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# Effectiveness of and user experience with web-based interventions in increasing physical activity levels in people with Multiple Sclerosis: A systematic review

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3

4 **Running Head:** Web-based interventions in MS

5 **Title:** Effectiveness and user experience of web-based interventions in increasing  
6 physical activity levels in people with Multiple Sclerosis: A comprehensive systematic  
7 review

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22

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25 University for her assistance with the design of the search strategy.

26 **Title:** Effectiveness and user experience of web-based interventions in increasing  
27 physical activity levels in people with Multiple Sclerosis: A comprehensive systematic  
28 review

29

30 **Abstract** 275 words

31 **Background:** Supporting people with MS to achieve and maintain recommended  
32 levels of physical activity is important but challenging. Web-based interventions are  
33 increasingly used to deliver targeted exercise programmes and promote physical  
34 activity.

35 **Purpose:** To systematically review current evidence regarding the effectiveness and  
36 user experience of web-based interventions in increasing physical activity in people  
37 with multiple sclerosis.

38 **Data Sources:** MEDLINE, EMBASE, CINAHL, AMED, PEDro, PsychInfo, Web of  
39 Sciences, The Cochrane Library and grey literature were searched from 1990-  
40 September 2016.

41 **Study Selection:** English language articles reporting use of web-based interventions  
42 to increase physical activity in adults with MS were included. Eligible quantitative  
43 studies were of any design and reported a measure of physical activity. Qualitative

44 studies exploring users' experiences, in any context were included. Of the 881  
45 articles identified, nine met the inclusion criteria.

46 **Data Extraction:** Two reviewers independently assessed methodological quality and  
47 extracted data using standardized critical appraisal and data extraction instruments  
48 from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review  
49 Instrument (JBI-MASTARI).

50 **Data Synthesis:** Meta-analysis of self-reported physical activity questionnaire data  
51 from four studies demonstrated a SMD of 0.67 95%CI [0.43, 0.92] indicating a  
52 positive effect in favour of the web-based interventions. Narrative review of  
53 accelerometry data from three studies indicated increases in objectively measured  
54 physical activity. No qualitative studies met the inclusion criteria.

55 **Limitations:** Of the nine included articles only two different interventions, used with  
56 people who were ambulant were reported.

57 **Conclusions:** Web-based interventions have a short term positive effect on self-  
58 reported physical activity in ambulant people with MS. Evidence is not currently  
59 available to support or refute their use in the long term or with people who are not  
60 ambulant.

61

62

63 **Keywords:** internet, multiple sclerosis, physical activity

64 **Abbreviations:** MS-multiple sclerosis

65 **Body of manuscript 4984 words**

66

67 **Introduction**

68 Multiple Sclerosis (MS) is a progressive neurological condition that can result in  
69 wide-ranging impairments that may impact negatively upon activity and participation  
70 levels. Evidence demonstrates that people with MS are more sedentary and  
71 physically inactive than those in the general population, even in the early stages of  
72 the disease.<sup>1,2</sup> This is thought to be due to a combination of factors which include the  
73 direct effect of MS-related impairments, and the general deconditioning and  
74 functional deterioration which occurs as the disease progresses.

75

76 It is now well established that targeted exercise and increased levels of physical  
77 activity can result in a range of physical<sup>3,4,5,6,7</sup> and emotional<sup>8,9</sup> benefits for people in  
78 the early stage of MS, although this is yet to be established for those in the  
79 progressive phase of the disease.<sup>10,11</sup> Such increases in physical activity are  
80 important to minimize the complications and comorbidities associated with living a  
81 more sedentary lifestyle.<sup>12</sup> Furthermore, recent literature has suggested possible  
82 neuro-protective properties of exercise in people with MS.<sup>13</sup> Accordingly, there has  
83 been an increased emphasis within clinical practice to incorporate exercise  
84 programmes, and facilitate engagement with physical activity.<sup>14</sup> This approach  
85 aligns with public health guidelines,<sup>15</sup> developed to promote physical activity  
86 participation in the general population at a sufficient level to achieve health benefits.

87

88 Evidence based physical activity guidelines recommend that people with MS who  
89 have mild to moderate disability should aim to participate in 30 minutes of moderate

90 intensity aerobic activity twice a week and progressive resistance training involving  
91 major muscle groups twice a week.<sup>16</sup> There are no current guidelines regarding the  
92 prescription of physical activity levels for people with MS who have higher levels of  
93 disability.

94

95 Ensuring that adequate levels of physical activity are sustained in the long term is  
96 challenging, both for people with MS and for those involved in their management.<sup>17</sup>

97 Choice of activity, advice and support, control over level of engagement<sup>18</sup> and the

98 ability to develop 'self-support' <sup>19</sup> have been identified as key factors to facilitate

99 participation with physical activity. The low levels of physical activity in people with

100 MS<sup>20</sup> has also prompted researchers to identify the barriers to participation that

101 people with MS experience. Fatigue, lack of time, and the effort and travel distance

102 required to access rehabilitation venues are reported as barriers.<sup>21,22</sup> In parallel,

103 health services across the world face ever-increasing financial pressures, enforcing

104 reconsideration of cost effective, evidence-based service delivery.

105

106 Innovations in technology, such as the use of the internet, are increasingly being

107 used as a method for delivering physical activity interventions. Reviews of such web-

108 based interventions in the general population, as well as in conditions such as

109 obesity, rheumatoid arthritis and diabetes, have indicated promising results.<sup>23,24</sup>

110 More recently, two systematic reviews of randomised controlled trial studies in MS,

111 evaluating a broad spectrum of telerehabilitation interventions (including gaming

112 interventions, telephone support and the use of pedometers), suggest that these

113 distance-based interventions may be effective in increasing physical activity, <sup>25,26</sup> but  
114 that further robust research in this area is needed. However, the broad nature of  
115 these reviews means that it is not possible to evaluate the effectiveness of specific  
116 types of telerehabilitation interventions. Qualitative work<sup>27</sup> and process evaluation  
117 questionnaires<sup>17</sup> have been undertaken to explore the feasibility and acceptability of  
118 such web-based interventions, and provide helpful information to guide their on-  
119 going development. User feedback is important to optimise their effectiveness in  
120 enabling people with MS to increase and sustain physical activity levels in the long  
121 term.

122

123 This systematic review focused on studies of any design that investigated the use of  
124 interventions delivered via the internet that aimed to increase physical activity (as  
125 defined by Casperson)<sup>28</sup> in people with MS. It sought to establish their effectiveness  
126 in increasing physical activity, over the short ( $\leq$  three months) and long term ( $>$  three  
127 months), <sup>25</sup> and whether levels of activity met MS specific guidance.<sup>16</sup> This  
128 systematic review was conducted according to an *a priori* published protocol ref  
129 CRD42016054084. <sup>29</sup>

130

131 The original aim of this systematic review was to comprehensively explore the use of  
132 web-based interventions in increasing physical activity levels in people with a  
133 diagnosis of multiple sclerosis (MS), including both qualitative and quantitative data.  
134 As the literature search only yielded quantitative papers, it was not possible to  
135 address the qualitative objectives. Therefore, only the quantitative elements of the

136 review are reported in this paper.

137

138 The quantitative objectives were to identify:

- 139 • The effectiveness of web-based interventions in enabling people with MS to  
140 increase their physical activity levels as evaluated by measures of physical  
141 activity.
- 142 • If short or long-term web-based interventions enable people with MS to  
143 achieve the physical activity levels recommended in guidelines for adults with  
144 MS whilst they are being used.
- 145 • If the use of web-based interventions enable people with MS to maintain  
146 recommended levels of physical activity after the intervention has ceased, at  
147 short and long-term follow-up.

148

## 149 **Methods**

### 150 **Data Sources and Searches**

151

152 Searches aimed to find both published and unpublished studies. A three-step search  
153 strategy was utilized. An initial limited search of MEDLINE, AMED and CINAHL was  
154 undertaken followed by an analysis of the text words contained in the title and  
155 abstract, and of the index terms used to describe articles. A second search using all



156 identified keywords and index terms was then undertaken across all included  
157 databases. Thirdly, the reference list of all identified reports and articles was  
158 searched for additional studies. Studies published in English since 1990 were  
159 considered for inclusion. This date restriction is in place as the World Wide Web was  
160 established in 1989, and therefore web-based interventions were not possible prior  
161 to this. Two independent reviewers screened abstracts and full text articles for  
162 eligibility for inclusion, and any duplicates were removed.

163

164 **Initial keywords used:**

- 165 1) Web-based OR internet-based OR www OR world wide web OR e-learning  
166 OR telerehabilitation OR telemedicine OR eHealth  
167 2) Multiple sclerosis OR MS OR neurological condition OR neurolog\*  
168 3) Physical activity OR exercise OR physical fitness OR walking OR motor  
169 activity OR rehabilitation OR physiotherapy

170

171 The full search strategy is provided in Appendix 1.

172

173 Databases searched were MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCO),  
174 AMED (EBSCO), PEDro, PsychInfo, Web of Sciences, The Cochrane Library, and  
175 The Cochrane Central Register of Controlled Trials (CENTRAL). The search for  
176 unpublished studies included hand searches of reference lists of all identified articles  
177 and searches using Google Scholar, Conference Papers Index and clinical trials  
178 registers via [www.controlled-trials.com](http://www.controlled-trials.com) and <http://clinicaltrials.gov>. In two cases,

179 authors were then contacted directly to request the full papers for inclusion.

180

## 181 **Study Selection**

182

183 This review considered studies that included adults over the age of 18 with a  
184 diagnosis of MS, regardless of MS type, time since diagnosis or level of disability. It  
185 considered both experimental and epidemiological study designs including  
186 randomized controlled trials, non-randomized controlled trials, quasi-experimental  
187 studies, before and after studies, prospective and retrospective cohort studies and  
188 case control studies.

189

190 Studies that investigated the use of web-based interventions that were exercise or  
191 lifestyle activity based, and/ or incorporated a behaviour change or coaching  
192 approach to increase physical activity were reviewed. Studies reporting an active  
193 comparator, usual care or waitlist control and those without such comparators were  
194 included. Interventions describing any regimen of frequency or intensity of delivery  
195 were included. Studies that described use of the Internet to deliver virtual  
196 assessments or gaming interventions (such as Wii or Xbox) were not included.

197

198 Studies were considered if they included measures of physical activity such as  
199 accelerometer, pedometer or Global Positioning System data or physical activity  
200 questionnaires. Adherence/ compliance outcomes, when measured alongside  
201 physical activity data were also included, for example by recorded numbers of logins  
202 to web-based interventions or completion of activity diaries. The purpose of this

203 review was not to evaluate the effectiveness of web-based interventions at the level  
204 of impairment, hence outcomes such as weight loss, reduced blood pressure,  
205 increased cardiovascular fitness or muscle strength were not considered.

206

### 207 **Data Extraction and Quality Assessment**

208

209 Papers selected for retrieval were evaluated by two independent reviewers using a  
210 two-stage process to assess relevance and quality. Standardized critical appraisal  
211 instruments from the Joanna Briggs Institute Meta Analysis of Statistics Assessment  
212 and Review Instrument (JBI-MAStARI) were used (accessed via  
213 <https://www.jbisumari.org/>). Any disagreements that arose between the reviewers  
214 were resolved through discussion, or with a third reviewer where required. The  
215 outcomes of the quality assessments were summarised by calculating the number of  
216 items that were marked as present for each study. In keeping with the aim to be as  
217 comprehensive as possible, a cut-off point for inclusion was not set for the quality  
218 review stage; however, the outcome of the quality assessment was considered when  
219 making inferences from the data synthesis.

220

221

222 Data were extracted from papers using the standardized data extraction tool from  
223 JBI-MAStARI. The data extracted included specific details about the interventions,  
224 populations, study methods and outcomes of significance to the review question and  
225 specific objectives.

226

227 **Data synthesis and Analysis**

228

229 Where possible, data were combined in statistical meta-analysis to obtain a pooled  
230 standardized mean difference with 95% confidence interval (95% CI). Where  
231 standard deviations were not reported, they were imputed from the reported  
232 standard error using the formula  $SD = SE \times \sqrt{N}$ .<sup>30</sup> Because of the small sample sizes  
233 and variability of sample characteristics within the studies,<sup>31</sup> a random-effects  
234 generic inverse variance analysis was undertaken. The pooled data set was  
235 analysed for heterogeneity using a combination of visual inspection and  
236 consideration of the chi-squared statistic, setting a P value of 0.10.<sup>32</sup> Where  
237 statistical pooling was not possible, the findings are presented in narrative form,  
238 including tables and figures to aid in data presentation.

239

240 **Results**

241 ***Study Selection***

242

243 One reviewer (RD) performed the searches in September 2016. In total, 881 records  
244 were identified, which after removal of duplicates resulted in 618 titles and abstracts  
245 being screened for eligibility. The results of the searches are presented in the study  
246 selection flow chart (Figure 1), with specific details of the included studies in Table 1.

247

248 Insert figure 1

249 Insert table 1

250

251 **Critical Appraisal Results**

252 Insert table 2

253 **Methodological quality**

254 Insert table 3

255

256 Summaries of the appraisal of study quality are included in tables 2 and 3. Standards  
257 of reporting were generally good with both case series articles being marked as 'Yes'  
258 for all questions. Within the randomised controlled trials, the median number of 'yes'  
259 scores was 10 of a possible 13 items (inter-quartile range 8.75-10.25). The most  
260 frequently omitted methodological items related to blinding of research assessors  
261 and management of incomplete outcome data. Blinding of both participants and

262 treating therapists was not reported to have been undertaken in any trial, a common  
263 finding in reviews of rehabilitation trials.<sup>40</sup>

264

265

## 266 **Description of the participants**

267

268 The total number of participants recruited from the included studies was 346.

269 Baseline characteristic data was available for 340 participants, of whom 68% were

270 female, with a mean (SD) age of 45.7 (9.4) years and disease duration of 8.9 (7.0)

271 years. Participants were ambulatory with the majority (75%) walking unaided.

272 Disability status was described using the Patient Determined Disease Steps (PDDS)

273 scale<sup>41</sup> in all but one study<sup>39</sup> where the Expanded Disability Status Scale<sup>42</sup> was

274 used. Four studies only included participants with a classification of Relapsing

275 Remitting MS.<sup>34,35,17,36</sup> The remaining studies included people with both progressive

276 and relapsing remitting sub-types<sup>1,37,38,2,39</sup> (four of which reported on the same study

277 sample). Tallner<sup>39</sup> excluded those with a primary progressive disease course. Eight

278 of the nine studies were based in the USA, with one in Germany.<sup>39</sup>

279

## 280 **Study designs**

281

282 Seven of the included articles report on RCTs of internet based interventions with

283 waitlist controls (Table 1).<sup>1,2,17,34,37,39</sup> Four of these<sup>1,2,37,38</sup> report different aspects of

284 the same study, and hence to avoid double counting of data, of these only Pilutti et

285 al<sup>37</sup> has been used within the meta-analysis. The other two included studies are

286 single group design where participants are the waitlist controls from previously

287 reported studies.<sup>35,36</sup> Only one of the studies<sup>39</sup> described their sample size  
288 calculation.

289

## 290 **Description of web-based interventions**

291

292 Eight of the nine articles report on studies that were part of the development process  
293 of a behavioural intervention designed to increase physical activity by promoting  
294 additional walking as part of everyday life. The intervention was initially trialled as a  
295 12-week multimedia internet intervention<sup>34,35</sup> that focused on four information  
296 modules based on the Social Cognitive Theory: Getting Started, Planning for  
297 Success, Beating the Odds and Sticking with it. Content of the modules was made  
298 accessible during the intervention period in a titrated fashion and was supported with  
299 group chat sessions and a telephone line and email address to provide direct contact  
300 with the study team. The professional background of the study team is not described.  
301 Subsequent studies<sup>17,36</sup> described the addition of seven one-to-one video coaching  
302 sessions via Skype with the aims of increasing participant website login, and  
303 reinforcing, and clarifying website content with them. The coach was a doctoral  
304 student with expertise in behavior change and experience in conducting physical  
305 activity research in people with MS. In these five-to-ten minute sessions the  
306 participant and coach reviewed and progressed goals and discussed strategies to  
307 aid behaviour change based on the website content that had already been accessed.  
308 <sup>17,36</sup> In the latest reported study,<sup>37</sup> the intervention was delivered over six months and  
309 included 15 of the video coaching sessions. Intervention group participants in this

310 study also wore a pedometer and completed a logbook and goal tracker spreadsheet  
311 to motivate and record physical activity as part of the programme.

312

313 Tallner et al <sup>39</sup> describe a different intervention approach delivered via the internet; a  
314 six-month, individually prescribed, twice-weekly strength training and weekly  
315 endurance training (jogging, walking, cycling or swimming) programme. The trainers  
316 were physical therapists or exercise therapists with experience of rehabilitation of  
317 people with MS and trained in the exercise prescription and study processes.

318 Participants received supervision, and had their exercise programmes progressed  
319 online using a standardized progression scheme, delivered via a messaging service  
320 in the web-based software (not in real time) with further email and telephone support  
321 if required. None of the articles published after the development of the TIDieR  
322 guidelines <sup>43</sup> made reference to them in reporting their interventions,<sup>2,39</sup> although a  
323 summary of the intervention components is provided within each article.

324

## 325 **Description of outcomes**

326

### 327 **Physical activity**

328

329 Physical activity was measured using both self-report and objective measures. Three  
330 different standardized and validated self-report measures were used. The Godin  
331 Leisure Time Exercise Questionnaire (GLTEQ) was reported in six articles,<sup>2,17,34-37</sup>  
332 the International Physical activity Questionnaire (IPAQ) in five,<sup>1,2,35,36,38</sup> (three of  
333 which report the same sample<sup>1,2,38</sup>) and the Baecke Questionnaire in one.<sup>39</sup> The



334 GLTEQ<sup>44</sup> includes three items that measure the frequency of light, moderate and  
335 vigorous leisure-time physical activity completed for at least 15 minutes over the  
336 previous seven days, which are weighted and summed (0-119). The IPAQ<sup>45</sup> has six  
337 items that measure the frequency and duration of vigorous, moderate and walking  
338 physical activity over a seven-day period which are then weighted and summed (0-  
339 117). The sport score of the Baecke Questionnaire<sup>46</sup> is the product of the frequency,  
340 intensity and duration of a participants reported sports activities. In each of these  
341 measures, higher values indicate increased levels of physical activity.

342

343 Accelerometers, worn at the waist during waking hours, were used to collect  
344 objective physical activity data over seven days in three studies<sup>35-37</sup> and are  
345 reported as part of a composite measure in a secondary analysis article.<sup>2</sup> The  
346 activity counts per day (for days when the accelerometers were worn for at least 10  
347 hours) were converted into minutes of moderate to vigorous physical activity (MVPA)  
348 per day using validated cut-off points.<sup>47,48</sup> In addition, pedometer steps-per-day  
349 data, as a descriptive measure of change in physical activity were available from  
350 intervention group participants in four studies<sup>17,35-37</sup> where higher numbers of steps  
351 per day demonstrate greater levels of activity. Although no MS specific step count  
352 recommendations are available, a value of 7100 steps/ day is suggested to equate to  
353 someone achieving 30 minutes MVPA from the healthy older adult and special group  
354 population literature.<sup>49</sup>

355

## 356 **Compliance**

357

358 Compliance with using the interventions was reported in six studies<sup>1,17,34-36,39</sup> as  
359 numbers or percentages of website logins or percentage of participants completing  
360 their prescribed programme.

361

### 362 **Process evaluation**

363

364 Process evaluation questionnaires were incorporated at the end of two studies.<sup>17,35</sup>  
365 Information regarding overall satisfaction of the intervention, the website and the  
366 staff delivering the programme was collected.

367

### 368 **Effectiveness of interventions in increasing physical activity levels**

369

370 Both self-report and objective data is available from the included studies and these  
371 will be presented separately.

372

### 373 **Self-report Physical Activity Questionnaires**

374

375 Self-reported physical activity questionnaire data was available from four different  
376 study samples (n=277 complete data sets). Participants in the intervention groups  
377 participated in significantly more self-reported physical activity compared with  
378 controls: p=0.001, d=0.77<sup>37</sup>; p=0.01, d=0.72<sup>34</sup>; p=0.001, d=0.33<sup>39</sup> and p<0.001,  
379 d=0.98,<sup>17</sup> which remained statistically significant at three-month, follow up (p<0.001,  
380 d=0.79). These data were pooled in a meta-analysis (figure 2). The pooled SMD

381 0.67 95%CI [0.43, 0.92] indicates a positive effect in favour of the web-based  
382 interventions.

383

384 Self-report physical activity questionnaire data was also available from the two single  
385 group studies. One, <sup>35</sup> the waitlist control group from the initial pilot study,  
386 demonstrated a small and non-significant increase in GLTEQ scores ( $p=0.07$ ,  $d=$   
387  $0.34$ ) and a significant improvement in IPAQ scores ( $p=0.03$ ,  $d= 0.43$ ). In the second  
388 follow-up single group study<sup>36</sup> a statistically significant and large increase in GLTEQ  
389 scores ( $p<0.0015$ ,  $d=0.83$ ) and IPAQ scores ( $p<0.001$ ,  $d=1.12$ ) was demonstrated  
390 on completion of the treatment period, which had not been seen in the period of no  
391 treatment.

392

### 393 **Accelerometry data**

394

395 Accelerometry data was only available from one RCT <sup>37</sup> and the two single group  
396 studies <sup>35,36</sup> and is therefore reported here narratively. Pilutti<sup>37</sup> presented  
397 accelerometry data which indicated that participants in the intervention group  
398 achieved a moderate but non-significant increase in time spent undertaking MVPA  
399 compared with controls ( $p=0.07$ ,  $d=0.43$ ). This equated to an average increase of  
400 just under six minutes a day of extra MVPA compared with controls. Reporting on  
401 the same study, Motl <sup>2</sup> conducted a secondary analysis in which a composite score  
402 of PA was created combining GLTEQ, IPAQ and accelerometry. This composite  
403 physical activity data was analysed using a one-way ANCOVA, controlling for  
404 baseline physical activity scores, and demonstrated that the intervention group had

405 significantly higher levels of physical activity compared with those in the waitlist  
406 control group after the six-month intervention ( $p < 0.001$ ,  $np^2 = 0.12$ ), which the authors  
407 report to be a “practically meaningful effect”.<sup>2</sup> The pre- and post-intervention  
408 accelerometer data from two single group studies<sup>35,36</sup> demonstrated statistically  
409 significant increases in both total activity (counts per day ( $p = 0.002$ ,  $d = 0.68$ )<sup>35</sup> and  
410  $p < 0.001$ ,  $d = 0.92$ <sup>36</sup>; and total step counts per day  $p < 0.001$ ,  $d = 1.03$ <sup>36</sup>).

411

412 Intervention group pedometer data were reported from three studies<sup>17,36,37</sup> all of  
413 whom report increases in weekly pedometer step counts. Two of the studies note  
414 that the increases occurred during the first six weeks of the 12-week interventions  
415 and were maintained to the end.<sup>17,36</sup> The magnitude of these increases range from  
416 22% or an average of 1387 steps per day<sup>35</sup> to 46% (1869 steps),<sup>36</sup> both in excess of  
417 the minimal clinically important difference which would indicate a change in  
418 ambulation and clinical/health outcomes in MS.<sup>50</sup> As there is no control-group  
419 pedometer data, it is not possible to comment on whether these increases were due  
420 to the intervention.

421

#### 422 **Achievement of recommended levels of physical activity**

423

424 Although all articles describe the importance of physical activity in people with MS  
425 and one<sup>39</sup> makes direct reference to exercise prescription recommendations<sup>51</sup> none  
426 report physical activity levels in line with recommendations for either the general<sup>52</sup> or  
427 MS<sup>16</sup> populations. Four<sup>17,34-36</sup> of the nine articles were however, published before  
428 the publication of the MS-specific guidelines. Detailed information regarding the type

429 and intensity of physical activity undertaken is only reported in one study,<sup>39</sup> where  
430 participants were individually prescribed strength and self-selected endurance-  
431 training programmes based on their fitness level. A standardized progression  
432 scheme was used to facilitate strength training overload, and guidance was given  
433 regarding endurance training intensity levels in line with recommendations.<sup>51</sup> There  
434 is no detail provided as to whether this was achieved or whether this data was  
435 collected.

436

437 Dlugonski et al<sup>17</sup> report intervention group pedometer data that demonstrated that  
438 the sample walked an average of 6368 steps per day in the final week of the 12-  
439 week intervention. Data from the follow-up single group study<sup>36</sup> however, report that  
440 67% of the participants exceeded 7100 steps/ day over a week; above the value  
441 suggested<sup>49</sup> to be required for accumulating 30 minutes of MVPA each day for older  
442 adults and special populations.

443

#### 444 **Maintaining physical activity levels in the short and long-term**

445

446 Compliance data was collected by six of the included studies and is summarized in  
447 table 4. In the U.S. behavioral intervention studies, compliance with the early stages  
448 of the intervention<sup>34,35</sup> decreased during the intervention periods, but this was  
449 demonstrated to be improved by the addition of video coaching sessions during  
450 development of the intervention programme.<sup>1,17,36</sup> In the German exercise-based  
451 study, however, although web-based one-to-one support was available for each  
452 participant, compliance with documented training sessions in the online activity

453 journal declined after four weeks, falling to 36% of documented sessions after three  
454 months. However, it is not possible to establish if participants were continuing to  
455 exercise and not documenting their engagement with the programme, or if they were  
456 no longer adhering to their exercise programme.

457

458 Only one study<sup>17</sup> collected follow up physical activity data (self-report physical  
459 activity at three months) which demonstrated that the increase in physical activity  
460 post intervention ( $p < 0.001$ ,  $d = 0.98$ ) was sustained at three months ( $p < 0.001$ ,  
461  $d = 0.79$ ).

462

### 463 **Process Evaluation**

464

465 Twelve of the 21 participants provided feedback in one study<sup>35</sup> and 21 of the 22 who  
466 completed the intervention in another.<sup>17</sup> Participants in both studies reported a high  
467 degree of satisfaction with the programme as a whole, the staff involved, and an  
468 overall willingness to recommend the intervention to others. They reported less  
469 satisfaction with the intervention website, citing disinterest<sup>35</sup> in the online group chat  
470 sessions, and difficult to use forum section, as reasons for this and suggested that  
471 the programme would benefit from more interaction with other participants.

472 **Discussion**

473

474 The purpose of this systematic review was to examine the effectiveness of web-  
475 based interventions in enabling people with MS to increase their physical activity  
476 levels. Further, to ascertain if any increases were in line with recommended levels  
477 for adults with MS<sup>16</sup> and were maintained at short and long term follow-up.<sup>25</sup> The  
478 review also set out to include a qualitative component, but as no studies were found  
479 that met the inclusion criteria, it is not possible to achieve this aim of the review.

480

481 **Effectiveness in enabling increased physical activity levels**

482

483 The results of the meta-analysis of self-report physical activity data demonstrated  
484 that web-based interventions had a moderate positive effect on physical activity in  
485 participants with mild disability. Self-report measures are recognised to have  
486 limitations in terms of social desirability and recall biases in their use.<sup>53</sup> Further, the  
487 GLTEQ measures only leisure-time exercise of longer than 15-minute duration and  
488 the Baecke Sports score, only time in recognised sports; neither therefore capture  
489 the important shorter bursts of activity that people engage in throughout their day. To  
490 our knowledge, there are no established minimal clinically important differences  
491 (MCID) for self-report measures of physical activity and hence understanding the  
492 meaningful change also remains difficult. These issues highlight the importance of  
493 collecting more complete, objective data to accurately picture a person's daily  
494 lifestyle activity and help provision of the most appropriate physical activity advice.

495

496 Participants in all included studies had minimal disability, with a high percentage  
497 reporting no limitations to walking. Hence, it is not possible to comment on whether  
498 such interventions would be effective for people with higher levels of disability.  
499 Indeed, results from a secondary analysis of data from Pilutti et al<sup>2</sup> demonstrated a  
500 disability x time effect suggesting that their six-month intervention was most effective  
501 for those whose mobility was least affected. Other analyses went further, suggesting  
502 a greater effect for people with Relapsing Remitting MS and normal weight. In many  
503 countries, the population of people with MS who access healthcare systems have  
504 typically higher levels of disability and as such, this raises the question whether web-  
505 based interventions can also be beneficial for this group. Further, it may also  
506 challenge current practice, pointing to provision of physical activity promotion and  
507 rehabilitation input at earlier stages of the disease.

508

509 Participants from most of the included studies completed the PAR-Q<sup>54</sup> , a tool  
510 designed to help people evaluate their medical fitness prior to engaging in physical  
511 activity. Whilst fitness to exercise is very important, none of the studies asked  
512 participants about their attitude or readiness to engage in increased physical activity.  
513 It may be important to incorporate such questions prior to using such interventions in  
514 practice, where targeting a population ready to engage may have greater clinical and  
515 cost benefits.

516

517 Walking was the most common type of physical activity encouraged in the included  
518 studies. In order to describe the amount of activity undertaken at recommended



519 levels, data was presented as steps per day or time spent undertaking MVPA. Those  
520 that reported time spent in MVPA calculated this according to defined cut-off points<sup>1</sup>  
521 of numbers of steps/ minute that would equate to MVPA. It is suggested that for  
522 people whose disability levels are higher, the increased effort of walking<sup>55</sup> may mean  
523 that the number of steps/ minute to reach MVPA is lower.<sup>2,48</sup> There is no available  
524 data regarding required numbers of steps per day for people with MS to achieve 30  
525 minutes of MVPA, so reference is made to 7100 steps per day over one week, the  
526 figure obtained from the older adult and special groups literature.<sup>49</sup> For those people  
527 where it is too challenging to engage in sufficient walking to achieve health benefits,  
528 accessing other types of physical activity to achieve an adequate duration and  
529 intensity of activity is important.<sup>1</sup> This was incorporated in to the Tallner<sup>39</sup>  
530 intervention, where choice of endurance activity included activities such as cycling,  
531 swimming and cross training.

532

### 533 **Achievement of recommended levels of physical activity**

534

535 Physical activity guidelines for people with MS with mild to moderate disability  
536 recommend that people should aim to undertake 30 minutes of moderate intensity  
537 aerobic activity twice a week and progressive resistance training involving major  
538 muscle groups twice a week.<sup>16</sup> The findings of this review are such that it is not  
539 possible to suggest whether web-based interventions facilitate people with MS to  
540 meet these guidelines. Although some<sup>17,35-37</sup> of the eight articles describing the US  
541 behaviour intervention development included accelerometer or pedometer data (that  
542 could be used to estimate time undertaking MVPA), none report whether any of the

543 web-based modules or coached sessions discussed or prescribed strength training.  
544 The final article<sup>39</sup> described a targeted exercise programme including both strength  
545 and endurance components that could therefore have facilitated meeting  
546 recommendations, but do not present data as to whether prescribed levels were  
547 achieved, sufficiently intensive, or performed for long enough.

548

549 One of the potential benefits of a web-based intervention is that it may be used to  
550 help people maintain activity levels in the long term. As such, the issue of  
551 compliance is an important one to consider. The importance of appropriate support  
552 to facilitate engagement with exercise is well recognised.<sup>56,39</sup> In the included studies  
553 such support was provided by: experienced doctoral students (whose clinical  
554 background in not stated) in the behavioural intervention studies;<sup>17,36,37</sup> and physical  
555 therapists or exercise therapists in the targeted exercise intervention study.<sup>39</sup> The  
556 opportunity to engage with web-based support through a messaging service, with  
557 email and telephone options as required, did not appear to help participants adhere  
558 to the programme in the latter study<sup>39</sup> where adherence with documenting training  
559 sessions had already begun to reduce after four weeks. During the development of  
560 the U.S behavioural intervention however, the addition of web-based individual  
561 coaching sessions as part of the intervention was demonstrated to be instrumental in  
562 increasing compliance.<sup>17</sup> It is perhaps the case therefore, that planned, face-to-face  
563 sessions were key to the delivery of successful online support. This gives rise to the  
564 question as to whether it was the coaching itself or its role within the intervention  
565 package that made the difference. A further area of note is whether measuring  
566 compliance as numbers of log-ins or attendance at a coaching session truly

567 represents the level of engagement with an exercise programme or indeed  
568 adherence with increased physical activity.

569

570 **Maintenance or physical activity levels in the short and long-term**

571

572 It is not possible to comment on whether the web-based interventions enabled  
573 people to sustain recommended levels of physical activity in the long-term due to the  
574 lack of data. Only one study<sup>17</sup> included any follow-up beyond the post intervention  
575 assessment and that was short term, at three months. The statistically significant  
576 increases in self-reported physical activity, which remained at three months is  
577 promising, but longer term follow-up data is required to enable thorough discussion  
578 of this issue.

579

580 **Strengths and limitations of this review**

581

582 One of the strengths of the review was that it set out to include both qualitative and  
583 quantitative studies of any design, not only randomised controlled trials. This  
584 systematic review has enabled clarification of the existing body of literature, which  
585 can be sometimes difficult given the wide-ranging publication sources. It has  
586 identified that, of the nine articles published, there is multiple secondary reporting of  
587 a single study, resulting in six independent data sets (two of which were single group  
588 studies). It has identified that the included studies, in essence, report on just two  
589 different interventions. The web-based intervention inclusion criterion was chosen  
590 because of the very distinct role such interventions can provide and the specific

591 challenges they present. This was in contrast to two previous technology based  
592 systematic reviews in MS <sup>25, 26</sup> and resulted therefore in this focused review only  
593 including a small number of studies, which could be considered a limitation.

594

## 595 **Conclusion**

596

597 This systematic review suggests that web-based interventions have a positive effect  
598 on self-reported physical activity in ambulant people with MS, in the short term.

599 There is insufficient evidence to comment on their effectiveness on objective  
600 physical activity data or whether increases in physical activity equate to disease  
601 specific or worldwide physical activity recommendations. Due to the lack of follow-up  
602 data, it is also not possible to suggest whether such interventions can have an effect  
603 on physical activity levels in the long-term. Similarly, it is not possible to comment on  
604 whether they can be effective for people with higher levels of disability, but it may be  
605 that web-based interventions have greatest impact on physical activity when used in  
606 the early stages of the disease.

607

## 608 ***Implications for practice and research***

609

610 Web-based interventions may be helpful in facilitating ambulant individuals with MS  
611 to increase their physical activity levels, at least in the short term. Evidence is not  
612 currently available to either support or refute the use of web-based interventions in  
613 enhancing physical activity levels in individuals with MS who are not ambulant. The  
614 importance of the user experience should be considered in the on-going

615 development and evaluation of web-based interventions in the MS population.  
616 Research into the short and long-term effectiveness of such web-based  
617 interventions, especially for those with higher levels of disability, is required. Finally,  
618 determining the most effective support methods to maximise compliance with web-  
619 based interventions is vital.

620

621 **Conflict of interest**

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623 The authors declare no conflict of interest.

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792 **Figure and table legends**

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794 **Figure 1:** Prisma Flow Diagram

795 **Table 1:** Summary of articles reporting included studies

796 **Table 2:** Methodological Quality Assessment: Case Series Designs

797 **Table 3:** Methodological Quality Assessment: Randomized Controlled Trial Designs

798 **Figure 2:** Meta-analysis of self-reported physical activity questionnaire data

799 **Table 4:** Compliance data reported

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**Table 1. Summary of articles reporting included studies**

<b>Study/ Year/ Country</b>	<b>Study design</b>	<b>Number of Participants (total, %female)</b>	<b>Disability level</b>	<b>Disease course</b>	<b>Intervention</b>	<b>Physical Activity Outcomes (all participants unless stated)</b>
Motl et al 2011 <sup>34</sup> USA	RCT with waitlist control	54, 90% (data reported from 48)	PDDS 0-5	RRMS	12-week multimedia internet intervention, twice weekly online chat sessions, patient forum, telephone and email support	GLTEQ, intervention group compliance
Dlugonski et al 2011 <sup>35</sup> USA *	Single group	21, 90% (control group from Motl et al 2011)	PDDS 0-5	RRMS	12-week multimedia internet intervention, twice weekly online chat sessions, patient forum, telephone and email support (same intervention as Motl et al 2011)	GLTEQ, IPAQ, 7-day accelerometer, compliance
Dlugonski et al 2012 <sup>17</sup> USA <sup>‡</sup>	RCT with waitlist control	45, 87%	PDDS 0-6	RRMS	12-week internet delivered behavioral intervention plus 7 video coaching sessions	GLTEQ, intervention group; pedometer, compliance
Motl and Dlugonski <sup>36</sup> 2011* USA	Interrupted time series Single group	18, 89% (control group from Dlugonski 2012)	PDDS 0-4	RRMS	12-week internet delivered behavioral intervention plus 7 web-based video coaching sessions (same intervention as Dlugonski et al 2012)	GLTEQ, IPAQ, 7 day accelerometer, pedometer, compliance
Pilutti et al 2014 <sup>37</sup> USA	RCT with waitlist control	82, 76% (data reported from 76)	PDDS 0-6	RRMS and progressive MS	6-month multi- component behavioral intervention plus 15 web-based video coaching sessions	GLTEQ, 7-day accelerometer, intervention group pedometer

WEB-BASED INTERVENTIONS IN MS

Study/ Year/ Country	Study design	Number of Participants (total, %female)	Disability level	Disease course	Intervention	Physical Activity Outcomes (all participants unless stated)
Klaren et al 2014 <sup>38</sup> USA†	RCT (secondary analysis)	70 (of the 82 in the Pilutti study) 78% female	PDDS 0-6	RRMS and progressive MS	6-month multi- component Behavioral Intervention plus 15 web-based video coaching sessions (same intervention as Pilutti et al 2014)	Question 7 of IPAQ
Sandroff et al 2014 <sup>1</sup> USA†	RCT with waitlist control (secondary outcomes)	Same 82 from Pilutti study, data reported from 76. 76% female	PDDS 0-6	RRMS and progressive MS	6-month multi- component behavioral intervention plus 15 web-based video coaching sessions (same intervention as Pilutti et al 2014)	IPAQ. Compliance
Motl et al 2015 <sup>2</sup> USA†	RCT with waitlist control	Same 82 from Pilutti study, data reported on 76 76% female	PDDS 0-6	RRMS and progressive MS	6-month multi- component behavioral intervention plus 15 web-based video coaching sessions (same intervention as Pilutti et al 2014)	Composite PA score from GLTEQ, IPAQ and 7-day accelerometer
Tallner et al 2016 <sup>39</sup> Germany	RCT with waitlist control	126, 75% (data reported from 108)	EDSS 0-4	RRMS and SPMS	6-month programme 2x week strength training, 2–3 sets per exercise. Endurance training x1 week. Home-based and supervised via the internet	Baecke Questionnaire, compliance

819 RCT: randomised controlled trial; EDSS: Expanded Disability Status Scale; PDDS: Patient Determined Disease Steps Scale; RRMS: relapsing  
820 remitting multiple sclerosis; MS: multiple sclerosis; SPMS: secondary progressive multiple sclerosis; GLTEQ Godin Leisure Time Exercise  
821 Questionnaire; IPAQ: International Physical Activity Questionnaire; PA Physical Activity.

822 \*waitlist in single group study following the main study, † studies report secondary outcomes or secondary analysis of the original sample data.

823 ‡ Data collected at baseline at post intervention except Dlugonski et al<sup>17</sup> where a three-month follow up was conducted.

824 **Table 2: Methodological Quality Assessment: Case Series Designs**

Quality Criterion	Dlugonski 2011 <sup>35</sup>	Motl and Dlugonski 2011 <sup>36</sup>	%
Clear inclusion criteria	Y	Y	100
Standard, valid and reliable measurement of the condition?	Y	Y	100
Consecutive and complete inclusion of participants	Y	Y	100
Clear reporting of demographic information	Y	Y	100
Clear reporting of clinical information	Y	Y	100
Clear reporting of outcomes or follow up results	Y	Y	100
Clear definition of the condition/disease of interest in the case series	Y	Y	100
Clear reporting of the presenting site(s)/clinic(s) demographic information	Y	Y	100
Appropriate statistical analysis	Y	Y	100
Total number of 'yes' scores (maximum 9)	9	9	

825

826 **Table 3: Methodological Quality Assessment: Randomized Controlled Trial Designs**

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Quality Criterion	Dlugonski 2012 <sup>17</sup>	Klaren 2014 <sup>38</sup>	Motl 2011 <sup>34</sup>	Motl 2015 <sup>2</sup>	Pilutti 2014 <sup>37</sup>	Sandroff 2014 <sup>1</sup>	Tallner 2016 <sup>39</sup>	Completion %
True randomization used for assignment of participants	Y	Y	Y	Y	Y	Y	Y	100
Concealment of allocation to treatment group	Y	Y	Y	U	Y	U	Y	71.42
Treatment groups similar at the baseline	Y	Y	Y	Y	Y	Y	Y	100
Blinding of participants to group assignment	N	N	N	N	N	N	N	0
Blinding of those delivering treatment to group assignment	N	N	N	N	N	N	N	0
Blinding of outcomes assessors to group assignment	U	Y	Y	U	U	N	Y	42.85
Identical group treatment other than the intervention of interest	Y	Y	Y	Y	Y	Y	Y	100
Complete follow up, or use of strategies to address incomplete follow-up	Y	Y	Y	N	N	N	N	42.85
Analysis of participants in the groups to which they were randomized	Y	Y	Y	Y	Y	Y	Y	100
Measurement of outcomes in the same way for treatment groups	Y	Y	Y	Y	Y	Y	Y	100
Outcomes measured in a reliable way	Y	Y	Y	Y	Y	Y	Y	100
Use of appropriate statistical analysis	Y	Y	Y	Y	Y	Y	Y	100
Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	Y	Y	Y	Y	Y	Y	Y	100
Total number of 'yes' scores (maximum 13)	10	11	11	8	9	8	10	

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831 **Table 4: Compliance data reported in six of the included studies**

Study	Compliance measure	Outcomes	Conclusions
Motl 2011 <sup>34</sup>	% participants logged in per week  Average (SD) number of weeks participants logged in	96% in weeks 1 and 2, declined throughout 12 weeks 52% in weeks 8, 10, 11 71(+/- 15%) over 12 week period  8.6 (+/- 3.0)	Very weak correlation with change in PA (r=0.10, p= 0.64)
Dlugonski 2011 <sup>35</sup>	% participants logged in per week  Average (SD) number of weeks participants logged in	76% week 1, 81% week 2, 52% weeks 10-12  7.5 (+/- 4.3) over the 12 weeks	Significant correlation between number of weeks logged on and change in accelerometer data (r=0.42, p=0.03) but not with changes IPAQ (r=0.10, p=0.32) or GLTEQ (r=0.08, p=0.36)
Dlugonski 2012 <sup>17</sup> (7 video coach sessions)	% participants logged in per week  Average (SD) number of weeks participants logged in  Average number of video coaching sessions attended	~73% participants logged in ≥ 10 weeks of the 12 week intervention  10 (+/- 2.7)  6.8 (range 6-7) 77% of participants attended all 7.	Weekly log in moderately and significantly correlated with change in weekly pedometer step counts between weeks 1 and 12 (r=0.43, p=0.05)  Negligible and non-significant correlation with weekly log in and change in self-report PA (r=-0.03, p=0.90)
Motl and Dlugonski 2011 <sup>36</sup> (7 video coach sessions)	Average (SD) number of weeks participants logged in Average (SD) Number of video coaching sessions attended	10.6 (+/- 3) of 12 week intervention  6.6 (+/- 0.6) scheduled sessions	Moderate and significant correlation between weekly log in and number of coaching session attended (r=0.45, p<0.05) and between weekly log in and change in GLTEQ score (r=0.51, p<0.05), but non-significant correlation with weekly log in and change in IPAQ score (r= 0.35, p=0.08)
Sandroff 2014 <sup>1</sup> (15 web-based video coach sessions)	% participants who participated in: all intervention features Website log in Uploading step counts Attended video coach sessions	overall compliance  88.6% 80% 88%	No further information regarding time points or possible correlations
Tallner 2016 <sup>39</sup>	% participants who documented at least 80% of prescribed training programme during: Month 0-3	73%	Gradual decrease in compliance from week 4 onwards. Along with reduced compliance was increase in dropout rate (0-3 months 14%, 4-6 months 39%)

WEB-BASED INTERVENTIONS IN MS

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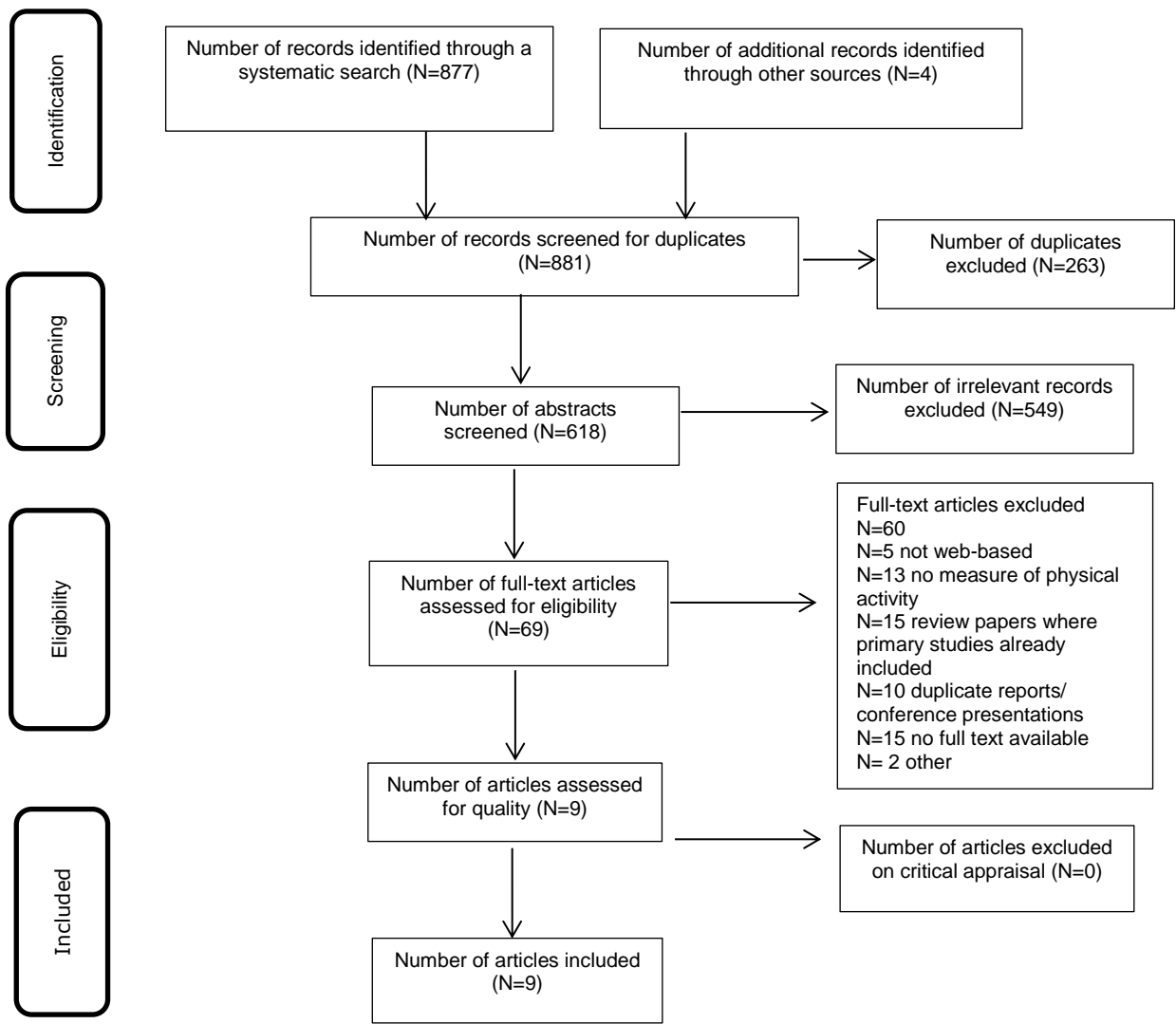
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	Months4-6	36%	
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833 **Figure 1: PRISMA<sup>33</sup> flow diagram of search and study selection**

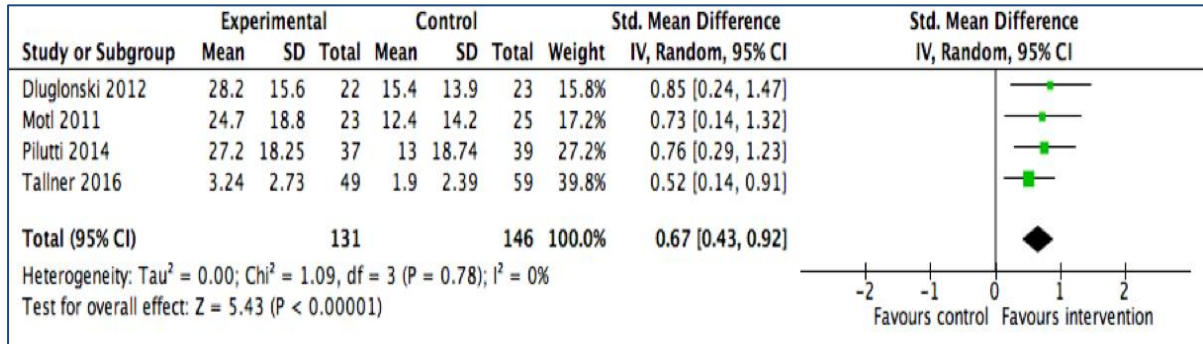
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883 **Figure 2: Meta-analysis of self-reported physical activity questionnaire data**

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887 Std: Standardised; IV: inverse variance; df: degrees of freedom; CI: confidence interval

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905 **Appendix I: Search strategy**

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 907 Medline (Ovid)  
 908 Search on 22/09/2016  
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Search	Query
#1	multiple sclerosis [tiab] OR multiple sclerosis [Mesh] OR MS [tiab] OR neurological condition [tiab] OR neurology* [tiab]
#2	internet [mesh] OR “web based” [tiab] OR “internet based” [tiab] OR telerehabilitation [tiab] OR telemedicine [tiab] OR www [tiab] OR “world wide web” [tiab] OR elearning [tiab] OR eHealth [tiab]
#3	#1 AND #2
#4	“Physical activity” [tiab] OR exercise [tiab] OR “physical fitness” [tiab] OR walking [tiab] or “motor activity” [tiab] OR rehabilitation [tiab] OR physiotherapy [tiab]
#5	#3 AND #4
Limit from 1990- current and English, language	

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