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Mental simulation practice has beneficial effects on patients' physical function following lower limb arthroplasty: a systematic review and meta-analysis

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#### 1 ABSTRACT

Objective: To determine the effectiveness of mental simulation practice (MSP) on measures
of physical function recovery in patients who have undergone a joint replacement surgery of
lower limbs.

5 Data sources: A systematic review was conducted using CINAHL, PubMed/MEDLINE,
6 Embase, SPORT Discus, PEDro, Cochrane Register of Controlled Trials and Google Scholar
7 from earliest record to 16<sup>th</sup> August 2019.

8 **Study Selections:** The following inclusion criteria were used to determine eligibility for 9 studies: 1) randomised and matched controlled trials recruiting male and female adults who 10 underwent primary unilateral joint arthroplasty; 2) the study examined effects of MSP 11 intervention on measures of physical function recovery (both performance-based and patient 12 self-reported); 3) measures of interest were compared between MSP and control groups. A 13 total of eight papers (seven studies) met the inclusion criteria and were included.

14 Data extraction: Data were extracted by one reviewer and checked by a second reviewer,15 independently.

Data Synthesis: When compared to standard physical therapy (SPT), MSP showed an effect 16 on physical function in general (effect size (ES) = 0.67, 95% CI 0.38 to 0.96, n = 7), maximal 17 voluntary strength of knee extensor muscles of the affected leg (ES = 1.41, 95% CI 0.64 to 18 2.18, n = 2), brisk walking speed (ES = 1.20, 95% CI 0.58 to 1.83, n = 2), brisk walking speed 19 with dual task (ES = 1.02, 95% CI 0.41 to 1.63, n = 2), timed up-to go test (ES = 0.96, 95% 20 CI 0.15 to 1.77, n = 3) and active flexion of the affected leg (ES = 0.70, 95% CI 0.29 to 1.11, 21 n = 4). Finally, meta-regression analysis revealed that effects of MSP were significantly 22 23 predicted only by total number of training sessions per study.

Conclusions: The present meta-analysis demonstrated that MSP intervention has multiple positive effects on measures of physical function recovery in patients who have undergone total knee or hip replacement surgery in comparison with SPT. Thus, MSP can be applied as an effective complementary therapy to SPT in physical rehabilitation of this specific population, especially in the early post-acute and acute phase.

#### 29 **PROSPERO registration number:** CRD42019118886

Key Words: motor imagery, action observation, strength, mobility, total knee replacement,
 total hip replacement

32 List of abbreviations:

33	OA	osteoarthritis
34	MSP	mental simulation practices
35	MI	motor imagery
36	AO	action observation
37	MI + AO	motor imagery combined with action observation
38	GI	guided imagery
39	ТКА	total knee arthroplasty
40	THA	total hip arthroplasty
41	SPT	standard physical therapy
42	TUG	timed up-to go test
43	TIDieR	template for intervention description and replication
44	GRADE	grading of recommendations assessment, development and evaluation system
45	ES	effect size
46	cES	composite effect size
47	MD	mean difference
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49		

#### 50 **Introduction**

Osteoarthritis (OA) represents one of the leading causes of disability among older 51 adult populations, where knee and hip OA are the most prevalent.<sup>1</sup> When conservative 52 treatments cannot help, replacement of the malformed joint is recommended. Joint 53 replacement surgery successfully relieves pain, corrects the deformity, and improves joint 54 function, activities of daily living, and thus, the patient's quality of life in general.<sup>2-4</sup> 55 Although peri-operative assessment of patients has considerably improved in the last few 56 decades.<sup>5,6</sup> a considerable reduction in quadriceps strength and overall physical function 57 persist a few months following major surgery.<sup>2,7</sup> Traditionally, post-rehabilitation practice 58 consists of conventional methods of physical exercises that mechanically stress the 59 musculoskeletal system.<sup>5,6</sup> However, improved knowledge and use of contemporary 60 technologies in recent years have yielded new evidence of fewer physically demanding 61 methods that could be feasible for specific populations, such as orthopaedic patients, who 62 63 cannot fully benefit and/or attend conventional physical therapies. Such methods are known as cognitive-based strategies; i.e., mental simulation practices (MSP) that are potentially 64 beneficial for the enhancement of various motor skills.<sup>8-10</sup> Hence, motor imagery (MI) and 65 66 action observation (AO) represent two of the most popular MSP practices used in clinical settings.<sup>8</sup> During MI, subjects mentally simulate a specific motor action without any actual 67 corresponding motor output,<sup>9</sup> while AO requires patients to observe action on video or watch 68 live actions performed by someone else.<sup>11</sup> Theory-based fundamental research postulates that 69 the same brain regions are activated during actual and imagined/observed movement.<sup>12</sup> While 70 the efficiency of both modalities has been proven when used either independently or 71 72 combined, in clinical settings, they are mostly practised as adjunct rehabilitation tools to conventional therapies.<sup>11,13,14</sup> Recently, a few original studies<sup>11,15–18</sup> aiming to investigate the 73 efficiency of clinical outcomes following lower limb joint replacement surgery have been 74

published. Examination of these studies reveals a high heterogeneity among types and 75 duration of MSP interventions, frequency of exposure, follow-up periods, and the variety of 76 physical function assessment tools used. There is a need to meta-analyse the observed effects 77 from the aforementioned studies to overcome these issues and determine the actual effects of 78 MSP on patients' physical function. Methodological discrepancies and inconsistencies in 79 findings regarding the effects of MSP interventions on physical function of patients following 80 major surgery of lower limbs make it difficult to draw any firm conclusions about their 81 effectiveness and dose-response relationships. For OA patients who have undergone knee 82 joint replacement surgery, the quadriceps strength is a major determinant of general physical 83 function,<sup>19</sup> while overall mobility assessed by walking speed and other functional tests have 84 been regarded as clinically essential measures.<sup>5,20</sup> Moreover, for a better understanding and 85 interpretation of patients' rehabilitation after major surgeries, the literature postulates that 86 both performance-based and patient self-report assessments should be considered.<sup>7,21,22</sup> 87 Therefore, the present systematic review with meta-analysis aimed to respond on the 88 following questions: 1) In patients who have undergone a joint replacement surgery of lower 89 limbs, will MSP intervention improve performance-based measures of strength, mobility and 90 self-reported measures of physical function, when compared to standard physical therapy 91 (SPT) alone? and 2) How is the MSP-performance relationship modified by key training 92 variables such as duration of the intervention, training frequency, and single training session 93 duration? 94

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#### 99 Methods

#### 100 **Protocol and registration**

101 This systematic review was performed according to the Preferred Reporting Items for 102 Systematic Review and Meta-Analysis guidelines.<sup>23</sup> The protocol was registered in the 103 prospective international register of systematic reviews, PROSPERO, and met all the 104 eligibility criteria for protocol registration (registration number: CRD42019118886).

#### 105 Search strategy and study selection

To identify all potentially relevant data from experimental studies, an initial systematic 106 literature search was conducted in January 2016 by one author (AP). Updated searches were 107 additionally conducted between 20th and 30th December 2018 and 15th August 2019 to include 108 new relevant studies by two authors (AP and ZM). Both initial and updated searches included 109 110 the following databases: CINAHL, PubMed/MEDLINE, Embase, SPORT Discus, PEDro, Cochrane Register of Controlled Trials and Google Scholar. Electronic databases were 111 searched using the following keywords or their combination: "motor imagery training", 112 "movement imagery", "mental practice", "mental simulation", "cognitive training", 113 "action observation", "strength", "force", "functional performance", "ROM", "pain", 114 "effects", "physical recovery", "rehabilitation", "mobility", "orthopaedic patients", "joint 115 116 replacement", "knee arthroplasty", "hip arthroplasty", "injury". In addition, citation tracking and manual reference list checks of included studies were performed. The language of eligible 117 publications was not restricted. Two reviewers (AP and ZM) independently assessed study 118 titles and abstracts to determine if they satisfied eligibility criteria, that were presented in 119 accordance to PICOS (patients' population/problem, intervention, comparison, outcome, 120 121 study design) guidelines. The following inclusion criteria were used: (1) Population: Studies recruiting male and female adults who underwent primary unilateral joint arthroplasty; (2) 122

Intervention: Mental simulation intervention. Given the specificity of rehabilitation 123 procedures and ethical issues, MSP was always delivered as an adjunct therapy to standard 124 physical therapy (SPT) and was compared with SPT intervention. (3) Comparison: Measures 125 of interest were compared: (i) in general between MSP and SPT (ii) between different MSP 126 practices, i.e., MI vs AO vs guided imagery vs MI+AO; and (iii) between different 127 128 rehabilitation phases such as a) acute rehabilitation (up to 3 weeks after surgery); b) early 129 post-acute rehabilitation (from 3 to 12 weeks) and; c) late post-acute rehabilitation phase (from 12 weeks to 12 months), respectively. (4) Outcome: i) performance-based measures of 130 physical function, such as maximal strength and mobility assessed by gait speed, timed up-to 131 132 go test (TUG), and flexibility measurements; and ii) physician-administered performance exam tests, such as Tinetti score and/or patient self-reported measures assessed through 133 questionnaires, such as the Oxford Knee Score, Lower Extremity Functional Score, Western 134 Ontario and McMaster Universities Osteoarthritis Index, Short Form 36 Health Survey, 135 Barthel and Lequesne indexes, respectively. Measurements were recorded for every reported 136 time point and categorised into aforementioned rehabilitation phases.<sup>5</sup> (5) Study Design: 137 Randomized and matched controlled trials published in peer-reviewed journals, required to be 138 no less than a week in duration and include one control group at least. 139

Studies were excluded according to the following criteria: (1) uncontrolled studies; (2) studies where arthroplasties were not performed on lower limbs; (3) studies where data about doseresponse relationship variables were not reported; and (4) studies from which we could not extract enough information to calculate effect size or include them in the analysis.

#### 144 **Data extraction**

Data were extracted by one reviewer (AP) and checked by a second reviewer (ZM), independently. Any disagreements between the reviewers were resolved by consensus or arbitration by a third reviewer (DT).<sup>9</sup> All studies reported means and standard deviations of

relevant outcomes. The Cochrane Consumers and Communication Review Group's 148 standardised protocol for data extraction was used to extract: (i) study characteristics, 149 including author(s), title, and year of publication; (ii) participant information, such as sample 150 151 size, age, type of surgery utilised, and gender; (iii) description of the intervention, including types of exercise, intensity, duration, and frequency; and (iv) study outcomes, including both 152 patient self-reported and performance-based measures of physical function. Outcomes of 153 interest were recorded for every reported time point and categorized into following 154 rehabilitation phases: a) acute rehabilitation (up to 3 weeks after surgery); b) early post-acute 155 rehabilitation (from 3 to 12 weeks) and; c) late post-acute rehabilitation phase (from 12 weeks 156 to 12 months), respectively, based on expert consensus on best practices for rehabilitation 157 after total hip and knee arthroplasty.<sup>5</sup> 158

The methodological quality of included studies was assessed using the PEDro scale.<sup>24</sup> 159 by two reviewers independently (AP and ZM). The PEDro scale consists of 11 items designed 160 for rating the methodological quality.<sup>24</sup> Each satisfied item contributes 1 point to the overall 161 PEDro score (range 0-10 points). However, item 1 was not included as part of the study 162 quality rating for this review, because it pertains to external validity,<sup>24</sup> which was beyond the 163 scope of the current review questions. Additionally, the Template for Intervention Description 164 and Replication (TIDieR) checklist was used to assess the completeness of intervention 165 descriptions for both the experimental and control groups<sup>25</sup>. The quality of evidence was 166 assessed by using the Grading of Recommendations Assessment, Development and 167 Evaluation (GRADE) system, where classifications were made as follows: "high quality", 168 "moderate quality", "low quality" and "very low quality".<sup>26</sup> However, several reasons might 169 lead to degradation of the quality of the evidence<sup>26</sup>, thus, in the current study we considered 170 the following criteria when assessing confidence in evidence: design limitation (if the 171 172 majority of studies in the meta-analysis had a PEDro score < 6; imprecision based on small sample size (< 300 for each pooled outcome); inconsistency of the results (substantial heterogeneity within effect estimates,  $I^2 \ge 50\%$ ); This review did not consider the indirectness criterion because the eligibility criteria ensured a specific population with relevant outcomes.

#### 176 Statistical analysis

The meta-analyses were performed using Comprehensive Meta-analysis software 177 (version 2.0; Biostat Inc., Englewood, NJ, USA). For all reported outcome measures, the 178 effect sizes (ES) or mean differences (MD), along with 95% CIs were calculated. If at least 179 two trials reported the same outcome and were considered homogenous, then a meta-analysis 180 was conducted and presented with a forest plot. Due to differences in outcomes assessed and 181 182 measurement scales used between studies, general physical function assessments and selfreported physical function tests were treated separately. Therefore, composite ES (cES) and 183 95% CI was calculated for each study to overcome problem of dependence from multiple 184 outcomes and pre-post evaluation periods.<sup>27</sup> A random-effects model of the meta-analysis was 185 used in all comparisons. In addition to ES, for maximal strength tests and mobility measures, 186 187 such as gait speed, TUG, joint flexion, and joint extension assessments were assessed across multiple studies and mean differences (MD) with 95% CI were calculated and presented in 188 their respective units. Thus, strength was presented in Nm/BMI, flexibility in degrees [°], gait 189 190 speed in m/s and time to complete the TUG test in seconds.

Furthermore, a random-effects meta-regression was performed to examine whether the effects of MPS on physical function, in general, were moderated by different training variables. Training variables were grouped according to the following: training volume (i.e. period, frequency, total number of training sessions) and time spent in training (i.e. total training, duration per study; total training duration per week, duration of single training session).

The publication bias was assessed by examining the asymmetry of the funnel plots 197 198 using Egger's test, and a significant publication bias was considered if the p value was <0.10. The magnitude of the MSP effects on outcome measures of interest was interpreted as 199 changes using the following criteria: trivial (<0.20), small (0.21–0.60), moderate (0.61–1.20), 200 large (1.21–2.00), very large (2.01–4.00), and extremely large (>4.00).<sup>28</sup> The  $I^2$  statistic was 201 used to investigate between-study heterogeneity; where values of 25%, 50% and 75% 202 represent low, moderate and high statistical heterogeneity, respectively.<sup>29</sup> Statistical 203 significance was set at the level of p < 0.05.<sup>28</sup> 204

#### 205 **Results**

The Egger's test was performed to provide statistical evidence of funnel plot asymmetry. Results indicated no publication bias for two meta-analysis only: physical function in general (p=0.568) and TUG (p=0.449), respectively. For all other analysis, the results indicated publication bias (p<0.10).

#### 210

#### **Study selection and characteristics**

Seven studies (eight journal articles) met all eligibility criteria and were included in 211 this systematic review and meta-analysis. The selection process was illustrated in Figure 1. A 212 total of 18,789 reports were identified across the databases in the initial search, and an 213 additional 34 papers were selected based on the reference list check. After duplicates were 214 215 removed, 7,567 reports remained. Based on a screening of the title and abstract, 6,586 articles were discarded (3,852 excluded after title analysis, 2,734 excluded after abstract analysis). 216 The full text of the 981 remaining articles was assessed in more detail for eligibility. Each 217 article was carefully read and coded for study characteristics, participant information, 218 description of the training intervention, and study outcomes. 973 articles did not meet the 219 inclusion criteria, while 8 articles that met the inclusion criteria were included in the 220

systematic review and meta-analysis. Majority of included studies were designed as randomised controlled studies  $(n=6)^{11,15,16,18,30-32}$ , whereas only one was a non-randomised controlled study.<sup>17</sup> Two different journal articles<sup>15,30</sup> reported divergent and valuable information from a single study. Thus, data from each article were extracted separately, then presented combined where applicable throughout this review.

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#### \*\*\*\* Figure 1 near here\*\*\*\*

The total number of patients in each study varied from  $20^{16}$  to 82,<sup>31</sup> with a total of 228 patients (41.7% males). All studies recruited older patients with 65.1 yrs. of age on average, scheduled for joint replacement primarily because of osteoarthritis of the knee (n=5)<sup>15,16,18,30,31</sup> or hip (n=3).<sup>11,17,33</sup>

A detailed description of the interventions is presented in Table 1. Briefly, for all 231 included studies, the experimental condition was an adjunct therapeutic tool to SPT. 232 Experimental conditions included SPT + motor imagery practice only  $(n=4)^{15,16,30,33}$  or SPT + 233 MI in combination with action observation (n=1),<sup>11</sup> SPT + action observation only  $(n=2)^{17,18}$ 234 or SPT + guided imagery practice only  $(n=1)^{31}$ . Studies differed in the focus of MSP. Thus, 235 the study of Moukarzel et al.<sup>16</sup> designed MI intervention to address three different objectives, 236 237 such as knee pain management, knee range of motion, and quadriceps strength. Paravlić et al.<sup>15,30</sup> focused on a strength task only, while two studies<sup>11,33</sup> included locomotor tasks only 238 (i.e., gait patterns). The studies also varied in the way researchers trained intervention 239 subjects. AO exercises in two studies<sup>17,18</sup> were provided by video clips of exercise that were 240 performed during SPT sessions and finally the guided imagery intervention was delivered 241 242 through audio scripts and designed to address patients' concerns and hopes about total knee arthroplasty (TKA), with a focus to facilitate mind-body connections and promote optimal 243 TKA outcomes. 244

\*\*\*\* Table 1 near here\*\*\*\*

245 246

The duration of the interventions varied from 10 days<sup>18</sup> to two months,<sup>11</sup> and the 247 individual training session duration varied from 15 to 30 minutes, respectively. On average, 248 20 sessions were delivered to patients (ranging between 9 and 35 sessions per single study). 249 The most frequent intervention was delivered twice per day<sup>17,18</sup> for 10 days in a row.<sup>18</sup> 250 251 Quality and completeness of reporting 252 Overall, the included studies were of moderate to high quality, with PEDro scores ranging from 5 to 10 (out of 10), with an average score of  $7.0 \pm 1.7$  (Table 2). 253 \*\*\*\* Table 2 near here\*\*\*\* 254 The completeness of intervention reporting was a higher for the experimental 255 conditions (mean: 77.1%; range from 25 to 100%) than for the control groups (mean: 72.9%; 256 range from 25 to 100%) (Figure 2). Compared to previously published data about the 257 completeness of intervention reporting in physiotherapy,<sup>34</sup> the current meta-analysis included 258 259 studies with sufficiently detailed exercise programme description.

260

#### \*\*\*\* Figure 2 near here\*\*\*\*

261 Effect of MSP interventions on physical performance in general

Meta-analysis of seven studies with a total of 228 patients showed a *moderate* effect (cES = 0.67, 95% CI 0.36 to 0.99, n = 7; p<0.001) on measures of physical fitness in general (Figure 3). The evidence was downgraded from high quality to low quality due to imprecision (sample size <300) and moderate to high heterogeneity ( $I^2 = 78\%$ ; p<0.001) (Table 3). Due substantial heterogeneity, sub-analysis and meta-regression analysis were performed. Sub-group analysis revealed that effects of the interventions had a tendency to be moderated by rehabilitation phase when data were collected (Q = 5.47; p = 0.065). In brief, a

*moderate* effect were observed following the acute phase (cES = 0.63, 95% CI 0.30 to 0.96, n 269 270 = 2, p < 0.001) and early post-acute phase (cES = 0.66, 95% CI 0.23 to 1.09, n = 5, p=0.003), while a trivial effect was observed following the late post-acute phase (ES = 0.17, 95% CI -271 272 0.13 to 0.47, n = 1, p=0.259). Additionally, when the effect of different types of MSP interventions was assessed, the sub-analysis revealed that the effects of intervention were 273 significantly moderated (Q = 19.25; p<0.001). In brief, a *moderate* effects were observed for 274 MI (ES = 1.05, 95 % CI 0.85 to 1.25, n = 3, p<0.001), MI + AO (ES = 0.63, 95 % CI 0.31 to 275 1.95, n = 1, p<0.001), and AO (ES = 0.63, 95 % CI 0.30 to 0.96, n = 2, p<0.001), while a 276 small negative effect was observed for GI (ES = -0.23, 95 % CI -0.75 to -0.29, n = 1, 277 p=0.382). Finally, sub-analysis revealed that there was no statistical difference in effects of 278 MI intervention on rehabilitation of physical function following TKA and THA (Q = 0.42; p< 279 280 0.517). In brief, a small effect was observed for TKA (ES = 0.56, 95 % CI 0.04 to 1.07, n = 4, 281 p=0.035), while a moderate effect was observed for THA (ES = 0.74, 95 % CI 0.53 to 0.95, n = 3, p<0.001). 282

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### \*\*\*\* Figure 3 near here\*\*\*\* \*\*\*\* Table 3 near here\*\*\*\*

285 *Effect of MSP interventions on maximal voluntary strength of knee extensor muscles* 

The summary effects showed that the MSP intervention had a *large* positive effect (ES = 1.38, 95% CI 0.73 to 2.03, n = 2; p<0.001) on measures of the maximal voluntary strength of knee extensor muscles of the affected leg following TKA (Figure 4a). In contrary, a *trivial* negative effect (ES = -0.05, 95% CI -1.14 to 1.03, n = 2, p=0.923) was observed for the unaffected leg. The evidence for both analyses was downgraded from high quality to moderate quality due to imprecision (sample size <300) (Table 3).

\*\*\*\* Figure 4 near here\*\*\*\*

#### 293 *Effect of MSP interventions on mobility*

The influence of MSP interventions on mobility was assessed with separate metaanalyses for gait speed, TUG, and flexibility to allow for the presentation of the results for each item individually, because of the clinical value of these tests.

297 The summary effects showed a *moderate* positive effect (ES = 0.67, 95% CI -0.38 to 1.72, n = 4; p=0.209) on measures of self-selected gait speed. A similar effect was observed 298 for self-selected gait speed during a dual task (ES = 0.75, 95% CI -0.89 to 2.38, n = 2, 299 p=0.331). The evidence of both analyses was downgraded from high quality to low quality 300 due to imprecision (sample size <300) and moderate to high heterogeneity (I<sup>2</sup> = 84 - 86%) 301 (Table 3). Moreover, a *moderate* positive effect were observed for brisk walking speed (ES =302 1.20, 95% CI 0.58 to 1.83, n = 2, p<0.001) and brisk walking speed with a dual task (ES = 303 304 1.02, 95% CI 0.41 to 1.63, n = 2, p=0.001), respectively (Figure 4b, c). The evidence for both 305 analyses was downgraded from high quality to moderate quality due to imprecision (sample size <300) (Table 3). 306

The summary effects showed a positive effect (ES = 0.96, 95% CI 0.15 to 1.77, n=3, p = 0.021) on measures of TUG test (Figure 4d). The evidence was downgraded from high quality to moderate quality due to imprecision (sample size <300) (Table 3).

The summary effects showed a *moderate* positive effect on measures of active (ES = 0.70, 95% CI 0.29 to 1.11, n = 4, p=0.001) and passive flexion (ES = 0.78, 95% CI -0.35 to 1.92, n = 3, p=0.176) of the affected leg, respectively. The evidence of both the active flexion and passive flexion was downgraded from high quality to moderate quality due to imprecision (sample size <300) (Table 3). Similarly, a positive effect (ES = 0.43, 95% CI -0.62 to 1.47, n = 2, p=0.423) was observed for active knee extension of the affected leg, where evidence was downgraded to moderate quality due to imprecision (sample size <300) (Table 3).

#### 317 *Effect of MSP interventions on self-reported physical function*

Pooled effect meta-analysis showed a *small* effect (cES = 0.51, 95% CI -0.36 to 1.38, 318 n = 4, p=0.254) on measures of self-reported physical function. The evidence was 319 320 downgraded from high quality to low quality due to imprecision (sample size <300) and high heterogeneity ( $I^2 = 85\%$ ; p<0.001) (Table 3). Due substantial heterogeneity, a sub-analysis 321 was performed. Sub-group analysis revealed that effects of the intervention had a tendency to 322 323 be moderated by rehabilitation phases when data were collected (Q = 5.26; p=0.072). In brief, *moderate* effects were observed following acute phase (cES = 0.73, 95% CI 0.22 to 1.23, n = 324 325 2, p=0.005), while *small* and *trivial* effects were observed following the early post-acute (cES = 0.29, 95% CI -1.64 to 2.22, n = 2, p=0.767) and late post-acute phases (cES = 0.00, 95% CI 326 -0.05 to 0.53, n = 1, p=1.000). 327

# Meta-regression analysis for training variables of physical function following mental simulation practice

Table 4 shows the results of the meta-regression for two subcategories of variables: training volume, and time spent in training. In the subcategory of training volume, only the total number of training sessions (per study) predicted the effect of MSP practice in general (p=0.042). Concerning the time spent in training, only the total training duration per study (p=0.075) showed a tendency to predict the effects of MSP on physical function in general. \*\*\*\* Table 4 near here\*\*\*\*

#### 337 **Discussion**

The present systematic review and meta-analysis confirms that MSP interventions can effectively improve both the patient self-reported and performance-based measures of physical function recovery in patients who have undergone a knee or hip joint replacement surgery. Moreover, a meta-regression analysis showed that the total number of training sessions per study predicted the effect size magnitude of MSP on physical function in general.

MSP intervention is potentially beneficial for the enhancement of various motor skills 343 and functional rehabilitation in patient populations.<sup>11,15,35</sup> However, previous reviews vielded 344 equivocal findings regarding the effectiveness of MSP on functional rehabilitation in 345 orthopaedic patients.<sup>36–38</sup> On the whole, these investigations differ in the aims being 346 determined, a targeted population chosen, and consequently, the overall methodology used.<sup>36–</sup> 347 For example, Zach et al.<sup>36</sup> meta-analyzed effects of MSP intervention on measures of 38 348 functional mobility, perceived pain, and self-efficacy in athletes following injury/or surgery 349 350 and concluded that MSP intervention might be beneficial for athletes recovering from injury. *Large* negative and *large* positive effects were found for pain and self-efficacy, respectively; 351 however, contrary to our study, the only small, nonsignificant effect was found for functional 352 mobility.<sup>36</sup> In a recently published review,<sup>37</sup> after summarizing the effects of psychological 353 interventions during the rehabilitation of patients after TKA and total hip arthroplasty (THA), 354 authors concluded that there is no enough evidence to support psychological interventions as a 355 rehabilitation practice tool in this specific population.<sup>37</sup> Conversely, by using a rigorous 356 methodological approach with a meta-analytic procedure, we found general improvements in 357 358 physical function following MSP intervention that on average ranged from 1 to 52%, when compared to SPT only. Our findings are aligned with one of the first systematic reviews with 359 the meta-analytical approach in the field<sup>39</sup> aiming to investigate mental practice enhance 360

performance in general. Driskell et al.<sup>39</sup> found that MSP has a positive effect on physical performance. Moreover, similar to current findings Driskell et al.<sup>39</sup> identified potentially moderating variables associated with MSP interventions, such as the duration of the practice, indicating that overall volume and duration of mental practice must be considered when designing MSP intervention.<sup>9,39</sup>

In the last two decades, there has been growing scientific interest in mental simulation 366 techniques and their potential effects in the field of neurorehabilitation practice.<sup>9,40–42</sup> A lot of 367 MI and AO based interventions have been successfully conducted and beneficial effects have 368 been proved in enhancing the performance of both symptomatic and asymptomatic 369 populations.<sup>9,40–42</sup> However, there is still debate about which of these techniques is more 370 efficient and in which modality, i.e., when used alone or combined.<sup>14,42,43</sup> Studies that have 371 been included in the current review differed in the type of MSP interventions, timing, 372 duration, and mode of delivery. That is why additional sub-group analysis and meta-373 regression analysis were applied and have made it possible to draw some valuable conclusions 374 375 for physiotherapeutic practice. When effects of different MSP types were analysed, our study showed that MI intervention seems to have the most substantial effect when compared to 376 MI+AO, AO, or GI alone. Ample physiological, behavioural, and neurophysiological 377 378 evidence suggests that imagined and/or observed movements are functionally equivalent to the real movements in terms of intention, planning, engagement of motor programs, duration, 379 and task difficulty.<sup>44,45</sup> Thus, one can argue that MSP intervention effectiveness relies on both 380 the neurophysiological and psychological factors.<sup>30,46,47</sup> Recently, an extensive review aimed 381 to summarise the theory of MI and AO research, concluded that concurrent AO+MI cannot 382 383 provide substantial evidence for more pronounced activity in motor regions of the brain compared to either MI or AO independently.<sup>14</sup> Aligned with the later review are results of 384 recent experimental study of Cuenca-Martinez et al.<sup>43</sup> that revealed that MI+AO does not lead 385

to higher autonomic nervous system response than MI alone while exercising functional and 386 387 straightforward movement tasks. Besides, it is worth to mention that the imagery ability may have had a significant impact upon its effectiveness because it is likely that someone who 388 cannot imagine performing a motor task will not benefit much from MI practice.<sup>48</sup> Thus, 389 given that only three studies<sup>15,16,31</sup> assessed patients' imagery ability while only one<sup>16</sup> 390 specified MI ability as exclusion criteria, it is possible that magnitude of patients ability to 391 imagine specified task might be accounted for effectiveness of MSP interventions 392 implemented.<sup>49,50</sup> In summary, our study showed that MI only was more effective than in 393 combination with AO, or AO and GI alone, respectively. However, given the gap in literature 394 395 regarding this question, research with high standards of methodological quality that directly compares the effectiveness of both MI and AO alone with its combination in rehabilitation of 396 397 orthopaedic patients is warranted.

Assessing the effectiveness of rehabilitation practice across different post-398 rehabilitation phases could provide more insight into the feasibility of MSP interventions in 399 400 patients' physical function recovery. In contrast to previous reviews in rehabilitation practice, we have provided evidence of MSP interventions' effectiveness across different post-401 rehabilitation periods, where the most substantial effect was observed after the application of 402 403 MSP in the early post-acute phase (i.e. from 3 to 12 weeks after surgery), followed by the acute phase (i.e. up to 3 weeks after surgery), and the late post-acute phase (i.e. from 12 404 weeks to 12 months). The observed differences in the magnitude of change across assessed 405 periods might be due to the fact that in patients following major surgery such as TKA or 406 THA, bodily pain combined with arthrogenic muscle inhibition induced by surgical trauma 407 seems to be the limiting factor for physical performance in the acute rehabilitation phase.<sup>2,51,52</sup> 408 In this period, joint structures are still in the process of healing their mechanical damage 409 induced by the surgery applied. When this initial stage of joint structure recovery ends, more 410

significant effects of MSP practice might be expected in the acute-post rehabilitation phase,
because more pronounced effects of actual physical practice can be accounted for overall
effects of rehabilitation.<sup>2,51,53</sup>

414 While perioperative rehabilitation following major surgeries has experienced a lot of positive changes in the last few decades,<sup>54–56</sup> there are still issues around patients' functional 415 recovery that could be improved. For OA patients who have undergone total knee 416 arthroplasty, recovery of quadriceps muscle strength has received considerable attention.<sup>19,57</sup> 417 Therefore, we conducted separate sub-analyses for clinically essential determinants of 418 419 patients' physical function. We found that MSP has a *large* effect on measures of the maximal 420 strength of knee extensor muscles of the affected leg, while a trivial negative effect was observed for the unaffected side. Furthermore, a *moderate* effect has been shown for self-421 selected gait speed, brisk walking speed, and TUG test, while for measures of flexibility, a 422 moderate positive effect was observed for active and passive flexions, respectively. The 423 improvements in these clinically essential measures of patients' physical function with MSP 424 425 might be prescribed to neural mechanisms, i.e., by regular activation of the cortical regions that are usually activated during real movements and consequently promote motor planning 426 and re-learning.<sup>40–42,44,58</sup> In the early post-surgery period, patients experience loss of more 427 than half of their pre-surgery strength,<sup>15,59</sup> that is likely a consequence of the alterations of 428 motor control at a central level induced by surgical trauma.<sup>2,59,60</sup> Paravlic et al.<sup>30</sup> found that 429 voluntary muscle activation accounted for 47% of the loss of knee extensor muscle strength at 430 one month after TKA. In later study,<sup>30</sup> both MI and SPT groups lost a significant amount of 431 strength when compared with pre-surgery values. However, the observed loss was lower in 432 the MI group which was accompanied by attenuated voluntary muscle activation.<sup>30</sup> Similar 433 findings were observed after intentional muscle disuse in healthy adults, where MI provided 434 evidence that neurological mechanisms contributed to the attenuation of muscle weakness and 435

voluntary muscle activation.<sup>58</sup> The higher attenuation of muscle strength, i.e., reduced 436 bilateral asymmetry, might be directly related to gait speed and performance on timed up-to 437 go test.<sup>15,61</sup> Comparable to effects were observed in patients after stroke<sup>35</sup> and Paravlic et al.<sup>15</sup> 438 found that increases in gait speed after MI intervention occurred mainly as a result of 439 increases in stride length, cadence, and consequently, decreases in both single and double 440 support phases during walking. Moreover, summarising the results of the included studies <sup>11,30</sup> 441 we found that MSP intervention has a positive effect on both the single and dual-task 442 conditions during self-selected and brisk walking speed, respectively. This finding is of great 443 importance, knowing that in everyday activities people often find themselves in situations 444 where postural adjustments and/or gait are overlapped with additional cognitive and/or motor 445 activity, such as talking on the phone, texting, avoiding obstacles, driving while talking, or 446 performing other cognitively demanding tasks that require directing attention between 447 448 simultaneous tasks. This simultaneous activity paradigm has gained a growing interest in neuroscience by focusing on ageing and neurodegenerative diseases.<sup>62</sup> Indeed, studies have 449 450 proved that simultaneous motoric and cognitive tasks affect gait speed and various qualitative parameters of walking in both healthy and symptomatic older adults.<sup>62,63</sup> For example, 451 findings from Toulotte et al.<sup>63</sup> revealed differences in gait parameters in healthy elderly 452 453 citizens who fall compared with those who do not. Mainly, differences were manifested as a reduction in gait speed, stride and step length, along with cadence, whereas step time and 454 single support time were longer under dual-task conditions than under single task.<sup>63</sup> Although 455 included studies in current review did not perform fall incidence analysis, we might assume 456 from observed results that MI intervention could potentially lead to a reduction of fall 457 incidence among TKA and THA patients and/or older adults in general, which remains to be 458 investigated.64 459

#### 460 Study limitations

Despite multiple benefits elucidated in the present systematic review and meta-461 analysis, some limitations must be outlined. First, external validity is limited to those patients 462 who were scheduled to TKA and THA, and not the orthopaedic population in general. 463 Secondly, we found that evidence was of only low to moderate quality due to imprecision (i.e. 464 small sample sizes) and inconsistency of the results (i.e. substantial heterogeneity within 465 effect estimates). Thirdly, the results of meta-regression analysis must be interpreted with 466 caution due to limited number of included studies. Our results, however, represent the best 467 468 estimate of effect size available, given the existing database, and provide the best evidence on which to base current decision-making. Finally, the possibility of negative result publication 469 bias is possible in this meta-analysis because studies reporting statistically significant or 470 positive results are more likely to be published in scientific journals compared to results 471 effects. 472 showing treatment no

#### 473 Conclusions

The present meta-analysis demonstrated that a MSP intervention has multiple positive 474 effects on measures of physical function recovery in patients who have undergone total knee 475 476 or hip replacement surgery in comparison with SPT, including beneficial effects on physical function in general, maximal strength of knee extensor muscles of affected leg, self-selected 477 478 gait speed, brisk walking speed, TUG test and active flexion. In addition, MI only showed to be more effective than in combination with AO, or AO and GI alone, where the largest effect 479 was observed after application of MSP in the acute phase, followed by early post-acute and 480 late post-acute phases, respectively. Finally, the total number of training sessions per study 481 significantly predicted effects of MSP on physical function in general. Thus, MSP 482 intervention seems to be an effective complementary therapy to standard physical therapy in 483 rehabilitation of patients after total knee and hip arthroplasty, especially in early post-acute 484 485 phase.

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#### Figure legends

Fig. 1 Flow diagram of the study selection process

Fig. 2 Percentage of studies achieving each TIDieR item of the experimental group and control group

Fig. 3 Effect of mental simulation practice interventions on physical performance in general

**Fig. 4** Effect of mental simulation practice interventions on: a) maximal voluntary strength of knee extensor muscles; b) brisk walking speed; c) brisk walking speed with dual task; and d) timed up-to go test