

Review

Virtual Reality Therapy for the Management of Chronic Spinal Pain: Systematic Review and Meta-Analysis

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Abstract

Background: The effectiveness of virtual reality (VR) therapy in adults with chronic spinal pain (CSP) is unclear.

Objective: This study was conducted to compare the effectiveness of VR therapy and other therapies in adults with CSP, especially patients with inflammation-related pain.

Methods: PubMed, Web of Science, Cochrane Library, Embase, and CINAHL databases were searched up to November 11, 2023. Randomized controlled trials (RCTs) comparing adults with CSP receiving VR therapy with those receiving other therapies were included. The trial registration platform as well as the reference lists of included studies and previous systematic reviews and meta-analyses were manually searched. Two independent reviewers performed study selection, data extraction, risk-of-bias assessment, and evaluation of the quality of the evidence. The weighted mean difference (WMD) was used as the effect size used to synthesize the outcome measure.

Results: In total, 16 RCTs involving 800 participants were included in this meta-analysis. The pooled data from 15 (94%) RCTs including 776 (97%) participants showed that VR therapy was superior in improving pain intensity (WMD=-1.63, 95% CI -2.11 to -1.16, $P<.001$, $I^2=90%$) and reducing inflammatory markers, including C-reactive protein (WMD=-0.89, 95% CI -1.07 to -0.70, $P<.001$, $I^2=0%$), tumor necrosis factor-alpha (WMD=-6.60, 95% CI -8.56 to -4.64, $P<.001$, $I^2=98%$), and interleukin-6 (WMD=-2.76, 95% CI -2.98 to -2.53, $P<.001$, $I^2=0%$). However, no significant differences were found in terms of the spinal range of motion (ROM), disability level, or fear of movement. In addition, 10 (63%) of the included RCTs had a high risk of bias.

Conclusions: VR therapy may be an effective and safe intervention for reducing symptoms in patients with CSP, as it is shown to exert significant analgesic effects and beneficial improvements in inflammatory factor levels. However, this approach may not have significant effects on the spinal ROM, disability level, or fear of movement. Notably, the quality of the evidence from the RCTs included in this study ranged from moderate to low. Therefore, we recommend that readers interpret the results of this study with caution.

Trial Registration: PROSPERO CRD42022382331; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=382331

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KEYWORDS

virtual reality; chronic spinal pain; inflammation-related pain; systematic review; meta-analysis

Introduction

Chronic spinal pain (CSP), which most commonly includes chronic low back pain (CLBP) and chronic neck pain (CNP), is the leading cause of years with disability worldwide [1,2] and constitutes the most frequent reason for patients to seek medical care in any given year. The lifetime prevalence of low back pain (LBP) is 84%; more specifically, the lifetime prevalence of CLBP is 23%, and LBP accounts for approximately 11%-12% of cases of disability [3]. CSP is recognized as a biopsychosocial syndrome [4]. Prolonged pain can lead to anxiety, depression, and other negative emotions and is particularly significant in patients with CSP, as it is associated with decreased quality of sleep and reduced physical activity, thus placing tremendous strain on health care systems and world economies [5].

Previous studies have reported that an intervertebral disc undergoes aging or pathological changes in the adjacent region in patients with CSP, exposing cells within the nucleus pulposus to macrophages, resulting in an inflammatory response that might trigger pain [6,7]. The guidelines recommend that nonsteroidal anti-inflammatory drugs (NSAIDs) be the primary choice for patients with chronic pain [8]. However, compared with a placebo, NSAIDs can reduce CSP by controlling the level of inflammation but do not achieve clinically important efficacy [9]. Additionally, long-term use may be associated with adverse effects (eg, gastrointestinal reactions, hepatic and renal damage, and cardiovascular risk) [10]. Several studies have shown that conventional nonpharmacological therapies, such as spinal manipulation, acupuncture, exercise therapy, yoga, and cognitive-behavioral therapy, are beneficial for reducing CSP and improving psychological symptoms but have limited effects (small to moderate) [11-14]. Effective cognitive-behavioral therapies are not widely accessible due to the reliance on therapist experience, and the long-term effectiveness of these therapies remains unclear [15]. Notably, the majority of patients with CSP have goals of pain management (using ongoing care) rather than “curing” (care with a specific end) for their therapeutic care because of the complexity of the causes of chronic pain [16]. Thus, pain management is as important as the control of inflammation levels for patients with CSP. There is an urgent need for an alternative analgesic nonpharmacological and anti-inflammatory strategy for patients with CSP.

Virtual reality (VR) is typically characterized by low cost, easy availability, reusability, and personalized customization; VR therapy has been used as an alternative approach for pain management in various populations, such as individuals with spinal cord injuries, burns, and phantom limb pain [17-19]. VR can be categorized into 2 types: nonimmersive virtual reality (NIVR) and immersive virtual reality (IVR). NIVR is managed using a computer or console gaming system and a 2D interface device (mouse, keyboard, or gamepad, joystick), and patients do not need to be fully immersed in a virtual environment for experience [20]. With the use of professional equipment,

hardware, and configuration of the corresponding software, IVR can mimic reality by enabling the user to interact with the virtual environment [21]. A recent study demonstrated that regular exercise with the use of VR might be related to a decrease in inflammation in participants undergoing chronic hemodialysis [22], and inflammatory arthritis–targeting innovative teaching approaches based on VR technology are considered feasible [23]. There is limited evidence regarding the beneficial effects of VR therapy on pain in patients with CNP [24] and CLBP [25,26]; furthermore, there is insufficient focus on inflammatory factors. Therefore, this study aimed to investigate the potential efficacy of VR in reducing pain intensity and the levels of inflammatory factors in patients with CSP, thereby providing an updated summary of the existing evidence.

Methods

Study Protocol and Registration

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The PRISMA checklist is given in [Multimedia Appendix 1](#). The study protocol was registered in the PROSPERO database (CRD42022382331). The *Cochrane Handbook for Systematic Reviews of Interventions* (version 5.1.0) was followed [27].

Search Strategy

Search Sources

PubMed, Web of Science, Cochrane Library, Embase, and CINAHL electronic databases were searched from inception to November 11, 2023, to identify relevant studies. The reference lists of the included studies, as well as systematic reviews and meta-analyses that examined the efficacy of VR in patients with CSP, were manually searched for additional eligible studies. The trial registration platform ClinicalTrials was also searched for ongoing studies that reported sufficient data on the efficacy of VR for CSP.

Search Terms

The studies on VR for CSP were identified by formulating appropriate search terms. These terms were selected based on the target population (spinal pain, neck pain, thoracic pain, back pain, LBP, sacral pain, and intervertebral disc pain), target intervention (eg, VR), and target study design (eg, randomized controlled trial [RCT]). The detailed search strategy is shown in [Multimedia Appendix 2](#).

Study Eligibility Criteria

The inclusion criteria were as follows:

- Participants: adults older than 18 years with chronic pain (more than 12 weeks) in the spinal region were included, except those who were receiving analgesic medication and who had cancer-related pain or neuropathic pain (eg, neuropathic pain after spinal cord injury, herniated disc with compression, sciatica, or lumbosacral radiculitis).

- Intervention: VR therapy.
- Comparisons: sham stimulation, usual care, and conventional treatment.
- Outcomes: pain intensity, inflammatory markers (eg, C-reactive protein [CRP], tumor necrosis factor-alpha [TNF- α], and interleukin [IL]-2, IL-4, and IL-6), fear of movement, spinal range of motion (ROM), and disability level.
- Study design: RCT.

No restrictions were imposed on language or publication date.

Study Selection

The retrieved studies were imported into Endnote X9 software (Clarivate), which was used to eliminate duplicate studies. Two independent reviewers (authors TTZ and FW) performed the initial screening of the literature by reading the titles and abstracts of all retrieved studies, and studies that did not meet the inclusion criteria were excluded. Next, the full texts of the remaining studies were screened. Any disagreements were resolved by negotiation and discussion with a third reviewer (author XZ).

Data Extraction

Two independent reviewers (authors FW and XL) extracted detailed information, including the name of the first author, the year and country of publication, the language of publication, study design, the number of included subjects (% female), diagnosis, and outcome indicators. Information about the characteristics of the interventions, including dose, frequency, and duration, was also collected for both the VR group and the control group. The sample size and mean (SD) of the outcome indicators in each group were collected. When the same group of participants was reported in different studies, the group with the largest sample size was selected for inclusion in this review to avoid duplicate publications [28]. For information that could not be confirmed, the authors were contacted by email. The 2 reviewers cross-checked the data at the end of the extraction, and any disagreements were resolved by negotiation.

Risk-of-Bias Assessment

The methodological quality of the included studies was independently assessed by 2 reviewers (authors XL and ZFH) using the Cochrane Risk of Bias tool, and the studies were classified as having a low, unclear, or high risk of bias [29]. Disagreements were resolved by consulting a third reviewer (author QD). The Egger test and funnel plots generated with Stata 14.0 software (StataCorp) were used to evaluate potential publication bias. The trim-and-fill method was used to adjust for funnel plot asymmetry due to publication bias [30].

Sensitivity analyses were performed by removing each study separately to assess the robustness of the results [29]. The overall strength of the evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) criteria [31].

Meta-Analysis and Subgroup Analysis

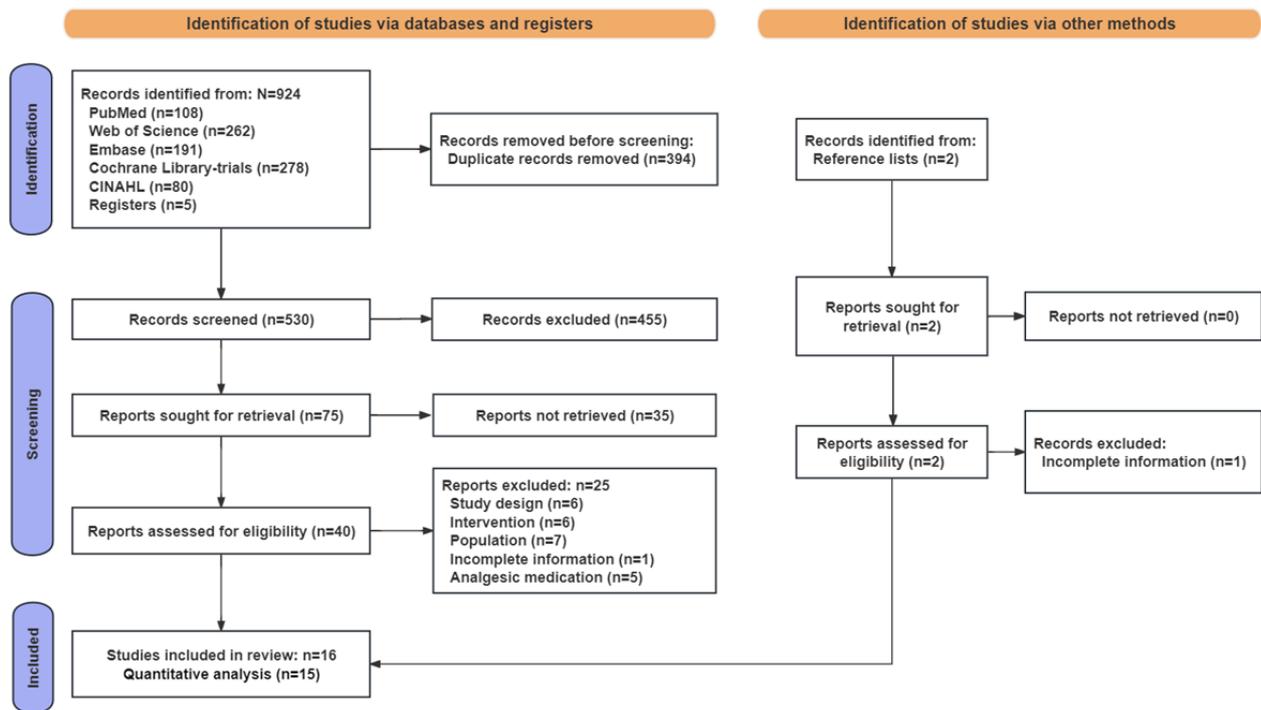
This systematic review and meta-analysis were performed using Review Manager software 5.4 (Informer Technologies) and Stata 14.0 software. Heterogeneity was tested using the I^2 statistic. A fixed effects model was selected for the outcome indicators if $I^2 < 50\%$, while a random effects model was used when there was significant statistical heterogeneity ($I^2 > 50\%$, $P < .05$). The effect size used to synthesize the outcome measure was the weighted mean difference (WMD). Three subgroup analyses were performed to explore the possible causes of heterogeneity among the studies: the region of CSP (CNP vs CLBP), VR types (IVR vs NIVR), and treatment duration (< 4 weeks vs ≥ 4 weeks).

Results

Search Results

A total of 924 records were obtained from the 5 databases and the trial registration platform. A total of 394 (42.6%) duplicates were identified and removed using Endnote X9 software. After screening the titles and abstracts, 40 (7.5%) of the remaining 530 RCTs were retained, and 490 (92.5%) were excluded for the following reasons: (1) the study population included patients without CSP, (2) the intervention did not use VR therapy, (3) the type of study was a non-RCT, (4) the information was incomplete, and (5) the patients also received analgesic medication. Of the 40 studies, 15 (38%) were retained after reading the full text and 25 (62%) were excluded for the following reasons: (1) the study population included patients without CSP, (2) the intervention did not use VR therapy, (3) the type of study was a non-RCT, (4) the information was incomplete, and (5) the patients also received analgesic medication. Two additional RCTs were retrieved from the reference lists of the included studies. One RCT was retained after the full text was read, and the other was excluded due to incomplete information. A total of 16 studies were included in this review, 15 (94%) of which reported sufficient data (eg, mean [SD], sample size) on the analgesic effect of VR for CSP. Therefore, 15 studies were included in the meta-analysis. The PRISMA flowchart of selecting the included studies is shown in Figure 1.

Figure 1. PRISMA flowchart: database and clinical trial register search and other sources. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis.



The CSP reported in the included studies included CLBP [32-43] and CNP [44-47]. All patients had chronic pain that persisted for more than 3 months. The sample size varied from 8 to 90

participants, and the mean age ranged from 18 to 85 years. The characteristics of all the studies are summarized in Table 1.

Table 1. Characteristics of the included studies [32-47].

First author	Patient characteristics			Outcome measures	Time points	Dropout rate (%)	Country, language
	Participants, n (% female)	Age (years), mean (SD)	Diagnosis				
Garcia et al [32]	T ^a : 179 I ^b : 89 (75) C ^c : 90 (78)	I: 51.5 (13.5) C: 51.4 (12.9)	CLBP ^d	DVPRS ^e , Pain Catastrophizing Scale (PCS), 8-item Chronic Pain Acceptance Questionnaire (CPAQ-8)	Baseline, -7, 0, 4, 7, 11, 14, 18, 21, 25, 28, 32, 35, 39, 42, 46, 49, 53, 56 days	I: 0 C: 0	United States, English
Nambi et al [33]	T: 60 I (VR ^f): 20 I (core stabilization [CS]): 20 C: 20	I (VR): 21.45 (1.50) I (CS): 21.39 (1.40) C: 20.97 (1.50)	CLBP	NPRS ^g , quality of life (physical fitness index)	Baseline, 4 weeks, 8 weeks, 6 months	I (VR): 0.05 I (CS): 0.05 C: 0	Saudi Arabia, English
Nambi et al [34]	T: 45 I (VR): 15 I (isokinetic training [IKT]): 15 C: 15	I (VR): 20.23 (1.60) I (IKT): 21.25 (1.20) C: 20.78 (1.60)	CLBP	NPRS	Baseline, 4 weeks	I (VR): 0 I (IKT): 0 C: 0	Saudi Arabia, English
Yalfani et al [35]	T: 25 I: 13 C: 12	I: 68.00 (2.94) C: 67.08 (2.90)	CLBP	VAS ^h , 36-item Short Form Health Survey (SF-36)	Baseline, 8 weeks	I: 0 C: 0	Iran, English
Park et al [36]	T: 24 I (NWE ⁱ): 8 I (lumbar stabilization exercise [LSE]): 8 C: 8	I (NWE): 44.12 (5.48) I (LSE): 43.37 (5.42) C: 45.50 (5.34)	CLBP	VAS	Baseline, 8 weeks	I: 0 C: 0	South Korea, English
Afzal et al [37]	T: 90 I: 45 (64.28) C: 45 (69.04)	I: 37.5 (12.5) C: 38.2 (11.8)	CLBP	VAS, Modified Oswestry Disability Index	Baseline, 4th, 8th, 12th sessions	I: 0.07 C: 0.07	Pakistan, English
Nambi et al [38]	T: 60 I (VRE ^j): 20 I (isokinetic exercise [IKE]): 20 C: 20	I (VRE): 23.2 (1.6) I (IKE): 22.9 (1.7) C: 22.8 (1.8)	CLBP	VAS, inflammatory biomarkers	Baseline, 4 weeks	I (VRE): 5 I (IKE): 5 C: 0	Saudi Arabia, English
Nambi et al [39]	T: 36 I (VR): 12 I (combined physical rehabilitation [CPR]): 12 C: 12	I (VR): 21.3 (2.6) I (CPR): 21.8 (2.2) C: 20.9 (2.8)	CLBP	Inflammatory biomarkers	Baseline, 4 weeks	I (VR): 0 I (CPR): 0 C: 0	Saudi Arabia, English
Nambi et al [40]	T: 54 I (VR): 18 I (CPR): 18 C: 18	I (VR): 22.3 (1.6) I (CPR): 21.4 (1.8) C: 21.9 (1.8)	CLBP	VAS, TSK-17	Baseline, 4 weeks	I (VR): 0 I (CPR): 0 C: 0	Saudi Arabia, English

First author	Patient characteristics			Outcome measures	Time points	Dropout rate (%)	Country, language
	Participants, n (% female)	Age (years), mean (SD)	Diagnosis				
Matheve et al [41]	T: 84 I: 42 (64) C: 42 (64)	I: 42.1 (11.5) C: 44.2 (11.9)	CLBP	NPRS, Roland-Morris Disability Questionnaire (RMDQ), PCS	Baseline, postintervention	I: 0 C: 0	Belgium, English
Stamm et al [42]	T: 22 I: 11 (73) C: 11 (55)	I: 75.00 (5.80) C: 75.50 (4.39)	CLBP	NRS ^k , Chronic Pain Grade Questionnaire (CPGQ), 12-item Short Form Health Survey (SF-12), Hannover Functional Ability Questionnaire for Measuring Back Pain-Related Disability (Ffb-H-R), TSK ^l -11	Baseline, 4 weeks	I: 0 C: 0	Germany, English
Monteiro-Junior et al [43]	T: 34 I: 17 (100) C: 17 (100)	T: 68 (4)	CLBP	NRS	Baseline, 8 weeks	I: 17.6 C: 5.8	Brazil, English
Cetin et al [44]	T: 41 I: 21 C: 20	I: 40.00 (11.88) C: 41.94 (10.76)	CNP ^m	Joint position sense error (JPSE), VAS, pressure pain threshold (PPT), SF-36	Baseline, 6 weeks	I: 19 C: 15	Turkey, English
Bahat et al [45]	T: 90 I (VR): 30 (63) I (laser): 30 (70) C: 30 (77)	I (VR): 48.00 (14.07) I (laser): 48.00 (17.41) C: 48.00 (17.76)	CNP	NDI ⁿ , VAS, EQ-5D, TSK-17, cervical range of motion (CROM), kinematic measures	Baseline, 4 weeks	I (VR): 16.6 I (laser): 13.3 C: 16.6	Israel, English
Nusser et al [46]	T: 55 I (VR): 17 (53) I (sensorimotor group [SM]): 16 (69) C: 18 (66)	I (VR): 51.2 (8.8) I (SM): 53.1 (5.7) C: 49.8 (8.1)	CNP	NRS, active cervical range of motion (ACROM), NDI	Baseline, 3 weeks	I (VR): 0 I (SM): 11 C: 10	Germany, English
Tejera et al [47]	T: 44 I: 22 (50) C: 22 (54.5)	I: 32.72 (11.63) C: 26.68 (9.21)	CNP	VAS, conditioned pain modulation (PPT), ACROM device, NDI, PCS, 11-item Spanish version of the TSK	Baseline, 4 weeks, 1 month, 3 months	I: 0 C: 0	Spain, English

^aT: total participants.

^bI: intervention group.

^cC: control group.

^dCLBP: chronic low back pain.

^eDVPRS: Defense and Veterans Pain Rating Scale.

^fVR: virtual reality.

^gNPRS: Numerical Pain Rating Scale.

^hVAS: Visual Analogue Scale.

ⁱNWE: Nintendo Wii exercise.

^jVRE: virtual reality exercise.

^kNRS: Numeric Rating Scale.

^lTSK: Tampa Scale for Kinesiophobia.

^mCNP: chronic neck pain.

ⁿNDI: Neck Disability Index.

The types of VR interventions included IVR [32,35,42,44-47] and NIVR [33,34,36-41,43], which were classified based on the degree of isolation participants experienced when interacting with the virtual environment during VR therapy. NIVR uses a wall-mounted screen or a computer monitor as the vehicle for VR content, while IVR uses a headset or head-mounted display [48]. Compared to NIVR, IVR can increase the user's sense of presence by improving immersion through the addition of auditory or haptic feedback [49]. The duration of a single VR session ranged from 2 to 40 minutes, and the frequency of

treatment ranged from 5 to 7 times a week; all the included studies ranged in duration from a single exercise session to 8 weeks. For the control groups, 5 (31%) studies performed conventional balance function training [33,34,38-40], 5 (31%) performed conventional physical therapy [36,37,41,46,47], 2 (13%) performed core training [43,44], and the remaining conducted treatments, including sham VR [32], conventional multimodal pain therapy [42], waiting lists [45], and standard care [35]. The intervention details are summarized in Table 2.

Table 2. Characteristics of the intervention protocols used in the included studies [32-47].

First author	Intervention group	Control group	Device	Duration
Garcia et al [32]	Ease VR ^a , IVR ^b , interactive, pain education, relaxation/interception, mindful escape, pain distraction games, dynamic breathing performed 56 times (2-16 minutes each time, average of 6 minutes, 1 time/day)	Sham VR, NIVR ^c , not interactive, displayed 2D nature footage with neutral music, 20 videos rotated over 56 sessions, performed 56 times (2-16 minutes each time, average of 6 minutes, 1 time/day)	Pico G2 4K all-in-one head-mounted VR device	8 weeks
Nambi et al [33]	VR group: sit in the virtual platform and select firing game executed by trunk movements (flexion, extension, and lateral flexion; 30 minutes/day, 5 times/week, for 4 weeks); heat modality (20 minutes); therapeutic ultrasound (25 minutes)	Conventional balance function training, traditional active balance exercise for abdominal and back muscles (5 times/week for 4 weeks); heat modality (20 minutes); therapeutic ultrasound (25 minutes)	VR group: Pro-Kin system PK 252 N (TecnoBody)	4 weeks
Nambi et al [34]	VRT: shooting game (30 minutes, 5 days/week, for 4 weeks); home-based exercise; hot-pack therapy (20 minutes); ultrasound (frequency 1 MHz, intensity 1.5 W/cm ² in continuous form for 5 minutes)	Conventional balance function training: standardized conventional exercises actively involving abdominal, deep abdominal, and back muscles (30 minutes/session, 5 days/week, for 4 weeks); hydrocollator packs (20 minutes/session); continuous ultrasound (frequency 1 MHz, intensity 1.5 W/cm ²) at the low back region (5 minutes, 5 days/week, for 4 weeks)	VRT: Pro-Kin system (TecnoBody)	4 weeks
Yalfani et al [35]	Fishing, boxing, tennis, football, bowling, beat saber, audio shield, and skiing (30 minutes, 3 times/week, for 8 weeks)	Standard care.	VR: HTC Vive virtual reality system	8 weeks
Park et al [36]	NWE ^d : using the Nintendo Wii exercise program, including the wakeboard, Frisbee dog, jet ski, and canoe games. Participants chose which Nintendo Wii sports program to perform and took a 2-minute break every 10 minutes (30 minutes/session, 3 times/week, for 8 weeks)	Conventional physical therapy: using physical agent modalities, such as a hot pack (30 minutes); interferential current therapy (15 minutes); deep heat with ultrasound (5 minutes)	VR: Nintendo	8 weeks
Afzal et al [37]	Kinetic exergames (trunk slide flexion, sitting to avoid obstacles, jumping and combined movement of arms, for 5 minutes); after 30 seconds of rest, play body ball game for 5 minutes (3 sessions/week for a total of 12 sessions); routine physical therapy	Conventional physical therapy: heat therapy for 10 minutes, hamstring stretching, back-strengthening exercises (3 sessions/week for a total of 12 sessions)	VR: nonimmersive system with a kinetic device (model V.2), incorporated with red-green-blue (RGB) cameras and time-of-flight (TOF) sensor, attached with a liquid crystal display (LCD) screen	4 weeks
Nambi et al [38]	VRE ^e : virtual training exercises performed in the upright position, a car race game chosen from the list of games, and training given to focus on the back muscles. The participant was asked to sit on the moving game chair and instructed to watch the game on the desktop monitor (30 minutes/session, 5 days/week, for 4 weeks); hydrocollator packs (20 minutes/session); continuous ultrasound (frequency 1 MHz, intensity 1.5 W/cm ²) at the low back region (5 minutes, 5 days/week, for 4 weeks)	Conventional balance function training: standardized conventional exercises actively involving abdominal, deep abdominal, and back muscles (30 minutes/session, 5 days/week, for 4 weeks); hydrocollator packs (20 minutes/session); continuous ultrasound (frequency 1 MHz, intensity 1.5 W/cm ²) at the low back region (5 minutes, 5 days/week, for 4 weeks)	VRE: Pro-Kin system (TecnoBody)	4 weeks

First author	Intervention group	Control group	Device	Duration
Nambi et al [39]	Virtual reality training (VRT): shooting game, sitting on a virtual platform and visualizing the game on the computer display screen (30 minutes each time, 5 times/week, for 4 weeks); heat modality (20 minutes); therapeutic ultrasound (frequency 1 MHz, intensity 1.5 W/cm ² ; 5 minutes); home-based exercise (10 repetitions, bottom-to-heel stretch, opposite arm/leg raise, back extension, bridging, knee rolling; 2 times/day for 4 weeks)	Conventional balance function training: active isotonic and isometric exercises for abdominal, deep abdominal, and back muscles (10-15 repetitions/day, 5 days/week for 4 weeks; stretching focused on each muscle group for 3 repetitions for 10 seconds per muscle group); heat modality (20 minutes); therapeutic ultrasound (frequency 1 MHz, intensity 1.5 W/cm ² ; 5 minutes); home-based exercise (10 repetitions, bottom-to-heel stretch, opposite arm/leg raise, back extension, bridging, knee rolling; 2 times/day for 4 weeks)	VR: Pro-Kin system PK 252 N (Pelvic Module balance trunk MF; TecnoBody)	4 weeks
Nambi et al [40]	VRT: shooting game, sitting on a virtual platform and visualizing the game on the computer display screen (30 minutes each time, 5 times/week, for 4 weeks); heat modality (20 minutes); therapeutic ultrasound (frequency 1 MHz, intensity 1.5 W/cm ² ; 5 minutes)	Conventional balance function training: active isotonic and isometric exercises for abdominal, deep abdominal, and back muscles (10-15 repetitions/day, 5 days/week for 4 weeks; stretching focused on each muscle group for 3 repetitions for 10 seconds per muscle group); heat modality (20 minutes); therapeutic ultrasound (frequency 1 MHz, intensity 1.5 W/cm ² ; 5 minutes)	VR: Pro-Kin system PK 252 N (Pelvic Module balance trunk MF; TecnoBody)	4 weeks
Matheve et al [41]	2 different games (2 minutes each); single-session intervention, 2 × 2 minutes of pelvic tilt exercises in the sagittal plane, with 30 seconds of rest in between, through a wireless motion sensor	Conventional physical therapy: 2 different games (2 minutes each); single-session intervention, 2 × 2 minutes of pelvic tilt exercises in the sagittal plane, with 30 seconds of rest in between	VR: wireless motion sensor (Valedo Pro, Hocoma)	Single exercise session
Stamm et al [42]	Multimodal pain therapy in VR (movement therapy and psychoeducation), training session including 12 exercises, structured as follows: (1) warm-up (training of upper and lower extremities), (2) main part (strengthening of abdominal and back muscles, core stability), (3) cool-down (stretching, progressive muscle relaxation), (4) psychoeducative units (topics: physiology of pain, pain management, stress management, everyday training), 3 times/week for 30 minutes	Conventional multimodal pain therapy: chair-based group exercises and psychoeducation in a group setting, 3 times/week for 30 minutes	VR: head-mounted display headset using the ViRST VR app	4 weeks
Monteiro-Junior et al [43]	Virtual physical training (8 exercises, 30 minutes each time, with 3 weekly sessions lasting 90 minutes each), lasted 8 weeks, 3 times weekly/session	Core training: postures adopted by participants for 15-30 seconds or according to the capacity of each; 10-15 seconds between postures (ie, bridges), with each performed 3 times, lasted 8 weeks, 3 times weekly/session	VR: Wii Balance Board (WBB; Nintendo)	8 weeks
Cetin et al [44]	VR exercises: VR apps that allowed neck movements in all directions, motor control (MC) exercises (20 minutes and then VR for 20 minutes, 5 repetitions for each exercise; 40 minutes/session, 3 sessions/week, for 6 weeks, total of 18 sessions)	Core training: strengthening of deep cervical flexors (DCF), deep cervical extensors (DCE), and axioscapular muscles; stretching exercises; and postural correction exercises (40 minutes, 10 repetitions for each exercise, 3 sessions/week, for 6 weeks, total of 18 sessions)	VR: Oculus Go VR glasses, 2 VR apps installed: "Ocean Rift" and "Gala 360"	6 weeks

First author	Intervention group	Control group	Device	Duration
Bahat et al [45]	VR group: kinematic home training and customized software with the virtual airplane controlled by head motion (5 minutes, 4 times/day, 20 minutes/day, 4 times/week, for 4 weeks)	Waiting list	VR: customized neck VR system (hardware including Oculus Rift DK1 head-mounted display equipped with 3D motion tracking; software developed using Unity-pro, version 3.5, Unity Technologies)	4 weeks
Nusser et al [46]	VR group: neck-specific sensorimotor training (NSST)— head-repositioning test (HRT), head-to-target test (HTT), dynamic exercise including 5 different trajectories (3 minutes given between tasks), training divided into 6 20minute sessions for a total of 120 minutes); standard rehabilitation program	Conventional physical therapy: different forms of general and neck-specific exercise therapies (strengthening, mobilization, relaxation, medical training therapy, functional gymnastics, aqua therapy, physical therapy, and traditional “back school”)	VR: modified VR system (Fraunhofer Institute für Graphische Datenverarbeitung), helmet (Schutzhelm uvex pheos alpine, Fürth), 3Space Fastrak System (Polhemus Inc)	3 weeks
Tejera et al [47]	VR mobile apps “Full Dive VR,” only lateral flexion movements of the neck; “VR Ocean Aquarium 3D”: flexion, extension, and rotation movements (3 series of 10 repetitions, with 30 seconds of rest between exercises)	Conventional physical therapy: flexion, extension, rotation, and tilt exercises (3 series of 10 repetitions, with 30 seconds of rest between exercises)	VR: VR Vox Play glasses with a head-mounted display clamping system (weight 330 g) with an LG Q6 smartphone attached, 2 VR mobile apps installed	4 weeks

^aVR: virtual reality.

^bIVR: immersive virtual reality.

^cNIVR: nonimmersive virtual reality.

^dNWE: Nintendo Wii exercise.

^eVRE: virtual reality exercise.

The risk of bias in the 16 (100%) studies included in the meta-analysis is presented in [Figure 2](#). Overall, 10 (63%) studies showed a high risk of bias. In addition, 15 (94%) RCTs generated an adequately randomized sequence, and 9 (60%) of them were analyzed using a blinded method for outcome

measurement. Ratings using the GRADE methodology for all outcome measurements were inconsistent and ranged from moderate to low quality ([Multimedia Appendix 3](#)). Therefore, the quality of evidence from most studies was classified as fair.

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

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Afzal et al (2022)	+	?	-	+	+	+	+
Bahat et al (2017)	+	+	-	+	+	+	+
Cetin et al (2022)	+	?	-	-	+	+	+
Garcia et al (2021)	+	?	+	+	+	+	+
Matheve et al (2020)	+	+	-	-	+	+	+
Monteiro-Junior et al (2015)	+	?	-	+	+	+	+
Nambi et al (2020)	+	?	-	+	+	+	+
Nambi et al (2021a)	+	?	?	?	+	+	+
Nambi et al (2021b)	+	?	?	+	+	+	+
Nambi et al (2021c)	+	+	?	+	+	+	+
Nambi et al (2022)	+	+	-	+	+	+	+
Nusser et al (2021)	+	?	-	-	+	+	+
Park et al (2013)	?	?	?	?	+	+	+
Stamm et al (2022)	+	?	-	-	+	+	+
Tejera et al (2020)	+	+	-	+	+	+	+
Yalfani et al (2022)	+	?	?	?	+	+	+

Primary Outcome

Pain Intensity

All 16 (100%) studies (800 patients) reported pain intensity: 9 (56%) used the Visual Analogue Scale (VAS) [34-38,40,44,45,47], 2 (13%) used the Numerical Pain Rating Scale (NPRS) [33,41], 3 (19%) used the Numeric Rating Scale (NRS) [42,43,46], and 1 (6%) used the Defense and Veterans Pain Rating Scale (DVPRS) [32]. The random effects model revealed that compared with the control treatment, the VR intervention significantly reduced pain intensity (WMD=-1.63, 95% CI -2.11 to -1.16, P<.001, I²=90%). Clinical differences between groups were significant, and as suggested, the minimal clinically important difference (MCID) threshold on the VAS for LBP was set at a 1.5-point reduction [50]. Given the significant heterogeneity observed (I²=90%), we performed subgroup analyses to investigate the source of heterogeneity

based on the different regions, VR types, and treatment durations.

VR had a good analgesic effect on both CNP and CLBP groups compared with the control group. The results did not significantly differ among the subgroups (WMD=-1.63, 95% CI -2.11 to -1.16); see Figure 3. Moreover, a total of 7 (44%) studies demonstrated that IVR significantly improved CSP (WMD=-1.50, 95% CI -2.45 to -0.55, P<.001, I²=80%) [32,35,42,44-47]. Another 8 (50%) studies showed that NIVR improved CSP substantially (WMD=-1.50, 95% CI -2.45 to -0.55, P<.001, I²=90%) [33,34,36-38,40,41,43]; see Figure 4. The subgroup analyses also revealed significant differences between treatment durations of <4 weeks (WMD=-1.41, 95% CI -2.12 to -0.69, P=.001, I²=0%) and ≥4 weeks (WMD=-1.65, 95% CI -2.16 to -1.14, P<.001, I²=91%) in terms of the analgesic effect of VR treatment on CSP (Multimedia Appendix 4).

Figure 3. Forest plots of the effect of VR compared with other treatments on pain intensity in patients with CSP: subgroup analysis of posttreatment effectiveness for different regions of spinal pain. CSP: chronic spinal pain; VR: virtual reality.

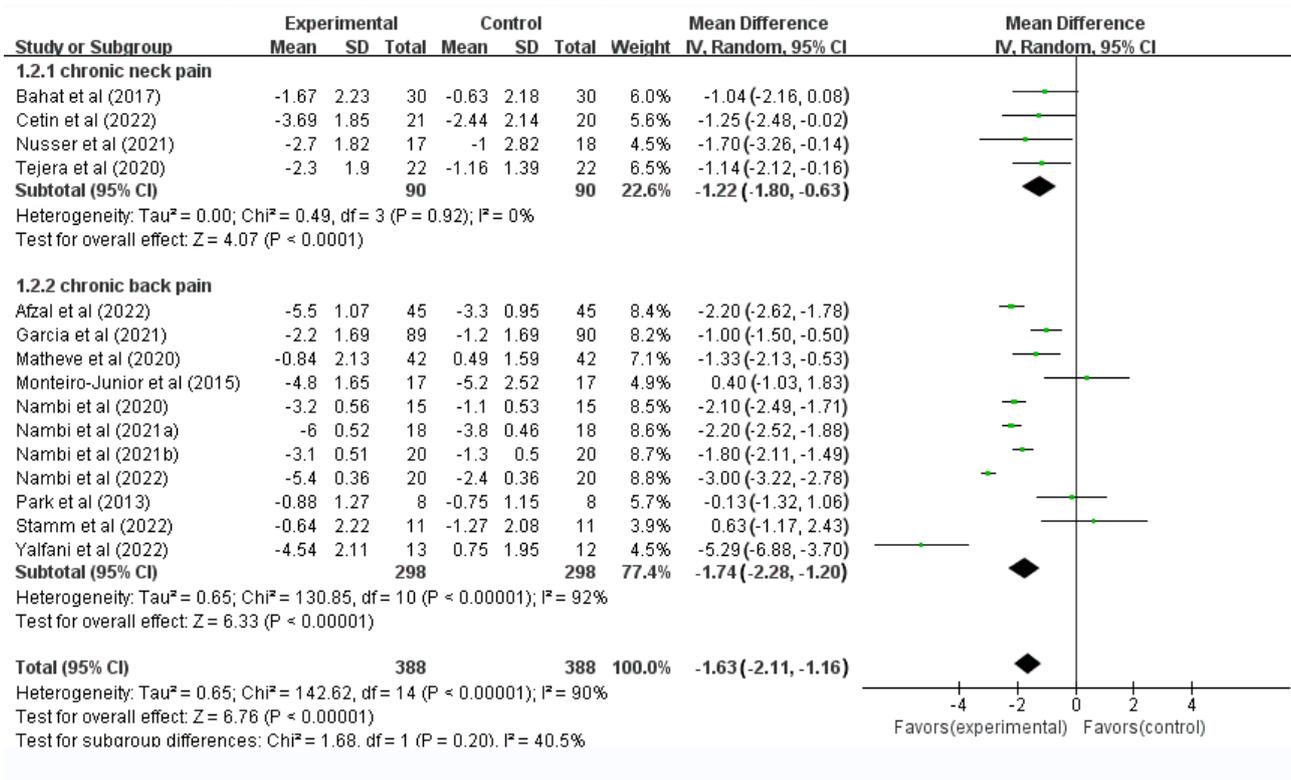
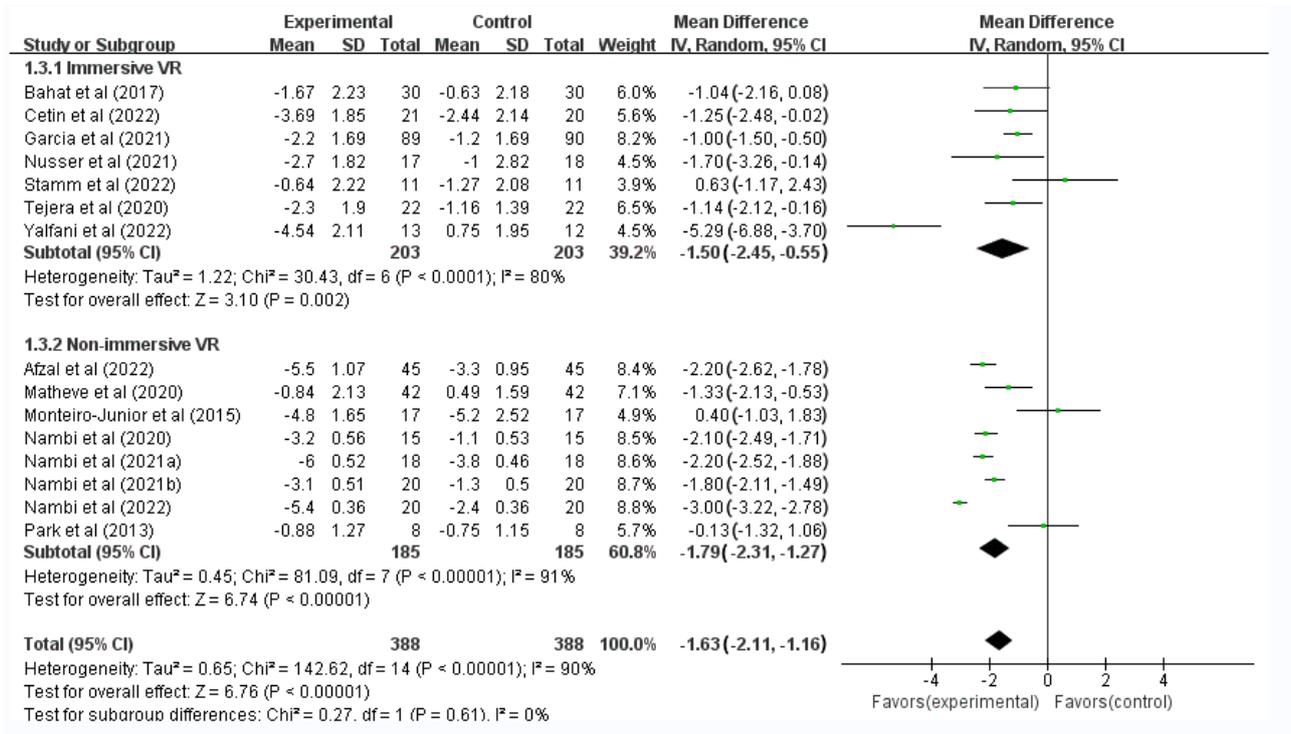


Figure 4. Forest plots of the effect of VR compared with other treatments on pain intensity in patients with CSP: subgroup analysis of posttreatment effectiveness for the VR intervention type. CSP: chronic spinal pain; VR: virtual reality.



Secondary Outcomes

Inflammatory Markers

Patients with CSP develop a systemic inflammatory response and have elevated levels of inflammatory markers in the blood

[51]. Two studies (62 patients) focused on the levels of inflammatory markers (eg, CRP, TNF- α , IL-2, IL-4, and IL-6) by collecting 10 mL of venous blood [38,39]. The results showed that VR therapy significantly improved the level of CRP (WMD=-0.89, 95% CI -1.07 to -0.70, $P<.001$, $I^2=0\%$),

TNF- α (WMD=-6.60, 95% CI -8.56 to -4.64, $P<.001$, $I^2=98\%$), and IL-6 (WMD=-2.76, 95% CI -2.98 to -2.53, $P<.001$, $I^2=0\%$). No significant differences were found between the IL-2 and IL-4 subgroups (Figure S1 in [Multimedia Appendix 5](#)).

Fear of Movement

Four studies (162 patients) reported fear of movement according to the 11-item or 17-item Tampa Scale of Kinesiophobia (TSK-11 or TSK-17, respectively) [42,47]. No significant differences were found in either the TSK-11 (WMD=-0.81, 95% CI -4.48 to 2.86, $P=.66$, $I^2=0\%$; Figure S2 in [Multimedia Appendix 5](#)) or TSK-17 (WMD=-9.66, 95% CI -22.01 to 2.68, $P=.13$, $I^2=97\%$; Figure S3 in [Multimedia Appendix 5](#)).

Spinal Range of Motion

Three studies reported changes in the ROM of the neck in 4 directions before and after the intervention [45-47]. No significant differences were found between the groups in terms of flexion (WMD=2.67, 95% CI -2.31 to 7.64, $P=.29$, $I^2=61\%$), extension (WMD=3.92, 95% CI -2.17 to 10.0, $P=.21$, $I^2=48\%$), right rotation (WMD=-0.22, 95% CI -4.38 to 3.95, $P=.92$, $I^2=0\%$), or left rotation (WMD=0.08, 95% CI -3.90 to 4.05, $P=.97$, $I^2=42\%$); see Figure S4 in [Multimedia Appendix 5](#).

Disability Level

Three studies (139 patients) reported disability levels in patients with CNP by using the Neck Disability Index (NDI) [45-47], a

10-item questionnaire that assesses self-reported disability related to CNP. Higher scores on the NDI indicate higher levels of disability. No significant differences were found in the pooled analysis of 3 (19%) studies (WMD=-2.66, 95% CI -5.47 to 0.15, $P=.06$, $I^2=48\%$); see Figure S5 in [Multimedia Appendix 5](#).

Adverse Events

One study reported that after 1 month of intervention, patients experienced nausea and motion sickness [32], two studies reported that there were no adverse events [33,37], and the remaining studies did not mention adverse events. The overall dropout rate was 4.25% (17/400) in the intervention group and 3.75% (15/400) in the control group.

Publication Bias and Sensitivity Analysis

The Egger test indicated significant publication bias in the results for pain intensity ($P=.03$; [Figure 5](#)). The sensitivity analysis for pain intensity revealed that removing each study separately did not significantly affect the pooled results, thus indicating that the results are robust ([Figure 6](#)). The trim-and-fill method was performed, and it was estimated that there were 4 missing studies. The pooled estimates (95% CIs) calculated for the fixed effects model and the random effects model were -2.30 (-2.42 to -2.18) and -2.06 (-2.50 to -1.61), respectively ([Figure 7](#)). No significant changes in the results were observed before or after pruning or filling, indicating that our results are robust and plausible.

Figure 5. Funnel plot of pain intensity in the VR group compared with the control group. VR: virtual reality; WMD: weighted mean difference.

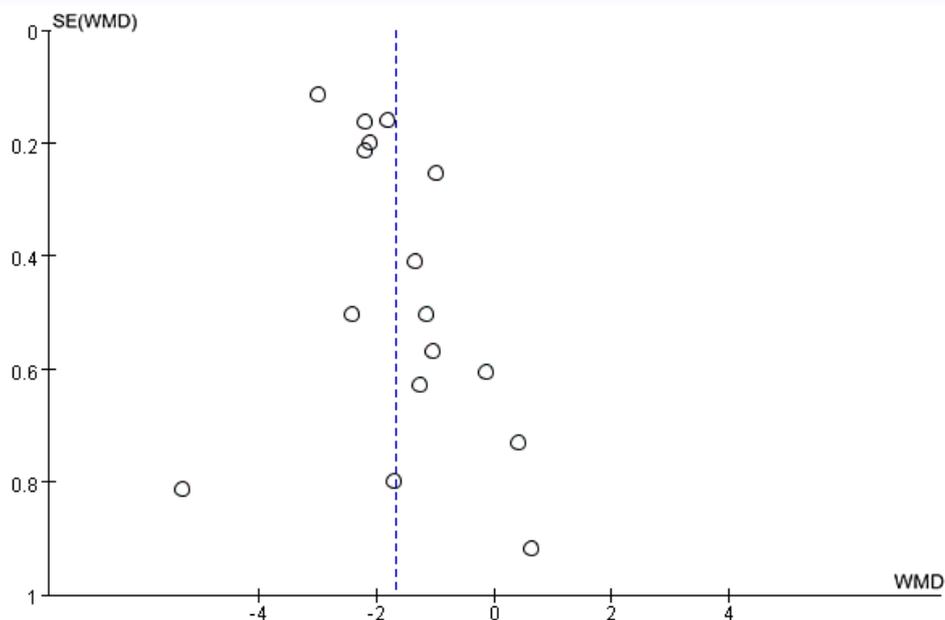


Figure 6. Sensitivity analysis of the included studies.

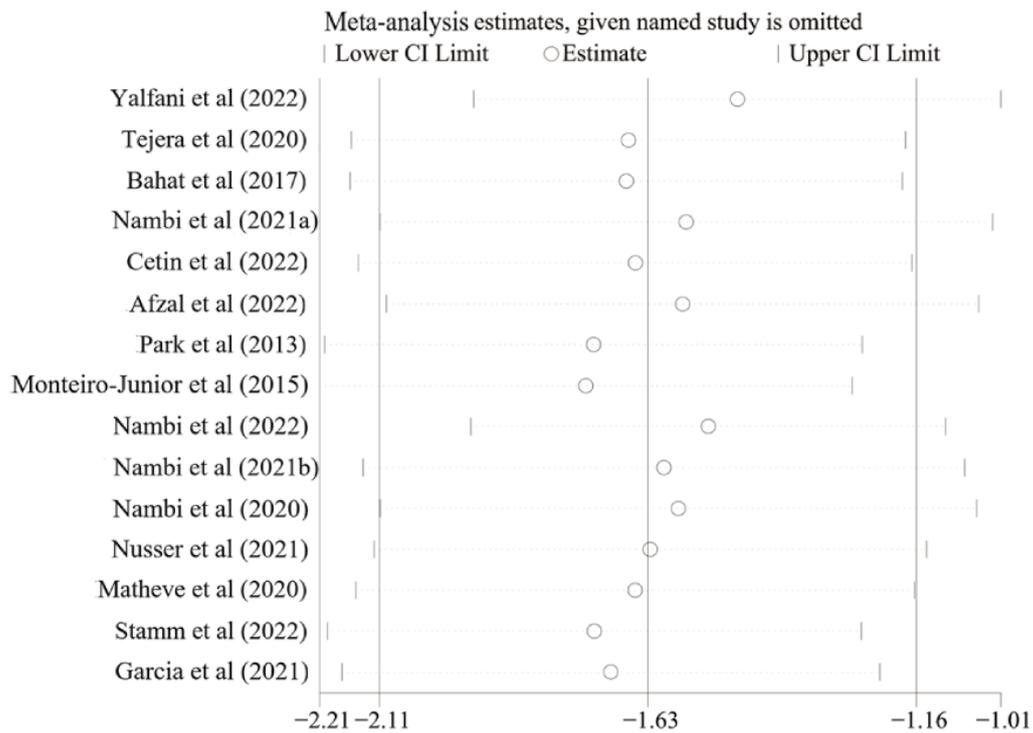
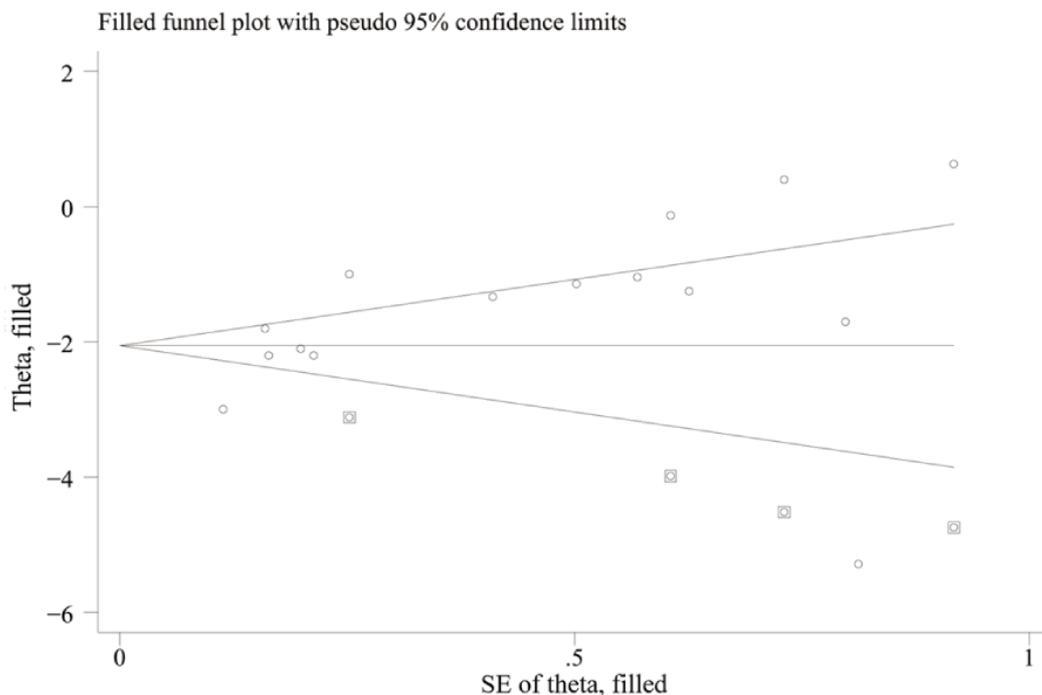


Figure 7. Trim-and-fill analysis to estimate the number of potentially missing studies about the effect of VR on CSP. Circles represent real studies, and squares represent studies estimated by this method. CSP: chronic spinal pain; VR: virtual reality.



Discussion

Principal Findings

The primary purpose of this meta-analysis was to compare the relative efficacy of VR therapy and other therapies (eg, conventional therapy, sham stimulation, and standard care) for

treating CSP. The results indicated that VR therapy can effectively relieve CSP. The results of subgroup analyses showed that VR is a beneficial pain management strategy for patients with CNP and CLBP. For different types of VR, subgroup analyses showed that compared to the control group, IVR and NIVR both significantly improved CSP. No statistically

significant differences were found between patients who underwent VR treatments for a duration of <4 weeks and a duration of ≥ 4 weeks. VR was associated with a significant improvement in inflammatory marker levels but not in the fear of movement, spinal ROM, or disability level. VR was found to be well tolerated among these patients.

Discussion of the Results

The primary result suggested that VR reduces self-reported pain intensity, which might be explained by several implicating mechanisms [52,53]. A previous study reported that abdominal muscle strength is significantly lower in people with LBP [54], and a lack of strength in the core trunk muscles can lead to a decrease in intra-abdominal pressure, affecting spinal stability [55]. VR, as a novel human-computer interaction approach, can stimulate and mobilize the sensory system during training and results in changes in neuroplasticity and enhanced performance of relevant muscle groups, promoting a new motor learning process and leading to increased spinal stability [37,56], which would benefit pain relief. Furthermore, previous studies have reported that an intervertebral disc undergoes aging or pathological changes in the adjacent region in patients with CSP, exposing cells within the nucleus pulposus to macrophages, resulting in an inflammatory response that might trigger pain [7,8]. VR therapy may enhance the activity of disc fibroblasts and increase the thickness of the multifidus muscle [39,57], which is beneficial for relieving pain intensity. Furthermore, pain is an unpleasant subjective sensation associated with actual or potential tissue damage and is correlated with the degree of patient attention given to the pain area [58-61]. The various virtual game environments and real-time feedback methods are the most eye-catching features in the VR training process; these methods can be used to attract the patient's visual and auditory attention to achieve motor performance, while relatively less attention has been given to the effects of VR on pain [62,63].

Although the high heterogeneity of the primary outcome and the results of the subsequent subgroup analyses suggest that the region of CSP, VR type, and treatment duration may play a role in the heterogeneity, the results of the sensitivity analysis indicate that these differences are more likely to be caused by 6 studies [33-35,37,38,40], which included participants of different ages.

VR therapy significantly improved the levels of inflammatory markers, including CRP, TNF- α , and IL-6. Numerous studies have previously reported an association between CSP and changes in inflammatory cytokines, such as IL-1 and TNF- α , which are thought to be closely related to the pathogenesis of disc herniation and degeneration [64,65]. Similarly, Nambi et

al [66] reported that 4 weeks of VR training could significantly decrease pain intensity, increase functional impairment, and improve CRP, TNF- α , IL-2, IL-4, and IL-6 levels. However, the limited number and low quality of the included studies need to be noted, and further RCTs with large samples and rigorous study designs are needed to elucidate these results.

Patients with CSP may engage in fear/avoidance behaviors to avoid pain and protect themselves by limiting spinal motion, which ultimately affects spinal mobility and the speed of movement [67,68], with the degree of pain catastrophizing being proportional to the degree of disability [69,70]. However, we found no statistically significant differences in fear avoidance beliefs after the VR intervention but at the 3-month follow-up [47]. A systematic review and meta-analysis reported that VR therapy enhances spinal ROM and physical functioning in patients with CNP [26]. We failed to observe significant differences in the spinal ROM or disability level after VR intervention compared to those in the control group, which may be attributed to the relatively short duration (0-8 weeks) of the VR intervention (the reported mean duration was 4.81 weeks).

Limitations

Several limitations need to be addressed in this meta-analysis. First, the pooled analysis of the studies may be imprecise due to the large heterogeneity and the low quality of evidence from most of the included studies, and the results should be interpreted with caution. Second, the optimal duration of treatment for CSP could not be determined. Third, the effectiveness of VR therapy in patients with CSP and its analgesic effects in long-term follow-up must be further explored in high-quality studies. Fourth, indicators related to quality of life, such as depression and anxiety, should be emphasized and investigated in depth in future studies of patients with CSP.

Conclusion

VR therapy is an innovative and effective analgesic method that has beneficial effects on inflammatory markers in patients with CSP compared to other therapies (sham stimulation, usual care, conventional treatment). However, this approach may not have significant effects on the fear of movement, spinal ROM, or disability level. Notably, the quality of the evidence from the RCTs included in this study ranged from moderate to low. Therefore, we recommend that readers interpret the results of this study with caution. Future trials with large sample sizes, rigorous designs, and long-term follow-up periods are needed to explore the clinical significance of these differences and key issues in patients with CSP and to elucidate the underlying mechanisms of VR.

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Data Availability

All data generated or analyzed during this study are included in this published paper and its supplementary information files.

Authors' Contributions

All authors contributed to the writing and redrafting of the manuscript. QD and XZ had the original idea. TZ and FW performed the literature search, XL and ZH assessed the risk of bias; YS, YF, and LZ rated the certainty of the evidence for each outcome; and XL and FW undertook data collection. The results were analyzed, interpreted, and discussed by XZ and QD. All authors contributed to the conception and design of the study, the analysis and interpretation of data, and the drafting and revising of the manuscript and have approved the final version.

Conflicts of Interest

None declared.

Multimedia Appendix 1

The PRISMA checklist. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

[\[DOCX File , 29 KB-Multimedia Appendix 1\]](#)

Multimedia Appendix 2

Search strategy for all electronic databases.

[\[DOCX File , 24 KB-Multimedia Appendix 2\]](#)

Multimedia Appendix 3

The GRADE criteria. GRADE: Grading of Recommendations, Assessment, Development and Evaluation.

[\[DOCX File , 22 KB-Multimedia Appendix 3\]](#)

Multimedia Appendix 4

Forest plots of the effect of VR compared with other treatments for pain intensity in patients with CSP: subgroup analysis of posttreatment effectiveness for treatment duration. CSP: chronic spinal pain; VR: virtual reality.

[\[DOCX File , 37 KB-Multimedia Appendix 4\]](#)

Multimedia Appendix 5

Forest plots of the effect of VR compared with other treatments for inflammatory marker level, fear of movement, spinal ROM, and disability level in patients with CSP. CSP: chronic spinal pain; ROM: range of motion; VR: virtual reality.

[\[DOCX File , 130 KB-Multimedia Appendix 5\]](#)

References

1. Chen S, Chen M, Wu X, Lin S, Tao C, Cao H, et al. Global, regional and national burden of low back pain 1990-2019: a systematic analysis of the Global Burden of Disease study 2019. *J Orthop Translat*. Jan 2022;32:49-58. [\[FREE Full text\]](#) [doi: [10.1016/j.jot.2021.07.005](https://doi.org/10.1016/j.jot.2021.07.005)] [Medline: [34934626](https://pubmed.ncbi.nlm.nih.gov/34934626/)]
2. de Campos TF, Elkins MR. Prevention of spinal pain. *J Physiother*. Jul 2021;67(3):158-159. [\[FREE Full text\]](#) [doi: [10.1016/j.jphys.2021.06.012](https://doi.org/10.1016/j.jphys.2021.06.012)] [Medline: [34127420](https://pubmed.ncbi.nlm.nih.gov/34127420/)]
3. Balagué F, Mannion AF, Pellisé F, Cedraschi C. Non-specific low back pain. *Lancet*. Mar 04, 2012;379(9814):482-491. [doi: [10.1016/S0140-6736\(11\)60610-7](https://doi.org/10.1016/S0140-6736(11)60610-7)] [Medline: [21982256](https://pubmed.ncbi.nlm.nih.gov/21982256/)]
4. Izzo R, Papolizio T, D'Aprile P, Muto M. Spinal pain. *Eur J Radiol*. May 2015;84(5):746-756. [doi: [10.1016/j.ejrad.2015.01.018](https://doi.org/10.1016/j.ejrad.2015.01.018)] [Medline: [25824642](https://pubmed.ncbi.nlm.nih.gov/25824642/)]
5. Ferreira ML, de Luca K. Spinal pain and its impact on older people. *Best Pract Res Clin Rheumatol*. Apr 2017;31(2):192-202. [doi: [10.1016/j.berh.2017.08.006](https://doi.org/10.1016/j.berh.2017.08.006)] [Medline: [29224696](https://pubmed.ncbi.nlm.nih.gov/29224696/)]
6. Khan AN, Jacobsen HE, Khan J, Filippi CG, Levine M, Lehman RA, et al. Inflammatory biomarkers of low back pain and disc degeneration: a review. *Ann N Y Acad Sci*. Dec 2017;1410(1):68-84. [\[FREE Full text\]](#) [doi: [10.1111/nyas.13551](https://doi.org/10.1111/nyas.13551)] [Medline: [29265416](https://pubmed.ncbi.nlm.nih.gov/29265416/)]
7. Ota Y, Connolly M, Srinivasan A, Kim J, Capizzano AA, Moritani T. Mechanisms and origins of spinal pain: from molecules to anatomy, with diagnostic clues and imaging findings. *Radiographics*. 2020;40(4):1163-1181. [doi: [10.1148/rg.2020190185](https://doi.org/10.1148/rg.2020190185)] [Medline: [32501739](https://pubmed.ncbi.nlm.nih.gov/32501739/)]
8. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain--United States, 2016. *JAMA*. Apr 19, 2016;315(15):1624-1645. [\[FREE Full text\]](#) [doi: [10.1001/jama.2016.1464](https://doi.org/10.1001/jama.2016.1464)] [Medline: [26977696](https://pubmed.ncbi.nlm.nih.gov/26977696/)]

9. Machado GC, Maher CG, Ferreira PH, Day RO, Pinheiro MB, Ferreira ML. Non-steroidal anti-inflammatory drugs for spinal pain: a systematic review and meta-analysis. *Ann Rheum Dis*. Jul 2017;76(7):1269-1278. [doi: [10.1136/annrheumdis-2016-210597](https://doi.org/10.1136/annrheumdis-2016-210597)] [Medline: [28153830](https://pubmed.ncbi.nlm.nih.gov/28153830/)]
10. Schjerning A, McGettigan P, Gislason G. Cardiovascular effects and safety of (non-aspirin) NSAIDs. *Nat Rev Cardiol*. Sep 2020;17(9):574-584. [doi: [10.1038/s41569-020-0366-z](https://doi.org/10.1038/s41569-020-0366-z)] [Medline: [32322101](https://pubmed.ncbi.nlm.nih.gov/32322101/)]
11. Chou R, Qaseem A, Snow V, Casey D, Cross JT, Shekelle P, Clinical Efficacy Assessment Subcommittee of the American College of Physicians; American College of Physicians; et al. American Pain Society Low Back Pain Guidelines Panel. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. Oct 02, 2007;147(7):478-491. [FREE Full text] [doi: [10.7326/0003-4819-147-7-200710020-00006](https://doi.org/10.7326/0003-4819-147-7-200710020-00006)] [Medline: [17909209](https://pubmed.ncbi.nlm.nih.gov/17909209/)]
12. Childs JD, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, et al. American Physical Therapy Association. Neck pain: clinical practice guidelines linked to the International Classification of Functioning, Disability, and Health from the Orthopedic Section of the American Physical Therapy Association. *J Orthop Sports Phys Ther*. Sep 2008;38(9):A1-A34. [doi: [10.2519/jospt.2008.0303](https://doi.org/10.2519/jospt.2008.0303)] [Medline: [18758050](https://pubmed.ncbi.nlm.nih.gov/18758050/)]
13. Malfliet A, Kregel J, Coppieters I, De Pauw R, Meeus M, Roussel N, et al. Effect of pain neuroscience education combined with cognition-targeted motor control training on chronic spinal pain: a randomized clinical trial. *JAMA Neurol*. Jul 01, 2018;75(7):808-817. [FREE Full text] [doi: [10.1001/jamaneurol.2018.0492](https://doi.org/10.1001/jamaneurol.2018.0492)] [Medline: [29710099](https://pubmed.ncbi.nlm.nih.gov/29710099/)]
14. Zhou L, Zhang R, Shang J, Kang L, Zhang Z, Zhang B, et al. Comparative effectiveness of non-pharmacological interventions in reducing psychological symptoms among patients with chronic low back pain. *Int J Surg*. Sep 27, 2023;110(1):478-489. [FREE Full text] [doi: [10.1097/JS9.0000000000000798](https://doi.org/10.1097/JS9.0000000000000798)] [Medline: [37755380](https://pubmed.ncbi.nlm.nih.gov/37755380/)]
15. Ho EK, Chen L, Simic M, Ashton-James CE, Comachio J, Wang DXM, et al. Psychological interventions for chronic, non-specific low back pain: systematic review with network meta-analysis. *BMJ*. Mar 30, 2022;376:e067718. [FREE Full text] [doi: [10.1136/bmj-2021-067718](https://doi.org/10.1136/bmj-2021-067718)] [Medline: [35354560](https://pubmed.ncbi.nlm.nih.gov/35354560/)]
16. Herman PM, Edgington SE, Ryan GW, Coulter ID. Prevalence and characteristics of chronic spinal pain patients with different hopes (treatment goals) for ongoing chiropractic care. *J Altern Complement Med*. Oct 2019;25(10):1015-1025. [FREE Full text] [doi: [10.1089/acm.2019.0247](https://doi.org/10.1089/acm.2019.0247)] [Medline: [31453711](https://pubmed.ncbi.nlm.nih.gov/31453711/)]
17. Ortiz-Catalan M, Guðmundsdóttir RA, Kristoffersen MB, Zepeda-Echavarría A, Caine-Winterberger K, Kulbacka-Ortiz K, et al. Phantom motor execution facilitated by machine learning and augmented reality as treatment for phantom limb pain: a single group, clinical trial in patients with chronic intractable phantom limb pain. *Lancet*. Dec 10, 2016;388(10062):2885-2894. [doi: [10.1016/S0140-6736\(16\)31598-7](https://doi.org/10.1016/S0140-6736(16)31598-7)] [Medline: [27916234](https://pubmed.ncbi.nlm.nih.gov/27916234/)]
18. Chi B, Chau B, Yeo E, Ta P. Virtual reality for spinal cord injury-associated neuropathic pain: systematic review. *Ann Phys Rehabil Med*. Jan 2019;62(1):49-57. [FREE Full text] [doi: [10.1016/j.rehab.2018.09.006](https://doi.org/10.1016/j.rehab.2018.09.006)] [Medline: [30312665](https://pubmed.ncbi.nlm.nih.gov/30312665/)]
19. Hoffman HG, Doctor JN, Patterson DR, Carrougher GJ, Furness TA. Virtual reality as an adjunctive pain control during burn wound care in adolescent patients. *Pain*. Mar 2000;85(1-2):305-309. [doi: [10.1016/s0304-3959\(99\)00275-4](https://doi.org/10.1016/s0304-3959(99)00275-4)] [Medline: [10692634](https://pubmed.ncbi.nlm.nih.gov/10692634/)]
20. Mirelman A, Rochester L, Maidan I, Del Din S, Alcock L, Nieuwhof F, et al. Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial. *Lancet*. Sep 17, 2016;388(10050):1170-1182. [doi: [10.1016/S0140-6736\(16\)31325-3](https://doi.org/10.1016/S0140-6736(16)31325-3)] [Medline: [27524393](https://pubmed.ncbi.nlm.nih.gov/27524393/)]
21. Collado-Mateo D, Merellano-Navarro E, Olivares PR, García-Rubio J, Gusi N. Effect of exergames on musculoskeletal pain: a systematic review and meta-analysis. *Scand J Med Sci Sports*. Mar 22, 2018;28(3):760-771. [doi: [10.1111/sms.12899](https://doi.org/10.1111/sms.12899)] [Medline: [28452070](https://pubmed.ncbi.nlm.nih.gov/28452070/)]
22. Turoń-Skrzypińska A, Rotter I, Przybyciński J, Szylińska A, Mińko A, Ciechanowski K, et al. Does exercising with the use of virtual reality during haemodialysis have an impact on plasma levels of interleukin 1 β , interleukin 6, and interleukin 8? *J Clin Med*. Aug 17, 2023;12(16):5358. [FREE Full text] [doi: [10.3390/jcm12165358](https://doi.org/10.3390/jcm12165358)] [Medline: [37629400](https://pubmed.ncbi.nlm.nih.gov/37629400/)]
23. Klemm P, Kleyer A, Tascilar K, Schuster L, Meinderink T, Steiger F, et al. A virtual reality-based app to educate health care professionals and medical students about inflammatory arthritis: feasibility study. *JMIR Serious Games*. May 11, 2021;9(2):e23835. [FREE Full text] [doi: [10.2196/23835](https://doi.org/10.2196/23835)] [Medline: [33973858](https://pubmed.ncbi.nlm.nih.gov/33973858/)]
24. Guo Q, Zhang L, Gui C, Chen G, Chen Y, Tan H, et al. Virtual reality intervention for patients with neck pain: systematic review and meta-analysis of randomized controlled trials. *J Med Internet Res*. Apr 03, 2023;25:e38256. [FREE Full text] [doi: [10.2196/38256](https://doi.org/10.2196/38256)] [Medline: [37010891](https://pubmed.ncbi.nlm.nih.gov/37010891/)]
25. Ahern MM, Dean LV, Stoddard CC, Agrawal A, Kim K, Cook CE, et al. The effectiveness of virtual reality in patients with spinal pain: a systematic review and meta-analysis. *Pain Pract*. Jul 2020;20(6):656-675. [doi: [10.1111/papr.12885](https://doi.org/10.1111/papr.12885)] [Medline: [32196892](https://pubmed.ncbi.nlm.nih.gov/32196892/)]
26. Brea-Gómez B, Torres-Sánchez I, Ortiz-Rubio A, Calvache-Mateo A, Cabrera-Martos I, López-López L, et al. Virtual reality in the treatment of adults with chronic low back pain: a systematic review and meta-analysis of randomized clinical trials. *Int J Environ Res Public Health*. Nov 11, 2021;18(22):11806. [FREE Full text] [doi: [10.3390/ijerph182211806](https://doi.org/10.3390/ijerph182211806)] [Medline: [34831562](https://pubmed.ncbi.nlm.nih.gov/34831562/)]

27. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev.* Oct 03, 2019;10(10):ED000142. [FREE Full text] [doi: [10.1002/14651858.ED000142](https://doi.org/10.1002/14651858.ED000142)] [Medline: [31643080](https://pubmed.ncbi.nlm.nih.gov/31643080/)]
28. Li X, Shen J, Liang J, Zhou X, Yang Y, Wang D, et al. Effect of core-based exercise in people with scoliosis: a systematic review and meta-analysis. *Clin Rehabil.* May 2021;35(5):669-680. [FREE Full text] [doi: [10.1177/0269215520975105](https://doi.org/10.1177/0269215520975105)] [Medline: [33356498](https://pubmed.ncbi.nlm.nih.gov/33356498/)]
29. Higgins JJPT, Savovi? J, Page M, Elbers R, Sterne J. Chapter 8: assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editors. *Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August)*. Hoboken, NJ. John Wiley & Sons; 2023;2023. URL: <https://training.cochrane.org/handbook/current/chapter-08>
30. Jennions MD, Møller AP. Publication bias in ecology and evolution: an empirical assessment using the 'trim and fill' method. *Biol Rev Camb Philos Soc.* May 2002;77(2):211-222. [doi: [10.1017/s1464793101005875](https://doi.org/10.1017/s1464793101005875)] [Medline: [12056747](https://pubmed.ncbi.nlm.nih.gov/12056747/)]
31. Schünemann H, Higgins JPT, Vist G, Glasziou P, Akl E, Skoetz N, et al. Chapter 14: completing 'summary of findings' tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editors. *Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023)*. Hoboken, NJ. John Wiley & Sons; 2023. URL: <https://training.cochrane.org/handbook/current/chapter-14>
32. Garcia LM, Birkhead BJ, Krishnamurthy P, Sackman J, Mackey IG, Louis RG, et al. An 8-week self-administered at-home behavioral skills-based virtual reality program for chronic low back pain: double-blind, randomized, placebo-controlled trial conducted during COVID-19. *J Med Internet Res.* Mar 22, 2021;23(2):e26292. [FREE Full text] [doi: [10.2196/26292](https://doi.org/10.2196/26292)] [Medline: [33484240](https://pubmed.ncbi.nlm.nih.gov/33484240/)]
33. Nambi G, Abdelbasset WK, Elsayed SH, Verma A, George JS, Saleh AK. Clinical and physical efficiency of virtual reality games in soccer players with low back pain. *Rev Bras Med Esporte.* Dec 2021;27(6):597-602. [FREE Full text] [doi: [10.1590/1517-8692202127062021_0034](https://doi.org/10.1590/1517-8692202127062021_0034)]
34. Nambi G, Abdelbasset WK, Elsayed SH, Alrawaili SM, Abodonya AM, Saleh AK, et al. Comparative effects of isokinetic training and virtual reality training on sports performances in university football players with chronic low back pain-randomized controlled study. *Evid Based Complement Alternat Med.* 2020;2020:2981273. [FREE Full text] [doi: [10.1155/2020/2981273](https://doi.org/10.1155/2020/2981273)] [Medline: [32617104](https://pubmed.ncbi.nlm.nih.gov/32617104/)]
35. Yalfani A, Abedi M, Raeisi Z. Effects of an 8-week virtual reality training program on pain, fall risk, and quality of life in elderly women with chronic low back pain: double-blind randomized clinical trial. *Games Health J.* Apr 2022;11(2):85-92. [doi: [10.1089/g4h.2021.0175](https://doi.org/10.1089/g4h.2021.0175)] [Medline: [35290742](https://pubmed.ncbi.nlm.nih.gov/35290742/)]
36. Park J, Lee S, Ko D. The effects of the Nintendo Wii exercise program on chronic work-related low back pain in industrial workers. *J Phys Ther Sci.* Aug 2013;25(8):985-988. [FREE Full text] [doi: [10.1589/jpts.25.985](https://doi.org/10.1589/jpts.25.985)] [Medline: [24259899](https://pubmed.ncbi.nlm.nih.gov/24259899/)]
37. Afzal MW, Ahmad A, Mohseni Bandpei MA, Gilani SA, Hanif A, Waqas MS. Effects of virtual reality exercises and routine physical therapy on pain intensity and functional disability in patients with chronic low back pain. *J Pak Med Assoc.* Mar 2022;72(3):413-417. [FREE Full text] [doi: [10.47391/JPMA.3424](https://doi.org/10.47391/JPMA.3424)] [Medline: [35320216](https://pubmed.ncbi.nlm.nih.gov/35320216/)]
38. Nambi G, Alghadier M, Kashoo FZ, Aldhafian OR, Nwihadh NA, Saleh AK, et al. Effects of virtual reality exercises versus isokinetic exercises in comparison with conventional exercises on the imaging findings and inflammatory biomarker changes in soccer players with non-specific low back pain: a randomized controlled trial. *Int J Environ Res Public Health.* Dec 28, 2022;20(1):524. [FREE Full text] [doi: [10.3390/ijerph20010524](https://doi.org/10.3390/ijerph20010524)] [Medline: [36612846](https://pubmed.ncbi.nlm.nih.gov/36612846/)]
39. Nambi G, Abdelbasset WK, Alqahatani BA. Radiological (magnetic resonance image and ultrasound) and biochemical effects of virtual reality training on balance training in football players with chronic low back pain: a randomized controlled study. *J Back Musculoskelet Rehabil.* 2021;34(2):269-277. [doi: [10.3233/BMR-191657](https://doi.org/10.3233/BMR-191657)] [Medline: [33285623](https://pubmed.ncbi.nlm.nih.gov/33285623/)]
40. Nambi G, Abdelbasset W, Alsubaie S, Saleh AK, Verma A, Abdelaziz MA, et al. Short-term psychological and hormonal effects of virtual reality training on chronic low back pain in soccer players. *J Sport Rehabil.* Mar 16, 2021;30(6):884-893. [doi: [10.1123/jsr.2020-0075](https://doi.org/10.1123/jsr.2020-0075)] [Medline: [33596538](https://pubmed.ncbi.nlm.nih.gov/33596538/)]
41. Matheve T, Bogaerts K, Timmermans A. Virtual reality distraction induces hypoalgesia in patients with chronic low back pain: a randomized controlled trial. *J Neuroeng Rehabil.* May 22, 2020;17(1):55. [FREE Full text] [doi: [10.1186/s12984-020-00688-0](https://doi.org/10.1186/s12984-020-00688-0)] [Medline: [32321516](https://pubmed.ncbi.nlm.nih.gov/32321516/)]
42. Stamm O, Dahms R, Reithinger N, Ruß A, Müller-Werdan U. Virtual reality exergame for supplementing multimodal pain therapy in older adults with chronic back pain: a randomized controlled pilot study. *Virtual Real.* Feb 11, 2022;26(4):1291-1305. [FREE Full text] [doi: [10.1007/s10055-022-00629-3](https://doi.org/10.1007/s10055-022-00629-3)] [Medline: [35194374](https://pubmed.ncbi.nlm.nih.gov/35194374/)]
43. Monteiro-Junior RS, de Souza CP, Lattari E, Rocha NBF, Mura G, Machado S, et al. Wii-workouts on chronic pain, physical capabilities and mood of older women: a randomized controlled double blind trial. *CNS Neurol Disord Drug Targets.* 2015;14(9):1157-1164. [doi: [10.2174/187152731566615111120131](https://doi.org/10.2174/187152731566615111120131)] [Medline: [26556092](https://pubmed.ncbi.nlm.nih.gov/26556092/)]
44. Cetin H, Kose N, Oge HK. Virtual reality and motor control exercises to treat chronic neck pain: a randomized controlled trial. *Musculoskelet Sci Pract.* Dec 05, 2022;62:102636. [doi: [10.1016/j.msksp.2022.102636](https://doi.org/10.1016/j.msksp.2022.102636)] [Medline: [35952621](https://pubmed.ncbi.nlm.nih.gov/35952621/)]
45. Sarig Bahat H, Croft K, Carter C, Hoddinott A, Sprecher E, Treleaven J. Remote kinematic training for patients with chronic neck pain: a randomised controlled trial. *Eur Spine J.* Jul 2018;27(6):1309-1323. [doi: [10.1007/s00586-017-5323-0](https://doi.org/10.1007/s00586-017-5323-0)] [Medline: [29018956](https://pubmed.ncbi.nlm.nih.gov/29018956/)]

46. Nusser M, Knapp S, Kramer M, Krischak G. Effects of virtual reality-based neck-specific sensorimotor training in patients with chronic neck pain: a randomized controlled pilot trial. *J Rehabil Med*. Mar 10, 2021;53(2):jrm00151. [[FREE Full text](#)] [doi: [10.2340/16501977-2786](https://doi.org/10.2340/16501977-2786)] [Medline: [33369684](#)]
47. Tejera DM, Beltran-Alacreu H, Cano-de-la-Cuerda R, Leon Hernández JV, Martín-Pintado-Zugasti A, Calvo-Lobo C, et al. Effects of virtual reality versus exercise on pain, functional, somatosensory and psychosocial outcomes in patients with non-specific chronic neck pain: a randomized clinical trial. *Int J Environ Res Public Health*. Aug 16, 2020;17(16):5950. [[FREE Full text](#)] [doi: [10.3390/ijerph17165950](https://doi.org/10.3390/ijerph17165950)] [Medline: [32824394](#)]
48. Comparcini D, Simonetti V, Galli F, Saltarella I, Altamura C, Tomietto M, et al. Immersive and non-immersive virtual reality for pain and anxiety management in pediatric patients with hematological or solid cancer: a systematic review. *Cancers (Basel)*. Mar 03, 2023;15(3):985. [[FREE Full text](#)] [doi: [10.3390/cancers15030985](https://doi.org/10.3390/cancers15030985)] [Medline: [36765945](#)]
49. Gupta A, Scott K, Dukewich M. Innovative technology using virtual reality in the treatment of pain: does it reduce pain via distraction, or is there more to it? *Pain Med*. Jan 01, 2018;19(1):151-159. [doi: [10.1093/pm/pxn109](https://doi.org/10.1093/pm/pxn109)] [Medline: [29025113](#)]
50. Ostelo RWJG, Deyo RA, Stratford P, Waddell G, Croft P, Von Korf M, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976)*. Jan 01, 2008;33(1):90-94. [doi: [10.1097/BRS.0b013e31815e3a10](https://doi.org/10.1097/BRS.0b013e31815e3a10)] [Medline: [18165753](#)]
51. Morris P, Ali K, Merritt M, Pelletier J, Macedo LG. A systematic review of the role of inflammatory biomarkers in acute, subacute and chronic non-specific low back pain. *BMC Musculoskelet Disord*. Mar 03, 2020;21(1):142. [[FREE Full text](#)] [doi: [10.1186/s12891-020-3154-3](https://doi.org/10.1186/s12891-020-3154-3)] [Medline: [32126991](#)]
52. Eccleston C, Fisher E, Liikkanen S, Sarapohja T, Stenfors C, Jääskeläinen SK, et al. A prospective, double-blind, pilot, randomized, controlled trial of an "embodied" virtual reality intervention for adults with low back pain. *Pain*. Oct 01, 2022;163(9):1700-1715. [[FREE Full text](#)] [doi: [10.1097/j.pain.0000000000002617](https://doi.org/10.1097/j.pain.0000000000002617)] [Medline: [35324507](#)]
53. Lier EJ, de Vries M, Steggink EM, Ten Broek RPG, van Goor H. Effect modifiers of virtual reality in pain management: a systematic review and meta-regression analysis. *Pain*. Aug 01, 2023;164(8):1658-1665. [[FREE Full text](#)] [doi: [10.1097/j.pain.0000000000002883](https://doi.org/10.1097/j.pain.0000000000002883)] [Medline: [36943251](#)]
54. Kato S, Murakami H, Demura S, Yoshioka K, Shinmura K, Yokogawa N, et al. Abdominal trunk muscle weakness and its association with chronic low back pain and risk of falling in older women. *BMC Musculoskelet Disord*. Jul 03, 2019;20(1):273. [[FREE Full text](#)] [doi: [10.1186/s12891-019-2655-4](https://doi.org/10.1186/s12891-019-2655-4)] [Medline: [31159812](#)]
55. Kitagawa R, Kato S, Demura S, Kurokawa Y, Shinmura K, Yokogawa N, et al. Efficacy of abdominal trunk muscles-strengthening exercise using an innovative device in treating chronic low back pain: a controlled clinical trial. *Sci Rep*. Dec 14, 2020;10(1):21883. [[FREE Full text](#)] [doi: [10.1038/s41598-020-78908-9](https://doi.org/10.1038/s41598-020-78908-9)] [Medline: [33318516](#)]
56. Mao Y, Chen P, Li L, Huang D. Virtual reality training improves balance function. *Neural Regen Res*. Oct 01, 2014;9(17):1628-1634. [[FREE Full text](#)] [doi: [10.4103/1673-5374.141795](https://doi.org/10.4103/1673-5374.141795)] [Medline: [25368651](#)]
57. Paalanne N, Niinimäki J, Karppinen J, Taimela S, Mutanen P, Takatalo J, et al. Assessment of association between low back pain and paraspinal muscle atrophy using opposed-phase magnetic resonance imaging: a population-based study among young adults. *Spine (Phila Pa 1976)*. Dec 01, 2011;36(23):1961-1968. [doi: [10.1097/BRS.0b013e3181fef890](https://doi.org/10.1097/BRS.0b013e3181fef890)] [Medline: [21289551](#)]
58. Currie SR, Wang J. Chronic back pain and major depression in the general Canadian population. *Pain*. Jan 2004;107(1-2):54-60. [doi: [10.1016/j.pain.2003.09.015](https://doi.org/10.1016/j.pain.2003.09.015)] [Medline: [14715389](#)]
59. Janssen SA, Arntz A. Anxiety and pain: attentional and endorphinergic influences. *Pain*. Aug 1996;66(2-3):145-150. [doi: [10.1016/0304-3959\(96\)03031-x](https://doi.org/10.1016/0304-3959(96)03031-x)] [Medline: [8880835](#)]
60. Turk DC. Understanding pain sufferers: the role of cognitive processes. *Spine J*. 2004;4(1):1-7. [doi: [10.1016/s1529-9430\(03\)00068-8](https://doi.org/10.1016/s1529-9430(03)00068-8)] [Medline: [14749188](#)]
61. Larson SL, Clark MR, Eaton WW. Depressive disorder as a long-term antecedent risk factor for incident back pain: a 13-year follow-up study from the Baltimore Epidemiological Catchment Area sample. *Psychol Med*. Mar 2004;34(2):211-219. [doi: [10.1017/s0033291703001041](https://doi.org/10.1017/s0033291703001041)] [Medline: [14982127](#)]
62. Huang Q, Lin J, Han R, Peng C, Huang A. Using virtual reality exposure therapy in pain management: a systematic review and meta-analysis of randomized controlled trials. *Value Health*. Mar 2022;25(2):288-301. [[FREE Full text](#)] [doi: [10.1016/j.jval.2021.04.1285](https://doi.org/10.1016/j.jval.2021.04.1285)] [Medline: [35094802](#)]
63. Gold JI, Belmont KA, Thomas DA. The neurobiology of virtual reality pain attenuation. *Cyberpsychol Behav*. Aug 2007;10(4):536-544. [doi: [10.1089/cpb.2007.9993](https://doi.org/10.1089/cpb.2007.9993)] [Medline: [17711362](#)]
64. Le Maitre CL, Hoyland JA, Freemont AJ. Catabolic cytokine expression in degenerate and herniated human intervertebral discs: IL-1beta and TNFalpha expression profile. *Arthritis Res Ther*. 2007;9(4):R77. [[FREE Full text](#)] [doi: [10.1186/ar2275](https://doi.org/10.1186/ar2275)] [Medline: [17688691](#)]
65. Phillips KLE, Jordan-Mahy N, Nicklin MJH, Le Maitre CL. Interleukin-1 receptor antagonist deficient mice provide insights into pathogenesis of human intervertebral disc degeneration. *Ann Rheum Dis*. Dec 2013;72(11):1860-1867. [doi: [10.1136/annrheumdis-2012-202266](https://doi.org/10.1136/annrheumdis-2012-202266)] [Medline: [23396662](#)]
66. Nambi G, Abdelbasset WK, Elsayed SH, Khalil MA, Alrawaili SM, Alsubaie SF. Comparative effects of virtual reality training and sensory motor training on bone morphogenic proteins and inflammatory biomarkers in post-traumatic osteoarthritis. *Sci Rep*. Oct 28, 2020;10(1):15864. [[FREE Full text](#)] [doi: [10.1038/s41598-020-72587-2](https://doi.org/10.1038/s41598-020-72587-2)] [Medline: [32985509](#)]

67. Matheve T, De Baets L, Bogaerts K, Timmermans A. Lumbar range of motion in chronic low back pain is predicted by task-specific, but not by general measures of pain-related fear. *Eur J Pain*. Jul 2019;23(6):1171-1184. [doi: [10.1002/ejp.1384](https://doi.org/10.1002/ejp.1384)] [Medline: [30793429](https://pubmed.ncbi.nlm.nih.gov/30793429/)]
68. Rudolfsson T, Björklund M, Djupsjöbacka M. Range of motion in the upper and lower cervical spine in people with chronic neck pain. *Man Ther*. Mar 2012;17(1):53-59. [doi: [10.1016/j.math.2011.08.007](https://doi.org/10.1016/j.math.2011.08.007)] [Medline: [21945295](https://pubmed.ncbi.nlm.nih.gov/21945295/)]
69. Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. Lancet Low Back Pain Series Working Group. What low back pain is and why we need to pay attention. *Lancet*. Jul 09, 2018;391(10137):2356-2367. [FREE Full text] [doi: [10.1016/S0140-6736\(18\)30480-X](https://doi.org/10.1016/S0140-6736(18)30480-X)] [Medline: [29573870](https://pubmed.ncbi.nlm.nih.gov/29573870/)]
70. Saavedra-Hernández M, Castro-Sánchez AM, Cuesta-Vargas AI, Cleland JA, Fernández-de-las-Peñas C, Arroyo-Morales M. The contribution of previous episodes of pain, pain intensity, physical impairment, and pain-related fear to disability in patients with chronic mechanical neck pain. *Am J Phys Med Rehabil*. Dec 2012;91(12):1070-1076. [doi: [10.1097/PHM.0b013e31827449a5](https://doi.org/10.1097/PHM.0b013e31827449a5)] [Medline: [23159953](https://pubmed.ncbi.nlm.nih.gov/23159953/)]

Abbreviations

- CLBP:** chronic low back pain
- CNP:** chronic neck pain
- CRP:** C-reactive protein
- CSP:** chronic spinal pain
- DVPRS:** Defense and Veterans Pain Rating Scale
- GRADE:** Grading of Recommendations, Assessment, Development and Evaluation
- IL:** interleukin
- IVR:** immersive virtual reality
- LBP:** low back pain
- NDI:** Neck Disability Index
- NIVR:** nonimmersive virtual reality
- NPRS:** Numerical Pain Rating Scale
- NRS:** Numeric Rating Scale
- NSAID:** nonsteroidal anti-inflammatory drug
- PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analysis
- RCT:** randomized controlled trial
- ROM:** range of motion
- TNF- α :** tumor necrosis factor-alpha
- TSK:** Tampa Scale of Kinesiophobia
- VAS:** Visual Analogue Scale
- VR:** virtual reality
- VRE:** virtual reality exercise
- WMD:** weighted mean difference

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