental practice for the upper-limb after stroke have shown it to be as
117 effective as some forms of physical practice upon impairments, and it appears
118 particularly efficacious if used alongside physical therapy.^{8,9,25,26} However, others
119 have reported no differences in activity limitations when compared to usual care
120 interventions,²⁷ suggesting that its effectiveness cannot be assumed. The most
121 recent Cochrane review of MP for the upper-limb after stroke was published in 2020⁸
122 and found that MP had a significant benefit upon upper-limb motor recovery and
123 activities. Further reviews largely support this finding,^{28,29} although the magnitude of

124 the effect appears to differ between studies. Even with the increase in available
125 trials, there is still uncertainty as to whether the changes elicited by MP could
126 specifically reduce activity limitations of the upper-limb, a recognised and shared
127 priority for people after stroke and clinicians³⁰. Furthermore, the optimal parameters
128 of use of MP for the upper-limb remain unclear. Specifically, the time period after
129 stroke during which MP might be most effective (when) and the effect of dose upon
130 activity limitations (how much)³¹ have not been identified.

131 Therefore, this review seeks to address this shortcoming by:

- 132 (i) examining the effectiveness of MP upon outcomes that specifically
133 measure activities and activity limitations,
- 134 (ii) describing when and in whom after stroke MP might have most benefit to
135 upper-limb activity outcomes
- 136 (iii) investigating if and how the dose affects the effectiveness of MP

137 The lack of clear guidance regarding how and in whom MP should be used
138 clinically may, in part, explain why despite its inclusion in stroke guidelines, MP is
139 reported to be rarely used in practice.³² The information generated by this review
140 will provide greater clarity for clinicians regarding how they might choose to use
141 MP in practice and identify clear indications of priorities for future research.

142 **Methods**

143 This review follows the Cochrane Reviews of mental practice and utilised the same
144 search criteria.⁸ It was registered with Prospero database of systematic reviews
145 (Prospero reference number: CRD42019126044) and followed published checklist
146 and guidance on systematic reviews (PRISMA and Cochrane).^{33,34}

147 Electronic searches of the following databases were completed: Cochrane Central
148 Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE , CINAHL,
149 PsycINFO, Scopus, Web of Science, the Physiotherapy Evidence Database (PEDro)
150 (<http://www.pedro.org.au/>), the specialist rehabilitation research databases CIRRIE
151 (<http://cirrie.buffalo.edu>) and REHABDATA (www.naric.com). The databases were
152 searched from the point of the last Cochrane review (November 2009) until 4th May
153 2020.

154 Search terms included: Arm; Practice; Stroke Rehabilitation; Imagination; Paresis;
155 Recovery of Function; Stroke

156 The search strategy is documented in appendix 1.

157 ***Screening and Selection***

158 Titles and abstracts were independently screened by two reviewers (RS and KJ).

159 Studies were included if: they were a parallel group randomised controlled trial;
160 participants were over 16 years of age with a confirmed diagnosis of stroke (clinical
161 criteria and/or scanning) and had a sensorimotor upper-limb involvement as a result
162 of their stroke; compared a MP intervention, defined as cognitive rehearsal of a
163 movement or task for the upper-limb,⁹ to conventional therapy, usual care, a defined
164 placebo intervention or no therapy; and the effects of MP could be delineated from
165 other interventions. Only studies whose full text was available in English and that
166 used outcomes that measured upper-limb activities before and after the intervention
167 were included. Upper-limb activities were defined according to the WHO criteria³⁵
168 and included lifting/carrying and putting down (d4300,4301, 4302, 4305) fine hand
169 use (d440) and hand and arm use (d445).

170 After title and abstract screening, the full text of selected studies were retrieved,
171 independently read and assessed for inclusion. Any papers where suitability was
172 unclear were reviewed by two reviewers (RS and KJ) and a decision made through
173 discussion.

174 ***Data Extraction***

175 Data was extracted by one reviewer (PB) into a data extraction spreadsheet which
176 was developed based on the Template for intervention description and replication
177 (TIDieR) checklist.³¹ Data extraction was checked by a second reviewer (RS).

178 The following data were extracted: citation details; aims; total number of participants;
179 number of groups; number in each group; number lost to attrition in each group;
180 randomisation; blinding; time since stroke; selection criteria; measurement schedule;
181 baseline arm function/score; frequency of MP sessions; duration of each MP
182 session; the length of the entire MP intervention; number of completed sessions;
183 total minutes of completed MP; duration and length of control intervention; baseline,
184 post intervention and follow-up (where available) point estimates and measures of
185 variability on outcome tools that measured activities or activity limitations. Where the
186 manuscript did not present data, the authors were contacted for this information.

187 ***Risk of bias (quality) assessment***

188 Two reviewers (RS and KJ) independently assessed the quality of all included
189 studies using the Physiotherapy Evidence Database (PEDro)³⁶ criteria scores.
190 Where possible, published assessments on the PEDro website were used to indicate
191 the quality of included studies. In the absence of published scores, PEDro scores
192 were independently assigned and then agreed by two reviewers (RS and KJ).

193 Scores indicated poor (less than 2), moderate (3-5) or high quality (6-10) trials.³⁶ Any
194 discrepancies were resolved by discussion.

195 **Analysis**

196 Studies were synthesised narratively and, where possible, meta-analysis of the
197 different continuous measures of upper-limb activity, presenting results as point
198 estimates and 95% confidence intervals (CI) was also undertaken by one reviewer
199 (AC). Funnel plots (plot of effect estimates from studies against a measure of
200 precision) were used to judge risk of publication bias. Weighted mean differences
201 (MD) were calculated where outcomes were measured on the same scale, with
202 standardised weighted mean differences (SMDs) calculated where outcomes were
203 measured on different scales for the same underlying construct.³⁴ Random-effects
204 models were estimated where SMDs were used to pool outcomes and fixed-effect
205 models where MD were synthesised. Heterogeneity was assessed through visual
206 inspection of forest plots and the calculation of the χ^2 and I^2 statistics. Sub-group
207 analyses explored the influence of time post stroke onset (using Stroke Recovery
208 and Rehabilitation Roundtable, SRRR classification),³⁷ severity of upper-limb
209 involvement at baseline (i.e. Action Research Arm Test; ARAT 0-20; 21-40; 41-57)
210 and the overall dose of mental practice delivered (minutes per day, calculated by
211 dividing the total number of minutes of MP reported to be delivered by the total
212 length of the MP intervention in days). This was categorised into low (below 25th
213 centile), medium (25-75th centile), high doses (above 75th centile).

214 Results were presented according to the Template for Intervention Description and
215 Replication (TIDieR),³¹ and comprised consideration of who and when (including
216 participant gender, the time since stroke using published criteria,³⁷ the participants'

217 cognitive function, and arm severity at baseline) and what and how much (the
218 viewpoint of MP, the simultaneous inclusion and the nature of other rehabilitative
219 interventions and the overall dose of MP provided).

220

221

222 **Results**

223 Initial searches yielded 1721 articles, which were reduced to 1239 after duplicates
224 were removed (see PRISMA diagram in Figure 1). After title, abstract, and then full
225 text screening, fifteen studies were selected for narrative review and presented in
226 Table 1.^{19,26,27,38-49} Four authors were contacted and asked to provide data which
227 would allow meta-analysis;^{44,46,47,49} one responded with data, another responded but
228 did not provide the data, two did not respond but the data for one of these two was
229 able to be extracted from Barclay-Goddard et al.'s (2011) Cochrane review.⁸ This left
230 12 studies that were suitable for meta-analysis.^{19,26,27,38-46} The characteristics and
231 main findings of included studies are presented in Table 1.

232 Figure 1 here

233 Figure 1 PRISMA diagram to show article flow through the review

234 TABLE 1 here

235 Table 1 Characteristics of included studies

236

237 **Quality:**

238 PEDRO scores are displayed in Table 1. Seven studies were either of
239 moderate^{19,26,38,39,44-46} or high quality^{27,40-43,48,49} whilst one was of poor quality.⁴⁷

240 **Outcomes:**

241 Nine^{19,26,27,38-41,45,49} studies utilised the Action Research Arm Test to indicate upper-
242 limb activity limitations as a primary or secondary outcome tool. The remaining six
243 studies used either the Wolf Motor Function Test,^{42,48} Jebsen-Taylor hand test,⁴³
244 Arm functional test - Functional Arm ability scale⁴⁶ or Motor activity log.^{44,47} As these
245 tools captured data predominantly at the level of activities they were collectively
246 pooled for analysis.^{19,26,27,38-46} Meta-analysis of these 12 studies revealed the
247 standardised weighted mean difference (SMD) for the overall effectiveness of MP
248 upon measures of activity limitation (shown in Figure 2) was 0.6 (95% confidence
249 intervals, CI: 0.32 to 0.88; n=328; I²=29%).

250

251 FIGURE 2 HERE

252 Figure 2 Forest plot to show the overall effectiveness of mental practice upon activity
253 limitations of the upper-limb

254

255 **Who and when?**

256 Fourteen of the 15 included studies presented demographic data and reported the
257 time since stroke (Table 1).^{19,26,27,38-46,48,50} There were more males than females
258 (males: 282; females: 183) and participants were a mean of 59.2 (SD: 4.9) years old.
259 Using standard criteria³⁷, eight studies were conducted in the chronic period^{26,38,39,42-}
260 ^{45,49}, two in the late sub-acute period^{27,41} with four being undertaken with people

261 predominantly in the early sub-acute period after stroke.^{19,40,46,48} Meta-analysis of 12
262 studies showed that MP had the largest benefit upon activity limitations in the early
263 subacute period (7 days to 3 months) after stroke (SMD:1.01, 95% CI: 0.53 to 1.5; 3
264 studies, n=76; I²=0%)^{19,40,46} followed by the chronic period (6 months and later; SMD:
265 0.65, 95% CI: 0.32 to 0.99; 7 studies, n=151 I²=0%)^{13,26,38,39,42-44} (Figure 3). Changes
266 in activity limitation after MP during the late sub-acute period (3 to 6 months) were
267 small and non-significant (SMD:0.09, 95% CI: -0.3 to 0.48, p=0.65; 2 studies, n=111
268 I²=0%).^{27,41}

269 FIGURE 3 HERE

270 Figure 3 Forest plot to show subgroup analysis (fixed effects) of time after stroke and
271 effectiveness of mental practice upon upper limb activities

272

273 All studies required participants to have no or very mild cognitive deficits in order to
274 take part. Ten from 15 studies screened people for cognitive dysfunction prior to
275 inclusion.^{26,27,38,39,41-44,46,49} Eight used the mini or full modified mental state
276 examination^{26,38,39,42-44,46,49} with cut-offs of 24 and 70 respectively. One used the
277 mental status questionnaire,²⁷ whilst another used the Wechsler Memory scale.⁴¹

278 For those eight studies (n=226) that reported baseline arm function using the
279 ARAT,^{19,26,27,38-41,45} most included participants who had moderate arm limitations
280 (median ARAT score: 25 range: 5-49). Only one study included participants who
281 would be classed as having severe arm limitations on the ARAT (mean ARAT score:
282 5)⁴¹. As presented in Figure 4, meta-analysis showed that MP had the greatest
283 benefit for those with the most severe upper-limb limitations (ARAT scores of 0-20;
284 weighted mean difference, WMD: 7.33, 95% CI: 0.94 to 13.72; 3 studies,³⁹⁻⁴¹ n=82;

285 I²=0%) followed by those with moderate limitations (ARAT scores from 21-40; WMD:
286 5.13, 95% CI: 2.88 to 7.39, 4 studies, ^{19,26,27,38} n=115; I²=0%). However, MP was not
287 effective in improving limitations in those with the most mild upper-limb involvement,
288 although this was only based on one study (ARAT scores from 41-57; WMD: 2.50,
289 95% CI: -4.38 to 9.38, p=0.48; 1 study, ⁴⁵ n=29).

290 FIGURE 4 HERE

291 Figure 4 Forest plot to show subgroup analysis (random effects) of the effects of
292 initial arm severity, measured using the ARAT, upon the effectiveness of mental
293 practice

294

295 ***What and how much?***

296 Ten studies did not clearly specify which perspective (first or third person) was used
297 during MP. Of the five studies that did, four solely utilised a first person
298 perspective^{19,39,41,48} whilst one used both first and third person.⁴³

299 In ten of the studies, MP was delivered in addition to conventional therapy/other
300 usual rehabilitation^{13,19,26,38-40,42,43,46,49} however there was little included detail of what
301 this comprised.

302 The mean length of the MP intervention was 4.7 weeks (SD: 1.9) with a median of 3
303 sessions (range 2-15) being provided each week. One study compared three
304 different durations of MP intervention so was excluded from this analysis.⁵⁰ The
305 mean duration of a typical MP session in the other 14 studies was 28.4 minutes (SD:
306 15.1).^{19,26,27,38-48} Dose was calculated to indicate the average amount of MP received
307 per day (total number of minutes of MP divided by the total length of the intervention

308 in days). The mean average dose was 20.3 minutes/day (SD: 14) from the 14
309 studies that used a single MP intervention^{19,26,27,38–48} (Table 1).

310 For meta-analysis, the data were split into low, medium and high doses using the
311 method of calculation described earlier. Two studies used a low dose of MP (≤ 6.6
312 minutes/day),^{26,43} five used a medium dose (6.7 to 32 minutes/day)^{13,38,39,42,44} whilst
313 five used a high dose (≥ 32.1 minutes/day).^{19,27,40,41,46} As shown in Figure 5, a lower
314 dose appeared to confer somewhat greater benefit to upper-limb function (SMD:
315 0.89, 95% CI: 0.04 to 1.74; 2 studies,^{26,43} n=25; I²=0%) than a medium (SMD: 0.61,
316 95%: 0.25 to 0.98; 5 studies,^{13,38,39,42,44} n=126 I²=0%) or high dose (SMD: 0.57, 95%
317 CI: 0.05 to 1.08; 5 studies,^{19,27,40,41,46} n=177; I²=60%).

318 FIGURE 5 HERE

319 Figure 5 Forest plot to show subgroup analysis of the effects of dose upon activity
320 limitations

321 Six of the 15 studies provided control treatments to match the time and attention
322 given the intervention group.^{19,27,38,43,44,48} They provided additional conventional
323 therapy,^{19,44} relaxation recordings,^{38,43} additional treatment based on the
324 neurodevelopmental technique,⁴⁸ or visual imagery training.²⁷ The remaining nine
325 studies did not detail the provision of additional control treatment.

326

327

328 Discussion

329 This systematic review evaluates the effectiveness of MP for the upper-limb after
330 stroke. It aimed to determine in whom and when after stroke it might have benefit

331 and to identify the dose of MP that might have the greatest effect. The main results
332 of this review were based on largely moderate to high quality trials and indicate that
333 MP can confer significant reductions in upper-limb activity limitations. Heterogeneity
334 in the meta-analyses were low (less than 29%) supporting the validity of these
335 results.

336 An important finding is that the magnitude of reported benefit of MP on upper-limb
337 activity limitations (SMD: 0.60, 95% confidence intervals, CI: 0.32 to 0.88; 12 studies,
338 n=328) exceeds that reported for other recognised upper-limb treatments in
339 comparable studies of people after stroke. These include repetitive task training
340 (SMD: 0.25, 95% CI: 0.01 to 0.49; 11 studies n=749)²⁴ and constraint induced
341 movement therapy (SMD: 0.24, 95% CI: -0.05 to 0.52; 42 studies, n= 1453)⁵¹.
342 Despite the apparent superiority of MP to other upper-limb interventions, MP is
343 reported to be used much less frequently than either repetitive task training or
344 constraint induced movement therapy in clinical practice.³² This indicates that further
345 work to support the implementation of MP into routine therapy practice is clearly
346 warranted.

347 The results of the current study are similar to that of the most recent Cochrane
348 review of MP for the upper-limb which reported analogous effect sizes of the overall
349 effectiveness of MP from 15 studies (SMD: 0.66, 95%CI: 0.39 to 0.94; n=397).⁹
350 However, a larger analysis reported a smaller effect (SMD: 0.36, 95% CI: 0.16 to
351 0.55; 18 studies, n=644).²⁸ The disparity between these two reviews may be
352 attributable to differences in the number of studies and participants included and the
353 analytical approach; Guerra et al. (2017)²⁸ pooled data from studies measuring both
354 impairment and activity limitations, whilst Barclay-Goddard et al. (2020) did not.⁹ The
355 findings could indicate a trend for lower effectiveness of MP on impairments in

356 comparison to activity limitations. However, this supposition is not supported in the
357 analysis of impairment outcomes by Barclay-Goddard et al. (2020) (SMD: 0.59,
358 95%CI: 0.30 – 0.87; 15 studies, n=397)⁹. This warrants further investigation.

359 ***Who? Patient selection and time since stroke***

360 All trials selected participants that had normal or only mild cognitive dysfunction after
361 stroke. The effect of reduced cognition upon the ability to undertake MP after stroke
362 remains uncertain. Several studies have shown that mental imagery after stroke may
363 take longer to complete when compared to healthy and/or younger controls^{20,21,52,53}
364 but no studies have provided explicit evidence of the minimal cognitive function
365 required to successfully complete MP. Future studies should therefore consider
366 broadening inclusion criteria to incorporate sub-groups of those after stroke with
367 moderate cognitive deficits to determine if they may benefit from MP.

368 None of the included trials stratified participants at baseline. As well as potentially
369 attenuating the estimates of effectiveness, the absence of stratification leads to
370 difficulty in knowing the optimal time after stroke and the severity of upper-limb
371 limitations that are likely to benefit most from MP. However, the sub-analyses
372 presented in this review suggest that MP delivered in the early subacute and chronic
373 phases after stroke and to those with the most severe arm deficits (scoring 0-20 on
374 the ARAT) may gain the most from MP.

375 Whilst others have found small differences between the effectiveness of MP
376 provided in the first six months after stroke or later⁹ (less than 6 months: SMD: 0.48,
377 95% CI: -0.04 to 0.99; 5 studies, n=188; ≥more than 6 months: SMD: 0.75, 95% CI:
378 0.44 to 1.06, 8 studies, n=179),⁹ our use of the SRRR criteria allowed more detailed
379 consideration of time periods. This revealed that the early subacute (seven days to

380 three months after stroke) group had the largest change in activity limitations after
381 using MP. The larger magnitude of changes during this early period is perhaps
382 unsurprising as the most rapid and the majority of endogenous plasticity, and thus
383 recovery of motor control, is typically observed in the first few weeks after stroke.^{37,54}
384 However, in line with the Barclay et al. (2020) review,⁹ a smaller but significant
385 benefit was also seen in people at least 6 months after stroke, suggesting that MP
386 may have different mechanisms of effect depending upon when after stroke it is
387 used. Collectively these results suggest that MP can improve upper-limb function at
388 multiple time points after stroke, and that work to understand the mechanism, and
389 potential differences in mechanisms, depending upon the time period in which it is
390 applied after stroke is warranted.

391 Our finding that those with the most severe deficits exhibited substantial and
392 significant benefit from MP is novel and is particularly noteworthy as this benefit (MD:
393 7.3, 95% CI: 0.94 to 13.7, $I^2=0\%$) exceeds the minimal clinically important difference
394 for the ARAT (5.7).⁵⁵ No other reviews of MP for the upper-limb have considered the
395 severity of upper-limb deficits upon the effectiveness of MP.^{9,28,56} Our finding
396 indicates that MP could provide a promising treatment for people with severe upper-
397 limb limitations, who typically cannot independently participate in other recognised
398 treatments (such as repetitive task training), as they have little voluntary movement.
399 The strength of this conclusion is limited by the wide confidence intervals, relatively
400 small number of studies in each subgroup, although heterogeneity was low, and
401 because the cut offs used in this analysis were arbitrarily assigned (ARAT scores:
402 severe: 0-20; moderate: 21-40; mild:41-57) to allow comparison. However, we chose
403 not to use more widely recognised ARAT cut off scores (severe: 0-10; moderate: 11-
404 56; mild: 57)⁵⁵ as this would mean all but one study⁴¹ would be considered to have

405 moderate limitations and so any subtleties in the response to MP would be missed.
406 Whilst analysing the severity of upper-limb limitations as we did is not standard, it
407 highlights that the effect of MP upon severe activity limitations after stroke is worthy
408 of further study in this group.

409 ***What and How much? Delivery and dose of MP after stroke***

410 In this review there was little indication to determine which perspective (first or third
411 person) used during MP was superior as most studies did not indicate the
412 perspective used. Mental imagery from a first person (egocentric) perspective is
413 generally agreed to be more effective than from a third person perspective and so is
414 more widely used in published research protocols⁷ but there is little empirical
415 evidence to support this.^{11,43} Few studies also indicated if or how MP training was
416 supervised. This is important as how MP is provided will have important time and
417 cost implications for therapy services, significantly influencing cost effectiveness.
418 Lack of detail regarding how MP is provided is a common criticism of studies
419 reporting MP interventions.⁵⁷ This could be remedied by adopting recognised
420 frameworks to deliver MP used in sport (e.g. Physical, Environment, Task, Timing,
421 Learning, Emotion and Perspective, PETTLEP)¹¹ and by the assiduous use of
422 intervention reporting guidelines in future studies (e.g. TIDieR).^{31,57}

423 Interestingly, all but one⁴¹ of the 15 included studies in this review delivered MP as a
424 single massed practice session on each day it was delivered. This contrasts with the
425 superiority of distributed over massed practice seen in motor learning⁵⁸ and the
426 findings of a small study in which distributed MP (20 minutes, three times a day,
427 n=13) produced significantly larger gains in upper-limb recovery after stroke when
428 compared to once daily therapy for 60 minutes (n=14).⁵⁹ This suggests that future

429 studies should consider delivering shorter but more frequent MP sessions to elicit
430 greater gains in function.

431 The meta-analysis of the dose delivered in this review indicated that a low or
432 medium dose (low: less than 6.6 minutes per day medium: more than >6.7 to less
433 than 32.1 minutes/day) appeared slightly more beneficial than higher doses of MP
434 (more than 32.2 minutes). If accurate, this indicates that MP could provide an
435 effective intervention without requiring substantial increases in therapist time and
436 costs. However, this is perhaps unlikely as these findings contradict the accepted
437 linear relationship between upper-limb therapy dose and response,⁶⁰ and instead
438 could be explained by the doses of MP delivered in all included studies being below
439 the amount needed to elicit optimal benefit. Other studies indicate that therapy for
440 the upper-limb must be delivered intensively in order to show an optimal benefit,^{61,62}
441 which is likely to comprise several hours of intensive daily treatment.^{60,63} In studies
442 included in this review, one hour was the maximum daily amount of MP delivered
443 and this was only delivered in two trials.^{41,46} Others have shown no significant
444 differences in outcomes between MP delivered for an hour a day when compared to
445 lower doses 20 and 40 minutes/day.⁴⁹ This suggests that future trials should
446 compare doses of a few minutes of MP to much more intensive practice akin to that
447 in studies of upper limb rehabilitation that have shown significant benefit. It is also
448 important to note that, both in this study and others, judgements of dose and
449 intensity were estimated solely from the duration that MP was provided. Detailing the
450 numbers of repetitions and the joints and movements targeted of mentally practiced
451 movements provided by the MP script would provide a more accurate estimation of
452 the intensity of training and should be reported in future studies, although it is

453 recognised that an individual's adherence to imagining movements cannot be
454 measured.

455 ***Limitations***

456 Funnel plots suggest that the findings of this systematic review may be skewed by
457 publication bias, with asymmetrical plots suggesting a lack of small studies showing
458 no benefit from the comparator interventions. Inevitably this can lead to
459 overestimation of the effectiveness of MP. Potential bias in the judgements of which
460 studies were included in the review may also skew results. Whilst data extraction
461 was checked, it was undertaken by one reviewer which may have introduced error.
462 Its wider validity is also restricted by the inclusion of only full-text articles available in
463 English and exclusion of articles that did not measure changes in activity limitations
464 of the upper-limb. The exclusion of studies that measured impairment was primarily
465 because a reduction in activity limitations is recognised to be more meaningful to
466 people after stroke than alterations in impairment.⁶⁴ Taken alongside the knowledge
467 that finding ways to effectively rehabilitate the upper-limb after stroke is a recognised
468 priority for both stroke survivors and clinicians³⁰ the focus upon activity limitations in
469 this review increases its clinical validity and ultimately its usefulness to clinicians and
470 people after stroke.

471 Interestingly, the studies included in this review did not always reflect the 'typical'
472 person who has had a stroke which limits the broader generalisability of the findings.
473 Included studies had relatively young participants with a mean age of 59 (SD: 5)
474 years and preferentially recruited males (there were almost 100 more males than
475 females). In Europe and Australasia, the average age for first stroke is markedly
476 older (around 70 years), stroke is more common in women than men,⁶⁵ and findings

477 between sexes are not directly transferable as females tend to have poorer
478 functional recovery.⁶⁶

479 A further limitation to the findings of this review is that no studies comprehensively
480 examined compliance and fidelity to the MP intervention; others have reported low
481 patient and therapist compliance to MP,⁶⁷ MP interventions are often not clearly
482 defined⁵⁷ and few therapists report using MP as part of therapy for the upper-limb
483 after stroke³² suggesting that the training and practical requirements of implementing
484 MP need to be considered alongside its clinical effectiveness.

485

486 **Conclusions**

487 The results of this systematic review and meta-analysis indicated that MP can
488 significantly improve activity limitations of the upper-limb after stroke and that it
489 appears more effective than several other, more frequently used interventions for the
490 upper-limb. This highlights that work is warranted to explore and support the
491 successful implementation of MP into clinical practice so that more people can
492 benefit from using it as part of their rehabilitation after stroke. The finding that MP
493 provides significant and substantial benefit that markedly exceeds the minimal
494 clinically important difference for the ARAT in those people after stroke with the most
495 severe limitations of the upper-limb is particularly novel and suggests that MP may
496 constitute a promising therapy for this subgroup.

497 Future trials should seek to stratify people based on the severity of upper-limb
498 function and/or their potential for recovery of the upper-limb to aid understanding of
499 who may benefit the most from MP. Further work is also needed to standardise the
500 delivery of MP; including identifying an optimal dose, standardising exactly how MP

501 is being used (first or third person viewpoints) and the number of repetitions of the
502 included movements in the MP intervention. This could be done by use of a detailed
503 intervention reporting tool³¹ and established MP intervention structure.¹¹

504

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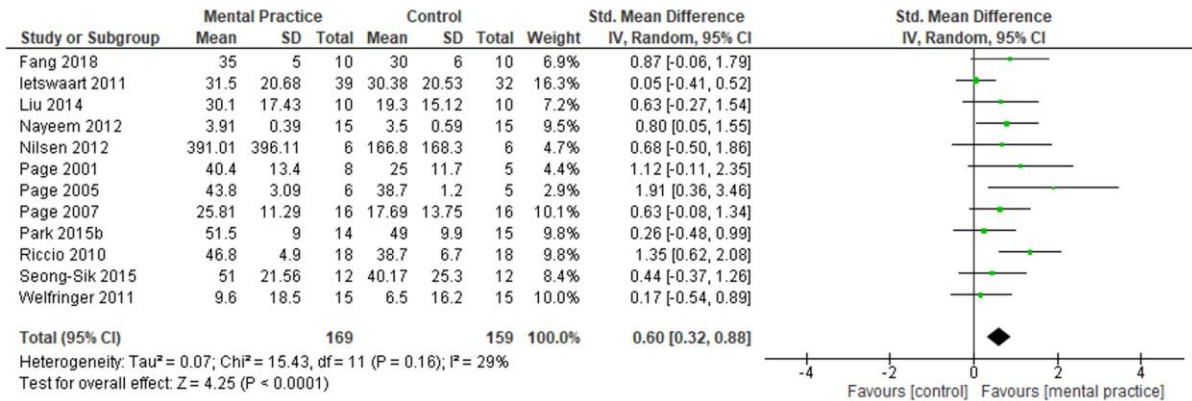
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698 Figure 1 NO LEGEND

699 Figure 2

700 Legend: Data in Nilsen et al (2012) are reversed so that improvement is indicated by a
 701 higher score.

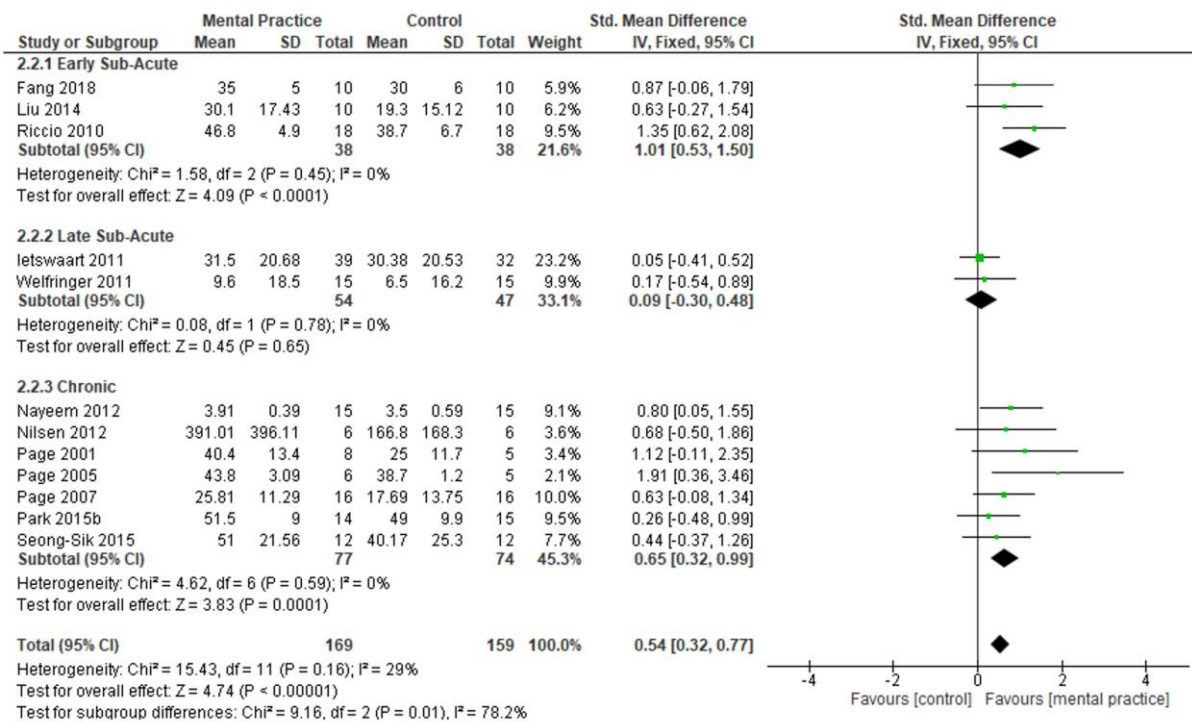
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705 Figure 3



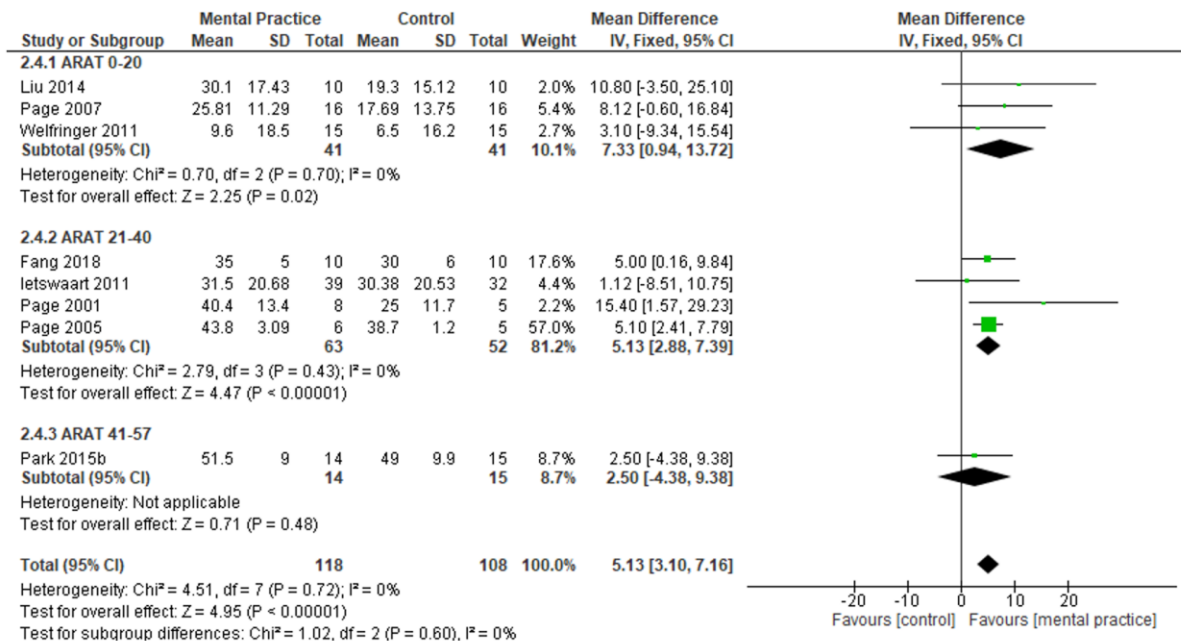
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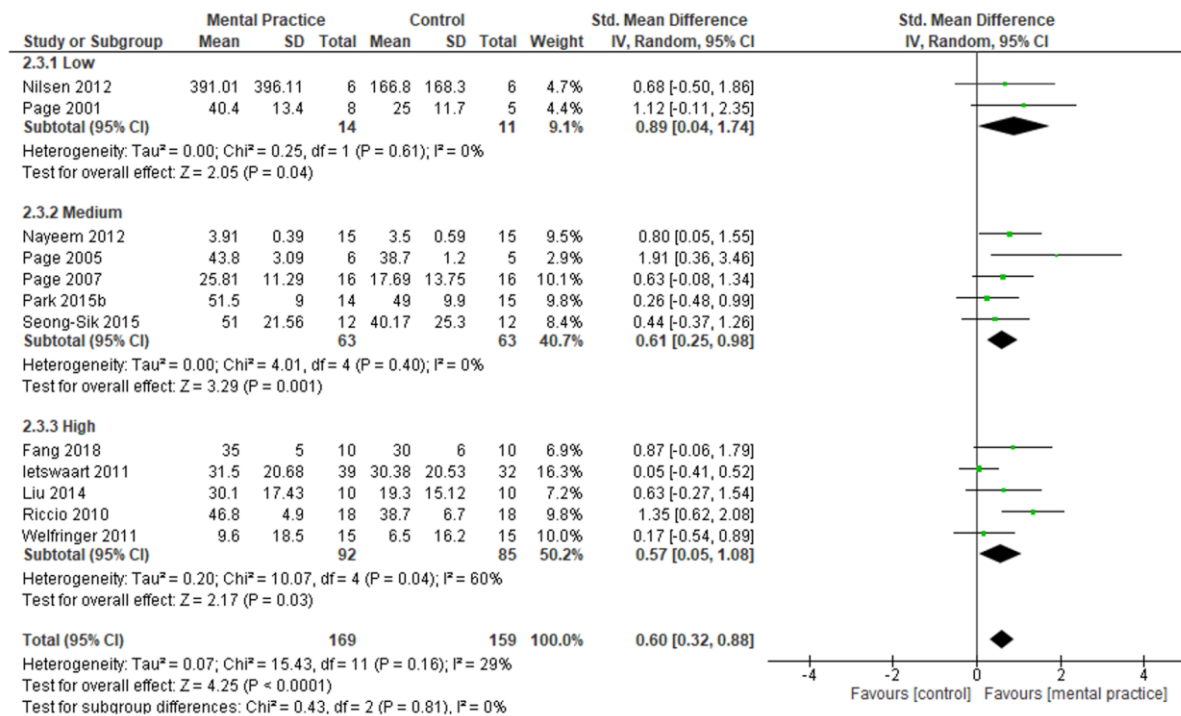
709 Legend: Data in Nilsen et al (2012) are reversed so that improvement is indicated by a
 710 higher score.

711 Figure 4



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713 Figure 5



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715 Legend: Data in Nilsen et al (2012) are reversed so that improvement is indicated by a
716 higher score

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718