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

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Abstract

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

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

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

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

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

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

Introduction

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

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

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

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

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

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

Material and Methods

Search strategy

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

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

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

Selection of studies

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

Data extraction and management

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

Assessment of methodological quality

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

Data analysis

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

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

Results

Study identification

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

Study design and sample characteristics

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

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

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

Effectiveness of EBGs on upper limb

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

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

Effectiveness of EBGs on lower limb

Three trials of PD individuals [31–33] and 3 of MS individuals [28,29,37] provided an intervention on balance rehabilitation [28,29,31–33,37]. Four trials compared EBGs to uncontrolled interventions [28,29,33,37], whereas 2 trials compared EBGs to a controlled intervention (e.g., conventional balance training) [31,32]. The EBG intervention used a commercial device (Wii Balance Board System [28,29,31]) or custom-designed devices and gaming solutions (modified Dance Dance Revolution [33,37] and a VR Balance training system [32]). The duration of EBGs ranged from 6 [32] to 48 [29] weeks and the number of sessions from 12 [32] to 48 [28]. The most commonly used outcomes were the Timed Up and Go test (TUG) [32,33,37], Berg Balance Scale (BBS) [31,32] and Choice Stepping Reaction Time test (CSRT) [33,37] (Table 1).

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

User compliance and technical feasibility

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

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

Safety

The number of reported adverse events did not significantly differ between the EG and CG (MD 0.17 [95% CI -0.02–0.36], $p=0.15$, $I^2=0.98$; Fig. 2C). However, 2/6 studies dealing with the lower limb [28,33] reported adverse events (i.e., knee and low back pain). One study reported that 8 participants' pre-existing pain was exacerbated during EG, which resulted in 2 cases of discontinued participation and one non-injurious fall [33], and the other study indicated that 24 (70%) participants had at least one adverse event [28].

Methodological quality

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

Discussion

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

Effectiveness of EBGs for the upper limb

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

Effectiveness of EBGs for the lower limb

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

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

User compliance and technical feasibility

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

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

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

Safety

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

Recommendation for EBGs at home in neurological diseases

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

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

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

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

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

Limitations

Despite the rigorous nature of the included research designs (i.e., RCT), the current results must be interpreted with caution. They may not be generalized to all neurological diseases because of the absence of studies featuring other pathologies besides stroke, PD and MS. In addition, participants presented no cognitive impairment and were younger and had a lower level of handicap than the global population. These factors have a strong impact on the implementation of home-based rehabilitation [43] and modify the impact of the intervention [33]. Concerning the risk of bias, several studies [27,32,35,36] recruited fewer subjects than the sample size calculation and reported difficulties with participant inclusion [36]. Finally, comparisons were difficult because of the heterogeneity between trials with regard to population type, study design, interventions and outcome measures, especially regarding the meta-analysis of effectiveness. For example, the interventions for the CG greatly varied, whether in conventional therapy in the content of the sessions, the location of the sessions (interventions in a centre [31]) or in a uncontrolled intervention for which usual care was not detailed at all.

Perspectives

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

Conclusion

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

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Conflict of interest: None declared.

Legends

Figure 1. Selection of studies in the review.

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

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

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Figure 1.

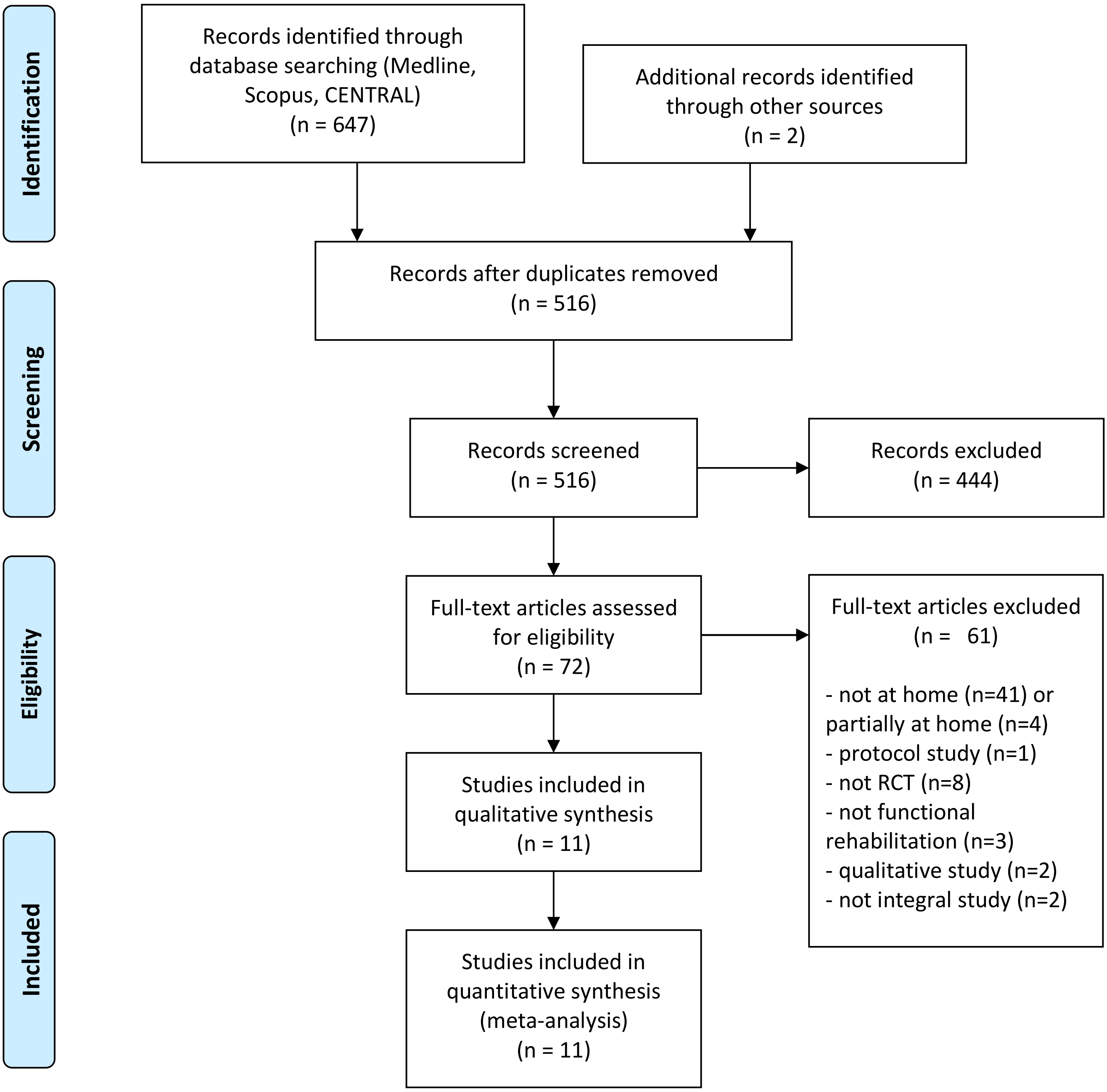
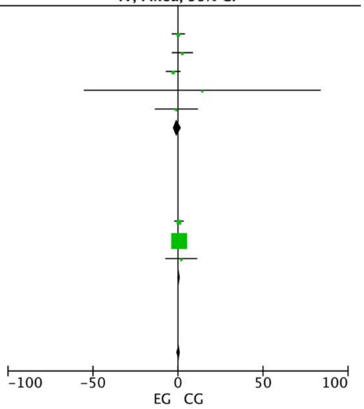

Identification
Screening
Eligibility
Included
Records identified through database searching (Medline, Scopus, CENTRAL) (n = 647)
Additional records identified through other sources (n = 2)
Records after duplicates removed (n = 516)
Records screened (n = 516)
Records excluded (n = 444)
Full-text articles assessed for eligibility (n = 72)
Full-text articles excluded (n = 61)
- not at home (n=41) or partially at home (n=4)
- protocol study (n=1)
- not RCT (n=8)
- not functional rehabilitation (n=3)
- qualitative study (n=2)
- not integral study (n=2)
Studies included in qualitative synthesis (n = 11)
Studies included in quantitative synthesis (meta-analysis) (n = 11)

Figure 2.

A

Study or Subgroup	EG Mean	EG SD	EG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Arm function								
Adie 2017	49.5	13.8	117	49.3	14.2	118	6.1%	0.20 [−3.38, 3.78]
Allen 2017	42.3	9.7	19	39.7	8.8	19	2.3%	2.60 [−3.29, 8.49]
Hoang 2015	26.8	5.4	28	29.6	8.3	22	4.9%	−2.80 [−6.80, 1.20]
Standen 2016	89.35	92.34	8	75.08	36	7	0.0%	14.27 [−55.05, 83.59]
Zondervan 2016	49.8	16.3	9	50.75	9	8	0.5%	−0.95 [−13.29, 11.39]
Subtotal (95% CI)			**181**			**174**	**13.7%**	**−0.50 [−2.88, 1.89]**
Heterogeneity: Chi² = 2.66, df = 4 (P = 0.62); I² = 0%								
Test for overall effect: Z = 0.41 (P = 0.68)								
1.1.2 Lower limb function (TUG)								
Hoang 2015	12.3	4.3	28	11.7	4.6	22	12.5%	0.60 [−1.90, 3.10]
Song 2017	9.72	2.14	28	9.02	1.7	25	72.8%	0.70 [−0.34, 1.74]
Yang 2015	20.7	11.4	11	18.8	10.7	12	1.0%	1.90 [−7.16, 10.96]
Subtotal (95% CI)			**67**			**59**	**86.3%**	**0.70 [−0.25, 1.65]**
Heterogeneity: Chi² = 0.07, df = 2 (P = 0.96); I² = 0%								
Test for overall effect: Z = 1.44 (P = 0.15)								
Total (95% CI)			**248**			**233**	**100.0%**	**0.53 [−0.35, 1.42]**
Heterogeneity: Chi² = 3.57, df = 7 (P = 0.83); I² = 0%								
Test for overall effect: Z = 1.19 (P = 0.24)								
Test for subgroup differences: Chi² = 0.83, df = 1 (P = 0.36), I² = 0%								

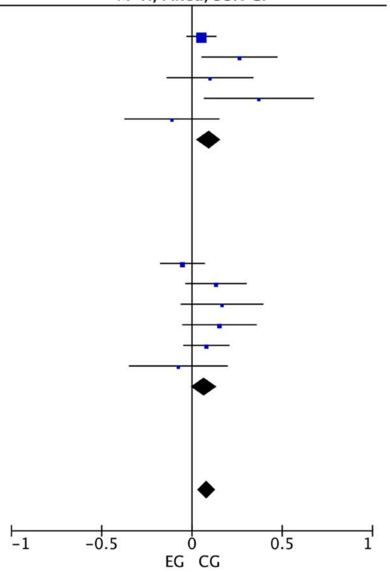
Mean Difference
IV, Fixed, 95% CI



B

Study or Subgroup	EG Events	EG Total	CG Events	CG Total	Weight	Risk Difference M-H, Fixed, 95% CI
2.2.1 upper limb						
Adie 2017	16	117	10	118	37.7%	0.05 [−0.03, 0.13]
Allen 2017	5	19	0	19	6.1%	0.26 [0.06, 0.47]
Nijenhuis 2016	1	10	0	10	3.2%	0.10 [−0.14, 0.34]
Standen 2016	8	17	1	10	4.0%	0.37 [0.07, 0.67]
Zondervan 2016	0	9	1	9	2.9%	−0.11 [−0.37, 0.15]
Subtotal (95% CI)		**172**		**166**	**53.9%**	**0.09 [0.03, 0.16]**
Total events	30		12			
Heterogeneity: Chi² = 9.25, df = 4 (P = 0.06); I² = 57%						
Test for overall effect: Z = 2.68 (P = 0.007)						
2.2.2 Lower limb						
Gandolfi 2017	2	38	4	38	12.2%	−0.05 [−0.17, 0.07]
Hoang 2015	5	28	1	22	7.9%	0.13 [−0.03, 0.30]
Prosperini 2013	2	12	0	18	4.6%	0.17 [−0.06, 0.39]
Song 2017	9	31	4	29	9.6%	0.15 [−0.05, 0.36]
Thomas 2017	2	25	0	25	8.0%	0.08 [−0.05, 0.21]
Yang 2015	1	11	2	12	3.7%	−0.08 [−0.35, 0.20]
Subtotal (95% CI)		**145**		**144**	**46.1%**	**0.07 [−0.01, 0.14]**
Total events	21		11			
Heterogeneity: Chi² = 6.88, df = 5 (P = 0.23); I² = 27%						
Test for overall effect: Z = 1.77 (P = 0.08)						
Total (95% CI)		**317**		**310**	**100.0%**	**0.08 [0.03, 0.13]**
Total events	51		23			
Heterogeneity: Chi² = 16.54, df = 10 (P = 0.09); I² = 40%						
Test for overall effect: Z = 3.18 (P = 0.001)						
Test for subgroup differences: Chi² = 0.31, df = 1 (P = 0.58), I² = 0%						

Risk Difference
M-H, Fixed, 95% CI



C

Study or Subgroup	EG Events	EG Total	CG Events	CG Total	Weight	Risk Difference M-H, Random, 95% CI
2.1.1 Upper limb						
Adie 2017	0	117	0	118	13.3%	0.00 [−0.02, 0.02]
Allen 2017	0	19	0	19	12.9%	0.00 [−0.10, 0.10]
Zondervan 2016	0	9	0	9	11.8%	0.00 [−0.19, 0.19]
Subtotal (95% CI)		**145**		**146**	**38.0%**	**0.00 [−0.02, 0.02]**
Total events	0		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 2 (P = 1.00); I² = 0%						
Test for overall effect: Z = 0.00 (P = 1.00)						
2.1.2 Lower limb						
Gandolfi 2017	0	38	0	38	13.2%	0.00 [−0.05, 0.05]
Hoang 2015	24	28	0	22	12.4%	0.86 [0.71, 1.00]
Prosperini 2013	5	18	0	18	11.4%	0.28 [0.06, 0.49]
Song 2017	8	31	0	29	12.2%	0.26 [0.10, 0.42]
Thomas 2017	0	15	0	15	12.7%	0.00 [−0.12, 0.12]
Subtotal (95% CI)		**130**		**122**	**62.0%**	**0.28 [−0.10, 0.65]**
Total events	37		0			
Heterogeneity: Tau² = 0.17; Chi² = 194.56, df = 4 (P < 0.00001); I² = 98%						
Test for overall effect: Z = 1.46 (P = 0.14)						
Total (95% CI)		**275**		**268**	**100.0%**	**0.17 [−0.02, 0.36]**
Total events	37		0			
Heterogeneity: Tau² = 0.07; Chi² = 359.13, df = 7 (P < 0.00001); I² = 98%						
Test for overall effect: Z = 1.73 (P = 0.08)						
Test for subgroup differences: Chi² = 2.12, df = 1 (P = 0.15), I² = 52.8%						

Risk Difference
M-H, Random, 95% CI

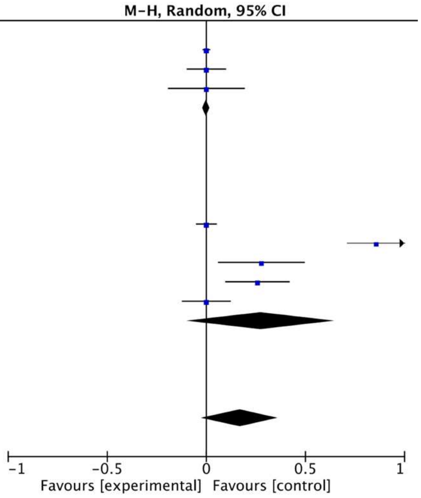
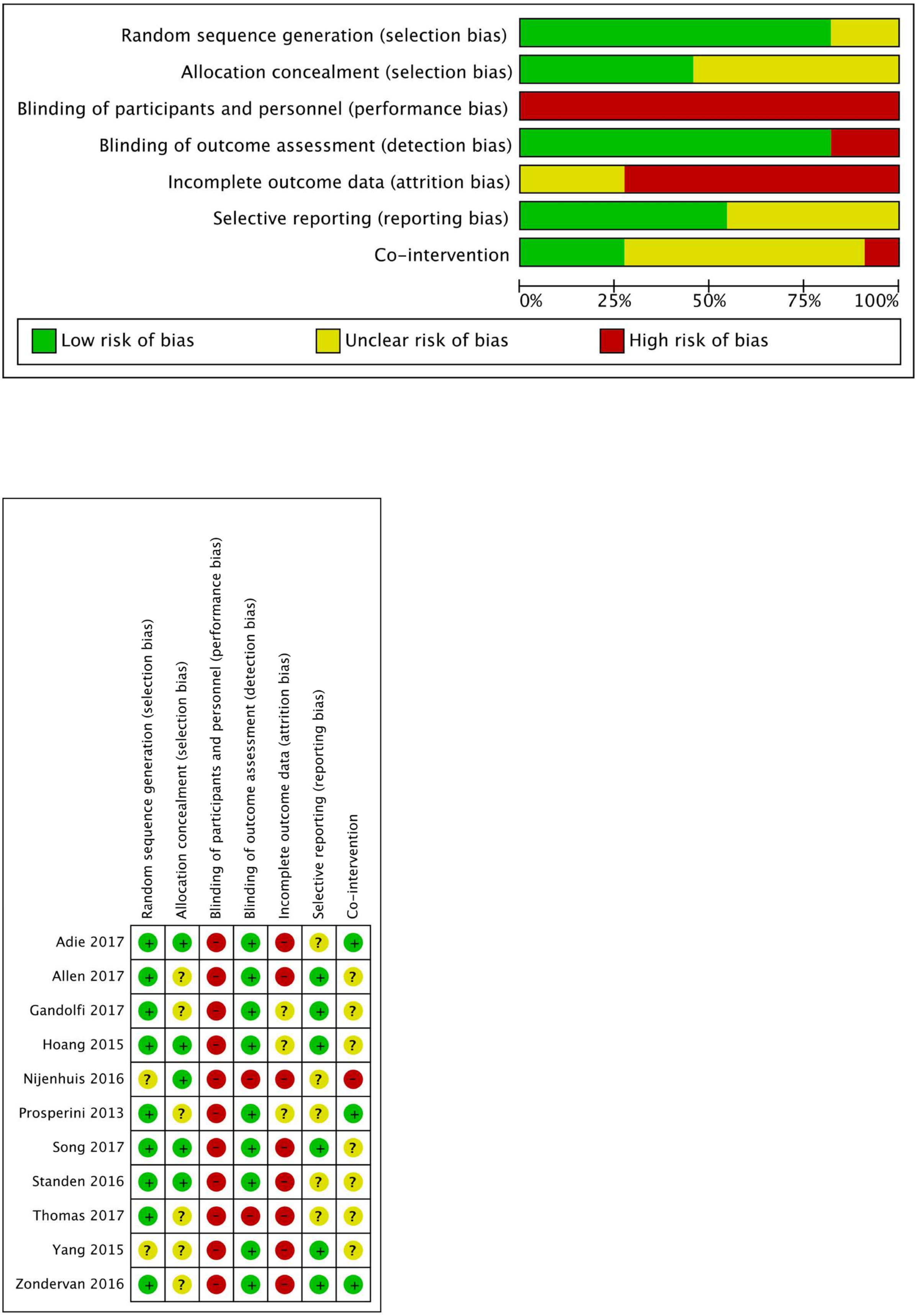


Figure 3.



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
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias
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^{TM} 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^{TM} 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.
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^{TM}) (n=38) CG: Sensory Integration Balance Training (SIBT) (n=38)	Commercial entertainment system: Nintendo Wii^{TM} 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) 15 EG: 9 (1 changed mind, 2 unable to contact participant, 2 participants' condition deteriorated, 4 no assessment) CG: 6 (4 changed mind, 2 participants deteriorated/deceased)	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^{TM} 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 6 EG: 6 patients, 2 of whom due to exacerbated pain where they had pre-existing lower back pain.	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: 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