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The effectiveness of virtual reality in patients with spinal pain: A systematic review and meta-analysis

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Abstract

Background: Virtual reality (VR) technologies have been shown to be beneficial in various areas of healthcare; to date, there are no systematic reviews examining the effectiveness of VR technology for the treatment of spinal pain.

Purpose: To investigate the effectiveness of VR technology in the management of individuals with acute, subacute, and chronic spinal pain.

Methods: Six electronic databases were searched until November 2019. Randomized controlled trials (RCTs) assessing the effectiveness of VR were eligible for inclusion. Two independent reviewers extracted the data, assessed the risk of bias for each study and the overall quality of evidence. Mean differences of outcomes were pooled as appropriate using random-effects models.

Results: Seven RCTs of high risk of bias met review criteria. Quality of evidence ranged from very low to low quality. In patients with chronic neck pain, VR improved GPE, satisfaction, and general health at short-term follow-up and general health and balance at intermediate-term follow up compared to kinematic training. VR improved pain intensity and disability at short-term and long-term follow-up compared to conventional proprioceptive training in patients with chronic neck pain. In patients with either subacute or chronic low back pain (LBP), VR improved pain, disability, and fear of movement compared to lumbar stabilization exercises and pain compared to conventional physical therapy (at short-term follow-up). In patients with chronic LBP, VR improved pain compared to lumbar stabilization exercises and fear of movement compared to conventional physical therapy (at short-term follow-up).

Conclusion: VR's potential for improvement in outcomes for spinal pain that demonstrated statistical and/or clinical significance (pain intensity, disability, fear of movement, GPE, patient satisfaction, general health status, and balance) highlights the need for more focused, higher-quality research on efficacy and effectiveness of VR for treatment of patients with spinal pain.

Introduction

Virtual reality (VR) is a new technology, which has been rapidly evolving over the past two decades [1, 2]. VR can be operationally defined as "simulations that make use of various combinations of interaction devices and sensory display systems" [3]. VR has been explored in a variety of fields and clinical applications, such as in treating phobias, akinesia in patients with Parkinson's disease, and phantom limb syndrome in patients with amputations [3-5]. Additional

patient populations that have demonstrated benefit from VR interventions include individuals with higher pain and physical dysfunction levels [6], higher anxiety [7], and those with a desire for an alternative to opioid analgesics [7, 8]. Overall, previous systematic reviews investigating the effectiveness of VR have suggested its usefulness in treating a variety of pain-related problems [9-11]. A recent systematic review found that VR has shown beneficial results in pain, anxiety, and stress in burn patients during physical rehabilitation and physiotherapy [12]. An additional systematic review found that VR is an effective intervention in acute inpatient medical settings for burn injury, eating disorders/obesity, and traumatic brain injury [13].

Distraction is one of the suggested mechanisms that explains the effects of VR on pain. By definition, distraction is "the engagement of cognitive and attentional resources that are necessary for pain processing" [3]. It is believed that the distractor (the VR program) diminishes the perception of pain by acting on the signaling pathways that lead to pain [4]. This suggests that VR may change the activity of the body's complex pain modulation system by decreasing the level of attention paid to the pain, causing the individual to no longer perceive a stimulus as painful. A majority of the previously published studies and reviews on the effects of virtual reality on pain focus on "pain resulting from acute and subacute conditions or pain-inducing therapies", such as pain associated with wound care following burn injuries, but do not examine the possible effects VR may have on spinal pain [9-11].

To our knowledge, no previous systematic review has specifically focused on the effectiveness of VR in patients with spinal pain (low back, thoracic, and neck pain). Spinal pain is a widely prevalent health condition and the worldwide leading cause of years lived with disability [14]. Various non-pharmacological treatments have been utilized for treatment of spinal pain but there is a lack of consensus on which conservative therapies are the most effective [2, 3] and results of meta-analyses suggest that, as a group, their effect sizes on pain and other outcomes are in the small to medium range. [2, 3]. The objective of this systematic review is to evaluate the evidence on the efficacy and effectiveness of VR for clinic and lab-based treatment of patients with spinal pain at short, intermediate, and long term follow-up.

Methods

Literature Search

The review was registered with the international prospective register of systematic reviews (PROSPERO) with the ID of 97253. The PRISMA Statement was used to guide the reporting of the present review [15]. PubMed, EMBASE, Scopus, CINAHL, PsycINFO, and Clinical.Trials.gov were searched from their inception up to November 2019, without language restrictions. The full search strategy is outlined in Appendix 1.

Study Selection

This review included randomized controlled trials (RCTs) that assessed the effectiveness of virtual reality for treatment of patients with spinal pain (neck pain, thoracic pain, or LBP). For eligibility, trials needed to meet the following criteria: (1) include male or female adolescents or adults, ages 12 to 80 years old, and (2) presenting with acute, subacute, or chronic spinal pain. Acute and subacute spinal pain was considered pain that has been present less than 12 weeks [16], whereas chronic spinal pain was defined as spinal pain lasting more than 12 weeks [16]. For this paper, spinal pain was defined as neck, thoracic, and LBP with or without radiating symptoms to the upper or lower extremities. No restrictions were placed on the setting, languages, or date of publication in the included studies. Studies that comprised of patients with serious spinal pathology (e.g. fractures, tumors, spinal cord injuries, and inflammatory diseases) were excluded. For the first screening, two pairs of independent reviewers evaluated the titles and abstracts for each possible study and excluded irrelevant studies (KK and CS, LD and AA). Two different reviewers then evaluated the full-text article and assessed whether the study fulfilled the inclusion criteria (MA and LD). When there was a disagreement, a decision made by a third reviewer was utilized (CS). Citations of the included studies were examined for additional studies to be included.

Intervention

The intervention investigated in this review, VR, is a relatively new technology that is operationally defined as "simulations that make use of various combinations of interaction devices and sensory display systems" to accomplish set goals [3]. As such, VR includes a broad construct with many variations and implementation methods. This systematic review maintained broad search criteria by considering VR as encompassing (1) methods such as head-mounted displays, curved displays with body motion sensors, video games, Nintendo Wii consoles, and

simulations and (2) technologies referred to as a simulated environment or as augmented reality. To be considered a simulated environment, the VR system used in a study had to (1) model a system or environment; (2) run interactively or non-interactively; and (3) utilize three-dimensional graphics and sensory feedback [17]. To be considered augmented reality, the system used in a study had to (1) combine real and virtual objects in a real environment; (2) run interactively and in real-time; and (3) register real and virtual objects with each other [18].

Comparison and Control Conditions

Comparison and control conditions accepted in this review included no treatment, waitlist control, treatment as usual *or* standard care (i.e. traditional physical therapy), minimal intervention (i.e. inert interventions or brief educational interventions/booklets), other types of exercise therapy, and all other interventions not including VR.

Outcomes

Primary outcomes included measures of pain intensity and disability. Secondary outcomes included specific function, general health status, future visits to healthcare professionals, return to work, patient satisfaction, adverse events, global perceived effect (GPE), balance, and fear of movement.

Risk of bias

The expanded version of the Cochrane Risk of Bias Assessment Tool from the Cochrane Back Neck group was used to measure the risk of bias of the included RCTs [16]. This tool was used to score each study on seven domains (random sequence generation, allocation concealment, selective reporting, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and other bias). Each domain was scored as “yes”, “no” and “unclear.” After, each study was scored in one of three categories: “high risk of bias”, “low risk of bias”, or “unclear” [29]. The scoring methods were informed by the Cochrane Handbook (Section 3.8). Scoring was conducted by two independent researchers before consensus was reached (KK and MA) [19]. For this review, after a consensus between the authors, we classified studies as having

low or high risk of bias based on critical key domains (random sequence, allocation concealment, and selective reporting). In cases in which a domain item was rated as "unclear" or "no" we rated the study as having a high risk of bias [19]. A similar criterion was adopted by a previous Cochrane Systematic Review [20].

Data Extraction

Information extracted from the studies included the following: publication data (authors and year), study setting, number and demographic characteristics of participants, details of the intervention and control conditions, risk of bias, measures used to assess primary and secondary outcomes, time of assessment (number of weeks after randomization), number of participants assessed, and results for the assessment for primary and secondary outcomes. Two review authors extracted data independently with minimal discrepancies that were resolved through discussion (with a third author when necessary) (MA and LD). Authors were contacted regarding insufficient information prior to the exclusion of the studies.

Data synthesis and statistical analysis

A narrative synthesis of the findings from the included studies was provided and structured around the study setting, study population, characteristics of participants, type of outcome, and intervention content. For each study, treatment effects measured by continuous variables were calculated using mean differences (MD) with 95% confidence intervals (95% CI), for either between-group differences in point estimates at specific time points or for between-group differences in change scores. Between-group differences were determined to be statistically significant if the p-value was less than 0.05.

Continuous data were converted to a common zero to 100-point scale (to account for trials assessing the same outcome on different scales). If there were multiple trials comparing the effects of a VR treatment with that of a comparison/control group of similar nature, and if these trials were sufficiently homogeneous (I^2 test <50% with no evident heterogeneity by visual inspection), we performed a meta-analysis using random-effects to obtain a pooled estimate of the effect with a 95% CI (note: this was only possible for the neck pain studies). Effects were summarized for the following time periods: short-term (closest to 4 weeks after randomization),

intermediate (closest to 6 months after randomization), and long-term (closest to 1 year after randomization) follow-up. [16]. Effect sizes were defined as being in one of three levels: small effect size (MD <10% of the scale), medium effect size (MD 10% to 20% of the scale) or large effect size (MD >20% of the scale) [21]. The effect was considered clinically important when the magnitude of the effect size was at least medium (>10% of the scale) [22].

The overall quality of the evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [23]. The quality of evidence was defined as "high quality" (further research is unlikely to change confidence in the estimate of effect), "moderate quality" (further research is likely to have an important impact on confidence in the estimate of effect and might change the estimate), "low quality" (further research is likely to have an important effect on confidence in estimate of effect and is likely to change the estimate), and "very low quality" (little confidence in the effect estimate) [24]. The quality of evidence for a given outcome was downgraded one level (e.g. from high to moderate, from low to very low) based on each of 5 factors: 1) Limitation in the design/implementation (≥25% of trials, had high risk of bias; 2) Inconsistency of results (≥25% of trials had results with large heterogeneity, I^2>50%); 3) Indirectness (when the trial context is not the same as the review question); 4) Imprecision (sample size <400 for each outcome); and 5) Publication bias (assessed using funnel plot analysis). Comparisons involving single RCTs were downgraded for imprecision and were not plotted. Review Manager (version 5.3) was used to assist in statistical analysis.

Results

Search selection

The initial search of the electronic databases yielded 583 potentially eligible studies following the removal of duplicate records. The screening of titles and abstracts led to full-text articles of 52 potentially eligible studies. From the 52, seven RCTs [25-31] (pooled sample = 311 participants) met the inclusion criteria and were included in the review. Primary reasons for study exclusion included characteristics such as non-randomized trials, serious spinal pathology, interventions failed to incorporate VR, publication was limited to a conference abstract, ongoing studies, and insufficient information. Excluded studies and the reason(s) they were excluded are

shown in Appendix 2. Ongoing studies are presented in Appendix 3. Figure 1 outlines the flow of studies through the review process. We did not identify additional citations from the reference lists of included studies.

Characteristics of included studies

In terms of the spinal pain location studied, four RCTs investigated LBP [25, 27, 29, 31] and three RCTs investigated neck pain [26, 28, 30]. There were no studies investigating the effects of VR in patients with thoracic spinal pain. Five of the seven studies included patients with chronic spinal pain [26-28, 30, 31] whereas two studies included participants with both subacute and chronic spinal pain [25, 29]. No included studies investigated acute pain. All included studies were published between 2013 and 2019 [25-31]. No studies reported if participants were taking pain medications during the course of the study. Two studies were conducted in Australia [28, 30], three in South Korea [25, 27, 31], one in Turkey [29], and one in Iran [26].

Based on available information, the participants in the LBP studies were 52.1 % male with an average age of 38.9 years and the participants in the neck pain studies were 36.6 % male with an average age of 42.7 years. Duration of intervention and number of sessions in the LBP studies ranged from two weeks to eight weeks (average of 5.5 weeks) and 10 to 24 sessions (average of 17.5 sessions). Duration of intervention and number of sessions in the neck pain studies ranged from four to five weeks (average of 4.3 weeks) and 4 to 64 sessions (average of 25 sessions). The neck pain studies included short and intermediate-term follow up assessments. The LBP studies included only short-term follow up assessments. Studies did not report if short-term outcomes were measured immediately in the lab post-intervention, later the same day, or a few days post-intervention. A comprehensive description of each study is available in Table 1.

Primary and secondary outcomes

All included trials measured pain intensity. Pain was measured with the visual analog scale (VAS) [32] in all trials, with higher scores indicating higher pain levels. Four included trials measured disability. Three trials measured disability with the Neck Disability Index (NDI) [26, 28, 30, 33], two trials measured disability with the Oswestry Disability Index (ODI) [25, 29, 34],

and one trial used the Roland Morris Disability Questionnaire (RMDQ) [25, 35] in addition to the ODI, with higher scores indicating higher levels of disability.

Two trials measured global perceived effect (GPE) with both trials using an 11-point scale from -5 to +5 [28, 30, 36], with higher scores indicating greater perceived effect. Four studies measured fear of movement. Fear of movement was measured with the Fear-Avoidance Beliefs Questionnaire (FABQ) [25, 37] and the Tampa Scale for Kinesiophobia (TSK) [28-30, 38]. Higher scores on the FABQ and TSK represent more strongly held fear-avoidance beliefs and kinesiophobia. Three trials measured general health status. General health status was measured with RAND Corporation health-related quality of life survey (RAND-36) [27, 39], EuroQol Group health-related quality of life instrument (EQ-5D) [30, 40], and Nottingham Health Profile (NHP) [29, 41]. Higher scores on the RAND-36 and EQ-5D indicate greater general health and health-related quality of life. Higher scores on the NHP indicate poorer perceived general health. Four trials measured balance, with three trials using single leg stance (SLS) [27-29, 42] and one trial using the Y Balance Test (YBT) [26, 43] as their measurement. Higher scores indicated greater balance. Two trials measured patient satisfaction with both using an 11-point scale from -5 to +5 [28, 30, 36]. Higher scores indicated greater satisfaction.

Intervention and comparisons: Neck pain

Virtual reality interventions administered in the trials investigating neck pain included programs using a head-mounted display with custom-designed software to track three-dimensional movements in real-time [28, 30] and a computer game operated by motions of the head detected by reflective markers [26]. These virtual reality-based interventions were either stand-alone treatments or paired with kinematic training. Comparisons administered in the studies investigating neck pain included kinematic training via a head-mounted laser [28, 30] and conventional proprioceptive training [26]. Kinematic training consists of active range of motion, quick movements of the neck, and accuracy training [40]. Conventional proprioceptive training consists of eye-follow, gaze stability, eye-head coordination, and position sense and movement sesnse practice with a head-mounted laser [26].

Intervention and comparisons: LBP

Virtual reality interventions administered in the trials investigating LBP included programs utilizing a Nintendo Wii system [25, 27], head-mounted displays [29], and horse simulator machines [31]. The VR studies using the Nintendo Wii sports system utilized a number of different game programs (e.g. the exercise program wakeboard, Frisbee dog, jet ski, and canoe games) [27]. These games require the participant to control a virtual player using a remote control with motion sensors. One study utilized the Nintendo Wii Fit yoga VR program which registers weight shifts on a motion-sensor controlled balance board [25]. The VR studies using head-mounted displays utilized an iPod and video glasses to play participants a video clip of walking through forest [29]. The VR studies using horse simulator machines involved having the participant sitting on a horse-shaped pommel that moves in conjunction with a video display [31].

All of the VR interventions used in the LBP studies were either stand-alone treatments or paired with traditional physical therapy or physical agent modalities. Comparisons administered in the trials investigating LBP included lumbar stabilization exercises (i.e., "contraction exercise for the transverse abdominis and multifidus followed by curl-ups in order to contract the rectus abdominis") [25, 27], physical agent modalities (hot pack, interferential current therapy, and deep heat with ultrasound) [27], no treatment [31], and traditional physical therapy (i.e., stabilization exercises and therapeutic modalities) [25, 29]. Traditional physical therapy consisted of a variety of exercises including bridges, planks, balancing on uneven surfaces, cat-camel mobility exercise, lumbar stretching, and a home exercise program [25, 29].

Risk of bias

The Cochrane Risk of Bias Tool was used to assess the risk of bias of the included studies. The results of this assessment are included in Figure 2. All seven of the studies included had a high risk of bias. The major limitations to study quality for the neck pain studies were random sequence generation, allocation concealment, and blinding of participants and personnel. The major limitations to study quality for the LBP studies were blinding of participants and personnel, incomplete outcome data, and selective reporting.

Treatment efficacy - neck pain (please see Table 2)

Virtual reality versus kinematic training

Primary outcomes (please see Figure 3)

Two trials were included in the meta-analysis comparing VR to kinematic training [28, 30]. The treatment approach for both trials involved flying a virtual airplane through the use of a customized neck VR system paired with a head-mounted display.

Based on low quality evidence, there was no statistically significant difference and no clinically important difference between VR and kinematic training for pain intensity (MD -9.08; 95% CI -21.84, 3.67; p=0.18) and disability (MD -2.24; 95% CI -6.38, 1.90; p=0.29) at short term follow up and for pain intensity (MD -6.90; 95% CI -16.05, 2.25; p=0.14) and disability (MD -4.30; 95% CI -10.57, 1.96; p=0.18) at intermediate term follow up.

Secondary outcomes (please see Figure 4)

Based on low-quality evidence there was a statistically significant difference but no clinically important effect in favor of VR compared to kinematic training for patient satisfaction [28, 30], global perceived effect [28, 30], and general health status [30] at short term follow up; and for balance [28] and general health status [30] at intermediate-term follow. There was no statistically significant difference and no clinically important difference between virtual reality and kinematic training for fear of movement [28, 30] and balance [28] at short term follow up (based on low quality evidence) and for fear of movement [28, 30] and GPE [28, 30] at intermediate-term follow up (based on very low to low quality evidence). Specific function, future visits to healthcare professionals, return to work, and adverse events were not reported in this comparison.

Virtual Reality versus conventional proprioceptive training

Primary outcomes

One trial that compared VR to conventional proprioceptive training was included in the analysis for pain intensity and disability [26]. The treatment approach for the included trial was a computer game operated by head movements detected by reflective markers on the participants' foreheads.

Based on low-quality evidence there was a statistically significant difference but no clinically important effect in favor of VR compared to conventional proprioceptive training for pain intensity (MD -8.88; 95% CI -14.20, -3.56; p<0.01) and disability (MD -7.14; 95% CI -10.51,-3.77; p<0.01) at short term follow up and for disability (MD -9.68, 95% CI -13.90, -5.46; p<0.01) at intermediate follow-up. There was a statistically significant difference and clinically important effect in favor of VR compared to conventional proprioceptive training for pain intensity (MD -10.60; 95% CI -17.56, -3.64; p<0.01) at intermediate follow-up.

Secondary outcomes

Based on low-quality evidence there was no statistically significant difference and no clinically important effect in favor of VR compared to conventional proprioceptive training for balance (MD -4.02; 95% CI -8.87, 0.83, p=0.10) at short term follow-up and for balance (MD -2.74, 95% CI -8.49, 3.01, p=0.35) at intermediate follow-up.

Treatment efficacy - low back pain (please see Table 3)

Virtual reality versus lumbar stabilization exercises

Primary outcomes

Two trials of patients with LBP that compared VR to lumbar stabilization were included in the analysis of pain intensity [25, 27]. A meta-analysis of the data was not completed due to the varying durations of pain investigated, with one study investigating chronic pain [27] and another investigating both subacute and chronic pain [25]. Both studies used a treatment approach utilizing a Nintendo Wii system. Based on low quality evidence there was a statistically significant and clinically important difference at short term follow up for pain intensity between VR and lumbar stabilization exercises for patients with subacute and chronic pain (MD -23.60; 95% CI -34.75, -12.45; p<0.01) [25]; and a statistically significant difference but no clinically important difference for patients with chronic pain (MD 10.00; 95% CI 0.34, 19.66; p=0.04) at short term follow up [27].

One trial comparing VR to lumbar stabilization was included in the analysis of disability [25]. Based on low-quality evidence there was a statistically significant difference and clinically important effect at short term follow up in favor of VR for disability (MD -21.59; 95% CI -38.65, -4.53; p=0.01).

Secondary outcomes

Based on low-quality evidence there was a statistically and clinically significant difference at short term follow up in favor of VR for low back pain vs lumbar stabilization for fear of movement [25]. There was no statistically significant difference and no clinically important difference for general health status and balance at short-term follow up [27]. Specific function, future visits to healthcare professionals, return to work, patient satisfaction, global perceived effect, balance, and adverse events were not reported in this comparison.

Virtual reality versus physical agent modalities

Primary outcomes

One trial of patients with LBP comparing VR combined with physical agent modalities to physical agent modalities was included in the analysis of pain intensity [27]. The VR treatment combined a program utilizing the Nintendo Wii system with the sports game with supplemental physical agent modalities. Based on low-quality evidence there was no statistically significant difference and no clinically important difference in favor of the combined VR/physical agent modalities treatment vs physical agent modalities alone at short term follow up for pain intensity (MD 1.20; 95% CI -8.67, 11.07; p=0.81). Disability was not reported in this comparison.

Secondary outcomes

Based on low-quality evidence there was no statistically significant difference and no clinically important difference for general health status and balance at short-term follow up [27]. Specific function, future visits to healthcare professionals, return to work, patient satisfaction, global perceived effect, fear of movement, and adverse events were not reported in this comparison.

Virtual reality versus conventional physical therapy

Primary outcomes

One trial of patients with LBP compared VR and conventional physical therapy and was included in the analysis of pain intensity [29]. The VR treatment approach consisted of a virtual walking program using a 3D television in close-range with an optoelectric based kinematic tracking system. Based on low-quality evidence there was a statistically significant and clinically important difference at short term follow up for pain intensity in favor of VR compared to conventional physical therapy (MD = -23.80; 95% CI -39.84 to -7.76; p<0.01) with chronic LBP. There was no statistically significant difference and no clinically important at short term follow up for disability (MD -4.15; 95% CI -8.89, 0.59; p=0.09).

Secondary outcomes

Based on low-quality evidence there was a statistically significant but not clinically important difference at short term follow up in favor of VR versus conventional physical therapy for fear of movement [29]. There was no statistically significant difference and no clinically important difference for general health status and balance at short-term follow up [29]. Specific function, future visits to healthcare professionals, return to work, patient satisfaction, global perceived effect, and adverse events were not reported in this comparison.

Virtual reality versus no treatment

Primary outcomes

One trial of patients with LBP compared VR to no treatment and was included in the analysis of pain intensity [31]. The VR treatment consisted of a VR-based horse-riding simulation. Based on low-quality evidence there was no statistically significant difference and no clinically significant difference at short term follow-up between VR and no treatment for pain intensity (MD based on % delta -16.77; 95% CI -42.73 to 9.19; p<0.21). Percentage delta was used for this comparison to account for the significant difference in baseline pain levels between the experimental and control groups. Disability was not reported in this comparison.

Secondary outcomes

No secondary outcomes were reported for this comparison.

Discussion

Summary of the main results

The objective of this review was to investigate the effectiveness of VR technology in the treatment of spinal pain. The effect of VR ranged from no statistical significance to clinical significance depending on the area of the spine being treated, the follow-up period being assessed, and the type of VR used. For patients with chronic neck pain, low-quality evidence suggests that VR may provide a clinically significant improvement over conventional proprioceptive training for pain intensity at intermediate follow-up. There were statistically significant, but not clinically significant, improvements over conventional proprioceptive training for pain intensity and disability at short term follow-up and disability at intermediate term follow-up and for global perceived effect, patient satisfaction, and general health status at short term and for general health status and balance at intermediate-term follow up compared to kinemtic training. For patients with subacute/chronic LBP, some clinically significant improvements at short-term follow up were observed for some VR programs (Nintendo Wii Fit yoga program and VR-based walking program) when VR was compared to lumbar stabilization exercises (i.e. for the outcomes of pain intensity, disability, and fear of movement) and when VR was compared to conventional physical therapy (i.e. for pain intensity as an outcome). We did not find a statistically significant difference between VR and physical agent modalities, and conventional physical therapy for all follow-up periods and outcomes tested.

Interpretation of the results and applicability of evidence

Despite the growing use of VR for spinal pain, evidence in this area remains limited. Our review identified seven VR studies of spinal pain that met our inclusion criteria. We felt that a systematic review of this limited evidence was warranted as it could provide summary of the current research and offer valuable suggestions for future research.

Our review found that the difference in effect between VR and other included interventions was often small and not clinically significant. Exceptions were that VR was found to yield clinically important differences when compared to conventional physical therapy (for pain intensity) and when compared to lumbar stabilization exercises (for pain intensity, disability, and fear of

movement) for LBP and when compared to conventional proprioceptive training (for pain intensity) for neck pain. In these studies, the effects obtained with VR were similar in magnitude to effect sizes reported for treatments such as manual therapy spinal mobilization compared to other active therapies (exercise, physical therapy) [44] and dry needling of the low back compared to acupuncture and sham needling [45].

VR is becoming more widely available in clinic settings where patients with spinal pain are treated. This is likely due to recent emergence of low-cost VR technologies [18]. A VR system poses a one-time cost to the clinic, and then it may be used repeatedly. The growing clinical use of VR underscores the need for more research in this area.

Future research needs to focus on several topics. First, in order to draw more definitive conclusions about the effects of VR in different populations with spinal pain we need more VR studies in patients with specific types of spinal pain, i.e. neck pain, thoracic spinal pain, and low back pain, and need to compare groups of patients with acute versus chronic pain in these areas. Further investigation into long-term VR treatment effects, (e.g. measured at 1 year follow up), would help determine if VR is a viable option for extended pain relief. Future studies could also investigate if VR booster treatment sessions would help patients achieve longer-term treatment effect.

Future studies also need to examine a wider range of key outcomes of VR treatments. These outcomes could include measures of specific function, future visits to healthcare professionals, return to work, adverse events, as well as a wider array of psychological and pain outcomes, such as pain interference.

Descriptions of VR treatments as well as comparison/control conditions could be improved in future studies by using the checklist and recommendations provided by TIDieR [46]. In terms of overall quality of evidence, it would be favorable to conduct future studies with decreased risk of bias particularly in the areas of random sequence generation, allocation concealment, and blinding of participants and personnel. Future studies are also needed to determine the optimal dose of VR treatments and to compare VR systems of varying sophistication and levels of

immersion. Such research could help tailor VR treatment protocols to optimize their treatment effects. In non-spinal related research, more immersive forms of VR have been found to be more likely to generate pain relief when compared to less immersive forms [10]. Future studies should also attempt to identify the key mechanism(s) by which VR can function to decrease pain (e.g. distraction).

If the field of VR for spinal pain is to advance, we need systematic programs of research. Researchers should start with small, high-quality pilot studies, "a methodological preface to a larger study designed to develop, adapt, or check the feasibility of methods and/or to provide evidence for calculating sample size in future research" [47]. After these pilot studies, the researchers should revise and refine their VR interventions and then continue to a larger, more resource-intensive, and methodologically rigorous efficacy studies conducted under ideal conditions in order to increase the likelihood that the intervention's effect will be demonstrated. Subsequent effectiveness research should be completed under 'real-world' conditions to help determine the intervention's effect in a clinical setting, making the results of a VR effectiveness study particularly relevant to practicing clinicians [48].

Comparison to other reviews

The results found in the past reviews and the present review differed. The current review determined there to be a small and often not clinically important difference between VR and the other intervention groups, with the exception of clinically important differences found for pain intensity, disability, and fear of movement across two LBP comparisons and pain intensity in one neck pain comparison. In contrast, past reviews exploring in-patient burn injury care, dental pain, post-surgical pain, port access pain, ischemic arm pain, eating disorders, and traumatic brain injury often determined VR to be a consistently clinically effective and safe strategy for the distraction from pain, increased patient satisfaction, and the reduction of anxiety. This difference between the results may be due to the fact that the most clear-cut and most promising results of VR have been found in studies of burn wound care with more mixed findings in other clinical pain populations such as the spinal pain conditions investigated in the present review [10].

Strengths and limitations

Strengths of this review, when compared to past reviews, are as follows. Our review assessed the quality of evidence for each outcome using GRADE, included only randomized controlled studies, had explicit inclusion and exclusion criteria, and included a sensitive search strategy. Another strength of this systematic review is the completion of a meta-analysis for neck pain studies. Many of the previously published reviews on VR are not systematic reviews [6, 9] and the few previously published systematic reviews did not include a meta-analysis [10-13]. Therefore, the quality and value of the current systematic review and meta-analysis are favorable. The review was limited by the low number of included studies, seven studies overall with two of those seven studies being included in the meta-analysis for neck pain, resulting in a smaller data pool and decreased power of the overall results. The review was also limited by the relatively young average age of the population studied (average of age of 38.9 years for LBP studies, and 42.7 years for neck pain studies). The results may not be applicable to younger or older populations. Another limitation is the lack of further psychological outcomes (i.e. anxiety, depression, stress) included in the review, however these outcomes were not found in the included studies and were considered to be outside the scope of this review. Lastly, heterogeneity among LBP studies prevented pooling of studies.

Conclusion

The results of this systematic review and meta-analysis of RCTs with low-quality evidence indicate there was a small effect size of VR for spinal pain which varied depending on the area of the spine treated, follow-up period, and type of VR utilized. Statically but not clinically significant effects were seen for neck pain, with the exception of a clinically significant effect for pain intensity in one comparison. For low back pain, clinically important short-term effects were demonstrated for pain intensity, disability, and fear of movement across two comparisons of VR to control conditions. VR's potential for improvement in outcomes for spinal pain that demonstrated statistical and/or clinical significance (pain intensity, disability, fear of movement, GPE, patient satisfaction, general health status, and balance) highlights the need for more focused, higher-quality research on efficacy and effectiveness of VR for treatment of patients with spinal pain.

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Appendix 1. Search strategy

Database: PubMed

#	Query
1	"pain"[MeSH Terms] OR pain[tiab] OR pains[tiab] OR painful[tiab] OR discomfort[tiab] OR "Back Pain"[Mesh] OR "Low Back Pain"[Mesh] OR suffering[tiab] OR sufferings[tiab] OR ache[tiab] OR aches[tiab] OR "Neck Pain"[Mesh] OR sore[tiab] OR soreness[tiab] OR analgesia[tiab]
2	"spine"[MeSH Terms] OR spine[tiab] OR spinal[tiab] OR "back"[MeSH Terms] OR back[tiab] OR backache[tiab] OR backaches[tiab] OR "neck"[MeSH Terms] OR neck[tiab] OR Neckache[tiab] OR Neckaches[tiab] OR cervical[tiab] OR cervicothoracic[tiab] OR lumbar[tiab] OR "lumbosacral region"[MeSH Terms] OR lumbosacral[tiab] OR Intervertebral[tiab] OR vertebral[tiab] OR vertebrae[tiab] OR Coccyx[tiab] OR Sacrum[tiab] OR sacral[tiab] OR sacrococcygeal[tiab] OR Lumbago[tiab] OR thoracolumbar[tiab] OR "Sciatica"[Mesh] OR sciatica[tiab] OR thoracic[tiab] OR dorsalgia[tiab] OR Cervicalgia[tiab] OR Cervicalgias[tiab] OR Cervicodynia[tiab] OR Cervicodynias[tiab]
3	"virtual reality"[mesh] OR “virtual reality”[tiab] OR “virtual realities”[tiab] OR VR[tiab] OR "computer simulated environment"[tiab] OR "Augmented reality"[tiab] OR "simulated reality"[tiab] OR "simulated environment"[tiab] OR “virtual simulation”[tiab] OR “virtual technology”[tiab] OR “virtual technologies”[tiab] OR “simulation technology”[tiab] OR “simulation technologies”[tiab]
4	#1 AND #2 AND #3

Database: Embase

#	Query
1	'pain'/exp OR pain:ab,ti OR pains:ab,ti OR painful:ab,ti OR discomfort:ab,ti OR 'backache'/exp OR 'low back pain'/exp OR suffering:ab,ti OR sufferings:ab,ti OR ache:ab,ti OR aches:ab,ti OR

	'neck pain'/exp OR sore:ab,ti OR soreness:ab,ti OR analgesia:ab,ti
2	'spine'/exp OR spine:ab,ti OR spinal:ab,ti OR 'back'/exp OR back:ab,ti OR backache:ab,ti OR backaches:ab,ti OR 'neck'/exp OR neck:ab,ti OR Neckache:ab,ti OR Neckaches:ab,ti OR cervical:ab,ti OR cervicothoracic:ab,ti OR lumbar:ab,ti OR 'lumbosacral region'/exp OR lumbosacral:ab,ti OR Intervertebral:ab,ti OR vertebral:ab,ti OR vertebrae:ab,ti OR Coccyx:ab,ti OR Sacrum:ab,ti OR sacral:ab,ti OR sacrococcygeal:ab,ti OR Lumbago:ab,ti OR thoracolumbar:ab,ti OR 'sciatica'/exp OR sciatica:ab,ti OR thoracic:ab,ti OR dorsalgia:ab,ti OR Cervicalgia:ab,ti OR Cervicalgias:ab,ti OR Cervicodynia:ab,ti OR Cervicodynias:ab,ti
3	'virtual reality'/exp OR ‘virtual reality’:ab,ti OR ‘virtual realities’:ab,ti OR VR:ab,ti OR ‘computer simulated environment’:ab,ti OR ‘Augmented reality’:ab,ti OR ‘simulated reality’:ab,ti OR ‘simulated environment’:ab,ti OR ‘virtual simulation’:ab,ti OR ‘virtual technology’:ab,ti OR ‘virtual technologies’:ab,ti OR ‘simulation technology’:ab,ti OR ‘simulation technologies’:ab,ti
4	#1 AND #2 AND #3

Database: Scopus

#	Query
1	TITLE-ABS-KEY(pain OR pains OR painful OR discomfort OR “Back Pain” OR “Low Back Pain” OR suffering OR sufferings OR ache OR aches OR “Neck Pain” OR sore OR soreness OR analgesia)
2	TITLE-ABS-KEY(spine OR spinal OR back OR backache OR backaches OR neck OR Neckache OR Neckaches OR cervical OR cervicothoracic OR lumbar OR "lumbosacral region" OR lumbosacral OR Intervertebral OR vertebral OR vertebrae OR Coccyx OR Sacrum OR sacral OR sacrococcygeal OR Lumbago OR thoracolumbar OR sciatica OR thoracic OR dorsalgia OR Cervicalgia OR Cervicalgias OR Cervicodynia OR Cervicodynias)
3	TITLE-ABS-KEY("virtual reality" OR “virtual realities” OR VR OR "computer simulated environment" OR "Augmented reality" OR "simulated reality" OR "simulated environment" OR “virtual simulation” OR “virtual technology” OR “virtual technologies” OR “simulation

	technology” OR “simulation technologies”)
4	#1 AND #2 AND #3

Database: CINAHL

#	Query
1	(MH "Pain+") OR (MH "Back Pain+") OR (MH "Low Back Pain") OR (MH "Neck Pain") OR AB (pain OR pains OR painful OR discomfort OR suffering OR sufferings OR ache OR aches OR sore OR soreness OR analgesia) OR TI (pain OR pains OR painful OR discomfort OR suffering OR sufferings OR ache OR aches OR sore OR soreness OR analgesia)
2	(MH "Spine+") OR (MH "Back") OR (MH "Neck") OR (MH "Lumbosacral Plexus+") OR (MH "Sciatica") OR AB (spine OR spinal OR back OR backache OR backaches OR neck OR Neckache OR Neckaches OR "cervical" OR cervicothoracic OR lumbar OR lumbosacral OR Intervertebral OR vertebral OR vertebrae OR Coccyx OR Sacrum OR sacral OR sacrococcygeal OR Lumbago OR thoracolumbar OR sciatica OR thoracic OR dorsalgia OR Cervicalgia OR Cervicalgias OR Cervicodynia OR Cervicodynias) OR TI (spine OR spinal OR back OR backache OR backaches OR neck OR Neckache OR Neckaches OR "cervical" OR cervicothoracic OR lumbar OR lumbosacral OR Intervertebral OR vertebral OR vertebrae OR Coccyx OR Sacrum OR sacral OR sacrococcygeal OR Lumbago OR thoracolumbar OR sciatica OR thoracic OR dorsalgia OR Cervicalgia OR Cervicalgias OR Cervicodynia OR Cervicodynias)
3	(MH "Virtual Reality+") OR AB (“virtual reality” OR “virtual realities” OR VR OR "computer simulated environment" OR "Augmented reality" OR "simulated reality" OR "simulated environment" OR “virtual simulation” OR “virtual technology” OR “virtual technologies” OR “simulation technology” OR “simulation technologies”) OR TI (“virtual reality” OR “virtual realities” OR VR OR "computer simulated environment" OR "Augmented reality" OR "simulated reality" OR "simulated environment" OR “virtual simulation” OR “virtual technology” OR “virtual technologies” OR “simulation technology”

	OR “simulation technologies”))
4	#1 AND #2 AND #3

Database: PsycInfo

#	Query
1	(DE "Pain" OR DE "Aphagia" OR DE "Back Pain" OR DE "Chronic Pain" OR DE "Headache" OR DE "Myofascial Pain" OR DE "Neuralgia" OR DE "Neuropathic Pain" OR DE "Somatoform Pain Disorder") OR AB (pain OR pains OR painful OR discomfort OR suffering OR sufferings OR ache OR aches OR sore OR soreness OR analgesia OR “back pain” OR “low back pain” OR “neck pain”) OR TI (pain OR pains OR painful OR discomfort OR suffering OR sufferings OR ache OR aches OR sore OR soreness OR analgesia OR “back pain” OR “low back pain” OR “neck pain”) OR KW (pain OR pains OR painful OR discomfort OR suffering OR sufferings OR ache OR aches OR sore OR soreness OR analgesia OR “back pain” OR “low back pain” OR “neck pain”)
2	(DE "Spinal Column") OR (DE "Back (Anatomy)")) OR (DE "Neck (Anatomy)") OR AB (spine OR spinal OR back OR backache OR neck OR neckache OR neckaches OR cervical OR cervicothoracic OR lumbar OR lumbosacral OR intervertebral OR vertebral OR vertebrae OR coccyx OR sacrum OR sacral OR sacrococcygeal OR lumbago OR thracolumbar OR sciatica OR thoracic OR dorsalgia OR cervicalgia OR cervicalgias OR cervicodynia OR cervicodynias) OR TI (spine OR spinal OR back OR backache OR neck OR neckache OR neckaches OR cervical OR cervicothoracic OR lumbar OR lumbosacral OR intervertebral OR vertebral OR vertebrae OR coccyx OR sacrum OR sacral OR sacrococcygeal OR lumbago OR thracolumbar OR sciatica OR thoracic OR dorsalgia OR cervicalgia OR cervicalgias OR cervicodynia OR cervicodynias) OR KW (spine OR spinal OR back OR backache OR neck OR neckache OR neckaches OR cervical OR cervicothoracic OR lumbar OR lumbosacral OR intervertebral OR vertebral OR vertebrae OR coccyx OR sacrum OR sacral OR

	sacrococcygeal OR lumbago OR thracolumbar OR sciatica OR thoracic OR dorsalgia OR cervicalgia OR cervicalgias OR cervicodynia OR cervicodynias)
3	(DE "Virtual Reality") OR AB (“virtual reality” OR “virtual realities” OR VR OR “computer simulated environment” OR “augmented reality” OR “simulated reality” OR “simulated environment” OR “virtual simulation” OR “simulation technology” OR “simulation technologies”) OR TI (“virtual reality” OR “virtual realities” OR VR OR “computer simulated environment” OR “augmented reality” OR “simulated reality” OR “simulated environment” OR “virtual simulation” OR “simulation technology” OR “simulation technologies”) OR KW (“virtual reality” OR “virtual realities” OR VR OR “computer simulated environment” OR “augmented reality” OR “simulated reality” OR “simulated environment” OR “virtual simulation” OR “simulation technology” OR “simulation technologies”)
4	#1 AND #2 AND #3

Database: ClinicalTrials.org

#	Query
1	(virtual reality OR virtual realities OR VR OR computer simulated environment OR Augmented reality OR simulated reality OR simulated environment OR virtual simulation OR virtual technology OR virtual technologies OR simulation technology OR simulation) | (pain OR pains OR painful OR discomfort OR suffering OR sufferings OR ache OR aches OR sore OR soreness OR analgesia) AND (spine OR spinal OR back OR backache OR backaches OR neck OR Neckache OR Neckaches OR cervical OR cervicothoracic OR lumbar OR lumbosacral OR Intervertebral OR vertebral OR vertebrae OR Coccyx OR Sacrum OR sacral OR sacrococcygeal OR Lumbago OR thoracolumbar OR sciatica OR thoracic OR dorsalgia OR Cervicalgia OR Cervicalgias OR Cervicodynia OR Cervicodynias)

Appendix 2. List of excluded studies/reasons for exclusion

1. Bolte B, de Lussanet M, Lappe M (2016) Virtual reality system for the enhancement of mobility in patients with chronic back pain. Int J Child Health Hum Dev 9(3):305-314.
   Reason for exclusion: Not RCT

2. Brodbeck D, Degen M, Stanimirov M, Kool J, Scheermesser M, Oesch P, Neuhaus C (2010) Augmented feedback system to support physical therapy of non-specific low back pain. Biomedical Engineering Systems and Technologies.
   Reason for exclusion: Not RCT

3. Chen KB, Sesto ME, Ponto K, Leonard J, Mason A, Vanderheiden G, Williams J, Radwin RG (2017) Use of Virtual Reality Feedback for Patients with Chronic Neck Pain and Kinesiophobia. IEEE Trans Neural Syst Rehabil Eng 25(8):1240-1248. doi: 10.1109/TNSRE.2016.2621886
   Reason for exclusion: Not RCT

4. Citrome L (2014) Ride ‘em cowboy! The therapeutics of virtual reality technology and simulation. Int J Clin Pract 68(8):931. doi: 10.1111/ijcp.12496.
   Reason for exclusion: Not RCT

5. Diers M, Zieglgänsberger W, Trojan J, Drevensek AM, Erhardt-Raum G, Flor H (2013) Site-specific visual feedback reduces pain perception. Pain 154(6):890-896. doi: 10.1016/j.pain.2013.02.022.
   Reason for exclusion: Not RCT

6. Evans R, Bronfort G, Keefe D, Taberko A, Hanson L, Haley A, Ma H, Jolton J, Yarosh L, Keefe F, Nam J (2017) Virtual reality environments for supporting mindfulness based healing of low back pain. BMC Complement Altern Med.
   Reason for exclusion: Not RCT

7. Emory University Woodruff Health Sciences Center (2005) Emory Begins NIH Study Using Virtual Reality Therapy For Back Pain. Orthop Today 25(2):116-116.
   Reason for exclusion: Not RCT

8. France CR, Thomas JS (2018). Virtual immersive gaming to optimize recovery (VIGOR) in low back pain: A phase II randomized controlled trial. Contemp Clin Trials 69:83-91.
   Reason for exclusion: Insufficient information

9. Guarino D, La Paglia F, Daino M, Maiorca V, Zichichi S, Guccione F, Pintabona A, Wiederhold M, Riva G, Wiederhold B, La Barbera D (2017). Chronic pain treatment through Virtual Reality. J Cyber Ther Rehabil.
   Reason for exclusion: Insufficient information

10. Harvie, D.S., M. Broecker, R.T. Smith, A. Meulders, V.J. Madden, and G.L. Moseley, *Bogus visual feedback alters onset of movement-evoked pain in people with neck pain.* Psychol Sci, 2015. 26(4): p. 385-92.
    Reason for exclusion: Other intervention

11. Hitzig S, Proulx K, Fuchs A, Wolfe D, Maltais D (2014) A Nintendo Wii-based rehabilitation program for spinal cord injury: Feasibility and outcomes. J Spinal Cord Med.
    Reason for exclusion: Serious spinal pathology

12. Igna R, Ştefan S, Onac I, Onac I, Ungur RA, Szentagotai Tatar A (2014) Mindfulness-based cognitive-behavior therapy (MCBT) versus virtual reality (VR) enhanced CBT, versus treatment as usual for chronic back pain. A clinical trial. Journal of Evidence-Based Psychotherapies 14(2):229-247.
    Reason for exclusion: Not RCT

13. Jordan M, Richardson EJ (2016) Effects of Virtual Walking Treatment on Spinal Cord Injury-Related Neuropathic Pain: Pilot Results and Trends Related to Location of Pain and at-level Neuronal Hypersensitivity. Am J Phys Med Rehabil 95(5):390-396. doi: 10.1097/PHM.0000000000000417.
Reason for exclusion: Serious spinal pathology.

14. Jordan M, Richardson EJ (2016) Effects of Virtual Walking Treatment on Spinal Cord Injury-Related Neuropathic Pain. Am J Phys Med Rehabil 95(5):390-396. doi: 10.1097/PHM.0000000000000417.
Reason for exclusion: Serious spinal pathology

15. Kaufman H (2012) From where we sit: Augmented reality for an active ageing European society. Journal of Cyber Therapy and Rehabilitation 5(1):35-37.
Reason for exclusion: Not RCT

16. Kumru H, Soler D, Vidal J, Pacual-Leone A, Valis-Sole J (2010). Quantitative sensory testing and contact heat evoked potentials before and after treatment in neuropathic pain after spinal cord injury. Eur J Pain Suppl.
Reason for exclusion: Serious spinal pathology

17. Le D, Sharar S, Hoffman H, Jensen M, Uso L, Opheim E, Patterson D, Bough D, Hoffer C (2011). A pilot study demonstrating effective virtual reality analgesia in the elderly. J Pain 12(4):P79.
Reason for exclusion: Not RCT

18. Li R, Wang NH, Yan X, Wei KL (2014). Comparison of postural control between healthy subjects and individuals with nonspecific low back pain during exposure to visual stimulus. Chin Med J 127(7):1229-1234.
Reason for exclusion: Not RCT

19. Lieberman I (2010). Point of view. Spine 35(4):E113.

Reason for exclusion: Not RCT

20. Mansour KB, Palazzo C, Dorner V, Poiradeau S, Ville I, Kadri A, Klinger E (2017) How new technologies can support patients adherence to home-based exercises? International Conference on Virtual Rehabilitation.
Reason for exclusion: Conference article

21. Mihajlovic Z, Popovic S, Brkic K, Cosic K (2017). A system for head-neck rehabilitation exercises based on serious gaming and virtual reality. Multimed Tools Appl 77(15):19113-19137.
Reason for exclusion: Not RCT

22. Ommaya AK, Adams KM, Allman RM, Collins EG, Cooper RA, Dixon CE, Fishman PS, Henry JA, Kardon R, Kerns RD, Kupersmith J, Lo A, Macko R, McArdle R, McGlinchey RE, McNeil MR, O'Toole TP, Peckham PH, Tuszynski MH, Waxman SG, Wittenberg GF (2013). Opportunities in rehabilitation research. J Rehabil Res Dev 50(6):vii-xxxii.
Reason for exclusion: Not RCT

23. Penn T, Browning W, France C, Hardee G, Zielke M, Trost Z (2017). Attitudes toward a virtual reality physical activity intervention among veterans with chronic low back pain. J Pain 18:S1-S1.
Reason for exclusion: Not RCT

24. Pozeg P, Palluel E, Ronchi R, Solcà M, Al-Khodairy AW, Jordan X, Kassouha A, Blanke O (2017). Virtual reality improves embodiment and neuropathic pain caused by spinal cord injury. Neurology 89(18):1894-1903.
Reason for exclusion: Serious spinal pathology

25. Romano DM (2005). Virtual reality therapy. Dev Med Child Neurol 47(9):580.
Reason for exclusion: Not RCT

26. Roosink M, McFadyen BJ, Hébert LJ, Jackson PL, Bouyer LJ, Mercier C (2015). Assessing the perception of trunk movements in military personnel with chronic non-specific low back pain using a virtual mirror. PLoS ONE 10(3):e0120251
Reason for exclusion: Not RCT

27. Roosink M, Robitaille N, Jackson PL, Bouyer LJ, Mercier C (2016). Interactive virtual feedback improves gait motor imagery after spinal cord injury: An exploratory study. Restor Neurol Neurosci 34(2):227-235.
Reason for exclusion: Serious spinal pathology

28. Salisbury DB, Parsons TD, Monden KR, Trost Z, Driver SJ (2016). Brain-computer interface for individuals after spinal cord injury. Rehabilitation Psychology 61(4):435-441.
Reason for exclusion: Serious spinal pathology

29. Sarig Bahat H, Chen X, Reznik D, Kodesh E, Treleaven J (2015). Interactive cervical motion kinematics: Sensitivity, specificity and clinically significant values for identifying kinematic impairments in patients with chronic neck pain. Man Ther 20(2):295-302.
Reason for exclusion: Other intervention, No measurement on the effectiveness of VR therapy.

30. Sarig Bahat H, Croft K, Hoddinott A, Carter C, Treleaven J (2016). Remote kinematic e-training for patients with chronic neck pain, a randomised controlled trial. Man Ther 25:e35.
Reason for exclusion: Preliminary mid-trial results

31. Soler D, Kumru H, Vidal J, Fregni F, Tormos JM, Navarro X, Leone AP (2010). Transcranial direct current stimulation (TDCS) and virtual reality (VR) techniques for treatment neuropathic central pain in spinal cord injury (NP-SCI). Eur J Pain Suppl 4(1):105-106.

Reason for exclusion: Serious spinal pathology

32. Suh HR, Lee SY (2018). A change in the size of the abdominal muscles and balance ability after virtual reality exercise in the elderly with chronic low back pain. Indian J Public Health Res Dev 9(9):1054-1059.
Reason for exclusion: Insufficient information

33. Thomas JS, France CR, Applegate ME, Leitkam ST, Walkowski S (2016). Feasibility and Safety of a Virtual Reality Dodgeball Intervention for Chronic Low Back Pain: A Randomized Clinical Trial. J Pain 17(12):1302-1317.
Reason for exclusion: Insufficient information

34. Trost Z, France C, Zielke MA, Hardee GM (2018). Wednesday, September 26, 2018 2:00 PM – 3:00 PM Integrating Technology into Practice: 2015 Research Grant: Development of a virtual reality graded exposure intervention for chronic low back pain: initial findings and future directions. Spine J
Reason for exclusion: Not RCT

35. Trost Z, Nowlin L, Guck A, Madi D, Davis M (2015). Exploring the role of pain-related fear and catastrophizing in response to a virtual reality gaming intervention for chronic low back pain. J Pain.
Reason for exclusion: Not RCT

36. Trost Z, Zielke M, Guck A, Nowlin L, Zakhidov D, France CR, Keefe F (2015). The promise and challenge of virtual gaming technologies for chronic pain: the case of graded exposure for low back pain. Pain Management 5(3):197-206.
Reason for exclusion: Not RCT

37. Villiger M, Bohli D, Kiper D, Pyk P, Spillmann J, Meilick B, Curt A, Hepp-Reymond MC, Hotz-Boendermaker S, Eng K (2013). Virtual reality-augmented neurorehabilitation

improves motor function and reduces neuropathic pain in patients with incomplete spinal cord injury. Neurorehabil Neural Repair 27(8):675-683.
Reason for exclusion: Serious spinal pathology

38. Wall TE (2015). The effects of the Nintendo™ Wii Fit on functional gait, balance and quality of life in ambulatory individuals with incomplete spinal cord injury. Dissertation Abstracts International: Section B: The Sciences and Engineering 76(2-B)
Reason for exclusion: Serious spinal pathology

Appendix 3. List of ongoing studies

1. Poiraudeau S (2015). Analgesic Effect of a Prototype Device of Virtual Reality in a Population of Patients With Chronic Low Back Pain. **ClinicalTrials.gov: NCT01407653.**

2. Kamil OH (2019). Effectiveness of Virtual Reality in Patients With Chronic Neck Pain. **ClinicalTrials.gov: NCT04014998.**

3. Cetin H (2019). Physical Therapy Using Virtual Reality/Augmented Reality. **ClinicalTrials.gov: NCT03874507.**

4. Binder D (2019). The Use of Virtual Reality for Lumbar Pain Management in an Outpatient Spine Clinic. **ClinicalTrials.gov: NCT03819907.**

5. Matheve T. Virtual Reality and Pain Perception During Exercises for Patients With Chronic Non-specific Low Back Pain. **ClinicalTrials.gov: NCT02679300.**

6. Iannaccone S. Virtual Reality Rehabilitation in Neck Pain Subjects. **ClinicalTrials.gov: NCT03987334.**

7. Bahat AS. VR Training for Pilots With Neck Pain. **ClinicalTrials.gov: NCT02979041**

Table 1. Characteristics of included studies.

Author	Participants	Pain Duration and Spine Region	Outcome measure	Intervention	Control	Number of Sessions / Duration of Intervention	Follow-up from Baseline
Kim et al. (2014) [33]	30 hospital patients; mean age, 47.4 y; 100% female	Subacute and chronic LBP	VAS pain scale, ODI, RMDQ, FABQ	VR-based Nintendo Wii Fit yoga program	Trunk stabilizing exercises + standard of care physical therapy	3, 30-minute sessions/week for 4 weeks	4 weeks
Park et al. (2013) [35]	24 tire factory workers; mean (SD) age, 44.3 (5.4) y	Chronic LBP	VAS pain scale, RAND-36, SLS	VR-based Nintendo Wii sports program + control treatment	Physical agent modalities, interferential current therapy, + deep heat with ultrasound	3, 30-minute sessions/week for 8 weeks	8 weeks
Rezaei et al. (2019) [34]	44 participants; mean (SD) age, 33.71 (9.7) y; 52% male	Chronic neck pain	VAS pain scale, NDI, YBT	VR-based computer game	Conventional proprioception training	8, 21-minute sessions over 4 weeks	4 weeks, 9 weeks
Sarig Bahat et al. (2018)	90 participants; mean (SD) age,	Chronic neck pain	VAS pain scale, NDI,	VR airplane flight via headset	Kinematic training via head-	4, 5-minute sessions/day, 4	4 weeks, 3 months

[38]	47.7 (6.4) y; 30% male		EQ-5D, GPE, TSK		mounted laser	times/week for 4 weeks	
Sarig Bahat et al. (2015) [36]	32 participants; mean (SD) age, 40.9 (13.4)	Chronic neck pain	VAS pain scale, NDI, GPE, SLS, TSK	VR airplane flight via headset + kinematic training via head-mounted laser	Kinematic training via head-mounted laser	4-6, 30-minute sessions over 5 weeks	5 weeks, 3 months
Yilmaz et al. (2017) [37]	44 patients referred by physicians for PT; mean (SD) age, 49.6 (7.45) y; 36% male	Subacute and chronic LBP	VAS pain scale, ODI, NHP, SLS, TSK	VR-based walking program + standard of care physical therapy	Standard of care physical therapy	5 sessions/week for 2 weeks, session time unclear	2 weeks
Yoo et al. (2014) [39]	47 volunteers from a local hospital; mean (SD) age, 20.6 (1.4) y; 100% male	Chronic LBP	VAS pain scale	VR-based horse riding simulation	No intervention	3, 10-40 minute sessions/week for 8 weeks	8 weeks

SD: standard deviation, y: years, PT: physical therapy, VR: virtual reality, VAS: visual analog scale, RAND-36: RAND Corporation health-related quality of life survey, EQ-5D: EuroQol Group health-related quality of life instrument, SLS: single leg stance, LBP: low

back pain, ODI: Oswestry Disability Index, RMDQ: Roland Morris Disability Questionnaire, FABQ: Fear-Avoidance Beliefs Questionnaire, NDI: Neck Disability Index, GPE: Global Perceived Effect, TSK: Tampa Scale for Kinesiophobia, NHP: Nottingham Health Profile, LSE: lumbar stabilization exercise. Higher scores on the VAS pain scale indicate greater pain levels. Higher scores on the RAND-36 represent greater functioning. Higher scores on the EQ-5D represent greater health-related quality of life. Higher scores on the ODI, RMDQ, and NDI represent greater disability. Higher scores on the FABQ and TSK represent more strongly held fear-avoidance beliefs and kinesiophobia. Higher scores on the GPE represent greater perceived improvements. Higher scores on the NHP represent poorer perceived health status. Higher scores on SLS indicate better balance.

Table 2. Summary of findings for neck pain

Comparison: Virtual reality (Head-mounted display) versus kinematic training for chronic neck pain				
Outcome (measure)	**N. of participants (n. of studies)**	**Mean Difference (95% CI), p-value**	**Interpretation**	**Quality of evidence (GRADE)**
Short-term follow-up				
Pain intensity (VAS 0-100)	122 participants (2 studies [36, 38])	MD = -9.08 (-21.84 to 3.67), p=0.18	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Disability (NDI 0-50, converted to 100)	122 participants (2 studies [36, 38])	MD = -2.24 (-6.38 to 1.90), p=0.29	No clinically important effect	⊕⊕⊖⊖ low[1,2]
GPE (-5 - +5, converted to 100)	122 participants (2 studies [36, 38])	MD = 4.88 (2.51 to 7.26), p<0.01*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Fear of movement (TSK 0-68, converted to 100)	122 participants (2 studies [36, 38])	MD = -1.75 (-6.78 to 3.28), p=0.49	No clinically important effect	⊕⊕⊖⊖ low[1,2]
General Health Status (EQ-5D 0-100)	90 participants (1 study [38])	MD = 9.54 (1.66 to 17.42), p=0.02*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Balance (SLS, seconds)	32 participants (1 study [36])	MD = 1.59 (-9.11 to 12.29), p=0.77	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Satisfaction (-5 - +5, converted to 100)	122 participants (2 studies [36, 38])	MD = 6.26 (3.90, 8.62), p<0.01*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Intermediate-term follow-up				
Pain intensity (VAS 0-100)	122 participants (2 studies [36, 38])	MD = -6.90 (-16.05 to 2.25), p=0.14	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Disability (NDI 0-50, converted to 100)	122 participants (2 studies [36, 38])	MD = -4.30 (-10.57 to 1.96), p=0.18	No clinically important effect	⊕⊕⊖⊖

				low[1,2]
GPE (-5 - +5, converted to 100)	122 participants (2 studies [36, 38])	MD = 12.27 (-3.89, 28.43), p=0.14	No clinically important effect	⊕⊖⊖⊖ very low[1,2,3]
Fear of movement (TSK 0-68, converted to 100)	122 participants (2 studies [36, 38])	MD = -0.84 (-5.39 to 3.70), p=0.72	No clinically important effect	⊕⊕⊖⊖ low[1,2]
General Health Status (EQ-5D, 0-100)	90 participants (1 study [38])	MD = 7.43 (0.25 to 14.61), p=0.04*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Balance (SLS, seconds)	32 participants (1 study [36])	MD = 15.99 (3.48 to 28.50), p=0.01*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Comparison: Virtual Reality (motion-detecting computer game) versus conventional proprioceptive training				
Outcome (measure)	**N. of participants (n. of studies)**	**Mean Difference (95% CI), p-value**	**Interpretation**	**Quality of evidence (GRADE)**
Short-term follow-up				
Pain intensity (VAS 0-100)	44 participants (1 study [34])	MD = -8.88 (-14.20 to -3.56), p<0.01*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Disability (NDI 0-50, converted to 100)	44 participants (1 study [34])	MD = -7.14 (-10.51 to -3.77), p<0.01*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Balance (YBT, centimeters)	44 participants (1 study [34])	MD = -4.02 (-8.87 to 0.83), p=0.10	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Intermediate-term follow-up				
Pain intensity (VAS 0-100)	44 participants (1 study [34])	MD = -10.60 (-17.56 to -3.64), p<0.01*	**Clinically important effect**	⊕⊕⊖⊖ low[1,2]
Disability (NDI 0-50, converted to 100)	44 participants (1 study [34])	MD = -9.68 (-13.90 to-5.46), p<0.01*	No clinically important	⊕⊕⊖⊖ low[1,2]

			effect	
Balance (YBT, centimeters)	44 participants (1 study [34])	MD = -2.74 (-8.49 to 3.01), p=0.35	No clinically important effect	⊕⊕⊖⊖ low[1,2]

Primary outcomes are highlighted in gray.

VAS: Visual Analog Scale, NDI: Neck Disability Index, GPE: Global Perceived Effect, TSK: Tampa Scale for Kinesiophobia, EQ-5D: EuroQol Group Health-Related Quality of Life instrument, SLS: Single leg stance, CI: confidence interval.

Short-term: Closest to 4 weeks, Intermediate-term: closest to 6 months

GRADE (Grading of Recommendations Assessment, Development, and Evaluation):

High quality: Further research is unlikely to change confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and might change the estimate

Low quality: Further research is likely to have an important effect on confidence in estimate of effect and is likely to change the estimate

Very low quality: Little confidence in the effect estimate

*: Statistical significance

[1]Downgraded one level due to limitations in the design/implementation

[2]Downgraded one level due to imprecision

[3]Downgraded one level due to inconsistency of result**s**

Table 3. Summary of findings for low back pain (LBP)

Comparison: Virtual reality (Nintendo Wii system) versus lumbar stabilization exercises for subacute and chronic LBP				
Outcome (measure)	**N. of participants (n. of studies)**	**Mean Difference (95% CI), p-value**	**Interpretation**	**Quality of evidence (GRADE)**
Short-term follow-up				
Pain intensity (VAS 0-100)	24 participants (1 study [35]), chronic LBP	MD = 10.00 (0.34 to 19.66), p=0.04*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Pain intensity (VAS 0-100)	30 participants (1 study [33]), subacute/chronic LBP	MD = -23.60 (-34.75 to -12.45), p<0.01*	**Clinically important effect**	⊕⊕⊖⊖ low[1,2]
Disability (RMDQ 0-24, converted to 100)	30 participants (1 study [33]), subacute, chronic LBP	MD = -21.59 (-38.65 to -4.53), p=0.01*	**Clinically important effect**	⊕⊕⊖⊖ low[1,2]
General health status (RAND-36, 0-100)	24 participants (1 study [35]), chronic LBP	MD = -8.75 (-24.32 to 6.82), p=0.27	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Balance (SLS)	24 participants (1 study [35]), chronic LBP	MD = -0.75 (-4.35 to 2.85), p=0.68	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Fear of movement (FABQ 0-96, converted to 100)	30 participants (1 study [33]), subacute/chronic LBP	MD = -23.36 (-34.06 to -12.66), p<0.01*	**Clinically important effect**	⊕⊕⊖⊖ low[1,2]
Comparison: Virtual reality (Nintendo Wii system) versus physical agent modalities for chronic LBP				
Outcome (measure)	**N. of participants (studies)**	**Mean Difference (95% CI), p-value**	**Interpretation**	**Quality of evidence**

Short-term follow-up				
Pain intensity (VAS 0-100)	24 participants (1 study [35]), chronic LBP	MD = 1.20 (-8.67 to 11.07), p=0.81	No clinically important effect	⊕⊕⊖⊖ low[1,2]
General health status (RAND-36, 0-100)	24 participants (1 study [35]), chronic LBP	MD = -3.75 (-21.87 to 14.37), p=0.68	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Balance (SLS)	24 participants (1 study [35]), chronic LBP	MD = -0.13 (-3.73 to 3.47), p=0.94	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Comparison: Virtual reality (Virtual walking program) versus conventional physical therapy for chronic LBP				
Outcome (measure)	**N. of participants (studies)**	**Mean Difference (95% CI), p-value**	**Interpretation**	**Quality of evidence**
Short-term follow-up				
Pain intensity (VAS 0-100)	44 participants (1 study [37]), chronic LBP	MD = -23.80 (-39.84 to -7.76), p<0.01*	**Clinically important effect**	⊕⊕⊖⊖ low[1,2]
Disability (ODI 0-50, converted to 100)	44 participants (1 study [37]), chronic LBP	MD = -4.15 (-8.89 to 0.59), p=0.09	No clinically important effect	⊕⊕⊖⊖ low[1,2]
General health status (NHP 0-100)	44 participants (1 study [37]), chronic LBP	MD = 55.16 (-11.96 to 122.28), p=0.11	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Balance (SLS)	44 participants (1 study [37]), chronic LBP	MD = 12.38 (-3.99 to 28.75), p=0.14	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Fear of movement (TSK 0-68, converted to 100)	44 participants (1 study [37]), chronic LBP	MD = -9.14 (-11.97 to -6.31), p<0.01*	No clinically important effect	⊕⊕⊖⊖ low[1,2]
Comparison: Virtual reality (Horse-riding simulator) versus no treatment for chronic LBP				
Outcome (measure)	**N. of participants (studies)**	**Mean Difference (95% CI), p-value**	**Interpretation**	**Quality of evidence**

Short-term follow-up				
Pain intensity (VAS 0-100)	47 participants (1 study [39]), chronic LBP	MD (reported in delta%) = -16.77 (-42.73 to 9.19), p<0.21	No clinically important effect	⊕⊕⊖⊖ low[1,2]

Primary outcomes are highlighted in gray.

VAS: Visual Analog Scale, ODI: Oswestry Disability Index, RMDQ: Roland Morris Disability Questionnaire, RAND-36: RAND Corporation Health-Related Quality of Life Survey, SLS: Single Leg Stance, FABQ: Fear-Avoidance Beliefs Questionnaire, TSK: Tampa Scale for Kinesiophobia, NHP: Nottingham Health Profile, CI: confidence interval

GRADE (Grading of Recommendations Assessment, Development, and Evaluation):

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Low quality: Further research is likely to have an important effect on confidence in estimate of effect and is likely to change the estimate

Very low quality: Little confidence in the effect estimate

*: Statistical significance

[1]Downgraded one level due to limitations in the design/implementation

[2]Downgraded one level due to imprecision

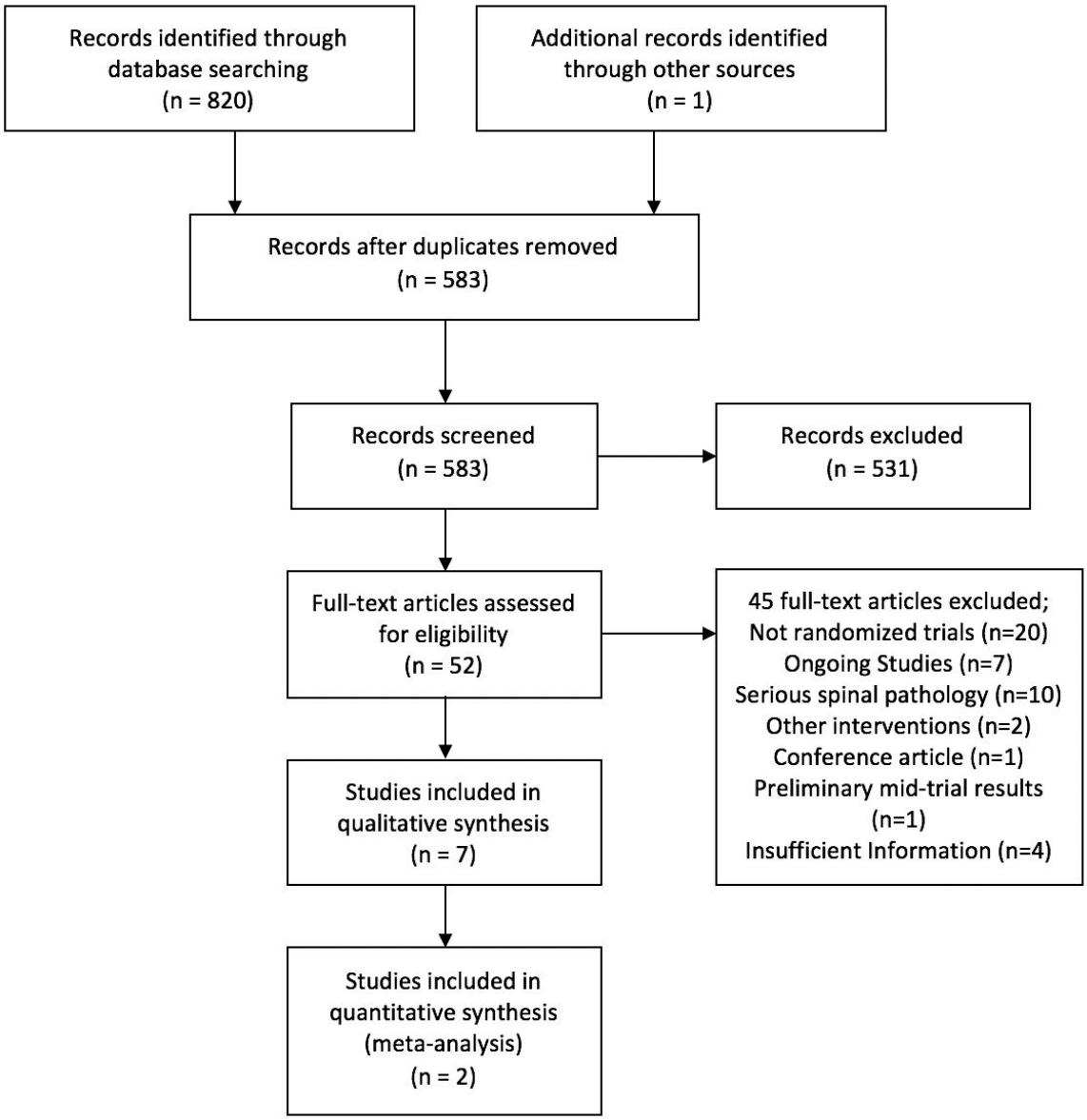

Figure 1. Flow diagram of review process

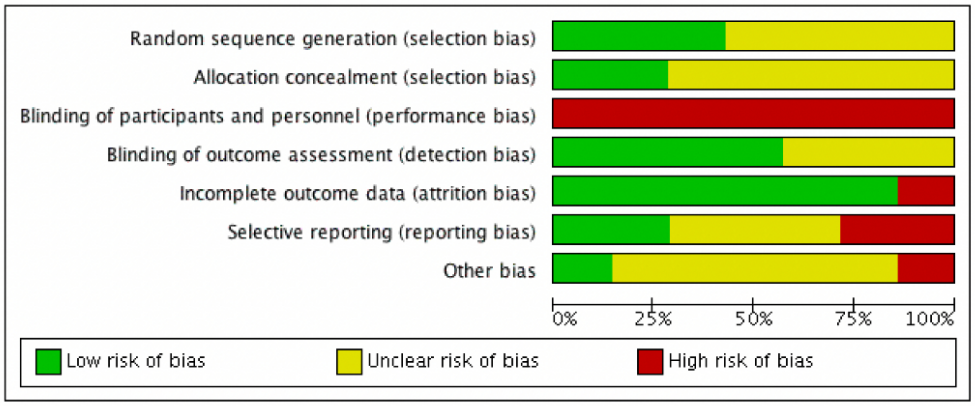

Figure 2 A. Cochrane risk of bias graph for included studies

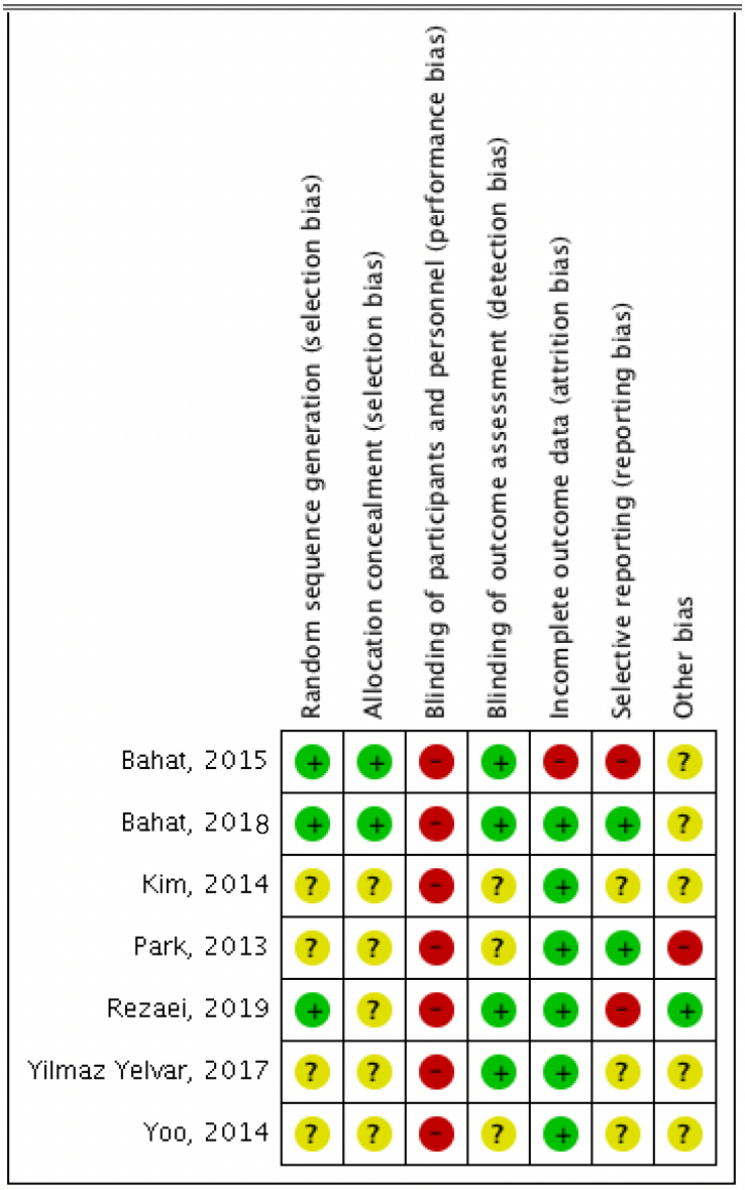

Figure 2 B. Cochrane risk of bias summary for included studies

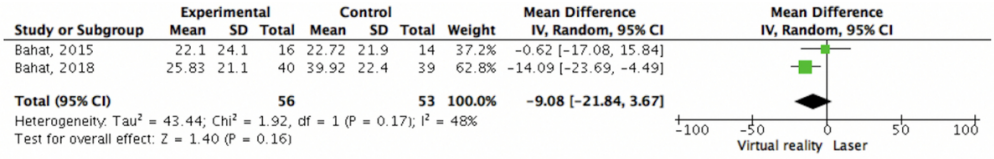

Figure 3 A. Outcome: Pain intensity at short-term follow up

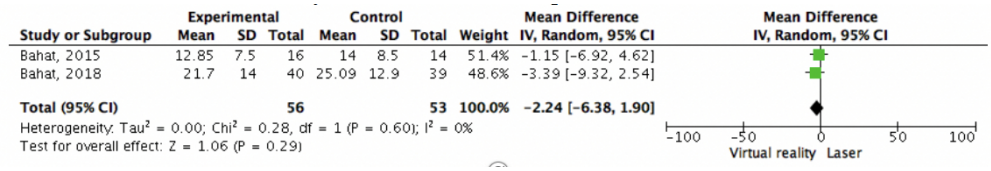

Figure 3 B. Outcome: Disability at short-term follow up

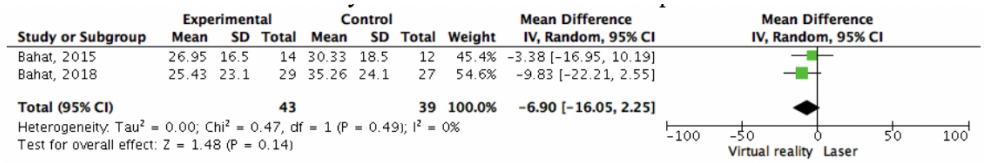

Figure 3 C. Outcome: Pain intensity at intermediate-term follow up

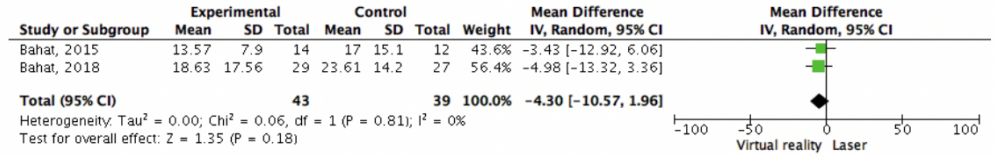

Figure 3 D. Outcome: Disability at intermediate-term follow up

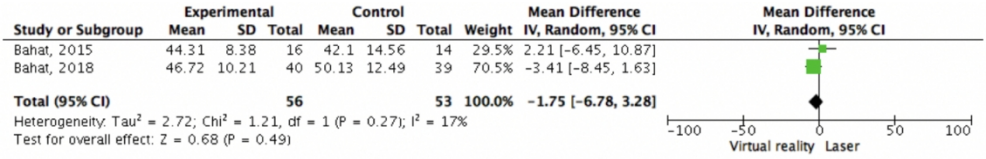

Figure 4 A. Outcome: Fear of movement at short-term follow up

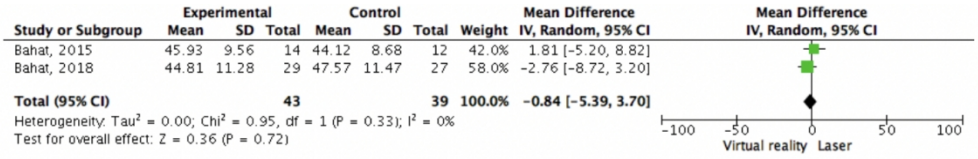

Figure 4 B. Outcome: Fear of movement at intermediate-term follow up

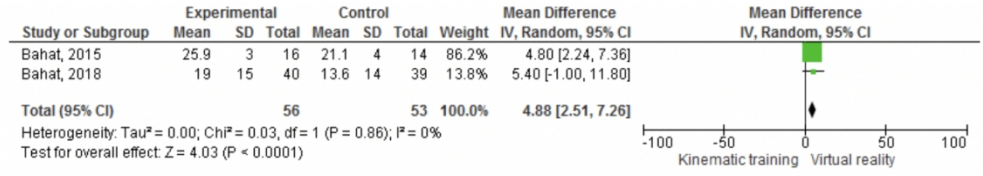

Figure 4 C. Outcome: Global perceived effect at short-term follow

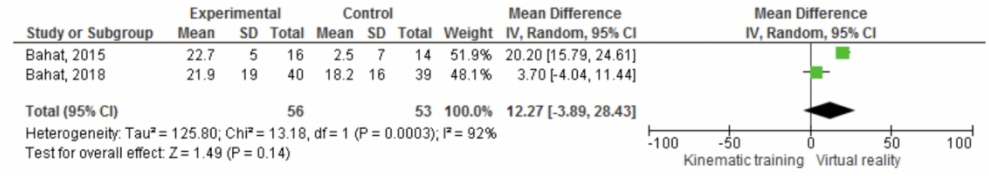

Figure 4 D. Outcome: Global perceived effect at intermediate-term follow up

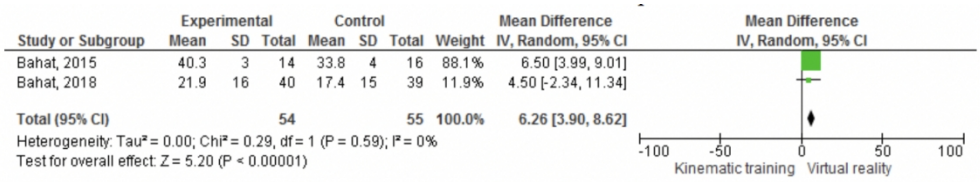

Figure 4 E. Outcome: Patient Satisfaction at short-term follow up