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Exergaming for Quality of Life in persons living with chronic diseases: A systematic review and meta-analysis

Running title: **Exergames for QoL in chronic diseases**

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Exergaming for quality of life in persons living with chronic diseases: A systematic review and meta-analysis

Abstract

Objective: To evaluate the evidence of effectiveness of exergame-based rehabilitative interventions on health-related quality of life (HRQoL) in persons with chronic diseases.

Type: Systematic review and meta-analysis.

Literature survey: Randomized and non-randomized controlled trials of exergame rehabilitation interventions in populations with chronic diseases reporting HRQoL outcomes were identified by searching PubMed, Scopus, Physiotherapy Evidence Database (PEDro), Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar, using keywords and MeSH terms for papers published between January 2005 and March 2019.

Methodology: Risk of bias was assessed by using the PEDro scale. The GRADE system was used to score the quality of evidence. Pooled effects were reported as standardized mean differences (SMDs) or weighted mean difference (MDs) and 95% confidence intervals (CIs), using a random-effects model. Heterogeneity was weighted by inconsistency I^2 tests.

Synthesis: Thirty-four trials were identified (1,594 participants). Overall, the evidence was low quality. Exergames significantly improved HRQoL in populations with chronic diseases, with a small effect size (32 studies; 1,544 participants; SMD 0.24; 95% CI 0.1 to 0.4; I^2 = 27%) and specifically in people with neurological disorders (20 studies, 956 participants, SMD 0.22; 95% CI 0.2 to 0.4; I^2 = 49%), rheumatologic diseases (four studies, 210 participants, SMD 0.39; 95% CI 0.1 to 0.7; I^2 = 4%), and cardiorespiratory and chronic metabolic conditions (five studies, 309 participants, SMD 0.23; 95% CI 0.0 to 0.5; I^2 = 0%). Exergaming interventions in health care settings demonstrated similarly small but positive effects (22 studies, 905 participants, SMD 0.30; 95% CI 0.1 to 0.5; I^2 = 41%), whereas those carried out in home-based contexts did not.

Conclusions: Exergame-based rehabilitative interventions performed in health care settings led to small but statistically significant improvements in HRQoL in persons with chronic diseases.

Keywords: Exergames; disability; chronic diseases; physical rehabilitation; quality of life

Introduction

Chronic diseases are health conditions characterized by long-term course and physical and/or mental impairments, representing one of the major challenges for health policies for their impact on financial and resource demand.[1] Chronic diseases contribute to the global burden of disability, due to their high impact in terms of disabling effects and the high prevalence of specific health conditions.[2] Persons with chronic disease must deal with medical therapy and lifelong treatments, pain, reduction in mobility, fatigue, social withdrawal, and psychological distress, which may further aggravate the subjective perception of burden. Although a number of care models for chronic diseases have been proposed and implemented, they are generally based on a patient-centered approach, requiring at the individual level the full health literacy, involvement, and empowerment of the patients, who should be asked to define the health related problems and actively self-manage their illness.[3] The assessment of health-related quality of life (HRQoL) has become one of the patient-reported outcome measures (PROMs) that is most used to evaluate the individual's point of view regarding the burden of a health condition and the subjective experience of disease, reflecting the individual's skills to cope with stressful events related to the illness.[4] Such measures of subjective perception and experience of disease are a multidimensional construct involving at least three main health domains (physical, psychological, and social functioning) and encompass the efficacy of treatments and need of care. HRQoL assumes a great relevance in clinical research of chronic diseases, mostly in those with bodily pain and psychological distress, that determines strong impairment of daily activities and social participation, and in which long-term treatments are often required.[5] HRQoL has been shown to be impaired in several chronic diseases[6], with poorer levels detected in individuals with two or more chronic conditions compared to a single one or to healthy persons.[7, 8]

The role of physical exercise in improving HRQoL has been investigated in healthy[9, 10] and clinical populations participating in different exercise-based rehabilitation programs.[11-13] Long-term rehabilitation programs for persons with chronic conditions are generally put in place to tackle the progression of the disease and minimize functional impairment, and they require strong adherence and motivation.

Virtual reality (VR), defined as *an advanced form of human–computer interface that allows the user to interact and be immersed in a computer-generated environment in a naturalistic fashion*,[14] represents a novel therapeutic approach (described as an "empowering environment") in which persons with disability can freely explore and act.[15] Exercise-based rehabilitation performed by means of VR games represents a promising technological strategy to enhance the interest of users by providing an easy and engaging setting, in which the key elements of gameplay (reward, challenge, feedback, choice, clear instructions, goals, and socialization) are combined with the main rehabilitative aims (motor skills learning, long-term retention, and transfer of skills).[16] Two distinct VR game technologies are employed in physical rehabilitation: the serious games - games actually developed to be used for rehabilitative purposes, which are currently expensive and hardly accessible - and exergames. Exergames are commercial videogame-based systems employed for the user to perform different physical activities and sports, thus increasing the energy expenditure and heart rate as a moderate–vigorous intensity exercise.[17] Although created as low-cost entertainment tools, they have gradually gained the interest of researchers because of their off-the-shelf applications in the prevention of and rehabilitation from different pathological conditions.[18-22] One of the crucial points of interest for health professionals is that exergames, because they are actually games, add attractiveness, fun, and enjoyment during the treatment, thus enhancing the individual's motivation, with potentially positive effects on dose-response, adherence to, and long-term effectiveness of the rehabilitation programs.[23, 24] Exergames have been shown to be not only at least as good as usual physical therapy, with comparable dose efficacy, but often more motivating and engaging than conventional rehabilitation programs for persons with physical impairments.[25] The impact of comprehensive rehabilitation by means of commercially available exergames on PROMs has not been investigated so far.

We, therefore, set out to determine whether and to what extent exergames have a positive impact on the general HRQoL of participants with chronic diseases. Moreover, because a number of previous investigations[22-25] elaborated on the possibility to extend the use of exergames for rehabilitation in a domestic setting, we further sought to detect whether home-based rehabilitative interventions performed by using exergames are as effective for HRQoL as those performed in health care centers.

Methods

Search strategy and article selection

A systematic review and meta-analysis was performed employing the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement.[26] A systematic search for relevant articles was carried out on PubMed, Scopus, Physiotherapy Evidence Database (PEDro), Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar, using keywords and MeSH terms for papers published from January 2005 to March 2019 (see **Supplementary file 1**). We chose to apply this time period restriction because the first console for active video games (Nintendo Wii™) was launched in 2005.

To avoid the risk of missing relevant articles, we also searched for additional papers through the reference lists of previously published reviews. One reviewer (GM) ran the search strategy and screened the initial titles after removing duplicates. Two authors (GM and LC) independently examined each potentially relevant article, using the following criteria as defined by the population, intervention, comparison, and outcome (PICO) model:[27] (i) Population: persons affected by chronic diseases; (ii) Intervention: "off the shelf" exergames (i.e., exergame-based interventions delivered by commercial devices); (iii) Comparison: conventional disease-related rehabilitation treatments; (iv): Outcomes: HRQoL, assessed by either widely accepted general questionnaires or specific questionnaires assessing HRQoL for specific diseases and conditions. Only papers published in peer-reviewed journals were included, if reporting findings from experimentally controlled studies (i.e., both randomized and non-randomized controlled trials). We excluded conference papers; articles published in languages other than English[28]; or unpublished data; as well as papers reporting findings of nonexperimental, observational studies or involving non-exergaming interventions (including the so-called action videogames). The search strategy was carried out from

December 2018 to March 2019.

Risk of bias and quality of the evidence assessment

Risk of bias in the included studies was assessed by the PEDro scale[29] by downloading the available scores on the website (https://www.pedro.org.au). If a trial had not been rated in the PEDro archive, two authors (GM and LC) independently scored the articles. The total score on the PEDro scale was interpreted as follows: 9–10, low risk of bias; 6–8, moderate risk of bias; studies with a score <6 were considered as carrying a high risk of bias. The Grading of Recommendation, Assessment, Development and Evaluation (GRADE) system was employed to score the quality level of the evidence.[30] The quality of the evidence of each outcome analyzed was downgraded from a high level or upgraded, according to predefined criteria.[31] Quality was downgraded by one place if there was evidence of: indirectness (e.g., indirect comparisons); substantial heterogeneity (Inconsistency statistic, I^2 >50%); imprecision (e.g., sample size ≤200 participants or 95% confidence interval (CI) crossing zero); publication bias demonstrated by asymmetry of funnel plots (if ≥10 trials were included),[32] or if most trials scored ≤6 on the PEDro scale. Conversely, the quality of the evidence was downgraded two places due to very large CIs (e.g., the upper or lower confidence limit crosses the standardized mean difference [SMD] of 0.5 in either direction), and imprecision.[31] The evidence was then ranked into four levels: very low, low, moderate, and high. Disagreements between authors were resolved by consensus and, if necessary, a third author was consulted (LP).

Data synthesis and statistical analysis

For each included article, we collected and recorded the following information in an electronic spreadsheet: (1) author(s)'s name and year of publication; (2) sample size of intervention and control group; (3) design and length of the study protocol; (4) topic (i.e., chronic disease/condition covered by the study: neurological diseases, rheumatologic conditions, cardiorespiratory and metabolic diseases, and other chronic health conditions producing chronic physical or psychological impairment); (5) characteristics of the interventions; (6) HRQoL assessment tools; (7) HRQoL post-intervention outcomes. Raw data (means and standard deviations, SDs) was extracted post-intervention or calculated from medians, standard errors, and 95% CI, *p* values, T values, or *F* values. In cases of missing data, a formal request was sent to the corresponding author of the considered study. Data was then analyzed using a generic inverse variance with random-effect models in Review Manager 5.3 (Cochrane Collaboration, 2014). To allow interpretation of the effect size of these changes, we calculated the SMD (95% CI) when homogeneous data was extracted from similar outcome measures[33] (i.e., for the meta-analyses on general HRQoL because the included studies used different assessment tools), and the weighted mean difference (MD, 95% CI) when data was extracted from the same outcome measure (i.e., for the meta-analyses, when the same HRQoL assessment tool was employed). Positive SMDs indicated a difference in results favoring exergames; by convention, an SMD of 0.20 was considered small, 0.50 medium, and an SMD ≥0.80 was defined as a large effect size.[34] Moreover, MDs were considered clinically meaningful for improvement of about 20% compared to the baseline condition.[35] Heterogeneity across the studies was assessed by I^2 statistic, which describes the percentage of variability in the point estimates.[36] We interpreted I^2 values as follows: 0%–40% as "might not be important"; 30%–60% as "may represent moderate heterogeneity"; 50%–90% as "may represent substantial heterogeneity"; 75%–100% showing "considerable heterogeneity." In cases of substantial heterogeneity, sensitivity analyses with a *leave-one-out* approach were performed to check whether the findings were driven by a single study.[37] Potential publication bias was determined by a visual inspection of the funnel plots and by the Egger's regression test. If not otherwise specified, values were expressed as mean ± SD.

Results

From 679 titles originally identified through database searching, and 24 additional titles identified from the reference lists of selected papers and previously published reviews, and after the exclusion of 27 articles published in languages other than English, we were able to assess 319 full-text articles for eligibility. **Figure 1** shows the process of study selection for the qualitative and quantitative syntheses.

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Qualitative data synthesis

Thirty-four studies (n = 1,594 participants) published between 2010 and 2019 fulfilled all the inclusion criteria and were included: 30 randomized controlled trials[38-67] and four controlled, cross-over trials.[68-71] **Table 1** summarizes the main characteristics of the included studies.

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Participants

Samples in the included studies ranged widely between 12[40] and 224 participants,[36] with a mean (±SD) of 54.4 ± 48.8. Twenty-one studies targeted persons affected by neurological disorders, such as stroke,[38, 40, 45, 51, 52, 61, 62, 64] Parkinson's disease,[46, 47, 53, 58, 60, 65] Alzheimer's disease,[55, 56] cognitive decline and mild cognitive impairment,[50, 57] multiple sclerosis,[69] Huntington's disease,[68] or tropical spastic hemiparesis.[42] Five studies targeted persons suffering from rheumatologic diseases, such as osteoarthritis,[44, 67] fibromyalgia,[39] ankylosing spondylitis,[48] and rheumatoid arthritis.[71] Five studies enrolled persons with chronic cardiorespiratory or metabolic conditions such as cystic fibrosis,[41] chronic respiratory diseases,[54] cardiovascular diseases,[43, 66] and type 2 diabetes.[49] The remaining three studies targeted persons with dizziness,[59] individuals undergoing hematopoietic stem cell transplantation,[63] and persons with schizophrenia.[70] (See **Table 1** for the samples' characteristics)

Exergame-based interventions and comparisons

The length of interventions ranged between two[61, 62] and 24 weeks,[66] with a mean (±SD) of 8.05 ± 4.3 weeks. Exergame-based interventions in 24 of the included studies were performed with the Nintendo Wii console, through the games available with the Wii platform (Wii Sports, Wii Fit, Wii Minisports).[38, 40-43, 45, 47, 49, 50, 53-64, 69-71] In nine studies, the exergame-based intervention was carried out using the Microsoft Kinect console (Xbox, Kinect Adventures, Kinect Sports, Light Race),[39, 44, 46, 48, 51, 52, 65-67] and one study used the Dance Dance Revolution game platform.[68]

Conventional disease-related rehabilitation treatments included conventional exercise-based rehabilitation training[38, 40, 42, 44, 46, 51, 55, 56, 58, 60, 63, 65, 71] and some specific rehabilitation programs.[43, 47, 50, 52-54, 57, 59, 60, 62, 64, 68] Interventions were carried out in clinical or rehabilitation care centers in all except 10 studies, in which exergame-based programs were performed at home, mostly unsupervised.[38, 41, 49, 55, 59, 66, 69, 70] Gandolfi and colleagues supervised each intervention section by telerehabilitation,[47] whereas Kloos and colleagues provided supervision from the researchers' supervision.[68] (See **Table 1** for the studies' characteristics)

HRQoL outcomes

HRQoL was the primary outcome in 17 studies[39, 40, 42, 44, 48- 50, 52, 57, 58, 63, 64, 66, 67, 69-71] and a secondary outcome in another 17 studies.[38, 41, 43, 45-47, 51, 53-56, 59-62, 65, 68] HRQoL was assessed through widely used general questionnaires, such as EuroQoL-5 Dimensions, 5item World Health Organization Well-being Index, World Health Organization-QoL Brief, and Short Form Health Survey at 36, 12, or 8 items,[38-40, 42, 44, 49, 52, 57, 59, 63, 67, 68, 70, 71] or through disease-specific questionnaires measuring the disease-specific burden on HRQoL.[41, 43, 45-48, 50, 51, 53-56, 58, 60-62, 64-66, 69] (See **Table 1** for the HRQoL assessment tools)

Risk of bias assessment

Risk-of-bias assessment of the included studies using the PEDro scale[29] yielded 20 studies, scoring from 6 to 8 at moderate risk of bias,[38-53, 55, 57, 60, 61, 64, 69] and the remaining 14, with a score <6, at high risk of bias.[44, 45, 54, 56, 58, 59, 62, 63, 65- 68, 70, 71] None of the included studies scored 9–10. (See **Table 1** for the total PEDro scores of the included studies)

Quantitative data synthesis

Data pooling from all the available studies that evaluated HRQoL outcomes (34 studies, 1,594 participants)[38-71] revealed a substantial heterogeneity across the trials (I^2 >50%). Sensitivity analyses were therefore conducted, which revealed that the pooled estimate was highly influenced by the study by Elshazly and colleagues[44] (40 participants). This study was removed, employing a *leave-one-out* approach. Moreover, visual inspection of the funnel plot suggested a potential publication bias in the small study by Fan and colleagues[45] (10 participants), which was, therefore, removed (see **Supplementary file 2**). After these corrections, data pooling revealed a small, statistically significant difference between exergame-based interventions and conventional disease-related rehabilitation therapies in favor of exergaming (SMD 0.24; 95% CI 0.1 to 0.4; I^2 = 27%). (See **Figure 1.1**)

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With reference to each disease area, in populations with neurological disorders (21 studies, 966 participants),[38, 40, 42, 45-47, 50-53, 55-58, 60-62, 64, 65, 68, 69] visual inspection of the funnel plot suggested a potential publication bias in the small study by Fan and colleagues[45] (10 participants) (see **Supplementary file 3**). After its removal, a significant statistical difference between groups in favor of exergame-based exercise was found, at a small effect size (SMD 0.22; 95% CI 0.2 to 0.4; I^2 = 49%) (see **Figure 1.2**).

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Data pooling from five studies reporting on HRQoL outcomes in rheumatologic diseases (250 participants)[39, 44, 48, 67, 71] showed excessive heterogeneity (I^2 >50%) across the trials. Sensitivity analyses were therefore conducted, which revealed that the pooled estimate was highly influenced by the study by Elshazly and colleagues[44] (40 participants) (see **Supplementary file 4**). This study was removed, employing a *leave-one-out* approach, resulting in low heterogeneity (I^2 = 4%) and a statistically significant difference between groups in favor of exergame-based exercise, at a small to moderate effect size (4 studies, 210 participants after sensitivity analyses; SMD 0.39; 95% CI 0.1 to 0.7; I^2 = 4%)[39, 48, 67, 71] (see **Figure 1.3**).

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In the meta-analysis of the studies reporting on HRQoL outcomes in cardiorespiratory and chronic metabolic conditions, pooled data from the five eligible studies (309 participants) revealed a statistically significant difference in favor of exergame-based exercise, at a small effect size (SMD 0.23; 95% CI 0.0 to 0.5; I^2 = 0%)[41, 43, 49, 54, 66] (see **Figure 1.4**).

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With reference to the three studies of exergame-based interventions for persons with neurological diseases, in which the SF-36 questionnaire was employed as the endpoint of treatment,[40, 42, 57] data pooling of each subcategory revealed a significant statistical difference between groups in favor of exergame-based intervention on all eight domains as follows: physical functioning (2 studies, 87 participants; MD 3.9; 95% CI 2.1 to 5.6), physical role (3 studies, 117 participants; MD 7.7; 95% CI 6.0 to 9.5), bodily pain (2 studies, 87 participants; MD 8.0; 95% CI 6.0 to 9.9), general health (3 studies, 117 participants; MD 4.5; 95% CI 2.5 to 6.5), vitality (3 studies, 117 participants; MD 10.4; 95% CI 8.5 to 12.3), social functioning (3 studies, 117 participants; MD 3.4; 95% CI 1.4 to 5.4), emotional role (2 studies, 104 participants; MD 6.0; 95% CI 4.0 to 8.0), and mental health (3 studies, 117 participants; MD 4.7; 95% CI 1.0 to 8.4) (see **Figures 2.1 to 2.8**). Sensitivity analyses were performed due to the excessive heterogeneity across the trials (I^2 >50%) for physical function, bodily pain, and emotional role (see **Supplementary file 5**). None of the MDs related to each of the SF-36 domains here analyzed can be considered clinically meaningful, because the 20% improvement cut-off was not achieved in any of them.[35]

----- Please, insert Figures 2.1 to 2.8 about here ----

Data pooling from reports (24 studies, 955 participants) in which the rehabilitation interventions in the form of exergames were performed in health care settings revealed a substantial heterogeneity (I^2 >50%). Sensitivity analyses were conducted, revealing that the aggregate estimate was highly influenced by the study by Elshazly and colleagues.[44] This study was therefore removed. Due to publication bias, the study by Fan and colleagues[45] was also removed (see **Supplementary file 6**). After their removal, data pooling showed a statistically significant difference between conventional disease-related rehabilitation treatments and exergame-based interventions performed in health care facilities, favoring the latter, at a small effect size (SMD 0.30; 95% CI 0.1 to 0.5; I^2 = 41%).[39, 40, 42, 43, 46, 48, 50-54, 56-65, 67] Conversely, data pooling from the 10 trials (639 participants) comparing home-based exergame interventions and conventional disease-related rehabilitation interventions did not reveal a significant difference between the two approaches (SMD 0.12; 95% CI –0.04 to 0.3; I^2 = 0%).[38, 41, 47, 49, 55, 66, 68-71] (See **Figures 3.1** and **3.2**)

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Table 2 reports the results of the GRADE assessment of the quality of evidence. The general and disease-related HRQoL outcomes were scored as having low to moderate (neurological diseases) quality of evidence, whereas the HRQoL outcomes depending on the intervention settings were scored as very low for home-based intervention and low for center-based intervention. Last, the quality of evidence for the SF-36 outcomes for neurological diseases was scored very low.

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Discussion

The aggregate estimates obtained indicate that exercise-based rehabilitation carried out by means of exergames can enhance HRQoL outcomes in people with chronic diseases in a manner similar to conventional disease-related rehabilitation interventions, as demonstrated by the small size of the difference between the two approaches. However, the overall low quality of the evidence for the majority of the outcomes considered prevents recommending this unconventional type of rehabilitation until a more robust body of evidence is gathered.

In general, there is increasing interest in probing the effect of rehabilitative interventions on PROMs. Their incorporation in clinical practice and research is important also for chronic conditions, where PROMs relating to HRQoL represent real key elements to estimate the physical and psychosocial burden of the disease and appraise the effects of treatments from the individual's perspective.[72] According to Fung and Hays, HRQoL represents the ultimate outcome of patient-centered care and is influenced by the quality of care as well as of social support and adherence to treatment, personal attitudes, beliefs, and individual needs.[73] Measuring HRQoL has been shown to drive positive effects on clinician–patient communication and relationship and enhance the user's health literacy and participation in the decision-making process,[74] thus potentially improving self-management of the disease. Personalized care planning for persons suffering from chronic conditions was shown to have positive effects on physical and mental health and on self-management skills, with greater effects from interventions that are more comprehensive, integrated, and engaging.[75, 76] Recently, a human-centered design, which encompasses the use of PROMs, was recommended in developing, implementing, and evaluating VR interventions in clinical trials.[77] HRQoL was set as the main endpoint of treatment in half of the studies included in our review (17 out of 34), thus testifying to the researchers' interest in customized care and users' perspective in physical rehabilitation of chronic diseases.

Conventional exercise-based rehabilitation for HRQoL has been shown to yield beneficial effects in persons affected by chronic disability, irrespective of the type and dose of exercise.[78-85] VR-based rehabilitation programs for persons with physical impairments were found slightly but significantly more effective than some conventional neurorehabilitation methods on motor control, balance, gait, and strength[86] and, specifically, for persons with post-stroke disability, improved walking speed, balance, and mobility.[87] They were also proposed as an effective, viable alternative to traditional rehabilitation programs for persons with multiple sclerosis.[88, 89] Compared to traditional rehabilitation approaches, exergame-based interventions (which are considered non-immersive VR systems) were found to improve to a significantly greater extent executive functions and visuospatial perception in adult populations with neurological disabilities and in children with neurodevelopmental disorders.[90] Nevertheless, the effect of non-immersive VR neurorehabilitation training on HRQoL has so far not been well debated, due to few, low-quality studies of the evidence also confirmed by our findings.[86] Indeed, two meta-analyses on VR-based interventions for specific neurologic disorders reported similar effects on HRQoL for VR and conventional physiotherapy in individuals with Parkinson's disease,[91] together with a lack of scientific evidence for VR-based interventions on HRQoL in post-stroke survivors.[92]

At a speculative level, we suggest that the positive effects on physical functioning from VR programs might be due to increased engagement and physical and cognitive fidelity ensured by the VR-based interventions, which add motivation and enjoyment, compared with overall repetitive and possibly less appealing conventional rehabilitation approaches.[93] Indeed, enjoyment during the rehabilitation sessions performed by means of VR has been indicated as an especial key element to increase users' adherence and engagement.[94] Several authors of the included studies describe exergame-based interventions as more engaging, motivating, and enjoyable than usual care, influencing participants' adherence to this form of unconventional rehabilitative protocols.[39, 40, 42-44, 45, 49, 51, 58, 63, 65, 68, 70] Noticeably, improvement in HRQoL by exergame-based intervention had been attributed merely to motivation, enjoyment, and compliance.[39, 42, 48, 49, 57, 64] However, the positive effect on HRQoL in populations with chronic conditions could also be driven by other determinants, such as improvement in motor functions, physical capability, activities of daily living, and fatigue,[38, 40, 41, 43-47, 49, 53-56, 59, 60, 62, 64, 65, 68, 69, 71] cognitive abilities,[51, 57, 66] and relief from pain,[39, 40, 42, 44, 48] depression,[50, 63, 67] and social withdrawal.[58, 70] Interestingly, the study carried out by Shimizu and colleagues on persons with schizophrenia objectively showed the effect of exergaming on prefrontal cortex activation, using functional near-infrared spectroscopy (fNIRS) imaging, thus potentially contrasting the typical schizophrenia-related reduction in blood flow in this brain region (the so-named hypofrontality) that has been hypothesized to be responsible for social withdrawal in schizophrenia.[70] In addition, prefrontal cortex activation is involved in executive functions, the cognitive skills involved in self-consciousness, planning, and acting in goal-directed behaviors, as well as in metacognition.[95] As previously reported, the improvement in executive functions produced by exergames could be related to the far transfer effect due to the dual-task performances required.[90] Future research should disentangle how those components influence HRQoL and in what measure; above all, it should identify which potentially relevant functional-mediators could be involved.

Because several previous studies have suggested that exergames might be a useful tool for home-based rehabilitation,[22, 96-99] we further analyzed the effects of exergame-based interventions on HRQoL both in home-based and health care center–based settings, compared with conventional rehabilitation therapies. Our findings pointed toward small but positive effects on HRQoL in health care center–based settings, which were, instead, not the case for home-based interventions. Indeed, the studies focused on home-based exergames interventions revealed some critical issues, such as higher cost,[38] lower training adherence,[41] higher risk of adverse effects,[69] and potential difficulty in objectively monitoring adherence to the specific exergame-based program.[66] Notably, beneficial effects, not limited to findings on HRQoL, were reported following exergames home-based interventions with either technicians'[47, 68] or caregivers' involvement.[41, 49, 55] According to Lohse and colleagues, video games designed for rehabilitation by allowing cooperation and competition with a partner (e.g., proximal socialization) can enhance learning, motivation, and engagement by means of human feedback and encouragement.[16] The results of the meta-analysis by Laver and colleagues on the use of VR-based rehabilitation programs (carried out by both off-the-shelf exergames and/or serious game devices) on post-stroke survivors showed a statistically nonsignificant trend, suggesting that higher dosage of interventions could be preferable for improving arm function and activities of daily living.[92] Our results further suggested a key role for the therapist's supervision during exergaming in enhancing patient-reported HRQoL: supervision not only represents a feedback regarding the way in which exergaming should be performed, but also involves advice on how to gain the targeted exercise intensity (least dose, frequency, and duration). Thus, we may hypothesize that a more controlled setting, such as exergame-based programs under therapists' supervision performed in a health care facility, might ensure better control over the variables related to the intensity of the rehabilitation program, along with other attributes of such a controlled setting (i.e., more attention, motivation, reinforcement, participants' adherence). Therefore, the visual, auditory, and haptic real-time feedback on users' performance given by the device could have a limited importance, in the absence of or with insufficient and ineffective clarifications given by humans. The latter findings open the possibility that exergaming in home-based rehabilitation settings may benefit from therapist–client interaction, or at least interaction with peers, to enhance not only the achievement of specific health goals, but also the individual's perception of physical, psychological, and social results.

Furthermore, only three of the included studies employed exergame-based group interventions.[39, 43, 65] Group-based exercise interventions showed controversial findings on HRQoL: they were proposed to enhance HRQoL among healthy elderly[100] persons with severe mental health disorders[101] and mitigate motor impairment and disease severity as well as enhance the HRQoL of persons with Parkinson's disease.[102] Conversely, no effect on HRQoL was found in persons with type 2 diabetes, if compared with individual counseling.[103] We may assume that group-based rehabilitation might enhance HRQoL, maximizing social communication and interactions in populations affected by chronic diseases, which are often limited in social contacts because of physical disability and high degrees of stigmatization. In addition, Lewis and Rosie proposed that interpersonal competition might facilitate motivation in virtual rehabilitation games programs for neurologic conditions.[104] Further and specific studies are needed to verify whether exergame-based rehabilitative interventions with group settings could have different effects on HRQoL compared to one-on-one approaches. In addition, a cost-effectiveness analysis was performed in the study by Adie and colleagues,[38] which revealed that exergame-based rehabilitations appear to be more expensive than conventional exercise interventions. Conversely, in the study by Gandolfi and colleagues,[47] exergame-based intervention combined with telerehabilitation monitoring was found to be less expensive than specific in-clinic sensory integration balance training. Moreover, Collado-Mateo and colleagues, del Corral and colleagues, and Mazzoleni and colleagues stated that exergame-based interventions were relatively affordable, including purchase costs ranging from 150 to 300 €/equipment.[39, 41, 54]

Study limitations

The present meta-analysis is not free of limitations. Among these are (1) the low quality of the evidence detected by the GRADE assessment, which limits the external validity of the pooled estimates here outlined, also considered that 14 trials carried a high risk of bias; (2) the lack of registration in a public registry prior to engaging in the present work; (3) the choice to employ five databases, excluding some relevant ones such as EMBASE; (4) the exclusion of articles written in languages other than English, which may have led to excluding possibly pertinent papers; (5) the heterogeneity of the clinical conditions here considered. As a final remark, the outcome chosen, HRQoL, which is intrinsically complex and characterized by multiple domains, may be poorly responsive to changes induced by rehabilitative interventions, which may explain the small magnitudes of effect observed.

Conclusions

Exergame-based rehabilitative interventions led to small, beneficial effects in enhancing self-reported HRQoL in people with chronic diseases. The overall low quality of the evidence calls for more powered and better controlled upcoming research to verify whether exergame-based interventions may be a viable alternative and/or complementary therapy to conventional rehabilitation treatments for people with chronic diseases. Moreover, the role played by the setting (i.e., home-based versus health care facility) and by the type and amount of supervision is still an open question that will need to be addressed in the near future.

Conflict of Interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Table 1. Characteristics and main findings of included studies.

AUTHOR(S), YEAR, COUNTRY	DESIGN, DISEASE AREA	RANDOMIZED SAMPLE SIZE, MEAN AGE, GENDER	INTERVENTION GROUPS PROTOCOL	EXERGAME SETTING	HRQoL ASSESSMENT TOOL	TIME OF ASSESSMENT	DROPOUTS	ADHERENCE (%)	PEDro TOTAL SCORE (/10)	MAIN RESULTS ON HRQoL
STUDIES ON POPULATION WITH NEUROLOGICAL DISORDERS										
Adie et al., 2016, United Kingdom	RCT, stroke	235 (≈ 67.3 ys.) 56% male	**ExBG** (N=117): Nintendo Wii Sports games (45 minutes/day for 6 weeks), plus conventional care (including physical rehabilitation). **Exergame intensity:** NR **NExBG** (N=118): individually tailored arm exercise (45 minutes/day for 6 weeks), plus conventional care (including physical rehabilitation).	Home-based, individually performed, not supervised	EQ-5D	T0 (pre-treatment) T1 (post-treatment, 6 weeks) T2 (follow-up, 6 months)	ExBG: 15 NExBG: 12	87.1%	7/10	Both the groups showed improved HRQoL rating, without differences between ExBG and NExBG.
da Silva Ribeiro et al., 2014, Brazil	RCT, stroke	30 (≈ 53.2 ys.) 36.7% male	**ExBG** (N=15): Nintendo Wii Sports (50 minutes/2 weekly sessions, for 8 weeks), plus 10 minutes/session of stretching exercises. **Exergame intensity:** NR **NExBG** (N=15): conventional care (physiotherapy, 60 minutes/2 weekly sessions, for 8 weeks)	Health facility, individually performed, supervised	SF-36	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 0 NExBG: 0	NR	7/10	Both the groups showed significant improvement in several HRQoL dimensions. A significant between-group difference was found for the domain physical functioning, in favor of the NExBG.
de Oliveira Arnaut et al., 2014, Brazil	RCT, Tropical Spastic Hemiparesis	12 (≈ 58 ys.) 33.4% male	**ExBG** (N=6): Nintendo Wii mini games (30 minutes/2 weekly sessions, for 8 weeks), plus conventional care (functional exercise protocol, 30 minutes/2 weekly sessions, for 8 weeks). **Exergame intensity:** NR **NExBG** (N=6): conventional care (functional exercise protocol, 30 minutes/2 weekly sessions, for 8 weeks)	Health facility, individually performed, supervised	SF-36	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 1 NExBG: 2	NR	6/10	The ExBG showed a significant improvement of the emotional aspects of HRQoL, compared with NExBG.
Fan et al., 2013, Taiwan	RCT, stroke	27 (≈ 64.4 ys.) 70% male	**ExBG** (N=7): Nintendo Wii Sports Resort (60 minutes/3 weekly sessions, for 3 weeks) **Exergame intensity:** NR **NExBG 1** (N=7): conventional care (occupational therapy, 60 minutes/3 weekly sessions, for 3 weeks) **NExBG 2** (N=7): placebo	Health facility, individually performed, supervised	SIS	T0 (pre-treatment) T1 (post-treatment, 4 weeks) T2 (follow-up, 8 weeks)	ExBG: 2 NExBG1: 2 NExBG2: 2 NExBG3: 1	NR	5/10	No significant difference was detected in HRQoL scores among groups, neither immediately after interventions, nor after follow-up.

			board game (60 minutes/3 weekly sessions, for 3 weeks) **NExBG 3** (N=6): no treatment							
Ferraz et al., 2018, Brazil	RCT, Parkinson's disease	72 (≈ 69 ys.) 59.7% male	**ExBG** (N=22): Microsoft Kinect Adventures (50 minutes/3 weekly sessions, for 8 weeks), plus drug therapy. **Exergame intensity:** NR **NExBG 1** (N=25): conventional care (functional training, 50 minutes/3 weekly sessions, for 8 weeks), plus drug therapy. **NExBG 2** (N=25): conventional care (bicycle exercise, 50 minutes/3 weekly sessions, for 8 weeks), plus drug therapy.	Health facility, individually performed, supervised	PDQ-39 EQ-5D	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 2 NExBG1: 3 NExBG2: 5	NR	7/10	A significant improvement in HRQOL was detected for ExBG and NExBG1, compared with NExBG2.
Gandolfi et al., 2017, Italy	RCT, Parkinson's disease	76 (≈ 68.6 ys.) 67.1% male	**ExBG** (N=38): Nintendo Wii (50 minutes/3 weekly sessions, for 7 weeks) plus drug therapy. **Exergame intensity:** NR **NExBG** (N=38): conventional care (sensory integration balance training, 50 minutes/3 weekly sessions, for 7 weeks) plus drug therapy.	Home-based, individually performed, tele-supervised	PDQ-8	T0 (pre-treatment) T1 (post-treatment, 7 weeks) T2 (follow-up, 11 weeks)	ExBG: 0 NExBG: 4	NR	7/10	Both groups showed an overall significant improvement of HRQoL.
Kloos et al., 2013, USA	Controlled, crossover, Huntington's disease	24 (≈ 50.7 ys.) 38.8% male	**ExBG** (N=13): Dance Dance Revolution (45 minutes/2 weekly sessions, for 6 weeks). **Exergame intensity:** NR **NExBG** (N=11): handheld video game (frequency NR, for 6 weeks)	Home-based, individually performed, supervised	WHOQOL-Brief	T0 (pre-treatment) T1 (post-treatment ExBG, 6 weeks) T2 (post-treatment NExBG, 12 weeks)	ExBG: 2 NExBG: 4	100%	3/10	No significant treatment effects observed for HRQoL between the ExBG and NExBG, and no significant differential treatment effects by disease severity.
Lee GH, 2016, South Korea	RCT, cognitive decline	30 (≈ 64.6 ys.) 60% male	**ExBG** (N=15): Nintendo Wii Fit and Wii Sports (40 minutes/3 weekly sessions, for 12 weeks), plus conventional care (cognitive rehabilitation program). **Exergame intensity:** NR **NExBG** (N=15): conventional care (conventional cognitive rehabilitation program, 3 weekly sessions, for 12 weeks)	Health facility, individually performed, supervised	QOL-AD	T0 (pre-treatment) T1 (post-treatment, 12 weeks)	NR	NR	6/10	After the intervention, HRQoL score in the ExBG improved signifi-cantly, while in the NExBG did not.
Lee HC et al., 2017, Taiwan	RCT, stroke	50 (≈ 57.5 ys.) 72.3% male	**ExBG** (N=26): Microsoft Kinect Xbox games (45 minutes/2 weekly sessions, for 6 weeks), plus conventional care (physical	Health facility, individually performed,	SIS	T0 (pre-treatment) T1 (post-treatment, 6 weeks) T2 (follow-up, 12	ExBG: 0 NExBG: 3	NR	6/10	In both groups, no significant improvement was observed in HRQoL.

			rehabilitation, 45 minutes/2 weekly sessions, for 6 weeks). **Exergame intensity:** NR **NExBG** (N=24): conventional care (physical rehabilitation, 90 minutes/2 weekly sessions, for 6 weeks)	supervised		weeks)				
Lee M et al., 2016, South Korea	RCT, stroke	26 (≈ 68.2 ys.) 69.2% male	**ExBG** (N=13): Microsoft Kinect (30 minutes/3 weekly sessions, for 8 weeks). **Exergame intensity:** NR **NExBG** (N=13): conventional care (group-based rehabilitation program, 30 minutes/3 weekly sessions, for 8 weeks).	Health facility, individually performed, supervised	SF-12	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 0 NExBG: 0	95.1%	8/10	There was a significant increase in HRQoL scores in the NExBG, including in Physical Component Summary score, whereas no significant increase was shown by the ExBG. There was no significant difference in HRQoL between the groups.
Liao et al., 2015, Taiwan	RCT, Parkinson's disease	36 (≈ 65.6 ys.) 47.3% male	**ExBG** (N=12): Nintendo Wii Fit (45 minutes/2 weekly sessions, for 6 weeks), plus treadmill training (15 minutes/ 2 weekly sessions) and drug therapy. **Exergame intensity:** NR **NExBG1** (N=12): conventional care (traditional exercise program, 45 minutes/2 weekly sessions, for 6 weeks), plus treadmill training (15 minutes/ 2 weekly sessions), and drug therapy. **NExBG 2** (N=12): fall prevention education plus drug therapy.	Health facility, individually performed, supervised	PDQ-39	T0 (pre-treatment) T1 (post-treatment, 6 weeks) T2 (follow-up, 7 weeks)	ExBG: 0 NExBG1: 0 NExBG2: 1	NR	7/10	Both the ExBG and NExBG1 showed significant improvements in HRQoL compared with NExBG2 at follow-up; however, there was no significant difference between the ExBG and NExBG1 in the HRQoL.
Padala et al., 2012, USA	RCT, Alzheimer's disease	22 (≈ 80.4 ys.) 27.3% male	**ExBG** (N=11): Nintendo Wii Fit (30 minutes/5 weekly sessions, for 8 weeks) **Exergame intensity:** NR **NExBG** (N=11): conventional care (walking program, 30 minutes/5 weekly sessions, for 8 weeks)	Health facility, individually performed, supervised	QOL-AD	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 1 NExBG: 1	NR	5/10	There were neither statistically significant differences between the groups, nor significant group-by-time interaction on HRQoL. However, intragroup analysis of NExBG showed improvement on the HRQoL.
Padala et al., 2017, USA	RCT, Alzheimer's disease	30 (≈ 73 ys.) 36.7% male	**ExBG** (N=15): Nintendo Wii (30 minutes/5 weekly sessions, for 8 weeks) **Exergame intensity:** NR **NExBG** (N=15): conventional care (walking program, 30 minutes/5 weekly sessions, for 8 weeks)	Home-based, individually performed, caregiver-supervised	QOL-AD	T0 (pre-treatment) T1 (post-treatment, 8 weeks) T2 (follow-up, 16 weeks)	ExBG: 4 NExBG: 4	95%	6/10	A significant intra-group improvement in the HRQoL was shown both in the ExBG and in the NExBG at 8 weeks, without inter-group differences. These effects were not sustained at 16 weeks.
			ExBG (N=39): Nintendo Wii							HRQoL was significantly

Park et al., 2017, South Korea	RCT, mild cognitive impairment	78 (≈ 67.2 ys.) 53.8% male	Sports (30 minutes/3 weekly sessions, for 10 weeks). **Exergame intensity:** NR **NExBG** (N=39): conventional care (cognition-specific computer training, 30 minutes/3 weekly sessions, for 10 weeks)	Health facility, individually performed, supervised	SF-36	T0 (pre-treatment) T1 (post-treatment, 10 weeks)	ExBG: 0 NExBG: 0	NR	7/10	higher in the ExBG, which showed higher improvement in vitality, role-emotional, bodily pain, and mental health scores compared with the NExBG. There was no significant difference in social functioning between the groups.
Pedreira et al., 2017, Brazil	RCT, Parkinson's disease	44 (≈ 63.6 ys.) 50% male	**ExBG** (N=22): Nintendo Wii (40 minutes/3 weekly sessions, for 4 weeks), plus drug therapy. **Exergame intensity:** NR **NExBG** (N=22): conventional care (physical therapy, 40 minutes/3 weekly sessions, for 4 weeks), plus drug therapy.	Health facility, individually performed, supervised	PDQ-39	T0 (pre-treatment) T1 (post-treatment, 4 weeks)	ExBG: 6 NExBG: 6	NR	4/10	ExBG showed an improvement in total HRQoL scores, while no differences were observed in the NExBG.
Prosperini et al., 2013, Italy	Controlled, cross-over, multiple sclerosis	36 (≈ 36.2 ys.) 30.6% female	**ExBG** (N=18): Nintendo Wii Fit (30 minutes/5 weekly sessions, for 12 weeks), plus conventional care. **Exergame intensity:** NR **NExBG** (N=18): conventional care.	Home-based, individually performed, not supervised	MSIS-29	T0 (pre-treatment) T1 (post-treatment ExBG, 12 weeks) T2 (post-treatment NExBG, 24 weeks)	ExBG: 1 NExBG: 1	NR	6/10	There were significant time x treatment interaction effects in HRQoL, indicating significant between-group differences over time in favor of ExBG.
Ribas et al., 2016, Brazil	RCT, Parkinson's disease	20 (≈ 61 ys.) 60% male	**ExBG** (N=10): Nintendo Wii Fit (30 minutes/2 weekly sessions, for 12 weeks) plus drug therapy. **Exergame intensity:** NR **NExBG** (N=10): conventional care (exercise program, 30 minutes/2 weekly sessions, for 12 weeks), plus drug therapy.	Health facility, individually performed, supervised	PDQ-39	T0 (pre-treatment) T1 (post-treatment, 12 weeks) T2 (follow-up, 20 weeks)	ExBG: 0 NExBG: 0	NR	7/10	No significant improvement in the HRQoL domains was reported by patients in either of the groups, without a group effect.
Saposnik et al, 2010, Canada	RCT, stroke	22 (≈ 61.3 ys.) 64% male	**ExBG** (N=11): Nintendo Wii Sports (eight 60 minutes sessions completed within 2 weeks, separated by ≥5 hours), plus conventional care (physiotherapy and occupational therapy). **Exergame intensity:** NR **NExBG** (N=11): recreational therapy (playing cards, bingo, Jenga), plus conventional care (physiotherapy and occupational therapy)	Health facility, individually performed, supervised	SIS	T0 (pre-treatment) T1 (post-treatment, 2 weeks) T2 (follow-up, 4 weeks)	ExBG: 2 NExBG: 3	76%	5/10	No significant differences between the groups were observed for HRQoL.
Saposnik et al, 2016, Canada	RCT, stroke	141 (≈ 62 ys.) 66.6% male	**ExBG** (N=71): Nintendo Wii Sports (ten 60 minutes sessions completed within 2 weeks), plus conventional care. **Exergame intensity:** NR **NExBG** (N=70): recreational	Health facility, individually performed, supervised	SIS	T0 (pre-treatment) T1 (post-treatment, 2 weeks) T2 (follow-up, 4 weeks)	ExBG: 17 NExBG: 12	NR	7/10	Participants in both groups had similar scores with respect to HRQoL at the end of the intervention, and 4 weeks post-intervention.

			therapy (playing cards, bingo, Jenga, or ball game), plus conventional care							
Şimşek & Çekok 2016, Turkey	RCT, stroke	44 (≈ 58 ys.) 69% male	**ExBG** (N=22): Nintendo Wii Sports and Wii Fit (45 to 60 minutes/3 weekly sessions, for 10 weeks). **Exergame intensity:** NR **NExBG** (N=22): conventional care (Bobath neurodevelopmental treatment, 45 to 60 minutes/3 weekly sessions, for 10 weeks)	Health facility, individually performed, supervised	NHP	T0 (pre-treatment) T1 (post-treatment, 10 weeks)	ExBG: 2 NExBG: 0	NR	7/10	A statistically significant difference was detected between pre- and post-treatment in HRQoL subscales and total mean difference values in both ExBG and NExBG, with none of the treatment superior to each other.
Tollár et al., 2019, The Netherlands	RCT, Parkinson's disease	74 (≈ 69.4 ys.) 48.6% male	**ExBG** (N=25): Microsoft Kinect Adventures (60 minutes/5 weekly, for 5 weeks), plus drug therapy **Exergame intensity:** HRR=110-140 beats/minute **NExBG 1** (N=25): conventional care (stationary cycling training, 60 minutes/5 weekly, for 5 weeks), plus drug therapy **NExBG 2** (N=24): wait-listed group, plus drug therapy	Health facility, individually performed, supervised	EQ-5D PDQ-39	T0 (pre-treatment) T1 (post-treatment, 5 weeks)	ExBG: 0 NExBG1: 0 NExBG2: 0	100%	5/10	HRQoL improved similarly in ExBG and NExBG1, with statistically significant differences as compared with NExBG2 (waiting list).
STUDIES ON POPULATION WITH RHEUMATHOLOGIC DISEASES										
Collado Mateo et al., 2017, Spain	RCT, fibromyalgia	83 (≈ 52.5 ys.) 0% male	**ExBG** (N=42): Microsoft Kinect (1 hour for 2 times/week, for 8 weeks). **Exergame intensity:** NR **NExBG** (N=41): conventional care	Health facility, group-based, supervised	EQ-5D	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 0 NExBG: 6	NR	7/10	The ExBG showed a significant improvement in 3 of the 5 dimensions of HRQoL (mobility, pain and discomfort, and anxiety and depression), compared with the NExBG.
Elshazly et al., 2016, Saudi Arabia	RCT, osteoarthritis	60 (≈ 59 ys.) gender NR	**ExBG** (N=20): Microsoft Kinect (15- to 30 minutes/3 weekly sessions, for 8 weeks), plus conventional care (exercise training). **Exergame intensity:** NR **NExBG 1** (N=20): sensory motor training (duration not reported/3 weekly sessions, for 8 weeks), plus conventional care (exercise training). **NExBG 2** (N=20): conventional care (exercise training, 22 minutes/3 weekly sessions, for 8 weeks).	Health facility, group-based, supervised	CDC-HRQOL	T0 (pre-treatment) T1 (during treatment, 4 weeks) T2 (post-treatment, 8 weeks)	ExBG: 0 NExBG1: 0 NExBG2: 0	NR	5/10	All the groups (ExBG, NExBG1, and NExBG2) showed significant improvement in HRQoL. ExBG showed more significant difference than the other two groups.
										In the ExBG, HRQoL

Karahan et al, 2016, Turkey	RCT, Ankylosing Spondylitis	60 (≈ 36.3 ys.) 78.3% male	**ExBG** (N=30): Microsoft Kinect (30 minutes/5 weekly sessions, for 8 weeks). **Exergame intensity:** NR **NExBG** (N=30): conventional care	Health facility, individually performed, supervised	ASQOL	T0 (pre-treatment) T1 (post-treatment, 8 weeks)	ExBG: 2 NExBG: 1	NR	6/10	significantly improved after eight weeks of the program, while in the NExBG remained unchanged. Significant differences between the two groups were shown in HRQoL, in favor of ExBG.
Wi[illegible] et al., 2013, South Korea	RCT, osteoarthritis	40 (≈ 75.2 ys.) 0% male	**ExBG** (N=20): Microsoft Kinect (30 minutes/3 weekly sessions, for 4 weeks), plus conventional care. **Exergame intensity:** NR **NExBG** (N=20): conventional care (15 minutes hot pack and 15 minutes electrical stimulation, for 4 weeks)	Health facility, individually performed, supervised	SF-8	T0 (pre-treatment) T1 (post-treatment, 4 weeks)	ExBG: 0 NExBG: 0	NR	4/10	The post-intervention HRQoL scores of ExBG were significantly higher than that pre-intervention. Moreover, ExBG's score was higher than that of the NExBG, although the differences were not significant.
Zernicke et al., 2016,	Controlled, cross-over, rheumatoid arthritis	30 (≈ 56 ys.) 17% male	**ExBG** (N=15): Nintendo Wii (30 minutes/3 weekly sessions, for 12 weeks), plus drug therapy. **Exergame intensity:** NR **NExBG** (N=15): conventional care (home-based physical activity program, 30 minutes/3 weekly sessions, for 12 weeks), plus drug therapy	Home-based, individually performed, not supervised	SF-36	T0 (pre-treatment) T1 (post-treatment ExBG, 12 weeks) T2 (post-treatment NExBG, 24 weeks)	ExBG: 1 NExBG: 2	NR	3/10	The mean changes of HRQoL results were without statistical significance between groups, indicating an equal effect of both treatments.
STUDIES ON POPULATION WITH CARDIORESPIRATORY AND METABOLIC CHRONIC CONDITIONS										
del Corral et al., 2017, Spain	RCT, cystic fibrosis	40 (≈ 11.8 ys) 47.5% male	**ExBG** (N=20): Nintendo Wii Sports (30- to 60-min sessions for 5 days/week, for 6 weeks). **Exergame intensity:** 70-80% maximal HR **NExBG** (N=20): conventional care (including daily exercise routine)	Home-based, individually performed, caregiver-supervised	CFQ-R	T0 (pre-treatment) T1 (post-treatment, 6 weeks) T2 (follow-up, 12 months)	ExBG: 3 NExBG: 2	95%	8/10	The ExBG showed significantly higher scores on HRQoL domain respiratory symptoms after the intervention compared with NExBG, with a further improvement in other domains after 12 months-follow up.
Dos Santos Ruivo et al., 2017, Ireland	RCT, cardiovascular diseases	32 (≈ 60 ys.) 81% male	**ExBG** (N=16): Nintendo Wii Sports (60 minutes/2 weekly sessions, for 6 weeks). **Exergame intensity:** 55-70% maximal HR **NExBG** (N=16): conventional care (cardiac rehabilitation program, 60 minutes/2 weekly sessions, for 6 weeks)	Health facility, group-based, supervised	MacNew Questionnaire	T0 (pre-treatment) T1 (post-treatment, 6 weeks) T2 (follow-up, 8 weeks)	ExBG: 1 NExBG: 3	96%	7/10	ExBG showed improved HRQoL following the intervention in physical, emotional and global domains. However, a post hoc age-adjusted analysis did not reveal any significant difference between exercise protocols.
Kempf & Martin, 2013, Germany	RCT, crossover, Type 2 diabetes	220 (≈ 61 ys.) 46% male	**ExBG** (N=120): Nintendo Wii (30 minutes/day, for 12 weeks). **Exergame intensity:** NR **NExBG** (N=100): conventional care.	Home-based, individually performed, not supervised	WHO-5	T0 (pre-treatment) T1 (post-treatment, 12 weeks) T2 (only for NExBG: post-treatment, 24 weeks)	ExBG: 27 NExBG: 17	NR	6/10	HRQoL significantly improved in the ExBG compared to the NExBG, which showed a slight decrease during waiting phase.

Mazzoleni et al., 2014, Italy	RCT, chronic respiratory diseases	40 (≈71.2 ys) gender NR	**ExBG** (N=20): Nintendo Wii (1 hour/day sessions for 1 week), plus conventional care (standard supervised pulmonary rehabilitation program). **Exergame intensity:** up to 80% maximal HR **NExBG** (N=20): conventional care (standard supervised pulmonary rehabilitation program, daily session for 3 weeks, including 30 minutes of exercise)	Health facility, individually performed, supervised	SGRQ	T0 (pre-treatment) T1 (post-treatment, 3 weeks)	ExBG: 1 NExBG: 0	NR	5/10	HRQoL improved significantly and at the same amount in both groups.
Vieira et al., 2017, Portugal	RCT, coronary artery disease	46 (≈ 57.6 ys.) 100% male	**ExBG** (N=15): Microsoft Kinect (90 minutes/3 weekly sessions, for 24 weeks). **Exergame intensity:** 65-70% maximal HR **NExBG 1** (N=15): conventional care (home-based paper booklet cardiac rehabilitation program, 90 minutes/3 weekly sessions, for 24 weeks) **NExBG 2** (N=16): education program	Home-based, individually performed, not supervised	MacNew Questionnaire	T0 (pre-treatment) T1 (during the treatment, 12 weeks) T2 (follow-up, 24 weeks)	ExBG: 4 NExBG1: 4 NExBG2: 5	77%	5/10	No significant differences were found in the analysis between the three groups in any of the dimensions and total scores of HRQoL in the different moments, and in the analysis of the variable difference.
STUDIES ON POPULATION WITH OTHER CHRONIC CONDITIONS										
Phillips et al., 2018, United Kingdom	RCT, dizziness	40 (≈ 47.5 ys.) 35% male	**ExBG** (N=21): Nintendo Wii Fit (two 30 minutes sessions/day, for 16 weeks). **Exergame intensity:** NR **NExBG** (N=19): conventional care (standard customized vestibular rehabilitation protocol, two 30 minutes sessions/day, for 16 weeks)	Health facility, individually performed, not supervised	SF-36	T0 (pre-treatment) T1 (during the treatment, 4 weeks) T2 (during the treatment, 8 weeks) T3 (during the treatment, 12 weeks) T4 (post-treatment, 16 weeks)	ExBG: 11 NExBG: 8	NR	4/10	For the ExBG, the HRQoL physical health score was significantly different at week 16 compared to baseline. Both groups significantly improved in HRQoL.
Schumacher et al., 2018, Germany	RCT, hematopoietic stem cells transplantation	42 (≈ 56.2 ys.) 59.5% male	**ExBG** (N=19): Nintendo Wii Fit and Wii Sports (30 minutes/5 weekly sessions, for 4 weeks). **Exergame intensity:** NR **NExBG** (N=23): conventional care (physiotherapy).	Health facility, individually performed, supervised	SF-36	T0 (pre-treatment) T1 (during the treatment, 2 weeks) T2 (post-treatment, 4 weeks) T3 (follow-up, 100 days after hematopoietic stem cells transplantation)	ExBG: 5 NExBG: 6	NR	5/10	For most domains of HRQoL, the ExBG reached higher scores compared with the NExBG. The only exception was physical functioning, with comparable results between the groups at post-intervention. At 100-days after bone transplantation follow-up, physical functioning and mental health remained stable in the NExBG,

										while increased in the ExBG, in which increased also vitality and social functioning.
Shimizu et al., 2017, Japan	Controlled, cross-over, schizophrenia	8 (≈ 46.7 ys.) 75% male	**ExBG**: (N=5) Nintendo Wii Sports Resort (60 minutes/2 weekly sessions, for 12 weeks). **Exergame intensity:** NR **NExBG** (N=3): conventional care (occupational therapy).	Home-based, individually performed, not supervised	SF-36	T0 (pre-treatment) T1 (post-treatment ExBG, 12 weeks) T2 (post-treatment NExBG, 24 weeks)	ExBG: 0 NExBG: 1	NR	5/10	A significant post-intervention positive effect was shown in HRQoL domains bodily pain, role emotional, and social functioning, in favor of ExBG.

Legend.
ASQOL: Ankylosing Spondylitis Quality of Life questionnaire; CDC-HRQOL: Centre for Disease Control-Health Related Quality of Life questionnaire; CFQ-R: Cystic Fibrosis Questionnaire-Revised; EQ-5D: EuroQoL-5 Dimensions; ExBG: Exergame-based intervention group; HRQoL: Health Related Quality of Life; HRR: Heart Rate Range; MSIS-29: Multiple Sclerosis Impact Scale; NExBG: non-Exergame-based intervention group; NHP: Nottingham Health Profile; PDQ-8: Parkinson's Disease Quality of Life questionnaire; PDQ-39: Parkinson's Disease Questionnaire-39; PEDro: Physiotherapy Evidence Database; QOL-AD: Quality of Life-Alzheimer's disease; RCT: Randomized Controlled Trial; SF-8: Short Form Health Survey 8-items; SF-12: Short Form Health Survey 12-item; SF-36: Short Form Health Survey 36-items; SGRQ: St. George's Respiratory Questionnaire; SIS: Stroke Impact Scale; WHO-5: 5-item World Health Organization Well-Being Index; WHOQOL-Brief: World Health Organization Quality of Life-Brief; ys.: years.

Table 2. Grades of Recommendation, Assessment, Development and Evaluation (GRADE) quality of evidence

Outcome	Design	Risk of bias (PEDro scale)	Indirectness	Inconsistency	Imprecision	Publication bias	Effect size	GRADE quality
HRQoL in people living with CDs I^2= 27%, SMD: 0.24, 95% CI 0.1 to 0.4	RCT x 32	-1[a]	-1[b]	0	0	0	0	Low
HRQoL in neurological diseases I^2= 49%, SMD: 0.22, 95% CI 0.02 to 0.4	RCT x 20	0	-1[b]	0	0	0	0	Moderate
HRQoL in rheumatologic conditions I^2= 4%, SMD: 0.39, 95% CI 0.1 to 0.7	RCT x 4	-1[a]	-1[b]	0	0	0	0	Low
HRQoL in cardiorespiratory and metabolic diseases I^2= 0%, SMD: 0.23, 95% CI 0.01 to 0.5	RCT x 5	-1[a]	-1[b]	0	0	0	0	Low
SF-36 domains in neurological diseases								
Physical functioning I^2= 0%, MD: 3.9, 95% CI 2.1 to 5.6	RCT x 2	-1[a]	-1[b]	0	-1[c]	0	0	Very low
Role physical I^2= 0%, MD: 7.7, 95% CI 6.0 to 9.5	RCT x 3	0	-1[b]	0	-2[d]	0	0	Very low
Bodily pain I^2= 0%, MD: 8.0, 95% CI 6.0 to 9.9	RCT x 2	-1[a]	-1[b]	0	-2[d]	0	0	Very low
General health I^2= 0%, MD: 4.5, 95% CI 2.5 to 6.5	RCT x 3	0	-1[b]	0	-2[d]	0	0	Very low
Vitality	RCT x 3	0	-1[b]	0	-2[d]	0	0	Very low

I^2= 0%, MD: 10.4, 95% CI 8.5 to 12.3								
Social functioning	RCT x 3	0	-1[b]	0	-2[d]	0	0	Very low
I^2= 0%, MD: 3.4, 95% CI 1.4 to 5.4								
Role emotional	RCT x 2	0	-1[b]	0	-2[d]	0	0	Very low
I^2= 0%, MD: 6.0, 95% CI 4.0 to 8.0								
Mental health	RCT x 3	0	-1[b]	0	-2[d]	0	0	Very low
I^2= 16%, MD: 4.7, 95% CI 1.0 to 8.4								
Center-based exergames *vs*. home-based exergames								
Center-based exergames	RCT x 22	-1[a]	-1[b]	0	0	0	0	Low
I^2= 41%, SMD: 0.30, 95% CI 0.1 to 0.5								
Home-based exergames	RCT x 10	-1[a]	-1[b]	0	-1[c]	0	0	Very low
I^2= 0%, SMD: 0.12, 95% CI -0.04 to 0.3								

Abbreviations. PEDro: Physiotherapy Evidence Database scale; **RCT:** Randomised Controlled Trial; **SMD:** Standardised Mean Difference; **MD**: Weighted Mean Difference; **CI:** Confidence Interval; **I^2:** Inconsistency Statistic; **HRQoL:** Health-related Quality of Life; **CDs:** Chronic Diseases.

[a] Downgraded one place as most of the trials scored ≤ 6 on the PEDro scale

[b] Downgraded one places due to indirect comparisons

Downgraded one places due to imprecision (less than 200 participants or 95% CI crossed zero)

[d] Downgraded two places due to very large confidence interval and imprecision

Figure 1. PRISMA flow chart for study selection

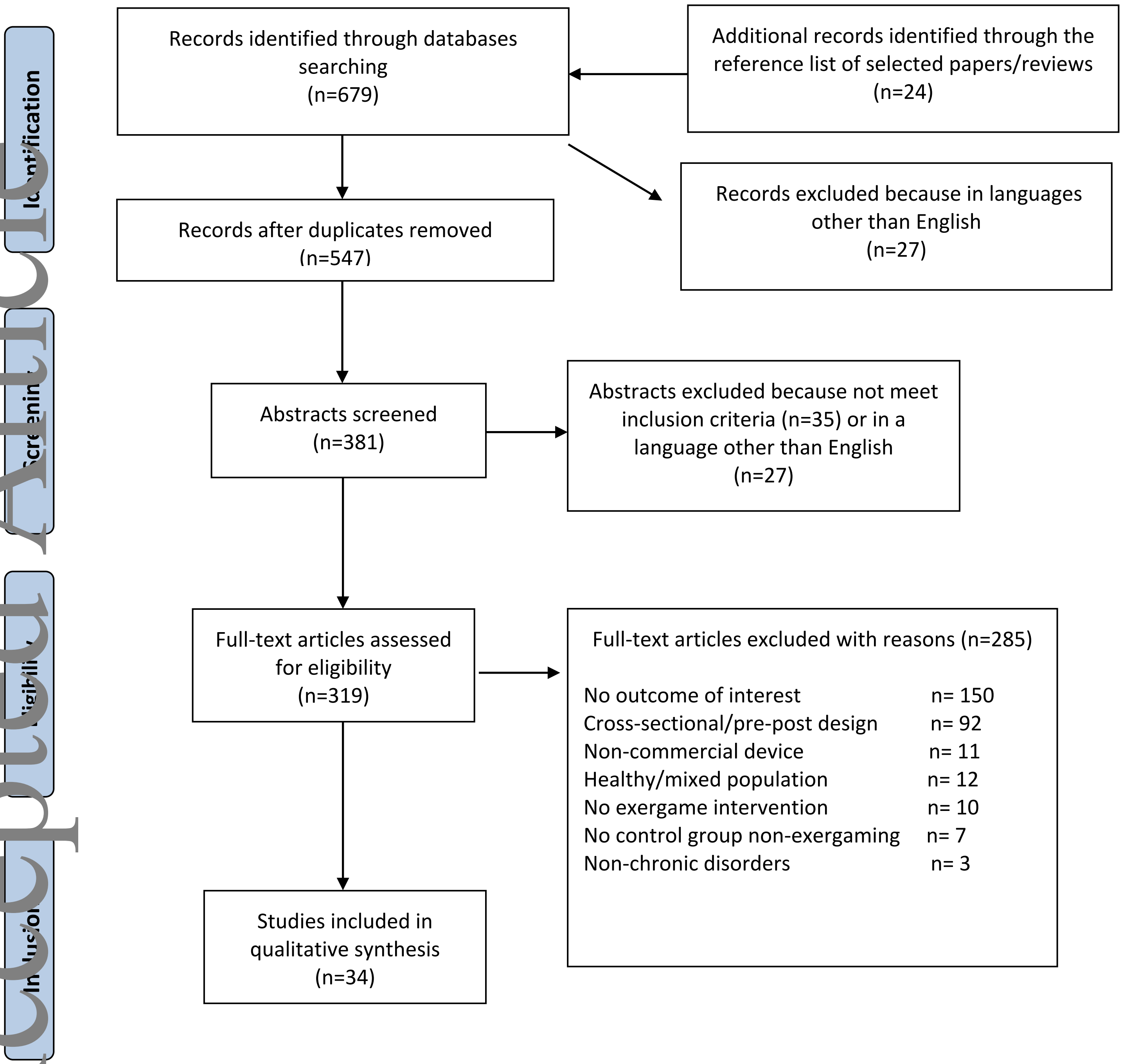


Figure 1.1 Forest plot of included studies on exergame-based interventions on HRQoL in populations living with chronic diseases

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Adie 2016	70.8	18.5	102	70.9	18.5	107	8.0%	-0.01 [-0.28, 0.27]
Collado-Mateo 2017	0.7	0.2	42	0.6	0.2	41	5.0%	0.50 [0.06, 0.93]
da Silva Ribeiro 2014	70.3	11.8	15	64.2	16.4	15	2.5%	0.42 [-0.31, 1.14]
de Oliveira Arnaut 2014	62.4	29.1	5	49.1	22.9	4	0.8%	0.44 [-0.90, 1.79]
del Corral 2017	82.1	16.3	20	79.4	13.7	20	3.1%	0.18 [-0.45, 0.80]
dos Santos Ruivo 2017	4.8	1.7	16	4.5	1.5	16	2.6%	0.18 [-0.51, 0.88]
Elshazly 2016	4.5	0.6	20	3.3	0.5	20		Not estimable
Fan 2013	55.6	13.4	5	35	11	5		Not estimable
Ferraz 2018	-33.9	25.2	20	-32.9	19.1	20	3.1%	-0.04 [-0.66, 0.58]
Gandolfi 2017	-24.2	14.8	36	-24.2	15.8	34	4.6%	0.00 [-0.47, 0.47]
Karahan 2016	-6.8	4.3	28	-10.3	6.4	29	3.9%	0.63 [0.10, 1.16]
Kempf & Martin 2013	47.6	9.1	93	45.3	10.8	83	7.5%	0.23 [-0.07, 0.53]
Kloos 2013	291.8	65.4	11	294.3	57	8	1.7%	-0.04 [-0.95, 0.87]
Lee GH 2016	89.9	10.6	13	93.7	9.9	13	2.2%	-0.36 [-1.13, 0.42]
Lee HC 2017	26.7	5	15	22.8	5.3	15	2.4%	0.74 [-0.01, 1.48]
Lee M 2016	63	18.1	26	63.1	11.6	21	3.5%	-0.01 [-0.58, 0.57]
Liao 2015	-68.8	20	12	-70.8	27.1	12	2.1%	0.08 [-0.72, 0.88]
Mazzoleni 2014	-31.5	10.5	19	-35.1	19.8	20	3.1%	0.22 [-0.41, 0.85]
Padala 2012	35.9	2.8	11	35.6	5.6	11	1.9%	0.07 [-0.77, 0.90]
Padala 2017	38.5	3.5	15	38.3	3	15	2.5%	0.06 [-0.66, 0.78]
Park 2017	75.4	10.6	39	69.5	3.6	39	4.7%	0.74 [0.28, 1.20]
Pedreida 2017	-24.2	16	19	-21.8	15.1	19	3.0%	-0.15 [-0.79, 0.49]
Phillips 2018	48.5	10	10	46.6	10.4	10	1.8%	0.18 [-0.70, 1.06]
Prosperini 2013	-69	21	18	-78	24	18	2.8%	0.39 [-0.27, 1.05]
Ribas 2016	-23.2	19.2	10	-14.9	14.2	10	1.7%	-0.47 [-1.36, 0.42]
Saposnik 2010	-8.3	15.1	9	-13.3	13.4	7	1.4%	0.33 [-0.67, 1.32]
Saposnik 2016	104	21.6	59	101.6	23.4	62	6.3%	0.11 [-0.25, 0.46]
Schumacher 2018	37.9	17.4	19	34.8	17.5	23	3.2%	0.17 [-0.43, 0.78]
Shimizu 2017	36.6	12.7	8	39.4	13.4	7	1.4%	-0.20 [-1.22, 0.82]
Simsek & Cekok 2016	-7	3.7	20	-8.5	3.1	22	3.2%	0.43 [-0.18, 1.05]
Tollar 2019	2.6	1.6	25	0.1	1.4	24	2.9%	1.63 [0.98, 2.29]
Viera 2017	6.2	0.8	11	5.8	1	11	1.9%	0.42 [-0.42, 1.27]
Wi 2013	24.1	4.6	20	23.1	3.6	20	3.1%	0.24 [-0.38, 0.86]
Zernicke 2016	6.2	0.8	11	5.8	1	11	1.9%	0.42 [-0.42, 1.27]
Total (95% CI)			**777**			**767**	**100.0%**	**0.24 [0.12, 0.37]**

Heterogeneity: Tau² = 0.03; Chi² = 42.49, df = 31 (P = 0.08); I² = 27%
Test for overall effect: Z = 3.79 (P = 0.0001)

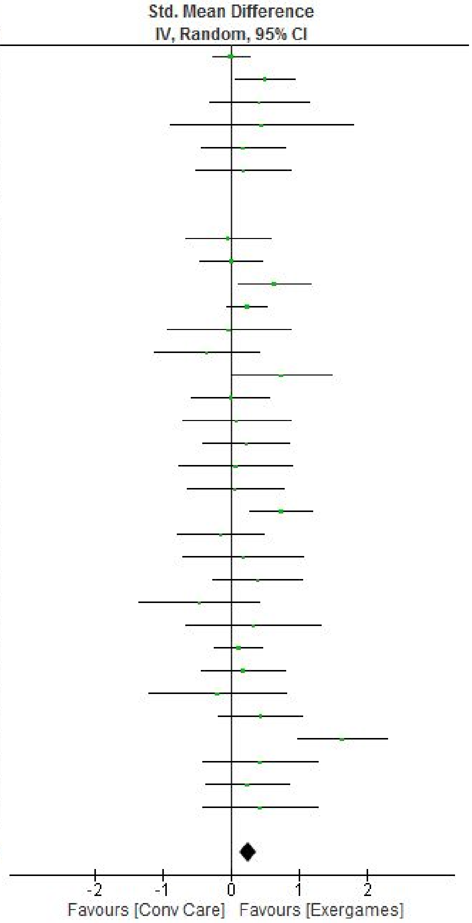


Figure 1.2. Forest plot of included studies on populations with neurological disorders

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Adie 2016	70.8	18.5	102	70.9	18.5	107	9.4%	-0.01 [-0.28, 0.27]
da Silva Ribeiro 2014	70.3	11.8	15	64.2	16.4	15	4.5%	0.42 [-0.31, 1.14]
de Oliveira Arnaut 2014	62.4	29.1	5	49.1	22.9	4	1.8%	0.44 [-0.90, 1.79]
Fan 2013	55.6	13.4	5	35	11	5		Not estimable
Ferraz 2018	-33.9	25.2	20	-32.9	19.1	20	5.3%	-0.04 [-0.66, 0.58]
Gandolfi 2017	-24.2	14.8	36	-24.2	15.8	34	6.9%	0.00 [-0.47, 0.47]
Kloos 2013	291.8	65.4	11	294.3	57	8	3.3%	-0.04 [-0.95, 0.87]
Le[illegible] GH 2016	89.9	10.6	13	93.7	9.9	13	4.1%	-0.36 [-1.13, 0.42]
Lee [illegible]C 2017	26.7	5	15	22.8	5.3	15	4.3%	0.74 [-0.01, 1.48]
[illegible]M 2016	63	18.1	26	63.1	11.6	21	5.8%	-0.01 [-0.58, 0.57]
Liao 2015	-68.8	20	12	-70.8	27.1	12	3.9%	0.08 [-0.72, 0.88]
[illegible]la 2012	35.9	2.8	11	35.6	5.6	11	3.7%	0.07 [-0.77, 0.90]
Padala 2017	38.5	3.5	15	38.3	3	15	4.5%	0.06 [-0.66, 0.78]
Pa[illegible] 2017	75.4	10.6	39	69.5	3.6	39	7.0%	0.74 [0.28, 1.20]
Pe[illegible]eida 2017	-24.2	16	19	-21.8	15.1	19	5.2%	-0.15 [-0.79, 0.49]
[illegible]sperini 2013	-69	21	18	-78	24	18	5.0%	0.39 [-0.27, 1.05]
Ribas 2016	-23.2	19.2	10	-14.9	14.2	10	3.4%	-0.47 [-1.36, 0.42]
[illegible]snik 2010	-8.3	15.1	9	-13.3	13.4	7	2.9%	0.33 [-0.67, 1.32]
Saposnik 2016	104	21.6	59	101.6	23.4	62	8.3%	0.11 [-0.25, 0.46]
Sim[illegible]ek & Cekok 2016	-7	3.7	20	-8.5	3.1	22	5.4%	0.43 [-0.18, 1.05]
Tollar 2019	2.6	1.6	25	0.1	1.4	24	5.0%	1.63 [0.98, 2.29]
[illegible] (95% CI)			**480**			**476**	**100.0%**	**0.22 [0.02, 0.42]**

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 37.31$, df = 19 (P = 0.007); $I^2 = 49\%$
Te[illegible] for overall effect: Z = 2.19 (P = 0.03)

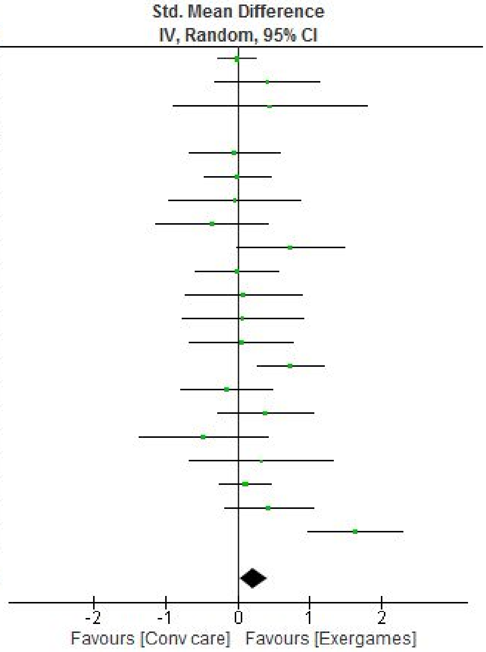


Figure 1.3 Forest plot of included studies on populations with rheumatologic diseases

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Collado-Mateo 2017	0.7	0.2	42	0.6	0.2	41	38.6%	0.50 [0.06, 0.93]
Elshazly 2016	4.5	0.6	20	3.3	0.5	20		Not estimable
Karahan 2016	-6.8	4.3	28	-10.3	6.4	29	26.6%	0.63 [0.10, 1.16]
Wi 2013	24.1	4.6	20	23.1	3.6	20	19.8%	0.24 [-0.38, 0.86]
Zernicke 2016	68	15	15	70	19	15	15.0%	-0.11 [-0.83, 0.60]
Total (95% CI)			**105**			**105**	**100.0%**	**0.39 [0.11, 0.67]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.14$, df = 3 (P = 0.37); $I^2 = 4\%$

Test for overall effect: Z = 2.70 (P = 0.007)

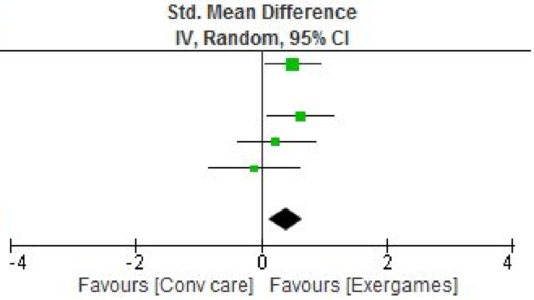
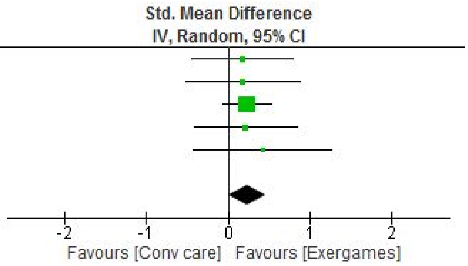


Figure 1.4 Forest plot of included studies on populations with cardiorespiratory and metabolic chronic conditions

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Std. Mean Difference IV, Random, 95% CI
del Corral 2017	82.1	16.3	20	79.4	13.7	20	13.0%	0.18 [-0.45, 0.80]
dos Santos Ruivo 2017	4.8	1.7	16	4.5	1.5	16	10.4%	0.18 [-0.51, 0.88]
Kempf & Martin 2013	47.6	9.1	93	45.3	10.8	83	56.9%	0.23 [-0.07, 0.53]
Mazzoleni 2014	-31.5	10.5	19	-35.1	19.8	20	12.6%	0.22 [-0.41, 0.85]
Viera 2017	6.2	0.8	11	5.8	1	11	7.0%	0.42 [-0.42, 1.27]
Total (95% CI)			**159**			**150**	**100.0%**	**0.23 [0.01, 0.45]**

Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 4 (P = 0.99); I² = 0%
Test for overall effect: Z = 2.02 (P = 0.04)



Figures 2.1 to 2.8 Forest plots assessing HRQoL domains through SF-36 questionnaire in neurological disorders

Figure 2.1 Physical functioning

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	94	12	15	65	21.5	15		Not estimable
de Oliveira Arnaut 2014	44	16.4	5	30	21.2	4	0.5%	14.00 [-11.26, 39.26]
Park 2017	75.5	4.2	39	71.7	3.5	39	99.5%	3.80 [2.08, 5.52]
Total (95% CI)			**44**			**43**	**100.0%**	**3.85 [2.13, 5.56]**

Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 4.40 (P < 0.0001)

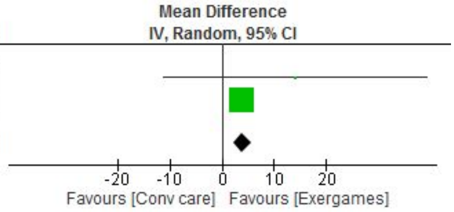


Figure 2.2 Role physical

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	65	38.7	15	55	39.2	15	0.4%	10.00 [-17.88, 37.88]
de Oliveira Arnaut 2014	45	51.2	5	18.8	23.9	4	0.1%	26.20 [-24.42, 76.82]
Park 2017	72.4	4.2	39	64.7	3.7	39	99.5%	7.70 [5.94, 9.46]
Total (95% CI)			**59**			**58**	**100.0%**	**7.73 [5.98, 9.48]**

Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 2 (P = 0.76); I² = 0%
Test for overall effect: Z = 8.65 (P < 0.00001)

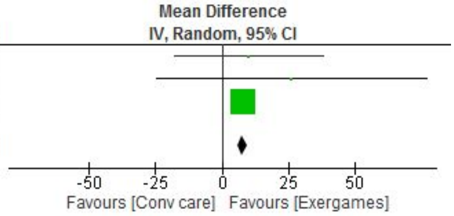


Figure 2.3 Bodily pain

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	64.4	7.5	15	66.9	4.7	15		Not estimable
de Oliveira Arnaut 2014	58	33.3	5	63.8	29.2	4	0.2%	-5.80 [-46.68, 35.08]
Park 2017	72.7	5.1	39	64.7	3.7	39	99.8%	8.00 [6.02, 9.98]
Total (95% CI)			**44**			**43**	**100.0%**	**7.97 [5.99, 9.94]**

Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 1 (P = 0.51); I² = 0%
Test for overall effect: Z = 7.91 (P < 0.00001)

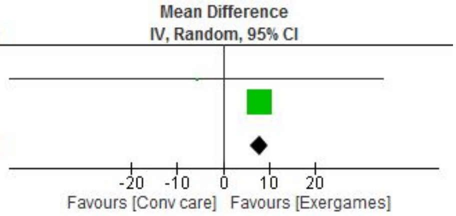


Figure 2.4 General health

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	63.7	19.4	15	61.3	19.4	15	2.0%	2.40 [-11.48, 16.28]
de Oliveira Arnaut 2014	61	11.4	5	54.5	10.4	4	1.9%	6.50 [-7.77, 20.77]
Park 2017	66.8	5	39	62.3	3.9	39	96.2%	4.50 [2.51, 6.49]
Total (95% CI)			**59**			**58**	**100.0%**	**4.50 [2.54, 6.45]**

Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 2 (P = 0.92); I² = 0%
Test for overall effect: Z = 4.52 (P < 0.00001)

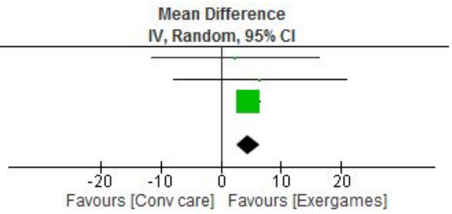


Figure 2.5 Vitality

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	87	14.1	15	71.3	24.5	15	1.7%	15.70 [1.39, 30.01]
de Oliveira Arnaut 2014	55	31.8	5	48.8	33.8	4	0.2%	6.20 [-37.09, 49.49]
Park 2017	72.6	4.8	39	62.3	3.7	39	98.1%	10.30 [8.40, 12.20]
Total (95% CI)			**59**			**58**	**100.0%**	**10.39 [8.50, 12.27]**

Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 2 (P = 0.75); I² = 0%
Test for overall effect: Z = 10.81 (P < 0.00001)

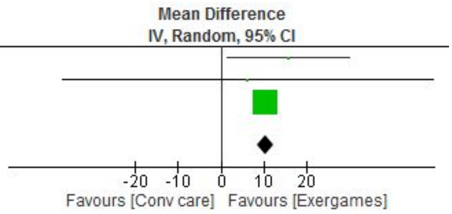


Figure 2.6 Social functioning

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	52.5	33.5	15	63.3	35.2	15	0.7%	-10.80 [-35.39, 13.79]
de Oliveira Arnaut 2014	72.5	37.9	5	78.1	35.9	4	0.2%	-5.60 [-53.99, 42.79]
Park 2017	79.2	5.3	39	75.7	3.6	39	99.2%	3.50 [1.49, 5.51]
Total (95% CI)			**59**			**58**	**100.0%**	**3.39 [1.39, 5.39]**

Heterogeneity: Tau² = 0.00; Chi² = 1.42, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 3.32 (P = 0.0009)

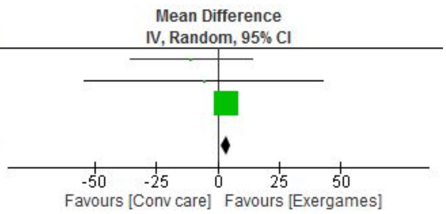


Figure 2.7 Role emotional

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	77.8	37.1	15	71.1	41.5	15	0.5%	6.70 [-21.47, 34.87]
de Oliveira Arnaut 2014	86.7	29.8	5	16.7	9.2	4		Not estimable
Park 2017	75.8	5.2	39	69.8	3.8	39	99.5%	6.00 [3.98, 8.02]
Total (95% CI)			**54**			**54**	**100.0%**	**6.00 [3.99, 8.02]**

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 5.84 (P < 0.00001)

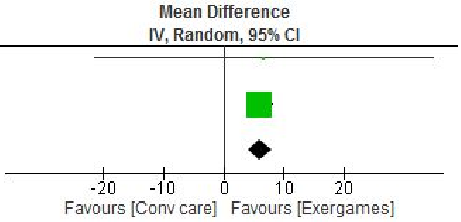


Figure 2.8 Mental health

Study or Subgroup	Exergames Mean	Exergames SD	Exergames Total	Conventional care Mean	Conventional care SD	Conventional care Total	Weight	Mean Difference IV, Random, 95% CI
da Silva Ribeiro 2014	60.8	10.1	15	60	12.9	15	16.9%	0.80 [-7.49, 9.09]
de Oliveira Arnaut 2014	76.8	21.1	5	82	9.5	4	3.1%	-5.20 [-25.91, 15.51]
Park 2017	88.6	6	39	82.7	3.7	39	80.0%	5.90 [3.69, 8.11]
Total (95% CI)			**59**			**58**	**100.0%**	**4.69 [1.00, 8.39]**

Heterogeneity: Tau² = 3.17; Chi² = 2.38, df = 2 (P = 0.30); I² = 16%
Test for overall effect: Z = 2.49 (P = 0.01)

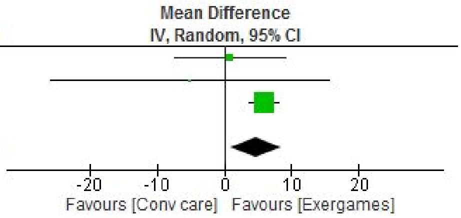


Figure 3.1 Forest plot of included studies employing center-based interventions

Study or Subgroup	Conventional care Mean	SD	Total	Center-based exergames Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Collado-Mateo 2017	0.7	0.2	42	0.6	0.2	41	7.0%	0.50 [0.06, 0.93]
da Silva Ribeiro 2014	70.3	11.8	15	64.2	16.4	15	4.1%	0.42 [-0.31, 1.14]
de Oliveira Arnaut 2014	62.4	29.1	5	49.1	22.9	4	1.6%	0.44 [-0.90, 1.79]
dos Santos Ruivo 2017	4.8	1.7	16	4.5	1.5	16	4.3%	0.18 [-0.51, 0.88]
Elshazly 2016	4.5	0.6	20	3.3	0.5	20		Not estimable
Fan 2013	55.6	13.4	5	35	11	5		Not estimable
Ferraz 2018	-33.9	25.2	20	-32.9	19.1	20	4.9%	-0.04 [-0.66, 0.58]
Karahan 2016	-6.8	4.3	28	-10.3	6.4	29	5.8%	0.63 [0.10, 1.16]
Lee GH 2016	89.9	10.6	13	93.7	9.9	13	3.7%	-0.36 [-1.13, 0.42]
Lee HC 2017	26.7	5	15	22.8	5.3	15	3.9%	0.74 [-0.01, 1.48]
Lee M 2016	63	18.1	26	63.1	11.6	21	5.4%	-0.01 [-0.58, 0.57]
Liao 2015	-68.8	20	12	-70.8	27.1	12	3.5%	0.08 [-0.72, 0.88]
Mazzoleni 2014	-31.5	10.5	19	-35.1	19.8	20	4.8%	0.22 [-0.41, 0.85]
Padala 2012	35.9	2.8	11	35.6	5.6	11	3.3%	0.07 [-0.77, 0.90]
Park 2017	75.4	10.6	39	69.5	3.6	39	6.7%	0.74 [0.28, 1.20]
Pedreida 2017	-24.2	16	19	-21.8	15.1	19	4.8%	-0.15 [-0.79, 0.49]
Phillips 2018	48.5	10	10	46.6	10.4	10	3.1%	0.18 [-0.70, 1.06]
Ribas 2016	-23.2	19.2	10	-14.9	14.2	10	3.0%	-0.47 [-1.36, 0.42]
Saposnik 2010	-8.3	15.1	9	-13.3	13.4	7	2.5%	0.33 [-0.67, 1.32]
Saposnik 2016	104	21.6	59	101.6	23.4	62	8.1%	0.11 [-0.25, 0.46]
Schumacher 2018	37.9	17.4	19	34.8	17.5	23	5.0%	0.17 [-0.43, 0.78]
Simsek & Cekok 2016	-7	3.7	20	-8.5	3.1	22	5.0%	0.43 [-0.18, 1.05]
Tollar 2019	2.6	1.6	25	0.1	1.4	24	4.6%	1.63 [0.98, 2.29]
Wi 2013	24.1	4.6	20	23.1	3.6	20	4.9%	0.24 [-0.38, 0.86]
Total (95% CI)			**452**			**453**	**100.0%**	**0.30 [0.12, 0.48]**

Heterogeneity: Tau² = 0.07; Chi² = 35.37, df = 21 (P = 0.03); I² = 41%
Test for overall effect: Z = 3.27 (P = 0.001)

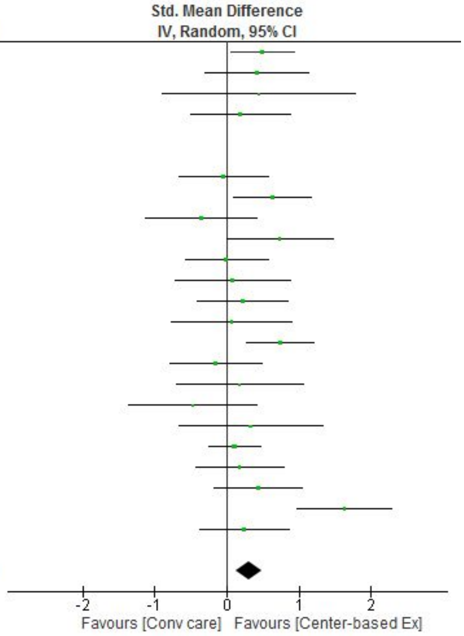


Figure 3.2 Forest plot of included studies employing home-based interventions

Study or Subgroup	Conventional care Mean	SD	Total	Home-based exergames Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Adie 2016	70.8	18.5	102	70.9	18.5	107	32.9%	-0.01 [-0.28, 0.27]
del Corral 2017	82.1	16.3	20	79.4	13.7	20	6.3%	0.18 [-0.45, 0.80]
Gandolfi 2017	-24.2	14.8	36	-24.2	15.8	34	11.0%	0.00 [-0.47, 0.47]
Kempf & Martin 2013	47.6	9.1	93	45.3	10.8	83	27.5%	0.23 [-0.07, 0.53]
Kloos 2013	291.8	65.4	11	294.3	57	8	2.9%	-0.04 [-0.95, 0.87]
Padala 2017	38.5	3.5	15	38.3	3	15	4.7%	0.06 [-0.66, 0.78]
Prosperini 2013	-69	21	18	-78	24	18	5.6%	0.39 [-0.27, 1.05]
Shimizu 2017	36.6	12.7	8	39.4	13.4	7	2.3%	-0.20 [-1.22, 0.82]
Viera 2017	6.2	0.8	11	5.8	1	11	3.4%	0.42 [-0.42, 1.27]
Zernicke 2016	6.2	0.8	11	5.8	1	11	3.4%	0.42 [-0.42, 1.27]
Total (95% CI)			**325**			**314**	**100.0%**	**0.12 [-0.04, 0.28]**

Heterogeneity: Tau² = 0.00; Chi² = 3.80, df = 9 (P = 0.92); I² = 0%
Test for overall effect: Z = 1.51 (P = 0.13)