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The Effectiveness of Serious Games in Alleviating Anxiety: Systematic Review and Meta-analysis

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Abstract

Background

Anxiety is a mental disorder characterized by apprehension, tension, uneasiness, and other related behavioral disturbances. One of the nonpharmacological treatments used for reducing anxiety is serious games, which are games that have a purpose other than entertainment. The effectiveness of serious games in alleviating anxiety has been investigated by several systematic reviews; however, they were limited by design and methodological weaknesses.

Objective

This study aims to assess the effectiveness of serious games in alleviating anxiety by summarizing the results of previous studies and providing an upto-date review.

Methods

We conducted a systematic review of randomized controlled trials (RCTs). The following seven databases were searched: MEDLINE, CINAHL, PsycINFO, ACM Digital Library, IEEE Xplore, Scopus, and Google Scholar. We also conducted backward and forward reference list checking for the included studies and relevant reviews. Two reviewers independently carried out the study selection, data extraction, risk of bias assessment, and quality of evidence appraisal. We used a narrative and statistical approach, as appropriate, to synthesize the results of the included studies.

Results

Of the 935 citations retrieved, 33 studies were included in this review. Of these, 22 RCTs were eventually included in the meta-analysis. Very low–quality evidence from 9 RCTs and 5 RCTs showed no statistically significant effect of exergames (games entailing physical exercises) on anxiety levels when compared with conventional exercises (P=.70) and no intervention (P=.27), respectively. Although 6 RCTs demonstrated a statistically and clinically significant effect of computerized cognitive behavioral therapy games on anxiety levels when compared with no intervention (P=.01), the quality of the evidence reported was low. Similarly, low-quality evidence from 3 RCTs showed a statistically and clinically significant effect of biofeedback games on anxiety levels when compared with conventional video games (P=.03).

Conclusions

This review shows that exergames can be as effective as conventional exercises in alleviating anxiety; computerized cognitive behavioral therapy games and exergames can be more effective than no intervention, and biofeedback games can be more effective than conventional video games. However, our findings remain inconclusive, mainly because there was a high risk of bias in the individual studies included, the quality of meta-analyzed evidence was low, few studies were included in some meta-analyses, patients without anxiety were recruited in most studies, and purpose-shifted serious games were used in most studies. Therefore, serious games should be considered complementary to existing interventions. Researchers should use serious games that are designed specifically to alleviate depression, deliver other therapeutic modalities, and recruit a diverse population of patients with anxiety.

Keywords: serious games, exergames, anxiety, computerized cognitive behavioral therapy games, biofeedback games, systematic reviews, meta-analysis, mobile phone

Introduction

Background

Anxiety is a normal response to situations in human life. However, excessive anxiety may be indicative of anxiety disorders, which are mental disorders characterized by apprehension, tension, uneasiness, and other related behavioral disturbances. They are potentially coupled with other physiological symptoms, such as shortness of breath, headaches, nausea, and abdominal pain [1,2]. Anxiety disorders include separation anxiety disorder, phobia, social anxiety disorder, panic disorder, and substance- or medicationinduced anxiety disorder [3]. Globally, the prevalence of anxiety disorders in the general population is estimated to be 26.9% [4]. Anxiety disorders affect all age groups, including children and adolescents [5], and can be debilitating in nature, causing significant impairment in one's social and professional functioning [6]. Evidence has revealed a strong association between anxiety and mortality rates among healthy individuals [7,8]. Anxiety contributes to a decrease in quality of life and other health-related problems [8]. Globally, over 45 million incidents are estimated to be attributed to anxiety disorders, which, in turn, are responsible for approximately 28.68 million disabilityadjusted life years [9,10].

Despite the prevalence of anxiety disorders, they often go undetected and undertreated [11]. Anxiety requires treatment and management because of the stimulation of the sympathetic system, which can lead to adverse effects. Treatments for anxiety disorders can be divided into pharmacological treatments (eg, psychotropic medications) and nonpharmacological treatments (eg, cognitive behavioral therapy [CBT]) [12,13]. Although the use of pharmacological treatments can be effective for the treatment of anxiety disorders, they can cause many adverse events and would not be effective for everyone. Therefore, nonpharmacological treatments have been used to reduce anxiety levels [14,15].

One of the nonpharmacological treatments used for reducing anxiety is serious games, which are games that have a purpose other than entertainment [16-19]. In recent years, the popularity and adoption of serious games have been on the rise because of their ability to educate and influence change in one's experience or behaviors [20,21]. Evidence suggests that serious games can enable players to experience more meaningful, engaging, and challenging learning when compared with traditional

interventions or other methods used to relieve anxiety [22].

Serious games come in a variety of types and formats, such as (1) exergames, or video games that entail physical exercises (eg, fitness and balance exercises) as part of the intended gameplay; (2) computerized CBT games, which are video games that provide CBT for the users; (3) biofeedback games, which are video games that use electrical sensors attached to the participant to receive information about the participant's body state (eg, electrocardiogram sensors) and seek to influence some of the player body's functions (eg, heart rate); (4) attention distraction games, which are video games that are used to direct a user's attention away from another focus or a given event; (5) brain training games, which are video games that aim to maintain or improve users' cognitive abilities (eg, working memory, executive function, processing speed, and attention), and (6) social skills training games that use computer-based games to improve social skills and mental health.

Research Gap and Aim

Various studies have assessed the effectiveness of serious games in alleviating anxiety. Examining and summarizing the evidence from these studies is critical to reach informed conclusions about the effectiveness of serious games in the treatment of anxiety disorders. Two published reviews summarized the evidence regarding the effectiveness of serious games on anxiety [16,17]. However, these reviews are undermined by certain shortcomings that limit the generalization of the findings. Specifically, these reviews (1) focused on only one type of serious games (ie, exergames) [16]; (2) included non-randomized controlled trials (RCTs) [16,17]; (3) focused on a specific age group (eg, adolescents) [17]; (4) did not search the main databases of the information technology and health care fields (eg, MEDLINE, PsycINFO, IEEE Xplore, and ACM Digital Library) [16,17], or (5) did not conduct meta-analyses [17]. To address the existing gaps in the literature, this review aims to assess the effectiveness of serious games in alleviating anxiety by summarizing the results of previous studies and providing an upto-date review.

Methods

We conducted a systematic review and meta-analysis per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (<u>Multimedia Appendix 1</u>) [23]. The protocol for this review was registered at PROSPERO (International Prospective Register of Systematic Reviews; ID: CRD42021264126).

Search Strategy

Search Sources We searched the following bibliographic databases to retrieve the relevant studies: MEDLINE (via Ovid), PsycINFO (via EBSCO), CINAHL (EBSCO), IEEE Xplore, ACM Digital Library, and Scopus. These databases were searched on June 29, 2021, by the first author (A Abdalrazaq). We also set up automatic alerts, as needed, to retrieve weekly searches for 12 weeks (ending on August 28, 2021). Furthermore, we searched *Google Scholar* to identify gray literature. We considered only the first 10 pages (ie, 100 hits), as Google Scholar retrieves a vast number of studies, and it organizes them based on their relevance. Finally, we conducted backward and forward reference list checking (ie, screening the reference lists of the included studies and relevant reviews and screening the studies that cited the included studies).

Search Terms Two experts in digital mental health were consulted before developing the search query for this review, and systematic reviews of relevance to this review were checked. The search terms were chosen based on the target intervention (eg, serious games and exergames), target outcome (eg, anxiety), and target study design (eg, RCT and clinical trial). Multimedia Appendix 2 summarizes the search query used for searching each of the 8 databases.

Study Eligibility Criteria

Only RCTs that assessed the effectiveness of serious games in alleviating anxiety levels were included in this study. Specifically, the target intervention in this review was serious games that were delivered on digital platforms such as computers, consoles (Xbox, PlayStation, etc), mobile phones, tablets, handheld devices, or any other computerized devices. Furthermore, gaming had to be an integral and primary component of the intervention. The serious games must have been used for therapeutic or preventive purposes.

Nondigital games and those used for other purposes, such as monitoring, screening, and diagnosis, were excluded. RCTs on whether there were parallel RCTs, cluster RCTs, crossover RCTs, or factorial RCTs were all included, but we excluded quasi-experiments, observational studies, and reviews.

The outcome of interest in this review was *anxiety level*, regardless of the outcome measures. We included the outcome data measured immediately after the intervention rather than the follow-up data. Trials in the English language were eligible for inclusion in this review, and all other languages were excluded. Conference abstracts and posters, commentaries, preprints, proposals, and editorials were excluded. RCTs published as journal articles, conference proceedings, and dissertations were included. No restrictions related to the population, year of publication, country of publication, comparator, or study settings were applied.

Study Selection

We identified relevant studies in the following steps. First, we exported the retrieved studies into EndNote X8 software to identify and eliminate duplicate entries. In the second step, 2 reviewers (A Abd-alrazaq and MA) independently screened the titles and abstracts of all the retrieved studies. Finally, the full texts of the studies included in the previous step were screened independently by 2 reviewers. The 2 reviewers resolved any disagreements through discussion. The interrater agreement in steps 2 and 3 were Cohen κ =0.81 and Cohen κ =0.93, respectively, indicating a perfect level of interrater agreement [24].

Data Extraction

Two independent reviewers used Microsoft Excel to extract the data from the included studies. Multimedia Appendix 3 shows the data extraction form that was used by the 2 reviewers to extract the data precisely and systematically from the included studies. We pilot-tested the form using the 5 included studies before proceeding. Disagreements between the reviewers were resolved via discussion. We observed an interrater agreement of 0.86, indicating a perfect level of agreement [24]. Where outcome data such as mean, SD, and sample size were unavailable, we contacted the corresponding

authors in an attempt to retrieve them. In this way, we managed to retrieve such information for an additional 5 studies.

Risk of Bias Appraisal

As recommended by the Cochrane Collaboration [25], the risk of bias was assessed by 2 independent reviewers using the Risk-of-Bias 2 (RoB 2) tool. This tool appraises the risk of bias in five domains in RCTs: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result [25]. The risk of bias judgments in these domains was used to determine the overall risk of bias for each included study. Disagreements in judgments between the 2 reviewers were resolved via discussion. Interrater agreement between the reviewers was perfect (Cohen κ =0.86) [24].

Data Synthesis

We used a narrative and statistical approach to synthesize the extracted data. Specifically, in our narrative synthesis, we describe the characteristics of the included studies, population, intervention, comparator, and outcome measures using texts and tables. The findings of the included studies were summarized and grouped according to the type of serious games (eg, exergames, computerized CBT games, and biofeedback games). We also conducted a meta-analysis, where at least 3 studies of the same type of serious games reported sufficient data (ie, mean, SD, and number of participants in each intervention group).

We used Review Manager (RevMan 5.4; The Cochrane Collaboration) to conduct the meta-analyses. The effect of each study and the overall effect was assessed using the standardized mean difference (SMD) because the type of data for the outcome of interest (anxiety level) was continuous, and the instruments used to evaluate the outcome were diverse among the included trials. We selected the random-effects model for the analysis because of the high clinical heterogeneity between the meta-analyzed studies in terms of serious game characteristics (eg, type, duration, frequency, and period), population characteristics (eg, sample size, mean age, and health condition), and outcome measures (eg, tools and follow-up period).

When the meta-analysis showed a statistically significant difference between the groups, we examined whether this difference was clinically important. We used the concept of *minimal clinically important difference* (MCID), which refers to the smallest change in a measured outcome that a patient would deem as worthwhile and substantial enough to warrant a change in a patient's therapy. MCID boundaries were calculated as -0.5 to +0.5 times the SMD of the meta-analyzed studies.

We calculated I^2 and a chi-square P value to examine the degree and statistical significance of heterogeneity, respectively, in the meta-analyzed studies. A chi-square P value of \leq .05 suggests heterogeneous meta-analyzed studies [26]. When I^2 ranged from 0% to 40%, 30% to 60%, 50% to 90%, and 75% to 100%, the degree of heterogeneity was judged as insignificant, moderate, substantial, or considerable, respectively [26].

We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to assess the overall quality of evidence resulting from meta-analyses [27]. The GRADE approach appraises the quality of evidence based on five domains: risk of bias, inconsistency (ie, heterogeneity), indirectness, imprecision, and publication bias [27]. The overall quality of the meta-analyzed evidence was appraised separately by 2 reviewers, and any differences in decisions were addressed by discussion. The reviewers' interrater agreement was deemed perfect (Cohen κ =0.96) [24].

Results

Search Results

As shown in Figure 1, we identified 935 records by searching 7 electronic databases. Of these records, we identified and removed 198 duplicates using EndNote software. The screening of the titles and abstracts of the remaining 737 records led to the exclusion of 649 citations because (1) they did not use serious games (n=319); (2) the anxiety level was not a measured outcome (n=98); (3) they were not RCTs (n=186); (4) they were not peer-reviewed articles, theses, or conference proceedings (n=29); and (5) they were published in languages other than English (n=17). Reading the full text of the remaining 88 publications led to the exclusion of 59 publications for the

following reasons: (1) the intervention did not use serious games (n=25), (2) the anxiety level was not a measured outcome (n=19), (3) they were not RCTs (n=13), and (4) they were published in a language other than English (n=2). We identified 4 additional RCTs through backward and forward reference list checking. A total of 33 RCTs were included in this review [28-60]. We conducted a meta-analysis when at least 3 studies of the same type of serious games reported sufficient data (ie, mean, SD, and number of participants in each intervention group). Therefore, 22 of the included RCTs were included in the meta-analysis [28-46,49-51].

Characteristics of Included Reviews

The included studies were published between 2012 and 2021 (<u>Table 1</u>). The year that witnessed the largest number of included studies was 2017 (n=8), followed by 2020 (n=6) and 2021 (n=6). The included studies were conducted in 16 different countries, as shown in <u>Table 1</u>. The country that published the largest number of included studies was the United States (n=6). All included studies were published in peer-reviewed journals, except for one that was a thesis. The trial type used in most of the included studies was parallel RCTs (n=31).

The sample size in the included studies ranged from 30 to 709, with an average of 112.8 (SD 93.2). The targeted participants were adults (aged >18 years) in 18 studies, adolescents (aged 12-18 years) in 5 studies, children (aged 5-11 years) in 5 studies, and both children and adolescents in 3 studies. Specifically, the mean age of participants reported in 31 studies ranged between 6.6 and 84.2 years, with an average of 34.7 (SD 22.4) years. The percentage of males reported in 31 studies ranged from 0% to 100%, with an average of 43.2% (SD 23.8%). The participants' health conditions varied between studies, and anxiety was the most common (n=7). The participants in most studies were recruited from clinical settings (n=22).

Only serious games were used as interventions in 28 of the included studies, whereas the remainder used serious games combined with other interventions (<u>Table 2</u>). Nintendo Wii Fit (n=5) was the most common game used in the included studies, followed by MindLight (n=4). We identified eight types of serious games based on the therapeutic modality that they deliver: exergames (n=13), computerized CBT games (n=6), biofeedback

games (n=5), attention distraction games (n=3), brain training games (n=2), social skills training games (n=2), exposure therapy games (n=1), and psychoeducation games (n=1). In 20 studies, games were designed with a *serious* purpose from the beginning (designed serious games); however, in the remaining 13 studies, they were not designed as serious games from the start but rather were used for a serious purpose (purpose-shifted games). The most common platforms used for playing games were computers (n=17) and video game consoles (n=8). The duration of the games in the included studies ranged from 5 to 150 minutes, but it was \leq 60 minutes in most studies (n=28). The frequency of playing the games varied between only one time throughout the study and once a day, but it ranged between once a week and 3 times a week in 24 studies. The intervention period ranged from 1 to 24 weeks, but it ranged from 1 to 10 weeks in 25 studies.

As shown in <u>Table 3</u>, the comparison groups received inactive interventions in 14 studies while they received active interventions in 21 studies (eg. conventional exercises, CBT programs, video games, medication, and psychotherapy). Note that the numbers do not add up because 2 studies delivered both active and inactive interventions as comparators. The duration of the active comparators ranged from 10 to 180 minutes. The frequency of the active comparators varied between only one time throughout the study and once a day, but it ranged between once a week and 3 times a week in about half of the studies (15/33, 45.5%. The period of active comparators varied between 1 week and 24 weeks. The outcome of interest (eg, anxiety level) was measured using 15 different tools, but the most common tools used by the included studies were the Spence Children's Anxiety Scale (SCAS; n=8) and the Hospital Anxiety and Depression Scale (n=7). The outcome of interest was measured immediately after the intervention in all included studies, and the most common follow-up period was 3 months (n=10). Participant attrition was reported in 32 studies, ranging from 0 to 335.

Results of Risk of Bias Appraisal

Approximately 70% (23/33) of the included studies generated an appropriate random allocation sequence for the randomization process. The allocation sequence in 14 studies was concealed until the participants were assigned to the interventions. The groups were comparable at baseline in the 29 studies. On the basis of these judgments, the risk of bias because of the

randomization process was rated as low in 12 studies (Figure 2).

Participants and those who were delivering the interventions were blinded to the assigned interventions during the trial in 4 and 5 studies, respectively. In 2 studies, there was a deviation from the intended intervention, which occurred because of the experimental contexts. An appropriate analysis (eg, intention-to-treat or modified intention-to-treat analyses) was used in 26 studies to estimate the effect of the intervention. According to these judgments, the risk of bias because of deviations from the intended interventions was low in 20 studies (Figure 2).

Outcome data were available for more than 95% of the participants only in 12 studies. There was evidence that the findings were not biased by the missing outcome data in only 7 studies. In 8 studies, the missing outcome data resulted from reasons that were documented and not related to the outcome. Accordingly, 27 studies were judged as having a low risk of bias in the *missing outcome data* domain.

Four studies assessed the outcome of interest (ie, anxiety levels) using inappropriate measures. The measurement methods were comparable across the intervention groups in all included studies. The assessor of the outcome was aware of the assigned interventions in the 20 studies. Given that the outcome measure was subjective in all studies, the assessment of the outcome could have been affected by knowledge of the intervention received. Accordingly, only 9 studies were rated as having a low risk of bias in the *measuring the outcome* domain (Figure 2).

There was a prespecified analysis plan (ie, protocol) for the 15 studies. Only 3 studies reported outcome measurements that differed from those specified in the analysis plan. In all studies, there was no evidence that they selected their results from many results produced from multiple eligible analyses of the data. Accordingly, the risk of bias because of the selection of the reported results was considered low in 15 studies (Figure 2).

In the last domain, *overall bias*, the risk of bias was considered high in 21 studies as they were judged as having a high risk of bias in at least one domain. Ten studies were judged to raise some concerns in the domain of *overall bias*, as they had some concerns in at least one of the domains and

were not at high risk for any domain. The 2 remaining studies were judged to be at low risk of bias for the domain of *overall bias*, given that it was rated as having a low risk of bias for all domains. Reviewers' judgments about each *risk of bias* domain for each included study are presented in <u>Multimedia</u>

<u>Appendix 4 [29-60]</u>.

Results of Studies

In this review, serious games were classified into eight types based on the therapeutic modality that they deliver: exergames [28-40], computerized CBT games [41-46], biofeedback games [47-51], attention distraction games [52-54], brain training games [55,56], social skills training games [57,58], exposure therapy games [59], and psychoeducation games [60]. The results of the included studies are shown in the following subsections based on the types of serious games.

Exergames

Exergames Versus Conventional Exercises In total, 9 studies compared the effects of exergames with conventional exercises on the level of anxiety [28-36]. While 7 studies did not find a statistically significant difference in the anxiety levels between the groups [30-36], the 2 remaining studies showed a statistically significant difference in the anxiety level between the groups (one of them favored exergames over conventional exercises [29] while the other favored conventional exercises over exergames [28]).

The results of the 9 studies were meta-analyzed as shown in <u>Figure 3</u> [28-36]. No statistically significant difference (P=.70) in the anxiety levels was found between the exergame group and conventional exercise group (SMD -0.07, 95% CI -0.45 to 0.30). The degree of evidence heterogeneity was substantial (P=.002; I²=67%). The quality of the evidence was very low, as it was downgraded by 6 levels because of a high risk of bias, heterogeneity, and imprecision (<u>Multimedia Appendix 5</u>).

We ran a sensitivity analysis, given that some effect sizes seem to be outliers. Specifically, we removed the study conducted by Adomaviciene et al [28] for two reasons: (1) the anxiety level at baseline was statistically higher (P<.001) in the exergame group (mean 9.16, SD 4.59) than in the conventional exercise

group (mean 5.52, SD 2.37) and (2) the comparator was conventional exercises guided by robotic devices, which is not the case in other studies. Although the degree of heterogeneity decreased significantly from 67% to 30% by excluding Adomaviciene et al [28], there was still no statistically significant difference (P=.18) in the anxiety levels between groups (SMD -0.18, 95% CI -0.45 to 0.08; Multimedia Appendix 6 [28-60]).

We also reran the meta-analysis after excluding another study [36] because the anxiety level at baseline was considerably higher in the conventional exercise group (mean 8.0, SD 9.1) than in the exergame group (mean 2.7, SD 2.0). Similar to the first sensitivity analysis, the degree of heterogeneity decreased significantly from 30% to 13% by excluding Vieira et al [36]; however, there was still no statistically significant difference (P=.38) in the anxiety levels between groups (SMD -0.11, 95% CI -0.35 to 0.13; Multimedia Appendix 6).

Exergames Versus No Intervention Five studies compared the effect of exergames with no intervention or inactive intervention on anxiety levels $[\underline{36}$ - $\underline{40}]$. Whereas 4 studies did not find a statistically significant difference in anxiety levels between the groups $[\underline{36}$ - $\underline{39}]$, the remaining study showed a statistically significant difference in the anxiety levels between the groups, favoring exergames over no intervention $[\underline{40}]$.

A meta-analysis of the results of the 5 studies showed no statistically significant difference (P=.27) in the anxiety levels between the exergame group and the no intervention group (SMD -0.23, 95% CI -0.63 to 0.18; Figure 4 [36-40]). The heterogeneity of the meta-analyzed evidence was substantial (P=.03; I²=63%). The quality of the evidence was very low, as it was downgraded by 6 levels because of a high risk of bias, heterogeneity, and imprecision (Multimedia Appendix 5).

We ran a sensitivity analysis because some effect sizes seemed to be outliers. Specifically, we excluded a study conducted by Thomas et al [37], given that the anxiety level at baseline was statistically higher (P=.01) in the exergame group (mean 8.53, SD 3.62) than in the control group (mean 6.27, SD 3.28). The degree of heterogeneity decreased significantly from 63% to 28% when excluding the results in Thomas et al [37]. The difference in anxiety levels between the groups was statistically significant (P=.02; SMD -0.38, 95% CI

Computerized CBT Games Six studies compared the effect of computerized CBT games with no intervention on anxiety levels [41-46]. While 3 studies did not find a statistically significant difference in anxiety levels between the groups [44-46], the 3 remaining studies showed a statistically significant difference in the anxiety levels between the groups, favoring computerized CBT games over no intervention [41-43].

The results of these 6 studies were included in the meta-analysis. Three of these studies assessed anxiety levels using 2 different measures (Acrophobia Questionnaire [AQ] and Beck Anxiety Inventory [BAI] [42], State-Trait Anxiety Inventory [STAI]-State and STAI-Trait [43], SCAS-Generalized Anxiety Disorder, and SCAS-Social Anxiety [46]). Therefore, we included the results of all these measures in the meta-analysis to form 9 comparisons (Figure 5 [41-46]). The meta-analysis showed a statistically significant difference in the anxiety levels (P=.01) between computerized CBT games and control groups, favoring computerized CBT games over no intervention (SMD - 0.36, 95% CI - .63 to - 0.08). This difference was also clinically important as the overall effect was outside the MCID boundaries (-0.18 to +0.18) and its CI neither crossed the *no-effect* line (zero effect) nor any of the 2 MCID boundaries. For this outcome, MCID boundaries were calculated as -0.5 to +0.5 times the SMD value (-0.36). The statistical heterogeneity of the evidence was considerable (P<.001; I²=84%). The quality of the evidence was very low, as it was downgraded by 5 levels because of a high risk of bias, heterogeneity, and imprecision (Multimedia Appendix 5).

It is noteworthy that 3 of the 6 studies in the group targeted adults [41-43] while the reminders targeted adolescents [44-46]. Therefore, we conducted a subgroup analysis to assess whether the effect of computerized CBT differs between adults and adolescents. The subgroup analysis showed that the

effect of computerized CBT on anxiety was statistically different (*P*<.001) between adults and adolescents (Figure 6 [41-46]). Specifically, while there was no statistically significant difference (P=.33) in the anxiety levels between the exergame group and the no intervention group among adolescents (SMD -0.06, 95% CI -0.18 to 0.06), there was a statistically significant difference in the anxiety levels (*P*<.001) between computerized CBT games and control groups among adults (favoring computerized CBT games over no intervention [SMD -0.68, 95% CI -1.02 to -0.34]). The statistically significant difference among adults was also clinically important as the overall effect was outside the MCID boundaries (-0.34 to +0.34) and its CI neither crossed the *no-effect* line (Zero effect) nor any of the 2 MCID boundaries. For this outcome, MCID boundaries were calculated as -0.5 to +0.5 times the SMD value (-0.68). The statistical heterogeneity of the evidence was substantial (P=.007; I²=71%). The quality of the evidence was very low, as it was downgraded by 4 levels because of a high risk of bias and heterogeneity (Multimedia Appendix 5).

Donker et al [42] used two different questionnaires to assess anxiety levels: BAI and AQ-anxiety. The BAI is used to measure general anxiety symptoms while AQ-anxiety measures a specific type of anxiety, which is height-related anxiety [61]. We performed a sensitivity analysis by excluding the AQ-related results reported by Donker et al [61] because all studies in the meta-analysis assessed general anxiety symptoms. The sensitivity analysis showed a significant decrease in the degree of heterogeneity (from 84% to 56%), and the difference in anxiety levels between the groups remained statistically significant (P=.01; SMD -0.23, 95% CI -0.41 to -0.05), favoring computerized CBT games over no intervention (Multimedia Appendix 6). This difference remained clinically important as the overall effect was outside the MCID boundaries (-0.12 to +0.12) and its CI did not cross the *no-effect* line (zero effect). We also performed a sensitivity analysis after excluding another study [44] because its sample size (n=30) was relatively small compared with other studies. However, the degree of heterogeneity and total effect size did not change significantly (Multimedia Appendix 6).

Biofeedback Games Biofeedback games were used as interventions in 5 studies [47-51]. Two studies examined the effect of a biofeedback game (MindLight) and conventional CBT on anxiety levels (measured by the SCAS) among children with anxiety [47,48]. Both studies found no statistically

significant difference in anxiety levels between the biofeedback game group and the conventional CBT group [47,48].

The 3 remaining studies examined the effect of biofeedback games and conventional video games on anxiety levels (measured by the SCAS) among children with anxiety [49-51]. While 2 studies did not find a statistically significant difference in anxiety levels between the groups [50,51], the remaining study showed a statistically significant difference in the anxiety level between the groups, favoring biofeedback games over conventional video games [49]. A meta-analysis of the results of these 3 studies demonstrated a statistically significant difference in the anxiety levels (P=.03) between the biofeedback game group and conventional CBT group, favoring biofeedback games over conventional video games (SMD -0.23, 95% CI -0.43 to -0.03; Figure 7 [49-51]). This difference was also clinically important as the overall effect was outside the MCID boundaries (-0.115 to +0.115) and its CI neither crossed the *no-effect* line (zero effect) nor any of the 2 MCID boundaries. For this outcome, MCID boundaries were calculated as -0.5 to +0.5 times the SMD value (-0.23). The heterogeneity of the evidence was considered insignificant (P=.38; $I^2=0\%$). The quality of the evidence was low, as it was downgraded by 2 levels because of a high risk of bias and imprecision.

Attention Distraction Games Distraction games were used as interventions in 3 studies. Attention distraction games were interventions in 3 studies [52-54]. While 2 studies found a statistically significant effect of attention distraction games [53,54], the remaining study did not [52]. Specifically, Marechal et al [52] compared the effect of attention distraction games with medication (ie, midazolam) on anxiety levels (measured by the Modified Yale Preoperative Anxiety Scale) among children undergoing general anesthesia for minor surgical procedures. No statistically significant difference (P=.99) in anxiety levels was detected between the 2 groups [52]. The second study examined the effect of attention distraction games (Angry Birds, Subway Surfers, or Snail Bob), medication (midazolam), and watching an informative cartoon on the anxiety level (measured by the Modified Yale Preoperative Anxiety Scale) among children undergoing adenoidectomy, adenotonsillectomy, or myringotomy [53]. The study showed a statistically significant difference (*P*<.001) in the anxiety level between the groups, favoring the attention distraction games over medication (midazolam) and

watching an informative cartoon. In the third study [54], the effect of an attention distraction game (SpaceBurgers) on anxiety levels (measured by Subjective Units of Distress) among children with otolaryngological issues was compared with topical analgesia. The study found a statistically significant difference (P<.001) in the anxiety levels between the groups, favoring attention distraction games over topical analgesia [54].

Brain Training Games Brain training games were interventions in 2 studies [55,56]. The first study compared the effect of a brain training game (Tetris) to eye movement desensitization and reprocessing therapy on the levels of trait anxiety (measured by STAI) among patients with posttraumatic stress disorder [55]. The study did not detect any statistically significant difference (P=.81) in the level of trait anxiety postintervention [55]. The second study compared the effects of a brain training game (Band Together) and traditional video games on the level of anxiety (measured by STAI) in patients with multiple sclerosis [56]. No statistically significant difference in the levels of state anxiety (P=.95) and trait anxiety (P=.75) between the 2 groups was detected.

Social Skills Training Games Social skills training games were an intervention in 2 studies [57,58]. The first study investigated the effect of a social skills training game (Adventures) on the anxiety level (measured by the Social Anxiety Scale for Children-Revised) among patients with social skills deficits in comparison with no intervention. The study showed no statistically significant difference (P=.10) in anxiety levels between the groups. In the second study, the effect of a social skills training game (Pegasys-Virtual Reality) and social effectiveness therapy on the anxiety level (measured by Social Phobia and Anxiety Inventory for Children) among children with social anxiety were examined. The study demonstrated no statistically significant difference (P=.23) in anxiety levels between the groups.

Other Types of Serious Games One study compared the effect of an exposure therapy game (Spider App) to an entertainment video game (Bubble Shooter) on anxiety levels among patients with arachnophobia [59]. No statistically significant difference in anxiety level was detected between the groups postintervention [59].

Litvin et al [60] examined the effect of a psychoeducation game (eQuoo),

conventional CBT, and no intervention on anxiety levels among healthy employees. The study did not find any statistically significant difference (P=.95) in anxiety levels between the 3 groups [60].

Discussion

Principal Findings

This review examined the effectiveness of serious games on anxiety levels, as reported by RCTs. Of the 33 RCTs included in the current review, 20 were included in 4 main meta-analyses. The review found no statistically significant effect of exergames on anxiety levels, though it showed a statistically significant effect of computerized CBT games and biofeedback games on anxiety levels. Owing to the paucity of evidence, no statistical analysis was carried out for other types of serious games included in this review.

Very low–quality evidence from 9 RCTs showed no statistically significant effect of exergames on anxiety levels as compared with conventional exercises. This insignificant effect can be attributed to the fact that exergames are comparable with conventional exercises; therefore, it should not be surprising that comparing the effect of 2 very similar interventions did not produce a significant difference. This indicates that conventional exercises are at least as effective as conventional exercises. Our findings are similar to those of previous reviews [16,62]. Specifically, a meta-analysis of 5 RCTs showed no statistically significant difference (P=.81) in anxiety levels between the exergames group and the usual care group (ie, conventional exercises) [16]. Similarly, no statistically significant difference (P=.12) in depression levels between the exergames group and conventional exercises was found in another meta-analysis of 7 RCTs [62].

Very low–quality evidence from 5 RCTs showed no statistically significant effect when compared with the effects of exergames on anxiety levels as opposed to no intervention. However, a sensitivity analysis of 4 RCTs showed a statistically and clinically significant effect of exergames on anxiety level when compared with no intervention.

This finding is consistent with that of a previous review $[\underline{16,62}]$. Specifically, a

meta-analysis of 8 studies showed a statistically significant difference (P=.004) in *depression* levels between the exergames group and the control group. In contrast, exergames have a statistically and clinically significant effect on *depression* levels when compared with no intervention, according to a meta-analysis of 8 studies [62].

Very low–quality evidence from 6 RCTs demonstrated a statistically and clinically significant effect of computerized CBT games on anxiety levels when compared with no intervention. A subgroup analysis showed that the effect of computerized CBT on anxiety was significantly higher among adults than among adolescents. However, this finding may not be generalizable to older adults as participants in all the 6 studies were, on average, \leq 41.3 years. To the best of our knowledge, no previous reviews have examined the effect of computerized CBT games on anxiety, although many reviews have assessed the effect of computerized CBT in general (ie, games are not part of the intervention) [63-66]. However, our findings are in line with a previous review focusing on depression, which found a statistically and clinically significant effect of computerized CBT games on depression level according to a meta-analysis of 6 RCTs.

Low-quality evidence from 3 RCTs showed a statistically and clinically significant effect of biofeedback games on anxiety levels when compared with conventional video games. It is worth mentioning that the studies used biofeedback games specifically for alleviating anxiety and recruited participants with anxiety. The generalizability of this finding may be limited because of the following reasons: (1) participants in the 3 studies were adolescents (10-13.3 years), (2) all studies were conducted in the Netherlands, and (3) there was a small number of studies included in the meta-analysis.

Meta-analyses were not conducted to assess the effect of other types of serious games because of the small number of studies. Individual studies found no statistically significant effect of brain training games, social skills training games, exposure therapy games, and psychoeducation games on anxiety levels. However, other studies have shown contradictory results regarding the effects of attention distraction games on anxiety levels.

Strengths This review can be considered more comprehensive than the 2 previous reviews [16,17] because it was not restricted to a certain type of serious games, age group, or comparator, and it searched the main databases in health and information technology fields. This review was conducted according to highly recommended guidelines (ie, PRISMA) and included only RCTs. Therefore, it can be considered a robust and high-quality review.

The risk of publication bias is not a concern in this review because we sought to retrieve as many relevant studies as possible by searching the most popular databases in information technology, health fields, and gray literature databases, conducting backward and forward reference list checking, using a comprehensive search query, and not restricting our search to a certain country, year, setting, population, and comparator.

There is no concern about the risk of selection bias in this review, given that 2 reviewers independently performed the study selection, data extraction, risk of bias assessment, and quality of evidence evaluation with a perfect interrater agreement for all processes. The quality of the evidence was appraised using the GRADE approach to enable the reader to draw more accurate conclusions. When possible, we synthesized data statistically, which improved the power of the studies and increased the estimates of the likely size of the effect of serious games on anxiety.

Limitations This review excluded studies that used serious games delivered on nondigital platforms and those used for other purposes (eg, screening or diagnosis). Therefore, this review cannot comment on the effectiveness of these types of serious games. This review focused on the effectiveness of serious games on anxiety only; thus, we cannot comment on the effectiveness of serious games on other diseases.

Numerous studies were excluded as they were quasi-experiments and written in languages other than English. Therefore, it is likely that we missed relevant studies. We excluded these studies because quasi-experiments have lower internal validity than RCTs [67] and, owing to practical constraints, it was not possible to translate all non-English studies. Participants in most studies did not have anxiety before the intervention; therefore, the effect of serious games could not be significant.

This review meta-analyzed postintervention data rather than follow-up data; thus, this review cannot comment on the long-term effects of serious games on anxiety. Postintervention outcome data were selected given that about half of the included studies (16/33, 48.5%) did not follow-up with participants to measure the outcome data, and the follow-up period in the other half of the studies (17/33, 51.5%) was not consistent between studies.

We used postintervention data for each group to assess the effect size for each meta-analyzed study rather than the pre–post intervention change for each group; therefore, it is likely that the effect size is overestimated or underestimated. We used postintervention outcome data because most studies did not report the SD for pre- or postintervention change for each group, and preintervention outcome data were significantly different between groups in only 2 studies [36,37].

Research and Practical Implications

Research Implications Although anxiety was one of the measured outcomes in all the included studies, only 6 studies targeted the recruitment of people experiencing anxiety. This may lead to a severe underestimation of the effect of serious games on anxiety levels. This finding is consistent with a similar study that investigated the effects of depression [62]. Similarly, we recommend purposefully recruiting participants who have anxiety and establishing a baseline to objectively assess the effectiveness of serious games in reducing anxiety levels.

We would like to point out that several studies recruited very small samples, with a minimum of only 30 patients. Gaining statistically reliable insights from such small samples can be difficult and may be an additional reason why our meta-analyses provide no conclusive answer to the question of whether serious games can improve or augment traditional anxiety treatment. Thus, we encourage researchers to recruit a sample size that is sufficient to achieve a power of at least 80%.

Most of the included studies were conducted in a clinical setting. Although this could offer a controlled environment to run the studies, it could also introduce stress to the participants because of the nature of such a setting. Conducting more studies in the community and educational settings could present different findings as people usually play games outside of the traditional clinical setting.

The current literature focused mainly on exergames and computerized CBT games, while the effect of other types of serious games was investigated in only a few studies. There are opportunities to enrich the body of evidence on the effectiveness of serious games delivered through other therapeutic modalities such as psychoeducation games, biofeedback games, exposure therapy games, and brain training games.

Although serious games can be used for several purposes and many diseases, we focused on serious games that were used for therapeutic or prevention purposes and anxiety only. Researchers should conduct systematic reviews to assess the effectiveness of serious games used for other purposes (eg, monitoring, screening, and diagnosing) and for other diseases.

In only 2 studies, the overall risk of bias was low given that most studies had issues in the randomization process, measurement of the outcome, and selection of the reported result. Outcome data were missing from several studies; therefore, they were not included in the meta-analyses. Accordingly, researchers should avoid the abovementioned biases by conducting and reporting RCTs according to recommended guidelines or tools (eg, RoB 2 [25]).

Finally, most of the included studies were conducted in high-income countries, which, in turn, can limit the generalizability of our findings to low-income nations. There is a need to conduct more studies in low-income countries, especially given the varying nature of their cultures, socioeconomic conditions, and sources of stress and anxiety (eg, overpopulated cities, poor socioeconomic areas, and refugee camps). Furthermore, more studies are needed to determine any variance in the effectiveness of serious games that are designed specifically to reduce and alleviate anxiety levels intergenerationally.

Practical Implications This review showed that exergames are as effective as conventional exercises in alleviating anxiety and that computerized CBT games and biofeedback games are more effective than no intervention and

conventional video games, respectively. However, health professionals and decision-makers should be careful when interpreting these findings for the following reasons: the quality of meta-analyzed evidence ranged from very low to low, the overall risk of bias was high in most of the included studies, the heterogeneity of the evidence was high in the 3 meta-analyses, participants in most studies did not have anxiety, and many studies did not use serious games that were designed specifically to alleviate anxiety. Accordingly, psychologists and psychiatrists should consider offering serious games as complementary and not a substitute for existing interventions until further, more robust evidence is available.

Although anxiety can be alleviated by many nonpharmacological interventions, there are no or few serious games that deliver nonpharmacological interventions other than exercises and CBT in this review. This may be attributed to the lack of such serious games in real life. Therefore, developers should consider developing serious games that deliver nonpharmacological interventions such as breathing techniques, mindfulness training, problem-solving, attention distraction, biofeedback, psychoeducation, relaxation-based exercises, and rational emotive behavioral therapy.

Only a handful (n=7) of studies used mobile devices (smartphones and tablets) as the platform for their intervention. Mobile devices are particularly appealing because they are cheaper than computers and more pervasive than gaming consoles. Moreover, mobile devices are more accessible than computers and gaming consoles; it is estimated that there are approximately 15 billion mobile devices and more than 7.1 mobile users worldwide in 2021 [68]. This could present a lucrative opportunity for app and game developers to develop serious games that target anxiety and can be played via mobile devices.

Few studies have been conducted in developing countries, and this may be attributed to the lack of serious games in these countries. Given that there is a greater shortage of mental health professionals in developing countries than in developed countries (0.1 per 1 million people [69] versus 90 per 1 million people [70]), it is likely that individuals in developing countries are more in need of serious games than those in developed countries. Therefore, more serious games should be developed to alleviate anxiety among people in

developing countries.

We would like to point out that a significant portion of the studies (n=12) investigated intervention methods using now-discontinued platforms: Wii (n=8, end of life in 2017), Kinect (n=5, end of life in 2017), and Nintendo DS (n=1, end of life in 2014). Only in one case, other platforms will readily fill the gap in only one case (using Tetris [52]). For interventions using Microsoft's Kinect sensor, computer vision-based pose estimation on mobile phones or desktop PCs could fill the gap but will result in a different setup. Finally, some of the included studies using Wiimote (Wii Remote) and none of the more specialized Wii input devices could be recreated using newer Nintendo controllers. These considerations raise a few questions of practical importance: (1) How well can studies relying on legacy and specialized hardware be reproduced? (2) How useful are interventions that rely on platforms designed to undergo comparatively short life cycles? (3) Are off-the-shelf video games (purpose-shifted games) adequate intervention tools?

We believe that some of the included studies relying on legacy hardware could probably be salvaged, following the comments outlined above, but caution should be taken to fall victim to the novelty effect of emerging game controllers and proprietary input devices. The video game industry evolves quickly and is known to experiment with novel technology to spirit gamers away from competitors. Consequently, purpose-shifted games are not only very prone to depreciate quickly, but the same is true for the platforms they were designed for. We believe that researchers in this space should best assume the role of game designers, who focus on the game mechanics and purpose. In the second step, researchers are probably best advised to seek the help of a professional software development company to bring out the product in a timely fashion.

In addition, although we cannot rule out that off-the-shelf games that have undergone, first, a purpose-shift to become a serious game and yet another one to become part of a therapy (eg, Tetris) have a measurable effect, we also have little reason to assume that they do. It seems tempting to explain the effects of serious games on anxiety by their distractive nature, but studies do not agree with this question.

There is also an urgent need for an inclusive approach when developing these

apps and games to include professionals from the gaming industry as well as mental health experts. Technologists and developers are usually very aware of the aforementioned concerns but need medical professionals to avoid falling prey to the temptation of purpose-shifting existing games or designing games for goals that are different from anxiety relief.

Conclusions

Evidence from this study suggests that serious games have the potential to reduce anxiety levels. Specifically, exergames can be as effective as conventional exercises in alleviating anxiety; computerized CBT games and exergames can be more effective than no intervention, and biofeedback games can be more effective than conventional video games. However, definitive conclusions regarding the effectiveness of serious games in reducing anxiety remain inconclusive, mainly because of the high risk of bias in the individual studies included, the low quality of meta-analyzed evidence, the low number of studies included in some meta-analyses, participants without anxiety in most studies, and using purpose-shifted serious games in most studies. Until further, more robust evidence is available, serious games should be deemed as complementary to existing interventions and not as a substitute for them. To obtain adequate and robust evidence, researchers should use serious games specifically designed to alleviate depression and deliver other therapeutic modalities, recruit patients with anxiety, and minimize the risk of bias by recommended guidelines for conducting and reporting RCTs (eg, RoB 2).

Abbreviations

AQ	Acrophobia Questionnaire
BAI	Beck Anxiety Inventory
CBT	cognitive behavioral therapy
GRADE	Grading of Recommendations Assessment, Development, and Evaluation

MCID minimal clinically important difference

PRISMA Preferred Reporting Items for Systematic Reviews and

Meta-Analyses

PROSPERO International Prospective Register of Systematic

Reviews

RCT randomized controlled trial

RoB 2 Risk-of-Bias 2

SCAS Spence Children's Anxiety Scale

SMD standardized mean difference

STAI State-Trait Anxiety Inventory

Multimedia Appendix 1

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.

Multimedia Appendix 2

Search strategy.

Multimedia Appendix 3

Data extraction form.

Multimedia Appendix 4

Reviewers' judgments about each risk of bias domain for each included study.

Multimedia Appendix 5

Grading of Recommendations Assessment, Development, and Evaluation profile for the comparison of serious games to control or conventional exercises for anxiety.

Multimedia Appendix 6

Sensitivity analyses.

Footnotes

Conflicts of Interest: None declared.

References

- 1. American Psychiatric Association . *Diagnostic and statistical manual of mental disorders* (DSM-5). 5th edition. Virginia: American Psychiatric Publishing; 2013.
- 2. Testa A, Giannuzzi R, Sollazzo F, Petrongolo L, Bernardini L, Daini S. Psychiatric emergencies (part I): psychiatric disorders causing organic symptoms. *Eur Rev Med Pharmacol Sci.* 2013;17 Suppl 1:55–64. http://www.europeanreview.org/article/3083. [PubMed: 23436668]
- 3. *American Psychiatric Association*. Washington, D.C: American Psychiatric Association; 2015. [2021-08-18]. What are anxiety disorders? https://www.psychiatry.org/patients-families/anxiety-disorders/what-are-anxiety-disorders.
- 4. Nochaiwong S, Ruengorn C, Thavorn K, Hutton B, Awiphan R, Phosuya C, Ruanta Y, Wongpakaran N, Wongpakaran T. Global prevalence of mental health issues among the general population during the coronavirus disease-2019 pandemic: a systematic review and meta-analysis. *Sci Rep.* 2021;11(1):10173. doi: 10.1038/s41598-021-89700-8. doi: 10.1038/s41598-021-89700-8 [PMCID: PMC8119461] [PubMed: 33986414] [CrossRef: 10.1038/s41598-021-89700-8] [CrossRef: 10.1038/s41598-021-89700-8]
- 5. Higa-McMillan CK, Francis SE, Rith-Najarian L, Chorpita BF. Evidence base update: 50

- years of research on treatment for child and adolescent anxiety. *J Clin Child Adolesc Psychol.* 2016;45(2):91–113. doi: 10.1080/15374416.2015.1046177. [PubMed: 26087438] [CrossRef: 10.1080/15374416.2015.1046177]
- 6. White SW, Simmons GL, Gotham KO, Conner CM, Smith IC, Beck KB, Mazefsky CA. Psychosocial treatments targeting anxiety and depression in adolescents and adults on the autism spectrum: review of the latest research and recommended future directions. *Curr Psychiatry Rep.* 2018;20(10):82. doi: 10.1007/s11920-018-0949-0. http://europepmc.org/abstract/MED/30155584 .10.1007/s11920-018-0949-0 [PMCID: PMC6421847] [PubMed: 30155584] [CrossRef: 10.1007/s11920-018-0949-0]
- 7. Janszky I, Ahnve S, Lundberg I, Hemmingsson T. Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49,321 young Swedish men. *J Am Coll Cardiol.* 2010;56(1):31–7. doi: 10.1016/j.jacc.2010.03.033. https://linkinghub.elsevier.com/retrieve/pii/S0735-1097(10)01562-7 [PubMed: 20620714] [CrossRef: 10.1016/j.jacc.2010.03.033]
- 8. Tolmunen T, Lehto SM, Julkunen J, Hintikka J, Kauhanen J. Trait anxiety and somatic concerns associate with increased mortality risk: a 23-year follow-up in aging men. *Ann Epidemiol.* 2014;24(6):463–8. doi: 10.1016/j.annepidem.2014.03.001.S1047-2797(14)00103-3 [PubMed: 24731699] [CrossRef: 10.1016/j.annepidem.2014.03.001]
- 9. GBD 2019 Diseases and Injuries Collaborators Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet.* 2020;396(10258):1204–22. doi: 10.1016/S0140-6736(20)30925-9. https://linkinghub.elsevier.com/retrieve/pii/S0140-6736(20)30925-9 [PMCID: PMC7567026] [PubMed: 33069326] [CrossRef: 10.1016/S0140-6736(20)30925-9]
- 10. Yang X, Fang Y, Chen H, Zhang T, Yin X, Man J, Yang L, Lu M. Global, regional and national burden of anxiety disorders from 1990 to 2019: results from the Global Burden of Disease Study 2019. *Epidemiol Psychiatr Sci.* 2021;30:e36. doi: 10.1017/S2045796021000275. http://europepmc.org/abstract/MED/33955350 .S2045796021000275 [PMCID: PMC8157816] [PubMed: 33955350] [CrossRef: 10.1017/S2045796021000275]
- 11. Quek TT, Tam WW, Tran BX, Zhang M, Zhang Z, Ho CS, Ho RC. The global prevalence of anxiety among medical students: a meta-analysis. *Int J Environ Res Public Health*. 2019;16(15):2735. doi: 10.3390/ijerph16152735. https://www.mdpi.com/resolver? pii=ijerph16152735 [PMCID: PMC6696211] [PubMed: 31370266] [CrossRef: 10.3390/ijerph16152735]

- 12. Park SC, Oh HS, Oh DH, Jung SA, Na KS, Lee HY, Kang RH, Choi YK, Lee MS, Park YC. Evidence-based, non-pharmacological treatment guideline for depression in Korea. *J Korean Med Sci.* 2014;29(1):12–22. doi: 10.3346/jkms.2014.29.1.12. https://jkms.org/DOIx.php?id=10.3346/jkms.2014.29.1.12 [PMCID: PMC3890462] [PubMed: 24431900] [CrossRef: 10.3346/jkms.2014.29.1.12]
- 13. Barlow DH. *Clinical handbook of psychological disorders: a step-by-step treatment manual. 6th edition.* New York: The Guilford Press; 2021.
- 14. Hardoerfer K, Jentschke E. Effect of yoga therapy on symptoms of anxiety in cancer patients. *Oncol Res Treat.* 2018;41(9):526–32. doi: 10.1159/000488989.000488989 [PubMed: 30086538] [CrossRef: 10.1159/000488989]
- 15. Stephens I. Medical yoga therapy. *Children (Basel)* 2017;4(2):12. doi: 10.3390/children4020012. https://www.mdpi.com/resolver?pii=children4020012 .children4020012 [PMCID: PMC5332914] [PubMed: 28208599] [CrossRef: 10.3390/children4020012]
- 16. Viana RB, Dankel SJ, Loenneke JP, Gentil P, Vieira CA, Andrade MD, Vancini RL, de Lira CA. The effects of exergames on anxiety levels: a systematic review and meta-analysis. *Scand J Med Sci Sports.* 2020;30(7):1100–16. doi: 10.1111/sms.13654. [PubMed: 32171032] [CrossRef: 10.1111/sms.13654]
- 17. Barnes S, Prescott J. Empirical evidence for the outcomes of therapeutic video games for adolescents with anxiety disorders: systematic review. *JMIR Serious Games*. 2018;6(1):e3. doi: 10.2196/games.9530. https://games.jmir.org/2018/1/e3/ v6i1e3 [PMCID: PMC5852274] [PubMed: 29490893] [CrossRef: 10.2196/games.9530]
- 18. Zayeni D, Raynaud JP, Revet A. Therapeutic and preventive use of video games in child and adolescent psychiatry: a systematic review. *Front Psychiatry.* 2020;11:36. doi: 10.3389/fpsyt.2020.00036. doi: 10.3389/fpsyt.2020.00036. [PMCID: PMC7016332] [PubMed: 32116851] [CrossRef: 10.3389/fpsyt.2020.00036] [CrossRef: 10.3389/fpsyt.2020.00036]
- 19. Michael DR, Chen SL. *Serious games: games that educate, train, and inform.* Michigan: Cengage Learning PTR; 2005.
- 20. Dias LP, Barbosa JL, Vianna HD. Gamification and serious games in depression care: a systematic mapping study. *Telemat Inform.* 2018;35(1):213–24. doi: 10.1016/j.tele.2017.11.002. doi: 10.1016/j.tele.2017.11.002. [CrossRef: 10.1016/j.tele.2017.11.002]

- 21. Chatham RE. Games for training. *Commun ACM*. 2007;50(7):36–43. doi: 10.1145/1272516.1272537. [CrossRef: 10.1145/1272516.1272537]
- 22. Lau HM, Smit JH, Fleming TM, Riper H. Serious games for mental health: are they accessible, feasible, and effective? A systematic review and meta-analysis. *Front Psychiatry.* 2017;7:209. doi: 10.3389/fpsyt.2016.00209. doi: 10.3389/fpsyt.2016.00209. [PMCID: PMC5241302] [PubMed: 28149281] [CrossRef: 10.3389/fpsyt.2016.00209] [CrossRef: 10.3389/fpsyt.2016.00209]
- 23. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ.* 2009;339:b2700. doi: 10.1136/bmj.b2700. http://europepmc.org/abstract/MED/19622552 . [PMCID: PMC2714672] [PubMed:
- http://europepmc.org/abstract/MED/19622552 . [PMCID: PMC2714672] [PubMed: 19622552] [CrossRef: 10.1136/bmj.b2700]
- 24. Landis JR, Koch GG. An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. *Biometrics.* 1977;33(2):363–74. [PubMed: 884196]
- 25. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JP. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:l4898. doi: 10.1136/bmj.l4898. [PubMed: 31462531] [CrossRef: 10.1136/bmj.l4898]
- 26. Deeks JJ, Higgins JP, Altman DG. Chapter 9: Analysing data and undertaking metaanalyses. In: Higgins JP, Green S, editors. *Cochrane handbook for systematic reviews of interventions. Version 5.0.1.* Sussex: John Wiley & Sons; 2008. pp. 243–96.
- 27. Schunemann HJ, Oxman AD, Vist GE, Higgins JP, Deeks JJ, Glasziou P. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S, editors. *Cochrane handbook for systematic reviews of interventions.* Sussex: John Wiley & Sons; 2008. pp. 359–87.
- 28. Adomavičienė A, Daunoravičienė K, Kubilius R, Varžaitytė L, Raistenskis J. Influence of new technologies on post-stroke rehabilitation: a comparison of Armeo spring to the Kinect system. *Medicina (Kaunas)* 2019;55(4):98. doi: 10.3390/medicina55040098. https://www.mdpi.com/resolver?pii=medicina55040098 medicina55040098 [PMCID: PMC6524064] [PubMed: 30970655] [CrossRef: 10.3390/medicina55040098]

- 29. de Carvalho MS, Carvalho LC, de Silva Menezes F, Frazin A, da Costa Gomes E, Iunes DH. Effects of exergames in women with fibromyalgia: a randomized controlled study. *Games Health J.* 2020;9(5):358–67. doi: 10.1089/g4h.2019.0108. [PubMed: 32379982] [CrossRef: 10.1089/g4h.2019.0108]
- 30. Meldrum D, Herdman S, Vance R, Murray D, Malone K, Duffy D, Glennon A, McConn-Walsh R. Effectiveness of conventional versus virtual reality-based balance exercises in vestibular rehabilitation for unilateral peripheral vestibular loss: results of a randomized controlled trial. *Arch Phys Med Rehabil.* 2015;96(7):1319–28.e1. doi: 10.1016/j.apmr.2015.02.032.S0003-9993(15)00289-0 [PubMed: 25842051] [CrossRef: 10.1016/j.apmr.2015.02.032]
- 31. Schumacher H, Stüwe S, Kropp P, Diedrich D, Freitag S, Greger N, Junghanss C, Freund M, Hilgendorf I. A prospective, randomized evaluation of the feasibility of exergaming on patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant*. 2018;53(5):584–90. doi: 10.1038/s41409-017-0070-8.10.1038/s41409-017-0070-8 [PubMed: 29335629] [CrossRef: 10.1038/s41409-017-0070-8]
- 32. Ruivo JM, Karim K, O'Shea R, Oliveira RC, Keary L, O'Brien C, Gormley JP. In-class active video game supplementation and adherence to cardiac rehabilitation. *J Cardiopulm Rehabil Prev.* 2017;37(4):274–8. doi: 10.1097/HCR.0000000000000224. [PubMed: 28350640] [CrossRef: 10.1097/HCR.000000000000224]
- 33. Mazzoleni S, Montagnani G, Vagheggini G, Buono L, Moretti F, Dario P, Ambrosino N. Interactive videogame as rehabilitation tool of patients with chronic respiratory diseases: preliminary results of a feasibility study. *Respir Med.* 2014;108(10):1516–24. doi: 10.1016/j.rmed.2014.07.004. https://linkinghub.elsevier.com/retrieve/pii/S0954-6111(14)00242-X [PubMed: 25087837] [CrossRef: 10.1016/j.rmed.2014.07.004]
- 34. Polat M, Kahveci A, Muci B, Günendi Z, Kaymak Karataş G. The effect of virtual reality exercises on pain, functionality, cardiopulmonary capacity, and quality of life in fibromyalgia syndrome: a randomized controlled study. *Games Health J.* 2021;10(3):165–73. doi: 10.1089/g4h.2020.0162. [PubMed: 33689452] [CrossRef: 10.1089/g4h.2020.0162]
- 35. Lin YT, Lee WC, Hsieh RL. Active video games for knee osteoarthritis improve mobility but not WOMAC score: a randomized controlled trial. *Ann Phys Rehabil Med.* 2020;63(6):458–65. doi: 10.1016/j.rehab.2019.11.008.

https://linkinghub.elsevier.com/retrieve/pii/S1877-0657(20)30022-1 .S1877-0657(20)30022-1 [PubMed: 31981832] [CrossRef: 10.1016/j.rehab.2019.11.008]

- 36. Vieira Á, Melo C, Machado J, Gabriel J. Virtual reality exercise on a home-based phase III cardiac rehabilitation program, effect on executive function, quality of life and depression, anxiety and stress: a randomized controlled trial. *Disabil Rehabil Assist Technol*. 2018;13(2):112–23. doi: 10.1080/17483107.2017.1297858. [PubMed: 28285574] [CrossRef: 10.1080/17483107.2017.1297858]
- 37. Thomas S, Fazakarley L, Thomas PW, Collyer S, Brenton S, Perring S, Scott R, Thomas F, Thomas C, Jones K, Hickson J, Hillier C. Mii-vitaliSe: a pilot randomised controlled trial of a home gaming system (Nintendo Wii) to increase activity levels, vitality and well-being in people with multiple sclerosis. *BMJ Open.* 2017;7(9):e016966. doi: 10.1136/bmjopen-2017-016966. https://bmjopen.bmj.com/lookup/pmidlookup?view=long&pmid=28954791 .bmjopen-2017-016966 [PMCID: PMC5623500] [PubMed: 28954791] [CrossRef: 10.1136/bmjopen-2017-016966]
- 38. Wagener TL, Fedele DA, Mignogna MR, Hester CN, Gillaspy SR. Psychological effects of dance-based group exergaming in obese adolescents. *Pediatr Obes.* 2012;7(5):e68–74. doi: 10.1111/j.2047-6310.2012.00065.x. [PubMed: 22767495] [CrossRef: 10.1111/j.2047-6310.2012.00065.x]
- 39. Jahouh M, González-Bernal JJ, González-Santos J, Fernández-Lázaro D, Soto-Cámara R, Mielgo-Ayuso J. Impact of an intervention with Wii video games on the autonomy of activities of daily living and psychological-cognitive components in the institutionalized elderly. *Int J Environ Res Public Health.* 2021;18(4):1570. doi: 10.3390/ijerph18041570. https://www.mdpi.com/resolver?pii=ijerph18041570 .ijerph18041570 [PMCID: PMC7915676] [PubMed: 33562249] [CrossRef: 10.3390/ijerph18041570]
- 40. Collado-Mateo D, Dominguez-Muñoz FJ, Adsuar JC, Garcia-Gordillo MA, Gusi N. Effects of exergames on quality of life, pain, and disease effect in women with fibromyalgia: a randomized controlled trial. *Arch Phys Med Rehabil.* 2017;98(9):1725–31. doi: 10.1016/j.apmr.2017.02.011.S0003-9993(17)30155-7 [PubMed: 28322760] [CrossRef: 10.1016/j.apmr.2017.02.011]
- 41. Cooney P, Jackman C, Coyle D, O'Reilly G. Computerised cognitive-behavioural therapy for adults with intellectual disability: randomised controlled trial. *Br J Psychiatry.* 2017;211(2):95–102. doi: 10.1192/bjp.bp.117.198630.S0007125000281877 [PubMed: 28596245] [CrossRef: 10.1192/bjp.bp.117.198630]
- 42. Donker T, Cornelisz I, van Klaveren C, van Straten A, Carlbring P, Cuijpers P, van Gelder JL. Effectiveness of self-guided app-based virtual reality cognitive behavior therapy for acrophobia: a randomized clinical trial. *JAMA Psychiatry.* 2019;76(7):682–90. doi: 10.1001/jamapsychiatry.2019.0219. http://europepmc.org/abstract/MED/30892564

- .2728184 [PMCID: PMC6583672] [PubMed: 30892564] [CrossRef: 10.1001/jamapsychiatry.2019.0219]
- 43. Fish MT, Russoniello CV, O'Brien K. The efficacy of prescribed casual videogame play in reducing symptoms of anxiety: a randomized controlled study. *Games Health J.* 2014;3(5):291–5. doi: 10.1089/g4h.2013.0092. [PubMed: 26192483] [CrossRef: 10.1089/g4h.2013.0092]
- 44. Fleming T, Dixon R, Frampton C, Merry S. A pragmatic randomized controlled trial of computerized CBT (SPARX) for symptoms of depression among adolescents excluded from mainstream education. *Behav Cogn Psychother*. 2012;40(5):529–41. doi: 10.1017/S1352465811000695.S1352465811000695 [PubMed: 22137185] [CrossRef: 10.1017/S1352465811000695]
- 45. Merry SN, Stasiak K, Shepherd M, Frampton C, Fleming T, Lucassen MF. The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ.* 2012;344:e2598. doi: 10.1136/bmj.e2598. http://www.bmj.com/lookup/pmidlookup?view=long&pmid=22517917 . [PMCID: PMC3330131] [PubMed: 22517917] [CrossRef: 10.1136/bmj.e2598]
- 46. Perry Y, Werner-Seidler A, Calear A, Mackinnon A, King C, Scott J, Merry S, Fleming T, Stasiak K, Christensen H, Batterham PJ. Preventing depression in final year secondary students: school-based randomized controlled trial. *J Med Internet Res.* 2017;19(11):e369. doi: 10.2196/jmir.8241. https://www.jmir.org/2017/11/e369/ v19i11e369 [PMCID: PMC5691241] [PubMed: 29097357] [CrossRef: 10.2196/jmir.8241]
- 47. Schoneveld EA, Lichtwarck-Aschoff AL, Granic I. Preventing childhood anxiety disorders: is an applied game as effective as a cognitive behavioral therapy-based program? *Prev Sci.* 2018;19(2):220–32. doi: 10.1007/s11121-017-0843-8. http://europepmc.org/abstract/MED/28956222 .10.1007/s11121-017-0843-8 [PMCID: PMC5801383] [PubMed: 28956222] [CrossRef: 10.1007/s11121-017-0843-8]
- 48. Tsui T. *Qspace*. Canada: Queen's University; 2016. [2022-02-08]. The efficacy of a novel video game intervention (MindLight) in reducing children's anxiety. https://gspace.library.gueensu.ca/handle/1974/14821.
- 49. Schoneveld EA, Malmberg M, Lichtwarck-Aschoff A, Verheijen GP, Engels RC, Granic I. A neurofeedback video game (MindLight) to prevent anxiety in children: a randomized controlled trial. *Comput Hum Behav.* 2016;63:321–33. doi: 10.1016/j.chb.2016.05.005. [CrossRef: 10.1016/j.chb.2016.05.005]
- 50. Wijnhoven LA, Creemers DH, Vermulst AA, Lindauer RJ, Otten R, Engels RC, Granic I.

- Effects of the video game 'Mindlight' on anxiety of children with an autism spectrum disorder: a randomized controlled trial. *J Behav Ther Exp Psychiatry.* 2020;68:101548. doi: 10.1016/j.jbtep.2020.101548.S0005-7916(18)30277-5 [PubMed: 32155470] [CrossRef: 10.1016/j.jbtep.2020.101548]
- 51. Scholten H, Malmberg M, Lobel A, Engels RC, Granic I. A randomized controlled trial to test the effectiveness of an immersive 3D video game for anxiety prevention among adolescents. *PLoS One.* 2016;11(1):e0147763. doi: 10.1371/journal.pone.0147763. https://dx.plos.org/10.1371/journal.pone.0147763 .PONE-D-15-29519 [PMCID: PMC4729475] [PubMed: 26816292] [CrossRef: 10.1371/journal.pone.0147763]
- 52. Marechal C, Berthiller J, Tosetti S, Cogniat B, Desombres H, Bouvet L, Kassai B, Chassard D, de Queiroz Siqueira M. Children and parental anxiolysis in paediatric ambulatory surgery: a randomized controlled study comparing 0.3 mg kg-1 midazolam to tablet computer based interactive distraction. *Br J Anaesth.* 2017;118(2):247–53. doi: 10.1093/bja/aew436. https://linkinghub.elsevier.com/retrieve/pii/S0007-0912(17)30086-7 [PubMed: 28100529] [CrossRef: 10.1093/bja/aew436]
- 53. Sakızcı Uyar B, Polat R, Bolat M, Donmez A. Which is good for pre-operative anxiety? Midazolam, video games or teaching with cartoons: a randomised trial. *Eur J Anaesthesiol.* 2021;38(7):744–50. doi: 10.1097/EJA.00000000001384.00003643-202107000-00008 [PubMed: 33186304] [CrossRef: 10.1097/EJA.0000000000001384]
- 54. Liu KY, Ninan SJ, Laitman BM, Goldrich DY, Iloreta AM, Londino 3rd AV. Virtual reality as distraction analgesia and anxiolysis for pediatric otolaryngology procedures. *Laryngoscope*. 2021;131(5):E1714–21. doi: 10.1002/lary.29148. [PubMed: 33017065] [CrossRef: 10.1002/lary.29148]
- 55. Butler O, Herr K, Willmund G, Gallinat J, Kühn S, Zimmermann P. Trauma, treatment and Tetris: video gaming increases hippocampal volume in male patients with combat-related posttraumatic stress disorder. *J Psychiatry Neurosci.* 2020;45(4):279–87. doi: 10.1503/jpn.190027. https://www.jpn.ca/lookup/pmidlookup? view=long&pmid=32293830 . [PMCID: PMC7828932] [PubMed: 32293830] [CrossRef: 10.1503/jpn.190027]
- 56. Bove R, Rowles W, Zhao C, Anderson A, Friedman S, Langdon D, Alexander A, Sacco S, Henry R, Gazzaley A, Feinstein A, Anguera JA. A novel in-home digital treatment to improve processing speed in people with multiple sclerosis: a pilot study. *Mult Scler*. 2021;27(5):778–89. doi: 10.1177/1352458520930371. [PubMed: 32584155] [CrossRef: 10.1177/1352458520930371]

- 57. Sanchez R, Brown E, Kocher K, DeRosier M. Improving children's mental health with a digital social skills development game: a randomized controlled efficacy trial of adventures aboard the S.S. GRIN. *Games Health J.* 2017;6(1):19–27. doi: 10.1089/g4h.2015.0108. [PubMed: 28051877] [CrossRef: 10.1089/g4h.2015.0108]
- 58. Beidel DC, Tuerk PW, Spitalnick J, Bowers CA, Morrison K. Treating childhood social anxiety disorder with virtual environments and serious games: a randomized trial. *Behav Ther.* 2021;52(6):1351–63. doi: 10.1016/j.beth.2021.03.003.S0005-7894(21)00047-2 [PMCID: PMC8531536] [PubMed: 34656191] [CrossRef: 10.1016/j.beth.2021.03.003]
- 59. Haberkamp A, Walter H, Althaus P, Schmuck M, Rief W, Schmidt F. Testing a gamified Spider App to reduce spider fear and avoidance. *J Anxiety Disord.* 2021;77:102331. doi: 10.1016/j.janxdis.2020.102331.S0887-6185(20)30145-6 [PubMed: 33166870] [CrossRef: 10.1016/j.janxdis.2020.102331]
- 60. Litvin S, Saunders R, Maier MA, Lüttke S. Gamification as an approach to improve resilience and reduce attrition in mobile mental health interventions: a randomized controlled trial. *PLoS One.* 2020;15(9):e0237220. doi: 10.1371/journal.pone.0237220. https://dx.plos.org/10.1371/journal.pone.0237220 .PONE-D-19-35191 [PMCID: PMC7467300] [PubMed: 32877425] [CrossRef: 10.1371/journal.pone.0237220]
- 61. Steinman SA, Teachman BA. Cognitive processing and acrophobia: validating the Heights Interpretation Questionnaire. *J Anxiety Disord.* 2011;25(7):896–902. doi: 10.1016/j.janxdis.2011.05.001. http://europepmc.org/abstract/MED/21641766 .S0887-6185(11)00091-0 [PMCID: PMC3152668] [PubMed: 21641766] [CrossRef: 10.1016/j.janxdis.2011.05.001]
- 62. Abd-Alrazaq A, Al-Jafar E, Alajlani M, Toro C, Alhuwail D, Ahmed A, Reagu SM, Al-Shorbaji N, Househ M. The effectiveness of serious games for alleviating depression: systematic review and meta-analysis. *JMIR Serious Games*. 2022;10(1):e32331. doi: 10.2196/32331. https://games.jmir.org/2022/1/e32331/ v10i1e32331 [PMCID: PMC8800090] [PubMed: 35029530] [CrossRef: 10.2196/32331]
- 63. Adelman CB, Panza KE, Bartley CA, Bontempo A, Bloch MH. A meta-analysis of computerized cognitive-behavioral therapy for the treatment of DSM-5 anxiety disorders. *J Clin Psychiatry.* 2014;75(7):e695–704. doi: 10.4088/JCP.13r08894. [PubMed: 25093485] [CrossRef: 10.4088/JCP.13r08894]
- 64. Christ C, Schouten MJ, Blankers M, van Schaik DJ, Beekman AT, Wisman MA, Stikkelbroek YA, Dekker JJ. Internet and computer-based cognitive behavioral therapy for anxiety and depression in adolescents and young adults: systematic review and meta-analysis. *J Med*

Internet Res. 2020;22(9):e17831. doi: 10.2196/17831.
https://www.jmir.org/2020/9/e17831/ v22i9e17831 [PMCID: PMC7547394] [PubMed: 32673212] [CrossRef: 10.2196/17831]

- 65. Newby JM, Twomey C, Yuan Li SS, Andrews G. Transdiagnostic computerised cognitive behavioural therapy for depression and anxiety: a systematic review and meta-analysis. *J Affect Disord.* 2016;199:30–41. doi: 10.1016/j.jad.2016.03.018.S0165-0327(16)30050-7 [PubMed: 27060430] [CrossRef: 10.1016/j.jad.2016.03.018]
- 66. Rooksby M, Elouafkaoui P, Humphris G, Clarkson J, Freeman R. Internet-assisted delivery of cognitive behavioural therapy (CBT) for childhood anxiety: systematic review and meta-analysis. *J Anxiety Disord.* 2015;29:83–92. doi: 10.1016/j.janxdis.2014.11.006.S0887-6185(14)00172-8 [PubMed: 25527900] [CrossRef: 10.1016/j.janxdis.2014.11.006]
- 67. Bhattacherjee A. *Social science research: principles, methods, and practices.* Tampa: USF Tampa Library Textbooks Collection; 2012.
- 68. Mobile statistics report, 2021-2025. *The Radicati Group.* 2021. [2022-02-08]. https://www.radicati.com/wp/wp-content/uploads/2021/Mobile Statistics Report, 2021-2025 Executive Summary.pdf.
- 69. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J, Ackerman I, Aggarwal R, Ahn SY, Ali MK, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Bahalim AN, Barker-Collo S, Barrero LH, Bartels DH, Basáñez MG, Baxter A, Bell ML, Benjamin EJ, Bennett D, Bernabé E, Bhalla K, Bhandari B, Bikbov B, Bin Abdulhak A, Birbeck G, Black JA, Blencowe H, Blore JD, Blyth F, Bolliger I, Bonaventure A, Boufous S, Bourne R, Boussinesq M, Braithwaite T, Brayne C, Bridgett L, Brooker S, Brooks P, Brugha TS, Bryan-Hancock C, Bucello C, Buchbinder R, Buckle G, Budke CM, Burch M, Burney P, Burstein R, Calabria B, Campbell B, Canter CE, Carabin H, Carapetis J, Carmona L, Cella C, Charlson F, Chen H, Cheng AT, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahiya M, Dahodwala N, Damsere-Derry J, Danaei G, Davis A, De Leo D. Degenhardt L, Dellavalle R, Delossantos A, Denenberg J, Derrett S, Des Jarlais DC, Dharmaratne SD, Dherani M, Diaz-Torne C, Dolk H, Dorsey ER, Driscoll T, Duber H, Ebel B, Edmond K, Elbaz A, Ali SE, Erskine H, Erwin PJ, Espindola P, Ewoigbokhan SE, Farzadfar F, Feigin V, Felson DT, Ferrari A, Ferri CP, Fèvre EM, Finucane MM, Flaxman S, Flood L, Foreman K, Forouzanfar MH, Fowkes FG, Fransen M, Freeman MK, Gabbe BJ, Gabriel SE, Gakidou E, Ganatra HA, Garcia B, Gaspari F, Gillum RF, Gmel G, Gonzalez-Medina D, Gosselin R, Grainger R, Grant B, Groeger J, Guillemin F, Gunnell D, Gupta R, Haagsma J, Hagan H, Halasa YA, Hall W,

Haring D, Haro JM, Harrison JE, Havmoeller R, Hay RJ, Higashi H, Hill C, Hoen B, Hoffman H, Hotez PJ, Hoy D, Huang JJ, Ibeanusi SE, Jacobsen KH, James SL, Jarvis D, Jasrasaria R, Jayaraman S, Johns N, Jonas JB, Karthikeyan G, Kassebaum N, Kawakami N, Keren A, Khoo J, King CH, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Laden F, Lalloo R, Laslett LL, Lathlean T, Leasher JL, Lee YY, Leigh J, Levinson D, Lim SS, Limb E, Lin JK, Lipnick M, Lipshultz SE, Liu W, Loane M, Ohno SL, Lyons R, Mabweijano J, MacIntyre MF, Malekzadeh R, Mallinger L, Manivannan S, Marcenes W, March L, Margolis DJ, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnulty JH, McDermott MM, McGill N, McGrath J, Medina-Mora ME, Meltzer M, Mensah GA, Merriman TR, Meyer A, Miglioli V, Miller M, Miller TR, Mitchell PB, Mock C, Mocumbi AO, Moffitt TE, Mokdad AA, Monasta L, Montico M, Moradi-Lakeh M, Moran A, Morawska L, Mori R, Murdoch ME, Mwaniki MK, Naidoo K, Nair MN, Naldi L, Narayan KM, Nelson PK, Nelson RG, Nevitt MC, Newton CR, Nolte S, Norman P, Norman R, O'Donnell M, O'Hanlon S, Olives C, Omer SB, Ortblad K, Osborne R, Ozgediz D, Page A, Pahari B, Pandian JD, Rivero AP, Patten SB, Pearce N, Padilla RP, Perez-Ruiz F, Perico N, Pesudovs K, Phillips D, Phillips MR, Pierce K, Pion S, Polanczyk GV, Polinder S, Pope CA, Popova S, Porrini E, Pourmalek F, Prince M, Pullan RL, Ramaiah KD, Ranganathan D, Razavi H, Regan M, Rehm JT, Rein DB, Remuzzi G, Richardson K, Rivara FP, Roberts T, Robinson C, De Leòn FR, Ronfani L, Room R, Rosenfeld LC, Rushton L, Sacco RL, Saha S, Sampson U, Sanchez-Riera L, Sanman E, Schwebel DC, Scott JG, Segui-Gomez M, Shahraz S, Shepard DS, Shin H, Shivakoti R, Singh D, Singh GM, Singh JA, Singleton J, Sleet DA, Sliwa K, Smith E, Smith JL, Stapelberg NJ, Steer A, Steiner T, Stolk WA, Stovner LJ, Sudfeld C, Syed S, Tamburlini G, Tavakkoli M, Taylor HR, Taylor JA, Taylor WJ, Thomas B, Thomson WM, Thurston GD, Tleyjeh IM, Tonelli M, Towbin JA, Truelsen T, Tsilimbaris MK, Ubeda C, Undurraga EA, van der Werf MJ, van Os J, Vavilala MS, Venketasubramanian N, Wang M, Wang W, Watt K, Weatherall DJ, Weinstock MA, Weintraub R, Weisskopf MG, Weissman MM, White RA, Whiteford H, Wiebe N, Wiersma ST, Wilkinson JD, Williams HC, Williams SR, Witt E, Wolfe F, Woolf AD, Wulf S, Yeh P, Zaidi AK, Zheng Z, Zonies D, Lopez AD, AlMazroa MA, Memish ZA. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2197-223. doi: 10.1016/S0140-6736(12)61689-4.S0140-6736(12)61689-4 [PubMed: 23245608] [CrossRef: 10.1016/S0140-6736(12)61689-4]

70. Oladeji BD, Gureje O. Brain drain: a challenge to global mental health. *BJPsych Int.* 2016;13(3):61–3. doi: 10.1192/s2056474000001240.

http://europepmc.org/abstract/MED/29093905 .S2056474000001240 [PMCID: PMC5618877] [PubMed: 29093905] [CrossRef: 10.1192/s2056474000001240]

Figure 1

Flowchart of the study selection process.

Table 1
Characteristics of studies and populations.

Study Year Country Publication RCTa type Sample Age type size, n (years), mean Adomaviciene 2019 Lithuania Journal Parallel 60 64.6 et al [28] Carvalho et al 2020 Brazil Journal Parallel 35 51.3 article	Sex (ma (%) 40 (66 0 ((
Adomaviciene 2019 Lithuania Journal Parallel 60 64.6 et al [28] article Carvalho et al 2020 Brazil Journal Parallel 35 51.3	40 (66
et al [28] article Carvalho et al 2020 Brazil Journal Parallel 35 51.3	(66
Carvalho et al 2020 Brazil Journal Parallel 35 51.3	
•	0 ((
Meldrum et al 2015 Ireland Journal Parallel 71 54.1 [30] article	27
Schumacher et 2018 Germany Journal Parallel 42 56.3	25
al [31] article	(59
Ruivo et al [32] 2017 Ireland Journal Parallel 32 59.9	26
article	(81
Mazzoleni et al 2014 Italy Journal Parallel 40 71.2	NR ^l
[<u>33</u>] article	
Polat et al [34] 2021 Turkey Journal Parallel 40 44.8 article	0 ((
Lin et al [35] 2020 Taiwan Journal Parallel 80 57.0	39
article	(48
Vieira et al [36] 2017 Portugal Journal Parallel 46 57.7 article	NR
Thomas et al 2017 United Journal Parallel 30 49.3 [37] Kingdom article	3 (1
Wagener et al 2012 United Journal Parallel 41 14.0	14

Study	Year	Country	Publication	RCT ^a type	Sample	Age	Sex
			type		size, n	(years),	(ma
						mean	(%)
[<u>38</u>]		States	article				(33 🔻
4							•

^aRCT: randomized controlled trial.

Table 2
Characteristics of interventions.

Study	Intervention	Serious game name	Serious game type	Serious game genre	P
Adomaviciene et al [28]	Serious game	N/A ^a	Exergame	Designed	C ₁
Carvalho et al	Serious game	Wii Fit Plus	Exergame	Purpose- shifted	W b: W pl
Meldrum et al [30]	Serious game	Wii Fit Plus	Exergame	Purpose- shifted	W ba Fa
Schumacher et al [<u>31</u>]	Serious game	Wii Fit, Wii Sports	Exergame	Purpose- shifted	W ba
Ruivo et al [<u>32]</u>	Serious game	Wii Sports	Exergame	Purpose- shifted	W K
Mazzoleni et al [<u>33</u>]	Serious game + pulmonary rehabilitation program	Wii Fit Plus	Exergame	Purpose- shifted	W ba W p]
Polat et al [34]	Serious game + cycling activity	Kinect Sports (Beach Volleyball)	Exergame	Purpose- shifted	C ₁
Lin et al [<u>35</u>]	Serious game + hot	Hot Plus	Exergame	Designed	Cı

^bNR: not reported.

Study	Intervention	Serious game	Serious game type	Serious	P
		name		game	
				genre	
	packs +				S€
	transcutaneous				
	electrical nerve				
	stimulation				•
◀					•

^aN/A: not applicable.

^bCBT: cognitive behavioral therapy.

^cVR: virtual reality.

^dEEG: electroencephalography.

^eEMDR: Eye Movement Desensitization and Reprocessing.

Table 3
Characteristics of comparators and outcomes.

Study	Comparator	Duration (minute)	Frequency (time per	Period (week)	Outcom
			week)		- 1
Adomaviciene et al [28]	Robot-assisted trainings	45	Once a day	2	HADS ^a
Carvalho et al	Conventional exercises	60	3	7	Fibromy
[<u>29</u>]					Questio
Meldrum et al [30]	Conventional exercises	15	5	6	HADS
Schumacher et al [31]	Conventional exercises (physiotherapy)	30	5	2	HADS
Ruivo et al [<u>32</u>]	Conventional exercises	60	2	6	HADS
Mazzoleni et al	Conventional exercises (pulmonary rehabilitation program)	60	7	3	STAI ^b
Polat et al [<u>34</u>]	Conventional exercises + cycling activity	35	3	4	HADS
Lin et al [<u>35</u>]	Conventional exercises +	20	3	4	HADS

Study	Comparator	Duration (minute)	Frequency (time per week)	Period (week)	Outcom
	hot packs + transcutaneous electrical nerve stimulation				
Vieira et al [<u>36</u>]	Conventional exercises, control	70-85	3	24	Depress and Stre
Thomas et al [37]	Control	N/A ^c	N/A	N/A	HADS
Wagener et al	Control	N/A	N/A	N/A	Behavio 🔻

^aHADS: Hospital Anxiety and Depression Scale.

Figure 2

Review authors' judgments about each risk of bias domain.

Figure 3

Forest plot of 9 studies comparing the effect of exergames to that of conventional exercises on the anxiety level $[\underline{28} - \underline{36}]$. Std: standardized.

Figure 4

Forest plot of 5 studies comparing the effect of exergames to that of no intervention on the anxiety level $[\underline{36}$ - $\underline{40}]$. Std: standardized.

^bSTAI: State-Trait Anxiety Inventory.

^cN/A: not applicable.

^dSCAS: Spence Children's Anxiety Scale.

^eCBT: cognitive behavioral therapy.

^fSPAI-C: Social Phobia and Anxiety Inventory for Children.

Figure 5

Forest plot of 6 studies (9 comparisons) comparing the effect of CBT games to that of no intervention on the severity of depressive symptoms [41-46]. CBT: cognitive behavioral therapy; Std: standardized.

Figure 6

Forest plot of 6 studies (9 comparisons) comparing the effect of CBT games to that of no intervention on the anxiety level among adults and adolescents [41-46]. CBT: cognitive behavioral therapy; Std: standardized.

Figure 7

Forest plot of 3 studies comparing the effect of biofeedback games to that of conventional video games on the anxiety level [49-51]. Std: standardized.