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1 **Exercise-based games interventions at home in individuals with a neurological disease: a**
2 **systematic review and meta-analysis**

3
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17

18

19 **Abstract**

20

21 **Objective.** The objective of this review was to summarize the current best evidence for the
22 effectiveness, feasibility, user compliance and safety of exercise-based games (EBGs),
23 including virtual reality and interactive video game interventions, for the rehabilitation of
24 individuals with neurological disorders at home.

25 **Material and methods.** We identified randomized controlled trials (RCT) evaluating the
26 effects of EBGs in neurological patients in home settings by searching 3 electronic databases
27 (MEDLINE, SCOPUS, CENTRAL Library) from inception to March 2018. All data
28 pertaining to participants, interventions, outcomes, supervision and cost-effectiveness were
29 independently extracted by 2 reviewers. Risk of bias was independently assessed by 2
30 reviewers.

31 **Results.** Reports of 11 RCT studies with heterogeneous populations (i.e., stroke, Parkinson
32 disease and multiple sclerosis) were included in the review. The treatment of experimental
33 groups included EBGs (i.e., commercially available games such as Nintendo Wii or Dance
34 Dance Revolution or custom-designed devices), and control groups received a controlled (i.e.,

35 conventional therapy) or uncontrolled (i.e., usual care) intervention. Across studies, EBGs at
36 home tended to have limited effects on upper and lower limbs. We demonstrated an increased
37 risk of participants dropping out of the program or discontinuing training in experimental
38 groups (n=51 participants) as compared with controls (n=23 participants). Few adverse events
39 (2 of 6 studies), such as minor musculoskeletal pain, were reported in balance training.

40 **Conclusions.** This systematic review reveals that EBGs seem a relevant alternative for
41 rehabilitation at home because the effectiveness of these interventions was at least equivalent
42 to conventional therapy or usual care. We give recommendations for the development of new
43 EBG therapies.

44

45 **Keywords:** home, neurological disorders, rehabilitation, virtual reality, interactive video
46 game

47

48

49 **Introduction**

50 According to the World Health Organization's guidelines (2006), all people with disabilities
51 should have access to rehabilitation services, including at discharge from hospital [1]. Early
52 home-based rehabilitation has been found to reduce disability and increase quality of life in
53 stroke survivors [2]. In this context, the development of new interventions such as exercise-
54 based games (EBGs) becomes an interesting approach to find alternative treatments for
55 various neurological pathologies and to continue rehabilitation or to maintain its benefits after
56 discharge from the hospital [3], specifically in settings where the access to therapy is limited
57 due to geographical or financial constraints [4].

58 EBGs include virtual reality (VR) and interactive video gaming (IVG) and are
59 presented as an incentive to increase physical activity [5]. These activities recently emerged
60 as modern non-pharmaceutical treatment approaches in neurological rehabilitation [6]. VR is
61 defined as “the use of interactive simulations created with computer hardware and software to
62 present users with opportunities to engage in environments that appear and feel similar to
63 real-world objects and events” [7] and features immersive systems such as Glasstron (Sony
64 Electronics, Tokyo/CAVE, VRCO, Virginia Beach, VA, USA), IREX (GestureTek
65 Technologies, Toronto, Canada) and PlayStation EyeToy (Sony Entertainment, Tokyo) [8].
66 Exercise through video games, also known as IVG or exergames, integrates physical activity
67 into a video game environment and requires active core and/or body movements to control the
68 in-game experience. Many technologies such as Nintendo Wii (Nintendo, Kyoto, Japan) and

69 Xbox Kinect (Microsoft®, Redmond, WA, USA) have quickly been adapted to clinical
70 settings.

71 EBGs offer the potential to provide 1) moderate intensity exercises [9], task-oriented
72 training and high repetition to maximize motor learning and neuroplasticity [10]; 2) increased
73 motivation and enjoyment for the patient; 3) lower costs as compared with robot-assisted
74 therapies, force plates, and computerized dynamic posturography; 4) the ability to be used
75 independently by the patient; and 5) suitability for personal use at home. Despite these
76 potential benefits, evidence supporting this approach for improving symptoms in neurological
77 disorders remains discussed in rehabilitation centers [4,8,13,17-19]. EBGs offer simple and
78 affordable virtual therapy alternatives in the field of rehabilitation and improve the functional
79 abilities of the patient in a wide variety of rehabilitation populations [3,11,12], especially in
80 Parkinson disease (PD) [13,14], multiple sclerosis (MS) [15] and stroke [16,17]. The positive
81 effects were often demonstrated when the EBG is used as an adjunct to standard clinical
82 treatment rather than as a single intervention [8,13,17,18]. In contrast, some authors showed
83 limited effects [4,19] and recommended the need for further high-quality studies to
84 demonstrate the efficacy of IVG in neurological rehabilitation [18]. Finally, feasibility has
85 already been established in people with PD [13], and these interventions can safely be used in
86 stroke patients because potential adverse events tend to be mild [17,18].

87 Qualitative studies conducted at home showed that IVG is acceptable to neurological
88 patients and their caregivers in home-based rehabilitation, and it increases motivation and
89 engagement in rehabilitation [20–23]. In parallel, a systematic review of older people reported
90 satisfactory effectiveness and feasibility of EBG systems in home settings [24]. In-home
91 systems for EBG rehabilitation are technologically and pragmatically feasible for individuals
92 affected by neurological disorders, yet most studies in this population were conducted in a
93 laboratory or clinical setting. The findings of these studies cannot be systematically
94 generalized to home environments, where there often are barriers to rehabilitation. The use of
95 EBGs at home for neurological rehabilitation shows great promise, but the development of
96 rehabilitation programs based on exergames at home remains challenging in terms of
97 adherence, user compliance, supervision, access and cost. To our knowledge, no systematic
98 review has been conducted to evaluate the implementation of EBGs in home settings and their
99 effectiveness in individuals with neurological disorders.

100 The objective of this review was to summarize the most reliable evidence for the
101 effectiveness, technical feasibility, user compliance and safety of EBGs as a tool for the
102 rehabilitation of people with neurological disorders in home-based settings.

103

104 **Material and Methods**

105 *Search strategy*

106 We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses
107 (PRISMA) [25] statement to structure this review. We identified the most relevant articles
108 within the Cochrane Central Register of Controlled Trials (CENTRAL; Cochrane Library),
109 MEDLINE (PubMed search engine) and SCOPUS online databases and by handsearching
110 reference lists. We performed all searches up to March 20, 2018. We initially developed
111 search strategies for MEDLINE before adapting them for use in the other databases
112 (Appendix A).

113 We searched the titles, keywords and abstracts of database entries by using the
114 following search strategy where * denotes a wildcard to allow for alternate suffixes: (stroke
115 OR hemipl* OR hemipar* OR parkinson* disease OR multiple sclerosis OR cerebrovascular
116 disease OR cerebral palsy OR brain injur* NOT child*) AND (virtual reality OR video gam*
117 OR Xbox OR Wii OR Kinect OR computer gam* OR exergame) AND rehabilitation. We
118 also searched the grey literature (i.e., general internet search engines) to avoid missing
119 relevant articles.

120 The inclusion criteria were randomized controlled trials (RCTs) of adults, full
121 scientific papers written in English, EBG intervention including VR or IVG, based in home
122 settings in neurological disorders, and functional rehabilitation with quantitative data. The
123 exclusion criteria were publication older than 10 years, intervention not fully at home,
124 qualitative data only, cognitive function assessment only, and incomplete access to the study
125 data.

126

127 *Selection of studies*

128 Two authors (AP, BB) independently screened all search results (title, abstract) to identify
129 suitable studies, then assessed all trials for eligibility based on the full text.

130

131 *Data extraction and management*

132 By using a pre-tested data collection form, 2 review authors (AP, BB) independently
133 extracted data including author names, trial setting, study population, intervention details,
134 outcome measures, results for effectiveness, supervision, compliance (i.e., drop-outs and
135 discontinued), cost of rehabilitation, technical feasibility and adverse events. Disagreements
136 regarding the selection of studies and data extraction were resolved by discussion or, if

137 necessary, with a third author (JCD). We contacted study authors for additional information
138 when necessary.

139

140 *Assessment of methodological quality*

141 The risk of bias in the selection, performance, detection, attrition and reporting in the studies
142 was assessed by using the Cochrane Collaboration Risk of Bias tool and classified as high,
143 low or unclear risk [26]. We also added a co-intervention as a supplementary category. Two
144 reviewers (AP and JCD) independently rated the studies, and any disagreements were
145 resolved by consensus with a third reviewer (BB).

146

147 *Data analysis*

148 We classified the data into subgroups to determine whether the outcomes varied according to
149 upper- or lower-limb rehabilitation. When a study showed more than one outcome measure
150 for the same domain, we included the most frequently used measure across studies. When the
151 meta-analysis was limited due to unacceptable heterogeneity or data access, we completed the
152 statistical analysis by a narrative summary of the study results.

153 Mean differences (MDs) with 95% confidence intervals (CIs) were calculated for all
154 variables with the same outcome measure. If studies used different outcomes that were
155 deemed comparable, standardized MDs (SMDs) with 95% CIs were calculated. Heterogeneity
156 was assessed with the I^2 statistic; $I^2 > 50\%$ was considered heterogeneous. Fixed and random
157 effects models were used to pool study results with low and high heterogeneity, respectively.
158 The meta-analysis and generation of forest plots involved using RevMan v5.3 (RevMan;
159 Cochrane, London, UK).

160

161 **Results**

162 *Study identification*

163 The initial search yielded 516 articles; 72 were obtained as full text, and reports for 11 studies
164 were eligible for inclusion in this review [27–37] (Fig. 1). The characteristics of excluded
165 studies are detailed in Appendix B.

166

167 *Study design and sample characteristics*

168 The demographic characteristics of participants were generally well documented in each
169 study; however, there were considerable variations among studies regarding sample sizes (18-

170 235), pathologies (stroke, PD, MS), disease duration (56.8 days–12.5 years), mean age (36–74
171 years) and level of disability. We found no study on cerebral palsy or brain injury.

172 The main characteristics of the interventions and outcomes and main findings of
173 studies are presented for upper-limb (arm or hand rehabilitation) [27,30,34–36] and lower-
174 limb (leg rehabilitation) [28,29,31–33,37] (Table 1). The EBG intervention (i.e., experimental
175 group [EG]), was compared with a control group (CG) with uncontrolled (i.e., usual care)
176 [28–30,33,36,37] or controlled (i.e., conventional therapy) interventions [27,31,32,34,35].
177 EBGs mainly featured IVG, and no study used a VR system.

178

179 *Effectiveness of EBGs on upper limb*

180 Four trials of stroke patients [27,34–36] and one of PD individuals [30] provided an
181 intervention for arm or hand rehabilitation. Two trials [30,36] compared EBGs to a CG with
182 uncontrolled intervention, and 3 trials [27,34,35] compared EBGs to a controlled intervention
183 focused on hand and arm exercises. To provide the interventions, the trials used commercially
184 available devices such as the MusicGlove [35] and Nintendo Wii [27] or custom-built devices
185 and gaming software such as SCRIPT dynamic orthosis coupled with SaeboMAS (Saebo Inc.,
186 Charlotte, NC, USA) [34], virtual glove [36] and a new exergame [30]. The duration of EBGs
187 ranged from 3 [35] to 12 [30] weeks and the number of sessions from 12 [32] to 42 [27]. To
188 determine the effectiveness of EBGs, studies used different outcomes: Action Research Arm
189 Test (ARAT) [27,34,35], Nine-Hole Peg Test (9HPT) [29,30,35,36], Box and Blocks Test
190 (BBT) [34,35], Fugl-Meyer Assessment [34,35], Motor Activity Log (MAL) [27,34–36] and
191 Stroke Impact Scale (SIC) [27,34] (Table 1).

192 The EG interventions did not provide significantly better results than those of the CG
193 with the ARAT and 9HPT (MD 0.05 [95% CI -2.88–1.89], p=0.68, I²=0.0) (Fig. 2A). For the
194 other outcomes, most studies seemed to show similar results (Table 1). The follow-up period,
195 ranging from 4 [35] to 24 [27] weeks, revealed no difference between the 2 groups in many
196 studies [27,34,35].

197

198 *Effectiveness of EBGs on lower limb*

199 Three trials of PD individuals [31–33] and 3 of MS individuals [28,29,37] provided an
200 intervention on balance rehabilitation [28,29,31–33,37]. Four trials compared EBGs to
201 uncontrolled interventions [28,29,33,37], whereas 2 trials compared EBGs to a controlled
202 intervention (e.g., conventional balance training) [31,32]. The EBG intervention used a
203 commercial device (Wii Balance Board System [28,29,31]) or custom-designed devices and

204 gaming solutions (modified Dance Dance Revolution [33,37] and a VR Balance training
205 system [32]). The duration of EBGs ranged from 6 [32] to 48 [29] weeks and the number of
206 sessions from 12 [32] to 48 [28]. The most commonly used outcomes were the Timed Up and
207 Go test (TUG) [32,33,37], Berg Balance Scale (BBS) [31,32] and Choice Stepping Reaction
208 Time test (CSRT) [33,37] (Table 1).

209 The EG interventions were not significantly better than those for the CG for the TUG
210 (MD 0.70 [95% CI -0.25–1.65], $p=0.15$, $I^2=0.0$; Fig. 2A). However, some studies reported
211 significantly better results for the EG than the controlled intervention (postural control, [28])
212 and uncontrolled intervention (BBS, [31]; CSRT, SST [37]) (Table 1). The long-term benefits
213 of EBGs were not superior to those of the CG [31,32].

214

215 *User compliance and technical feasibility*

216 The characteristics of user compliance and technical feasibility of EBGs are presented in
217 Table 2. The training duration was assessed by using logbooks and diaries and was reported
218 for 6 studies [27–29,33–35]. The training duration of EBGs ranged from 7.75 hr [33] to 27.3
219 hr [28], with some EG patients not reaching the recommendations of the intervention [34] and
220 others exceeding the number of prescribed sessions [30]. The number of dropouts and
221 discontinued interventions was higher with the EG than CG: 51 and 23 cases, respectively
222 (MD 0.09 [95% CI 0.03–0.13], $p=0.001$, $I^2=0.0$; Fig. 2B).

223 Concerning technical feasibility, many studies used custom-designed devices and
224 gaming solutions (Table 2). Some EBGs were developed for only studies [30,32-34,37] and
225 require specific equipment or informatics development, so they are difficult to access for all
226 patients. Finally, we found a lack of details on the set-up of the equipment (time, easy to use
227 for the patient) or game development software (program, sets of system requirement,
228 connection problem). Interventions were generally supervised by telephone calls and home
229 visits (Table 2) [27–30,33,36,37]. Finally, 3 trials using the Nintendo Wii system analyzed the
230 cost of EBGs [27,29,31] and showed that EBGs were more [27] or less [31] expensive than
231 the CG (Table 2).

232

233 *Safety*

234 The number of reported adverse events did not significantly differ between the EG and CG
235 (MD 0.17 [95% CI -0.02–0.36], $p=0.15$, $I^2=0.98$; Fig. 2C). However, 2/6 studies dealing with
236 the lower limb [28,33] reported adverse events (i.e., knee and low back pain). One study
237 reported that 8 participants' pre-existing pain was exacerbated during EG, which resulted in 2

238 cases of discontinued participation and one non-injurious fall [33], and the other study
239 indicated that 24 (70%) participants had at least one adverse event [28].

240

241 *Methodological quality*

242 Figure 3 shows the risk of bias in the included studies. All trials used random sequence
243 generation with web services [27,36], computer-generated tables [28–33,37] or concealed
244 envelopes [34]; only one study used a centralized randomization protocol [38]. All studies
245 showed some performance bias due to the difficulty of blinding participants and therapists to
246 group allocation. However, 9 studies used blinded assessors [27,28,30–33,35–37]. For these
247 studies, the risk of detection bias was deemed low. Seven studies [27,30–33,35,36] described
248 a sample size calculation, but 4 [27,32,35,36] recruited fewer participants than the theoretical
249 calculation. Most studies recruited broadly similar numbers into each trial arm. Three of 5
250 trials [27,34,35] tracked time of intervention for both groups (EBGs and conventional
251 therapy) and one study revealed a significant difference in co-intervention dosage [34]. The
252 co-intervention constant was generally poorly described.

253

254 **Discussion**

255 This first review of EBGs in neurological diseases in home-based settings highlights that the
256 effectiveness of interventions was not superior to other interventions. The user compliance in
257 this type of intervention seemed limited and we found a lack of information regarding
258 technical feasibility. EBGs were not significantly associated with adverse events, despite
259 minor events reported in balance training. Interpreting the results was difficult because of the
260 heterogeneity of the studies.

261

262 *Effectiveness of EBGs for the upper limb*

263 The EBG interventions for the upper limb mainly focused on arm and hand rehabilitation in
264 stroke patients. The effects provided by EBG at home were limited to the upper limb because
265 these interventions were not superior to usual care or conventional therapy. In the literature,
266 the reported effects of IVG for the upper limb in stroke rehabilitation centers are similar [4],
267 and the impact of other home-based therapy programs for upper-limb recovery in stroke
268 patients remains unclear [39].

269

270 *Effectiveness of EBGs for the lower limb*

271 The EG and CG with a controlled intervention (i.e., conventional therapy) showed
272 improvements in most clinical assessments (Table 1), but the groups did not differ for the
273 most frequently reported outcomes. Some studies reported a positive and superior effect of
274 EBGs on balance as compared with other therapies [31] or to usual care [28,37]. In the
275 literature, IVG could improve balance impairments in patients with neurological diseases
276 [11,40], but this result was not found in the meta-analysis. EBGs have already been
277 considered as an alternative to conventional therapy in center rehabilitation [3,11–
278 13,15,16,19], but further studies with more homogenous data are needed to determine the
279 efficiency of EBGs at home.

280 EBGs show interesting promise regarding its long-term benefits, but these benefits
281 were not found superior to the CG. However, the evidence regarding long-term follow-up is
282 too weak to draw definitive conclusions.

283

284 *User compliance and technical feasibility*

285 Most studies reported satisfying acceptance of EBG interventions by patients, who considered
286 them engaging and enjoyable [20,22,23,28,34,36]. Despite this, the drop-out rate was
287 unexpectedly higher for the EG than CG in this review of only RCT studies (Fig. 2). Even
288 though most of the concerned patients claimed that they abandoned the intervention because
289 of external causes, some of the reasons for their abandonment may be directly related to the
290 EBGs [36]. Many participants declined or discontinued the intervention because of 1)
291 technological issues (e.g., lack of Internet connection or connection between computer and
292 technologies) [30,31], 2) lack of space to dedicate to EBGs at home [30], and 3)
293 discouragement when confronted with technological devices [31,32]. Home interventions are
294 commonly obstructed by physical and social environment (e.g., distractions at home, family
295 support) and self-efficacy (e.g., symptoms and impairments of the disease) [41–43], but they
296 eliminate the transport problems that are often associated with intervention dropouts in
297 rehabilitation centers [31]. EBG-specific barriers also emerged during the intervention [44]:
298 1) belief that EBGs increase risk factors (e.g., higher blood pressure, falls, etc.) [20,23], 2)
299 lack of customization and negative feedback of commercial games [23], 3) childish design of
300 the games [20], 4) lack of accessibility to technology (e.g., lack of space, internet connection)
301 [23].

302 Most studies supervised the interventions by combining home visits and phone calls
303 [27–30,33,36,37], whereas others solely relied on home visits [32,34] or phone calls [35].

304 Home visits included an initial visit to install the EBG and a final visit to collect data and
305 assessment. Contacts were generally planned once a week; however, participants could
306 request extra home visits or phone calls if required. Gandolfi et al. used video calls with
307 Skype software (Skype Technologies) during the entire session and 1 physiotherapist
308 supervised 2 patients in real time to reduce the cost of the EBG [31]. Indeed, the cost of the
309 intervention was often due to the number of contacts with health professionals [27]. Few
310 studies incorporated cost-effectiveness in the analysis and most did not provide details on
311 whether the technology was acquired through loan or purchase. Cost-effectiveness should be
312 incorporated in future trials [45].

313

314 *Safety*

315 Despite the significant lack of risks associated with EBGs, 2 studies found a high number of
316 minor musculoskeletal pain events with use of the Wii for balance rehabilitation [28,33].
317 Many studies mentioned injuries associated with specific IVG tools, such as “Wii-itis” or
318 “Nintendinitis,” even in healthy populations [46,47]. However, the risk of EBG training-
319 related injuries should be offset by its benefits in balance training, which must be carefully
320 considered in future studies.

321

322 *Recommendation for EBGs at home in neurological diseases*

323 Future studies in home settings should integrate the multiple observations reported in the
324 literature to ensure optimal EBG design [48].

325 The optimal dose for rehabilitation therapy remains unknown, but the delivered dose
326 of intervention affects the outcome [49] and a positive correlation exists between training
327 duration and training-induced changes in arm and hand function [34]. A minimal dose of 15
328 to 16 hr over the intervention period is suggested to increase the chances of reaching
329 clinically relevant treatment effects [17,50]. The training duration of EBGs was often less
330 than these recommendations (Table 2) and perhaps EBGs in neurological disorders may be
331 more efficient if patients followed the optimal dose for EBG.

332 In our study, 5 trials used commercially available games including the Wii system
333 [27–29,31] and MusicGlove [35], whereas 6 trials used custom-designed devices and/or
334 gaming software [30,32–34,36,37]. No study used immersive-type VR systems, probably
335 because of the higher costs than non-immersive VR systems and the inadequacy for home-
336 based settings. Most IVG systems for neurorehabilitation were commercial devices [3,11]
337 despite the recommendations to use custom game systems for neurological diseases [13].

338 Custom-designed EBGs could improve the effectiveness of and compliance with
339 interventions by focusing on the following issues [13]: 1) targeting specific clinical features
340 of neurological disease and use task-specific training in activities of daily living, 2) providing
341 easier objectives than commercial games and including explicit instructions and goals, 3)
342 providing appropriate, neutral feedback, 4) featuring a large variety of attractive exercises to
343 prevent boredom and abandonment [51], and 5) slowly and sparingly introducing more
344 cognitively demanding aspects. Most studies in our review did not specify whether they
345 complied with these recommendations. In parallel, a large number of pilot studies in home
346 settings have proposed new promising interventions [52,53] or interesting technological
347 developments [54,55] for neurological patients.

348 The rate of participant drop-outs and discontinued interventions raises an essential
349 question: how to manage the involvement of subjects in the intervention? To this extent,
350 future research should integrate realistic outcome expectations, verify the
351 acceptability/feasibility of the program with the relatives and incorporate effective behavior
352 change strategies. Another possibility would be to incorporate wireless monitoring in the
353 EBG system so that the user's compliance can be monitored from afar and timely feedback or
354 problem solving can be provided. The option to have multiple players interacting together
355 within a game-based task could also increase adherence [56]. Patients reported positive
356 feedback when offered the opportunity to share treatment with their social entourage in the
357 context of games [20,23,57].

358

359 *Limitations*

360 Despite the rigorous nature of the included research designs (i.e., RCT), the current results
361 must be interpreted with caution. They may not be generalized to all neurological diseases
362 because of the absence of studies featuring other pathologies besides stroke, PD and MS. In
363 addition, participants presented no cognitive impairment and were younger and had a lower
364 level of handicap than the global population. These factors have a strong impact on the
365 implementation of home-based rehabilitation [43] and modify the impact of the intervention
366 [33]. Concerning the risk of bias, several studies [27,32,35,36] recruited fewer subjects than
367 the sample size calculation and reported difficulties with participant inclusion [36]. Finally,
368 comparisons were difficult because of the heterogeneity between trials with regard to
369 population type, study design, interventions and outcome measures, especially regarding the
370 meta-analysis of effectiveness. For example, the interventions for the CG greatly varied,
371 whether in conventional therapy in the content of the sessions, the location of the sessions

372 (interventions in a centre [31]) or in a uncontrolled intervention for which usual care was not
373 detailed at all.

374

375 *Perspectives*

376 This review was focused on functional abilities, but neurological patients also present
377 cognitive disorders. Several studies have shown an improvement in cognitive functions with
378 IVG in a centre [58] or in a home-based setting [59,60]. In our review, one study revealed a
379 positive effect of EBG on cognitive performance [30].

380

381 **Conclusion**

382 This systematic review reveals that EBG seems to be a relevant alternative for rehabilitation
383 in the home for people with neurological diseases because the effectiveness of these
384 interventions was at least equivalent to conventional therapy or usual care. Technical
385 feasibility and user compliance were also debatable because of many dropouts and
386 discontinued interventions in the EG. Despite the statistically significant lack of risk
387 associated with EBG, this review also reported the existence of adverse events (i.e., minor
388 musculoskeletal pain) with balance training. This review has identified several important
389 considerations regarding the design of EBG interventions at home for patients with
390 neurological diseases, and we recommend these strategies to reduce usability barriers and to
391 use facilitators to increase patient participation. Future studies should include supervision,
392 cost-effectiveness and follow-up analyses to provide more accurate recommendations for
393 further studies of EBG at home.

394

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396 commercial, or not-for-profit sectors.

397 **Conflict of interest:** None declared.

398

399 **Legends**

400 Figure 1. Selection of studies in the review.

401 Figure 2. Forest plot of pooled results for A) effectiveness, B) user compliance and C) safety.

402 Figure 3. Risk of bias. Judgement of each risk of bias is presented as percentage.

403

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589

Figure 1.

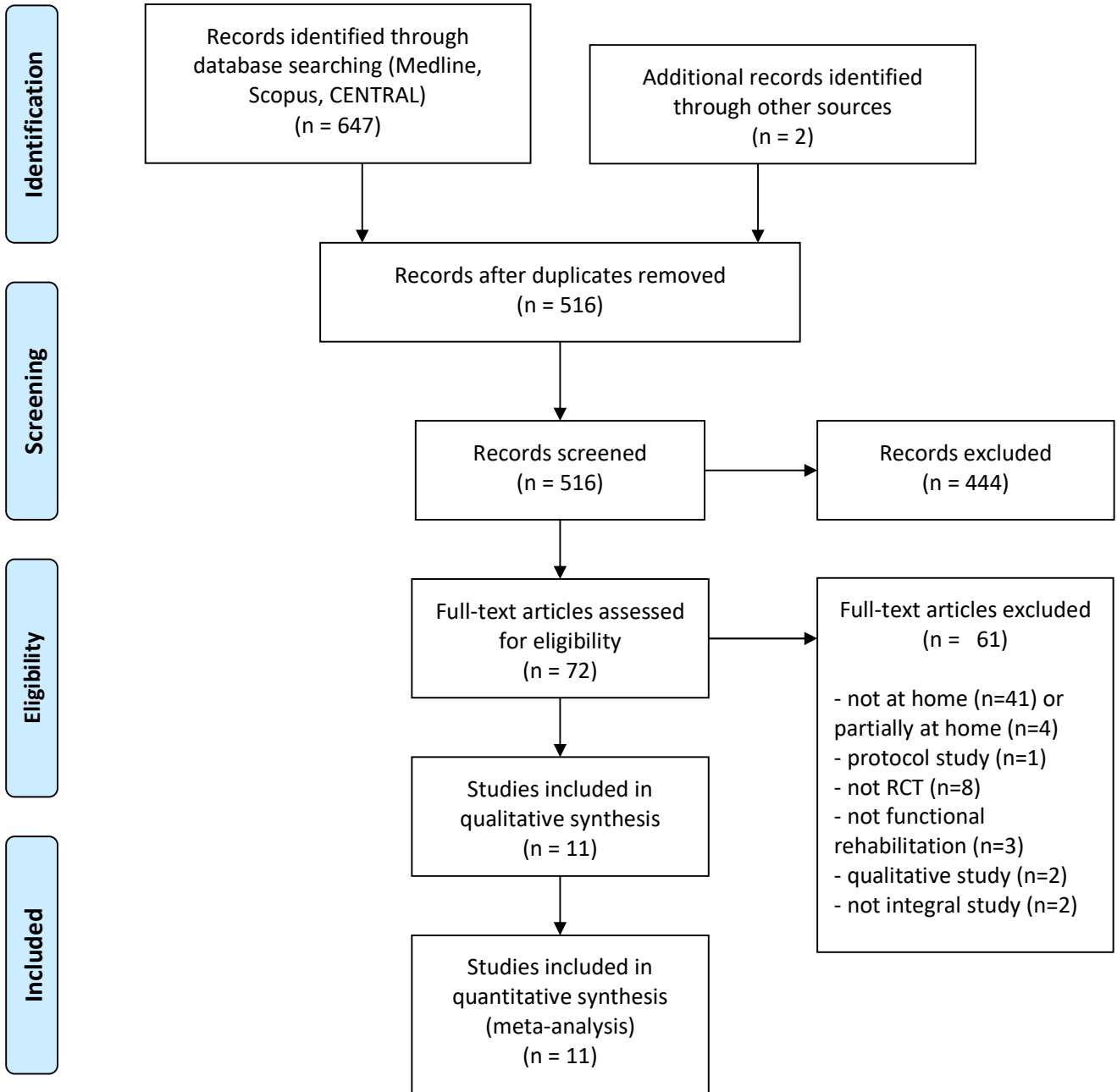
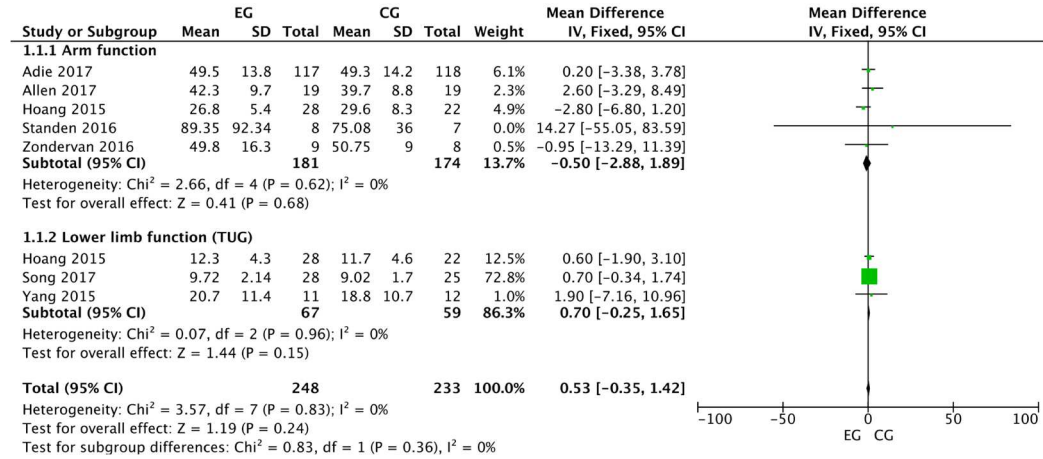
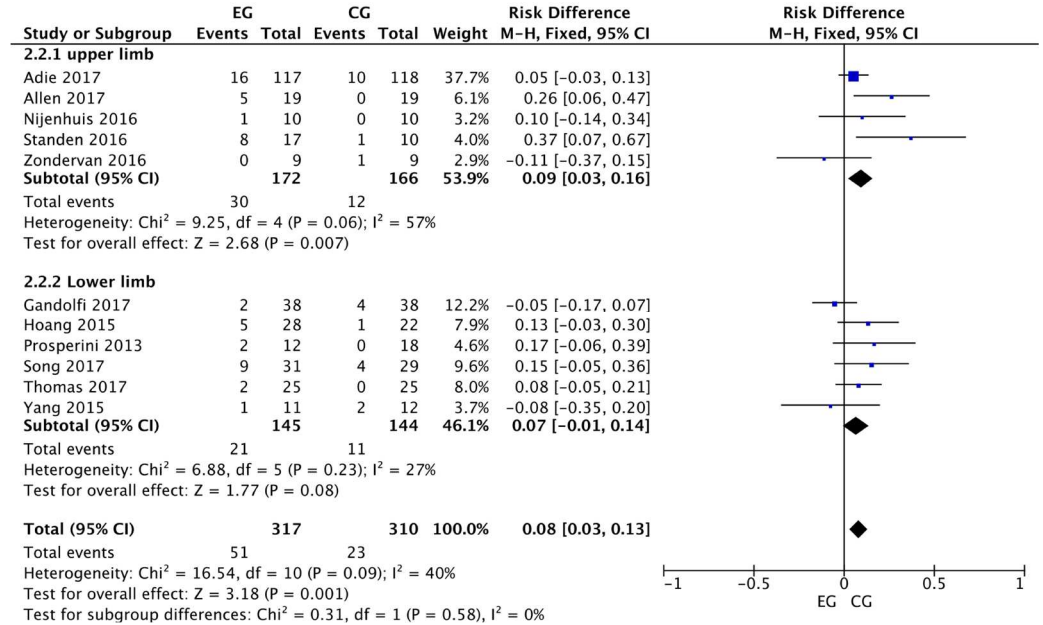


Figure 2.

A



B



C

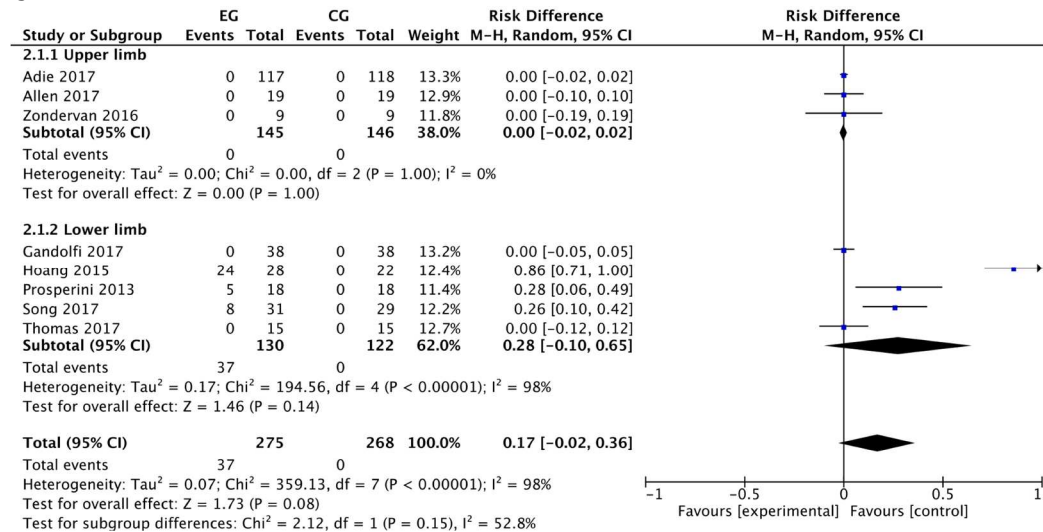
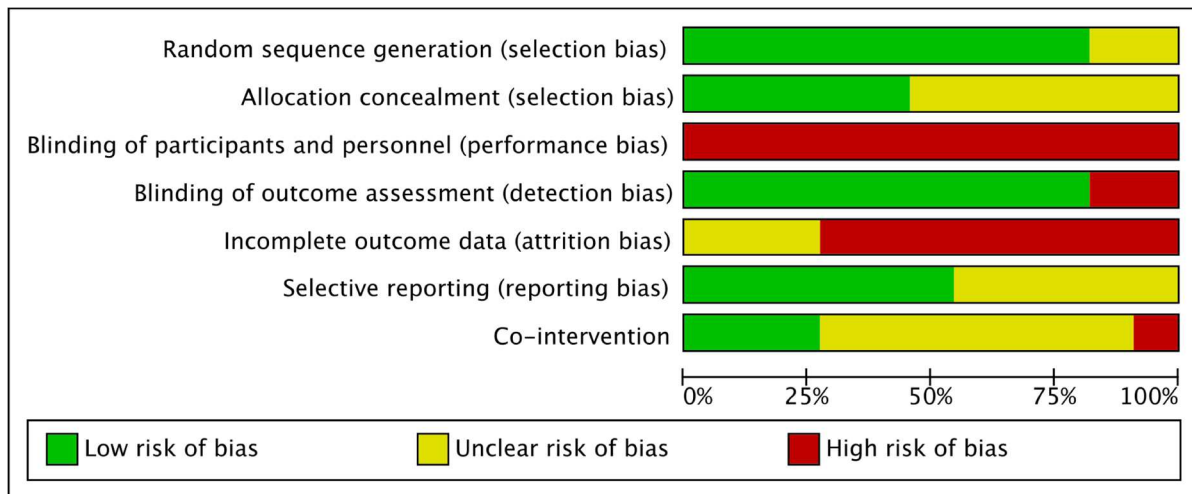


Figure 3.



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Co-intervention
Adie 2017	+	+	-	+	-	?	+
Allen 2017	+	?	-	+	-	+	?
Gandolfi 2017	+	?	-	+	?	+	?
Hoang 2015	+	+	-	+	?	+	?
Nijenhuis 2016	?	+	-	-	-	?	-
Prosperini 2013	+	?	-	+	?	?	+
Song 2017	+	+	-	+	-	+	?
Standen 2016	+	+	-	+	-	?	?
Thomas 2017	+	?	-	-	-	?	?
Yang 2015	?	?	-	+	-	+	?
Zondervan 2016	+	?	-	+	-	+	+

Table 1. Intervention, outcome and major findings of **exercise-based games (EBGs)** interventions (**main outcome in bold**).

Authors, country	Design, study duration	No. randomized (no. of dropouts) Age (SD), sex	Disease, duration, level of disability	Groups	EBG system and game	No of sessions, frequency and length	Outcome measure	Major findings
Upper-limb intervention								
EBG vs controlled intervention								
Adie, 2017 United Kingdom	RCT, multicentric, Intervention: 6 wk Follow-up: 24 wk	235 (26) 67.3 (13.4) 104/131 (W/M)	Stroke 56.8 d	EG: Wii sports games + usual care (n=117) CG: arm exercises (Graded Repetitive Arm Supplementary Program) + usual care (n=118)	Commercial entertainment system: Nintendo Wii™ 3 games: bowling, tennis, golf, baseball	42 sessions up to 45 min/d, 6 wk	ARAT, MAL, COPM, SIC, MRS, EQ-5D 3L	- Both groups had improved arm function at ST and LT. - No significant difference between groups at ST and LT.
Nijenhuis, 2016 Netherlands	RCT, multicentric Intervention: 6 wk Follow-up: 8 wk	20 (1) 60 y 9/10 (W/M)	Stroke 11.5 mo	EG: Saebomas (n=10) CG: Conventional therapy (n=10)	Custom-designed device: SCRIPT dynamic wrist and hand orthosis, Saebomas and a touchscreen computer displaying gaming exercises	36 sessions 30 min/d, 6 d/wk, 6 wk	ARAT, BBT, Fugl-Meyer Grip strength, MAL, SIC, IMI	- Both groups showed moderate improvements on most clinical assessments. - No significant difference between groups at ST and LT.
Zondervan, 2016 USA	RCT, crossover Intervention: 3 wk Follow-up: 4 wk	18 (1) 59,5 y 7/10 (W/M)	Stroke 4.3 y	EG: MusicGlove (n=9) CG: Conventional therapy (tabletop exercises) before Music Glove Therapy (n=9)	Commercial device: MusicGlove	9h of therapy 3h/wk, 3 wk	BBT, MAL, 9-HPT, ARAT, GDS, Fugl-Meyer score (upper limb), NIHSS, MAS	- Both groups significantly improved their BBT score, but no significant difference was found between groups. - EG exhibited significantly greater improvements than CG in MAL at LT.
EBG vs uncontrolled intervention								
Standen, 2017 United Kingdom	RCT Intervention: 8 wk	27 (9) 61 (13) y 11/16 (W/M)	Stroke 22 wk WMFT: 2.6	EG: Virtual glove (n=17) CG: Usual care (n=10)	Custom-designed device: virtual glove (hand-mounted power unit, with four diodes tracked using Wiimote™ controllers). 3 games: Spacerace, Spongeball, Balloonpop	24 sessions 20 min max/session, 3 times/day, 8 wk	WMFT, 9-HPT, MAL, NEADL	- Significantly greater change from baseline in the EG on WMFT at midpoint and two subscales of MAL at final.

Allen, 2017 Australia	RCT Intervention: 12 wk	38 (1) 68.4 (8.5) y 15/23 (W/M)	PD 8.3 y MDS- UPDRS motor exam: 41.3	EG: Exergame custom- developed by research team (n=19) CG: usual care and activities (n=19)	Custom-designed device and gaming software Exergames focused on coordinated movements of arm and hand, developed by the research team for the trial using Unity game development software 2 exergames: 'Marshmallow' and 'Chicken' 12 games per exergame	36 sessions 3 d/week, 12 wk	9-HPT , Hand reaction time and dexterity tests, MoCA, TMT, PDQ-39, MAM-36	- No significant difference between groups except for tapping tasks: EG showed better speed and increased errors. - EG showed improved performance in TMT-A compared to CG.
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Lower limb intervention

EBG vs controlled intervention

Gandolfi, 2017 Italia	RCT, multicentric Intervention: 7 wk Follow-up: 4 wk	76 (6) 68.2 (8.3) y 25/51 (W/M)	PD 6.8 y UPDRS score: 44.1	EG: TeleWii training (Nintendo Wii™) (n=38) CG: Sensory Integration Balance Training (SIBT) (n=38)	Commercial entertainment system: Nintendo Wii™ 10 games	21 sessions 50 min/session, 3 d/wk, 7 wk	BBS , ABC scale, Gait (10- Meter Walk Test; dynamic gait index), PDQ-8, Falls (number)	- Improvement for both groups in all outcome measures at ST and LT, except for fall frequency. Greater effect in EG for BBS than CG at ST.
Yang, 2016 United Kingdom	RCT Intervention: 6 wk Follow-up: 2 wk	23 (3) 74 (7.3) y 9/14 (W/M)	PD 8.8 y Hoehn Yahr scale: 3	EG: VR balance training (n=11) CG: Conventional balance training (n=12)	Custom-designed device and gaming software: VR Balance training system (touchscreen computer and wireless balance board). 3 programs (basic learning, indoor daily tasks and outdoor daily tasks) and 9 games	12 sessions 50 min/session, 2 d/wk, 6 wk	BBS , Gait (Dynamic Gait Index), TUG, PDQ-39, UPDRS-III	- Improvement for both groups in the BBS, Gait, TUG and PDQ-39 at ST and LT. - No significant difference for all outcomes found between groups at any assessment point.

EBG vs uncontrolled intervention

Song, 2017 Australia	RCT Intervention: 12 wk	60 (7) 66,5 (7) y 36/24 (W/M)	PD 8 y MDS- UPDRS Part III: 33	EG: Modified DDR + usual healthcare (n=31) CG: No intervention + usual healthcare (n=29)	Custom-designed device: modified DDR including a computer connected to the television or monitor and a custom-made step mat	36 sessions 15 min/session, 3 d/wk, 12 wk	CSRT , FGA , TUG, Hip abductor muscle power, MoCA, TMT, Falls (number and FES-I)	- No significant difference between EG and CG for all outcomes except TUG (in favour of CG). EG perceived improvements in mobility.
Hoang, 2014 Australia	RCT Intervention: 12 wk	50 (6) 52.4 (11.8) y 38/12 (W/M)	MS 12.5 y EDSS: 4.2	EG: Modified DDR (n=28) CG: No intervention (continued usual physical activity) (n=22)	Custom-designed device and gaming software: Step training system (modified DDR) combined with Stepmania open-source software (www.stepmania.com), step pad, computer and TV. 2 games	24 sessions at least 30- min/session, 2d/wk, 12 wk	CSRT , SST , Balance test (postural sway), Gait (10-m walk, 6-minute walk), TUG & DT TUG, Cognition (SDMT, TMT), 9-HPT, MSFC, Falls (number)	- EG performed significantly better in CSRT, SST and tests of sway with eyes open, 9-HPT, single and dual task gait speed and MSFC score than CG. No effect of falls.

Prosperini, 2013 Italia	Pilot RCT, 2- periods crossover Intervention: 12 wk (2 periods of 12 wk)	36 (2) 36.2 (8.7) 25/11 (W/M)	MS 10.8 y EDSS: 3.25	Group A: 12-week WBBS training, then 12- week observational period Group B: Reverse order compared to Group A n=18 per group	Commercial device: Nintendo® Wii Balance Board with Wii Fit® 7 games	48 sessions 30 min/session, 4 d/wk, 12 wk	Static standing balance, Gait (FSST; 25-Foot Walking Test), MSIS-29, Falls (self-reported number)	- EG performed better in COP path, FSST, 25-FWT, and MSIS-29 than CG.
Thomas, 2017 United Kingdom	Pilot RCT, mixed methods Intervention: 24 or 48 wk by gps	30 (2) 49.3 (8.7) 27/3 (W/M)	MS 47% < 6 y	EG: Mii-vitaliSe program (Wii balance + usual care) immediately (n=15) CG: Mii-vitaliSe program after a 6-month delay (n=15)	Commercial device: Nintendo® Wii Balance Board with Wii Fit® Games: Wii Fit Plus, Wii Sports and Wii Sports Resort	EG: 12 months CG: 6 months	Accelerometry, 2MWT, Step Test, Steady Stance Test, iTUG, Gait Stride- time Rhythmicity, static posturography, 9HTP, HADS, EuroQOL-5D-5L, MSIS29, FSI, SF-36, SCI-ESES, MSSE	Unclear

RCT, randomized controlled trial; EG, experimental group; CG, control group; EBG, exercise-based game; WBBS, Wii Balance Board System; SIBT, Sensory Integration Balance Training; DDR, Dance Dance Revolution; ST, short-term, LT, long-term.

2MWT, 2 Minute Walking Test; 9-HPT, Nine-Hole Peg Test; ABC scale, Activities-Specific Balance Confidence; ARAT, Action Research Arm Test; BBT, Box and Blocks Test; BBS, Berg Balance Scale; COPM, Canadian Occupational Performance measure; CSRT, Choice Stepping reaction time; EQ-5D 3L, standardized quality of life questionnaire; FGA, Functional Gait Assessment; FES-I, Fall Efficacy Scale–International Questionnaire; GDS, Geriatric Depression Scale; FSST, Four-Step Square Test; GLTEQ, Godin Leisure-Time Exercise Questionnaire; HADS, Hospital Anxiety and Depression Scale; IMI, Intrinsic Motivation Inventory; MAL, Motor Activity Log; MAM-36, Manual Ability Measure; MAS, Modified Ashworth Spasticity scale; MoCA, Montreal Cognitive Assessment; MRS, Modified Rankin Scale; MSIS, Multiple Sclerosis Impact Scale; MSFC, Multiple Sclerosis Functional Composite; MMSE, Mini Mental State Examination; NEADL, Nottingham Extended Activities of Daily Living; NIHSS, National Institute of Health Stroke Scale; PDQ-39, Parkinson’s Disease Quotation; QoL, Quality of Life; SCI-ESES, Spinal Cord Injury Exercise Self-Efficacy Scale; SDMT, Simple Digit Modality test; SIC, Stroke Impact Scale; SST, Stroop Stepping Test; TMT, Trail Making Test; TUG, Timed Up and Go; UPDRS, Unified Parkinson’s Disease Rating Scale; WMFT, Wolf Motor Function Test

Table 2. Characteristics of safety and feasibility of EBG interventions.

Authors	Screened training	Training duration (SD)	Cost of rehabilitation (SD)	Supervision	No. of dropouts Discontinued	Adverse events
Upper-limb intervention						
EBG vs controlled intervention						
Adie, 2017 United Kingdom	Diary: duration exercise, adverse events, home visits	EG: 37 (16.2) min per session Total: 1020 (721) min (17 h) CG: 32 (11.9) min per session Total: 998 (554) min (16.6 h)	EG : 1106 (1656) £ CG : 730 (829) £	Phone call: once per week Home visit: to collect the Wii system or to provide arm exercise instructions	11 EG: 7 (4 changed mind, 1 moved away, 1 unable to contact participant, 1 participant's condition deteriorated) CG: 4 (3 changed mind, 1 participant's condition deteriorated)	No adverse event
Nijenhuis, 2016 Netherlands	Diary: frequency and duration of training	EG: 118min/wk, total: 11.8 h CG: 189 min/wk, total: 18.9 h Variation duration: 13 to 423 min/wk	N	Home visit: once per week Researchers monitored progress and adjusted training programs remotely via a secured website	1 EG: 1 withdrawal during intervention (shoulder pain due to external cause) CG: 0	NR
Zondervan, 2016 USA	Logbook: duration of training Number of grips recorded using a laptop	EG: 10 h CG: 8.1 h	N	EG: Phone call at least once per week CG: Self-guided therapy (booklet of tabletop exercises for home therapy)	1 EG: 0 CG: 1 withdrawal from study with no assessment	No adverse event
EBG vs uncontrolled intervention						
Standen, 2017 United Kingdom	A log of when the system was in use was stored on the computer: games played, scores. The frequency of use of the glove was collected by the software	NR	N	EG: Home visits: Initial instruction by a therapist and subsequent support, then once per week or every 2 weeks. No limit on the number of visits per patient. Total of visits: 78 visits from the research team in addition to data collection visits. Phone calls: At the patient's request CG: Visits to collect data only	9 EG: 4 patients did not receive allocated intervention, 4 withdrawals CG: 1 withdrew as found measures onerous	NR
Allen, 2017 Australia	Logbook.	34.9 (97%) of the prescribed 36 exergame sessions were completed	N	Home visits: Two initial home visits, then a third visit at 6 weeks (possible extra home visits if required by the	1 EG: 1 for family reasons CG: 0	No adverse event

10 participants (53%) completed more sessions than the prescribed amount

patient)
Phone call: every 2 weeks

4
EG: (2 for family reasons + 2 health problems unrelated to the intervention)

Lower-limb intervention

EBG vs controlled intervention

Gandolfi, 2017 Italia	Self-reported log	NR	EG: 23.299€ CG: 28.899€	Skype™ video call during the entire duration of the session/one physiotherapist assigned to 2 patients	6 EG: 2 CG: 4 patients withdrew for medical reasons or because of transportation issues	No adverse event
Yang, 2016 United Kingdom	NR	NR	N	EG: Supervised by a home physiotherapist to ensure the appropriate execution of VR programs CG: The control group received conventional balance training by direct manual management from a home physiotherapist	3 EG: 1 withdrew from study (preference for CG) CG: 1 withdrew from study for personal reasons and 1 readmission	NR

EBG vs uncontrolled intervention

Song, 2017 Australia	Logbook: completed exercise, adverse events	31 (86%) of the prescribed 36 exergame sessions were completed Total: 7.75 h	N	Home visit: Two initial home visits + Additional visit at Week 6 Phone call: every 2 weeks	7 EG: 3 withdrawals (unclear reasons) CG: 3 withdrawals (unclear reasons) and 1 partial follow-up due to injury	8 participants' pre-existing pain (e.g. lower back pain, knee pain, foot pain) was exacerbated during EG One fall during game
Hoang, 2014 Australia	NR	EG: 71 min/wk (60 SD) Total: 14.2 h	N	Phone call: one in the first two weeks Home visit: one to install system	6 EG: 6 patients, 2 of whom due to exacerbated pain where they had pre-existing lower back pain. CG: 5 withdrew due to family reasons or a relapse of MS. CG: 1 withdrew to attend re-assessment due to health issue.	No adverse event
Prosperini, 2013 Italia	Logbook: recording of training, and falls or adverse event	Group A: 27.5 h (17.1) Group B: 27.1 h (15.9)	N	Home visits: initial session, then supervision every 4 weeks Phone call: once a week Supervised by trained physiotherapists	2 EG: 2 CG: 0	24 (70%) patients reported at least 1 adverse event 5 adverse events (knee and back pain) reported from mild (n=3) to moderate (n=2) level
Thomas, 2017 United Kingdom	Daily play log: adverse events, games played, training screened, intensity, enjoyment and fatigue rating (on a scale of 1–10), reasons for non-use, free text comments	The Wii was used in around 30% of days during the first 6 months of using the Wii (delayed and immediate groups combined) and 19% of days in the second 6 months (immediate group).	Estimated cost of providing Mii-VitaliSe: £684/pers	Home visits: 3 Phone calls or email: 10	2 EG: 2 withdrawals for medical reasons CG: 0	No adverse event

NR: not reported; EG: experimental group; CG: control group