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Review Article

The Use of Virtual Reality in Back Pain Rehabilitation: A Systematic Review and Meta-Analysis

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Abstract: **This systematic review aimed to synthesize the existing evidence of extended reality (XR) on pain and motor function outcomes in patients with back pain. Following the Cochrane guidelines, relevant articles of any language were selected by 2 independent reviewers from CINAHL, Cochrane, Embase, Medline and Web of Knowledge databases. Of 2,050 unique citations, 24 articles were included in our review. These studies included a total of 900 back pain patients. Despite broader XR search, all interventions were virtual reality (VR) based and involved physical exercises (n = 17, 71%), hippotherapy (n = 4, 17%), motor imagery (n = 1, 4%), distraction (n = 1, 4%), and cognitive-behavior therapy (n = 1, 4%). Sixteen controlled studies were included in a meta-analysis which suggested that VR provides a significant improvement in terms of back pain intensity over control interventions (Mean Difference: -0.67; 95% CI: -1.12 to -0.23; I^2 = 85%). Almost all included studies presented high risk of bias, highlighting the need to improve methodology in the examination of VR interventions. While the specific set of studies showed high heterogeneity across several methodological factors, a tentative conclusion could be drawn that VR was effective improving back pain intensity and tends to have a positive effect on improving other pain outcomes and motion function.**

Perspective: ***Extended reality technologies have appeared as interesting nonpharmacological options for the treatment of back pain, with the potential to minimise the need for opioid medications. Our systematic review summarised existing applications of extended reality for back pain and proposed a few recommendations to direct further studies in the field.***

Key words: *Virtual reality, back pain, motor function, immersion, rehabilitation.*

Back pain continues to be a global issue with serious health and economic consequences, and has been the greatest contributor to years lived with disability over the last 30 years.[138] Its prevalence increases regardless of age, sex, race, socioeconomic status, and world region.[46,142] Numerous factors can be attributed to the heterogeneous presentation of back pain. These include difficulty in accurate diagnosis, prognosis and availability of effective treatment options that reduce the reliance on invasive surgical and opiate-based pharmacological intervention.[26,40,44,48,80] Back pain rehabilitation is also time consuming and patients may lack the motivation necessary to complete the whole course of treatment.[126] Furthermore, biopsychosocial interactions known to influence chronic back pain

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have led to a paradigm shift towards personalized intervention strategies that prioritize a multidimensional treatment approach.[141]

Within the last decade, promising treatment modalities have adopted new technologies at increasing rates to improve pain and motor function outcomes in rehabilitation. These advancements provide clinicians and patients greater scope in the design and development of engaging interventions, offering greater flexibility over conventional methods. The umbrella term of extended reality (XR) encompasses the spectrum of immersive experiences made possible between physical and virtual environments or mixed realities. The use of XR technologies is becoming a more popular option for people suffering from acute and chronic pain. This growing popularity is partly facilitated by the accessibility of new, affordable, wireless head-mounted displays that offer high-quality immersive experiences.

XR can be used for pain modulation through at least four different ways. First, it distracts the brain's attention away from the noxious signals ascending from the body towards other sensations.[22,38,57] Second, by engaging the working memory (ie, the part of the short-term memory that keeps track of time) it creates the illusion of time acceleration, thereby shortening the duration of pain episodes.[47,62,120] Third, it induces the illusion of ownership of a virtual body using multisensory correlations to manipulate body perception for pain conditions that involve altered body image.[56,81,82,97] And finally, it can be used as gamification to increase motivation and engagement in specific behavioural activities or movement strategies through progressive challenge, achievement of game objectives, and in-games rewards.[49,74,101,130]

While the effectiveness of XR on different conditions associated with pain have been reviewed (including musculoskeletal disorders,[30,78] spinal cord injuries,[1,34,35] neurological diseases,[39,105] phantom limb,[53] burn injuries,[76,113] and dental treatment[79]), the effectiveness of XR on back pain has received relatively less attention. A single narrative review[129] provides a preliminary assessment of the potential size and scope of available research literature to describe the theoretical basis of the therapeutic effects of virtual reality on back pain, but aims and key methodological differences across clinical trials raises the need for a more systematic approach. Therefore, we aimed to systematically review the existing evidence for the current application of interventions across the XR spectrum in improving pain and motor function outcomes in individuals with back pain.

Methods

Terminology

The Reality-Virtuality Continuum introduced by Milgram et al.[90] in 1994 aims to cover all possible configurations of environments composed of real and virtual content, and classifies interactions into five categories based on the level to which virtual and/or real content are integrated: reality; augmented reality; augmented virtuality; mixed reality; and VR (Fig 1). Located at the extreme left of the continuum, reality is defined as any environment consisting exclusively of real content,[91] while VR is defined as an entirely computer-generated virtual environment [7] without means to connect with the real world or see it. [11] Between these 2 extremes, mixed reality bridges the space between wholly real and virtual experiences and includes augmented reality and augmented virtuality. Augmented reality aims to augment user perception and comprehension of reality by overlaying virtual content within the real-world view,[11] whereas augmented virtuality aims to enhance virtual environments with the integration of content from the real world.[10,11]

Along the reality-virtuality continuum, different input and output technologies can be exploited to deliver an inclusive, extensive, and surrounding illusion of the reality to stimulate user's sense of immersion.[117,127] Immersion can be regarded as a quality of the system's technology, an objective measure of the extent to which the system presents a vivid virtual environment while shutting out physical reality.[31] Input devices (such as joystick, keyboard, handheld controllers, wearable finger tracking glove, motion trackers, etc.) send signals to the system about the action of the user, while output devices (such as headphones, pressure pads, sensing gloves, visual stimuli projected on a wall, computer screen, googles or head mounted display, etc.) provide the users with feedback to stimulate their senses.[8]

The intensity of immersion is influenced by the feeling of presence (psychological sense of being in the virtual environment), the degree of realism (degree of agreement between user's expectations and the actual experience in the virtual world), and the level of reality (level at which the user feels the immersion as authentic).[10,28,117,127] A perfectly immersive experience requires the highest level of attention by stimulating all senses allowing the user to interact with the virtual world exactly as they would with the real world.[11]

Although many factors influence the level of immersion, 3 main categories of systems have previously been described[11,28, 71,109]:

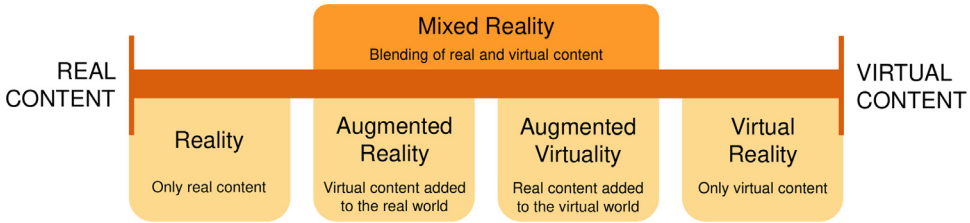

Figure 1. Reality-virtuality continuum inspired and modified from Milgram and Kishino.90.

- Low-immersive systems use desktops or handheld displays to provide a limited field of view of the virtual environment.[11,28,71,109] They are not associated with tracking systems and visual experience does not need to match proprioceptive feedback.[11,71]
- Moderate-immersive systems may involves a large and concave screen with a projection system that provide the user a broad field of view, similar to a large screen movie experience.[11,28,71] They may be associated with a tracking system.[11]
- High-immersive systems consist of head mounted display or surround-screen that completely fill the use's field of view.[11,28,71,109] They involve body motion capture system to closely match visual experience with proprioceptive feedback for optimal sensorimotor integration.[11,71]

Search Strategy

Using the Cochrane Guidelines,[61] pertinent studies (irrespective of published language) were extracted from the following databases: CINAHL, Cochrane, Embase, Medline (Pubmed) and Web of Science between database inception and January, 2019. The search strategy focused on keywords related to "back pain" and "virtual and mixed realities." An example of the full search strategy is presented in **Table S1** (see Supplemental digital content). Following January 2019, results of the search were automatically updated through email alerts provided by the selected databases until September 2020. In addition, the reference lists of included articles, pertinent reviews, and article references that cited an eligible study, were also screened. To identify in-progress or unpublished studies, the following clinical registries were consulted: ClinicalTrials.gov, Health Services Research Projects in Progress and the International Standard Randomized Controlled Trial Number Register. The current review has been reported following the statements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines (PRISMA)[92] and A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2).[116] Our review protocol was registered in PROSPERO (CRD42020161376).

Study Selection

References were gathered and duplicates were removed using EndNote (version X9, Thomson Reuters, 2019). In an initial screening, 2 independent reviewers (MB and AS) selected eligible studies based on titles and abstracts. A second independent screening (MB and AS) was then conducted on full texts. In the event of disagreement, a third author was consulted (JT). To be selected, a study had to include adult (≥18 years old) participants with back pain. A study that included participants with neck pain was excluded. Articles that included patients with spinal cord injury were excluded; this population has already been the subject of recent systematic reviews and/or meta-analyses.[1,34,35] All study designs that evaluated the effect of XR on pain and/or motor function outcomes were selected. The presence of a comparator (placebo, standard therapy, no treatment, gold standard, inactive controls, active controls, etc.) was not required for study inclusion.

Data Extraction

2 authors (MB and AS) extracted data independently for each included study using a standard data extraction spreadsheet (Microsoft Excel, Microsoft Corporation, Washington, United States). Discrepancies were resolved by consensus with a third author (JT). The following entries were included in the data extraction sheet: study characteristics (title, authors, journal, year, study design); methods (inclusion/exclusion criteria, number of patients and control included in the analysis, randomization, allocation concealment, and blinding methods); participants (pain condition, age, sex); intervention (devices used, number and duration of session, follow-up); outcomes (pain and motor function measurements); statistical analyses; results; and adverse events.

Risk of Bias

2 review authors (MB and AS) independently assessed the risk of bias of included articles. In the event of a disagreement, a third author (JT) was consulted. The second version of the Cochrane risk-of-bias tool for randomized trials (RoB 2)[125] was used to assess randomized controlled trials. This tool included 5 domains evaluating source of bias arising from the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. The Risk Of Bias In Non-Randomized Studies-of Interventions (ROBINS-I)[124] was used to assess risk of bias in the results of non-randomized studies. In the ROBINS-I tool, the risk of "Bias due to confounding" (domain 1) was considered low if the authors controlled the diagnosis of back pain and its severity (eg, with inclusion and exclusion criteria for a more homogenous population). For both tools, the judgement "Low risk of bias", "High risk of bias", "Some concerns"/"Moderate", "Unclear risk of bias"/"No information", for each item was followed by a description of the observations that support the judgement. Data was imported into the Robvis web app to create the risk-of-bias plots for the ROBINS-I and RoB 2 tools.[87]

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, intervention, and main results. In the meta-analysis, a random-effects model was used selected chose based on two criteria: 1) presence of a control group and an experimental group; 2) the most consistent measurement tool across studies. Accordingly, we included controlled before and after

studies and randomized control trials (RCTs) that used pain scales – numeric rating scale (NRS) or visual analog scale (VAS) – to measure pain intensity immediately after the intervention period. Due to a lack of studies that collected data at different post-trial follow-up times (eg, 6 months after the intervention), data collected during post-trial follow-up was not considered. The raw 0- to100-point scale scores were converted to a common 0- to 10-point scale by dividing by 10. For each individual study, the standardized mean difference was calculated as the difference between the experimental group (which used XR application) and the control group immediately after the intervention period. The treatment effect size was calculated for each study using reported sample sizes, means, and standard deviations after treatment for each group (experimental and control groups), with 95% confidence interval. When this information was not available, authors were contacted. The individual effect sizes are weighted according to the reciprocal of their variance (calculated as the square of the standard error given in the individual study).[36] Statistical heterogeneity is characterized by the observed intervention (experimental vs control) effects being more different from each other than 1 expected due to chance alone[54] and was assessed by calculating I^2, which is used to determine the percentage of the variation caused by heterogeneity within the sample of included studies. The most common classification of I^2 consider values lower than 25% as "small" heterogeneity, values between 25% and 50% as "medium", and higher than 50% as "large".[55] Publication bias for the pain intensity outcome was inspected using funnel plots with pseudo 95% confidence limits. Eight subgroup analyses were conducted to investigate how treatment effect varies across different subgroups of patients. Subgroups were chosen based on the sources of heterogeneity observed during the data extraction process: 1) the study design: controlled before-after studies vs RCTs; 2) the type of intervention: exercise vs horse riding simulation vs motor imagery/distraction/cognitive vs behavioral therapy; 3) the type of intervention for the control group: no intervention vs traditional physical therapy session; 4) the type of pain scale used: VAS vs NRS; 5) the duration of the intervention: short-term (≤12 sessions) vs long-term (>12 sessions); 6) the risk of bias due to deviations from the intended interventions: low risk of bias vs moderate/some concerns/unclear risk of bias; 7) the pain intensity scores at baseline: presence vs absence of difference in between the experimental and the control groups; 8) the level of immersivity of the experimental group: low vs moderate vs high. All analyses were conducted with Review Manager (RevMan) software version 5.4, 2020 (Cochrane Collaboration, Copenhagen, Denmark,). Forest plots were used to assess and visualize the pooled estimates and corresponding 95% confidence limits. A P <0.05 was considered statistically significant. Due to the variability in outcome assessments, no meta-analysis was done for motor function.

Results

Article Selection

Our search strategy yielded 2,050 unique citations from which 76 articles were reviewed. Of these, 24 studies fulfilled our selection criteria and were included in the systematic review,[5,25,52,60,63-65,70,72,73,84-86,93,96,100,106,128,130,143,144,146,147] while 52 were excluded for the following reasons: thesis (n = 1), [119] dataset (n = 1), [20] commentary (n = 1), [29] recruitment advertisement (n = 1),[111] unable to reach the authors for more information (n = 1),[50] no outcome of interest (n = 2),[43,126] no population of interest (n = 3),[58,69,94] review (n = 4),[24,135,136,140] game prototype (n = 6),[3,4,17,18,95,103] clinical trial protocol (n = 7),[19,32,45,83,98,107,145] no intervention of interest (n = 12), [6,13,15,16,21,37,77,110,121,123,137,139] and abstract (n = 13),[23,33,42,51,59,68,89,99,122,131,133,134]. Preliminary results from excluded abstracts can be found in Supplemental digital content (**Table S2**).

Characteristics of Included Studies

The characteristics of the 24 studies published in peer review journals are summarized in (Tables 1 and 2**)**. These articles included a total of 900 back pain patients (523 included in experimental groups and 377 included in control groups). They were published in English between 2013 and 2020. The experimental designs identified included 1 case study (4%), 4 uncontrolled before-after studies (17%), 3 controlled before-after studies (12%), and 16 RCTs (67%). All interventions were VR-based and involved physical exercises (71%),[5,52,63-65,70,72,84-86,93,96,106,128,130,146] hippotherapy (17%),[25,73,100,144] motor imagery (4%),[143] distraction (4%),[147] and cognitive behavioral therapy (4%).[60] The systems used to generate and display virtual environments varied highly across studies, with 75% of studies using moderate levels of immersion (eg, VR-based Kinect games). Low (eg, VR-based tablet games) and high (eg, VR-based exercise with a VR headset) levels of immersivity were associated with 17% and 8% of studies, respectively. In controlled studies (ie, RCTs and controlled before-after studies), VR interventions were often compared to control cohorts that consisted of a conventional application of physical therapy (68%), or no intervention (32%). Three studies added comparison cohorts that were not VR based, including: mindfulness-based cognitive behavior therapy,[60] lumbar stabilization exercises,[65] and isokinetic training.[96] Of the included studies, 50% applied interventions on a short-term intervention periods (≤12 sessions), compared to long-term intervention periods (>12 sessions). Half of the included studies mentioned receiving funding from non-profit organizations[5,27,52,63-65,86,96,100,130,144,147] and two stated that they did not have a funding source.[128,146] For the remaining studies, this information was not provided.[25,60,70, 72,73,84,85,93,106,143]

Fourteen RCTs[52,65,70,72,73,84,86,93,96,100,128,130,143,144,146,147] and 2 controlled before-after[25,60] studies were included in the meta-analysis (Fig 2).

Table 1. Methodological Description of Included non-RCTs

Author, Y (study design)	Population Group (n), % male	Mean Age (mean ± SD years)	Type of env. (level of immersivity)	Input device / Output Device (type of feedback)	Intervention (exercises involved)	Period (follow-up)	Pain and Motor Function Outcome	Main Findings
Alemanno et al. [5] 2019 (uncontrolled before and after study)	cLBP (20), 45%	47.5±15.3	VR-based Khymeia exercises program (moderate)	Polhemus G4 tracking system / Large 2D screen (visual, acoustic)	To regain a correct body image by improving the control of trunk movements (trunk rotation, flexion and extension realized in standing, sitting, and kneeling positions).	12 sessions of 1 hour over 4 – 6 weeks (NA)	-Pain scale: NRS -Pain questionnaires: MPQ-PRI, BPI, MPQ-NWC -Physical tests: maximal and average trunk's range of motion	-CWG: significant reductions in all pain outcomes (P <.001). -CWG: significant improvement in trunk functionality (P <.05).
Chen et al. [25] 2016 (controlled before-after study)	-EG: NS cLBP (10), NIA -EC: NS cLBP (9), NIA	-EG: NIA -CG: NIA	VR-based horse-riding simulator (moderate)	None / horse simulator and 2D screen (visual, motion-haptic)	To improve back pain, balance, and strength with: -EG: a horse-riding simulator (rhythmical equine movement) and an exercise program (core strengthening). -CG: an exercises program (core strengthening).	12 sessions of 30 minutes over 4 weeks (NA)	-Pain scale: VAS -Physical tests: limit of stability	-CWG: significative improvement of all outcomes after all interventions (P <.05). -CBG: no significant difference for all outcomes (P >.05).
Hennessy et al. [52] 2020 (uncontrolled before-after study)	cLBP (12), 33%	54.3±5.1	VR-based graded exposure (high)	HTC-Vive tracking system and pelvic mechanism for movement detection / self-driven KineAssist- MX treadmill and HTC-Vive headset (visual, acoustic, motion-haptic)	To provide progressive movement challenges to practice real-world movement tasks (reaching, bending and long-lasting loads).	3 sessions of 6 minutes over 1 wk (3 – 5 days after the last session)	-Pain scales: MPQ-sf VAS, expected pain -Pain questionnaire: MPQ-sf PRI -Motor function scale: RPE	-CWG: no significant difference for all pain questionnaires and scale (P >.05), expect for expected pain, which significantly increased over the sessions (P <.05) -CWG: RPE significantly increased over the sessions (P =.009)
Igna et al. [60] 2014 (controlled before-after study)	-EG1: cBP (35), NIA -EG2: cBP (25), NIA -CG: cBP (25), NIA	-EG-1: NIA -EG-2: NIA -CG: NIA	VR-based CBT using SnowWorld (high)	Headset tracking system and joystick / VR headset (visual, acoustic)	To decrease catastrophizing beliefs and maladaptive strategies of coping with pain, as well as to increasing healthy beliefs and coping strategies of pain control (none).	-EG-1: 6 VR-based CBT sessions and 10 PHM sessions over 2 – 3 weeks (NA) -EG-2: 6 MCBT sessions and 10 PHM sessions over 2 – 3 weeks (NA) -CG: 10 PHM sessions over 2 – 3 weeks (NA)	-Pain scales: VAS, PCS, PASS -Pain questionnaires: MPQ, CPAQ	-CWG: significant improvement of PCS and VAS for all groups (P <.05) after the intervention. -CBG: significantly greater improvement of CPAQ and VAS for EG-2 compared to CG (P <.05).
Jansen-Kosterink et al. [64] 2013 (uncontrolled before-after study)	cLBP (4) and cNSP (6), 20%	54.9±11.8	VR-based PlayMancer progressive exergame (moderate)	MoCap tracking system and treadmill / Large 2D screen (visual)	To improve pain intensity, pain disability, motor skills, and physical condition (walking, overhead reaching, neck mobility).	4 – 8 sessions of 45 – 60 minutes over 4 weeks (NA)	-Pain scale: VAS -Pain questionnaire: PDI -Physical tests: 6MWT, WV, OR, CROM	-CWG: no significant difference for all outcomes (P >.05) except CROM that improved significantly (P =.03) after the intervention.

(continued on next page)

Table 1. Continued

Author, Y (study design)	*Population Group (n), % male*	*Mean Age (mean ± SD years)*	*Type of env. (level of immersivity)*	*Input device / Output Device (type of feedback)*	*Intervention (exercises involved)*	*Period (follow-up)*	*Pain and Motor Function Outcome*	*Main Findings*
Jansen-Kosterink et al. [63] 2015 (controlled before-after study)	-EG: cLBP (44), 59% -CG: cLBP (24), 42%	-EG: 43.4±11.6 -CG: 43.5± 13.7	VR-based telemedicine exercise program (low)	None / 2D laptop screen (visual, acoustic)	To improve back pain with: -EG: a mix of conventional and telemedicine rehabilitation program (NIA). -CG: traditional physical therapy sessions (NIA).	-EG: 16 sessions of CRP and 5 sessions of telemedicine over 7 weeks (2 after the last session) -CG: 21 sessions of CRP over 7 weeks (2 months after the last session)	-Pain scale: VAS -Physical test: AEBT	-CWG: significant improvement of VAS for all groups (P <.05) and no significant difference of AEBT for all groups (P >.05). -CBG: no significant difference for all outcomes (P >.05).
Matheve et al. [85] 2018 (uncontrolled before-after study)	NS cLBP (10), 20%	35.5±NIA	VR-based ValedoMotion exercise system (moderate)	Wireless motion tracking sensor / 2D screen (visual)	To improve LBP with general conditioning (cycling, stepping, cross-trainer), MCE (pelvic tilts, repositioning, stability exercises), and home exercises (functional exercises). Over the weeks, VR-based pelvic tilts exercises were gradually introduced to MCE and home exercises.	36 sessions of 2 hours over 18 weeks (NA)	-Pain scale: NRS -Motor function scale: PSFS	-CWG: significant improvement of NRS (P =.011) and PSFS (P <.001) after the intervention.
Peterson et al. [106] 2018 (case series)	cLBP (3), 0%	45.0±23.0	VR-based telerehabilitatio n home exercise program a physical therapist (low)	None / 2D screen (visual, acoustic)	To improve cLBP with a home exercise program (motor control and endurance of trunk muscles exercises) and telemedicine session with a physical to provide relevant feedback to the patients (education, CBT, exercise progression, and problem solving of barriers).	4 telerehabilitation sessions of 7 – 28 minutes over 12 months (NA)	-Pain scale: NRS -Pain questionnaire: PSEQ	-CWG: all patients reported a trend toward reduction or maintenance of a low daily NRS. -CWG: all patients improved their PSEQ score.

6MWT, 6 minute walking test; AEBT, Åstrand ergometer bicycle test; BPI, brief pain inventory; CBG, comparison between the groups (difference pre/post intervention of control group vs experimental group); cBP, chronic back pain; CBT, cognitive behavior therapy; CG, control group; cLBP, chronic low back pain; cNSP, chronic neck/shoulder pain; CPAQ, chronic pain acceptance questionnaire; CRP, conventional rehabilitation program; CROM, cervical range of motion; CWG, comparison within group (pre vs post intervention); EG, experimental group; Env., environment; MCBT, mindfulness-based cognitive behavior therapy; MCE, motor control exercises; MPQ, McGill pain questionnaire; MTS, motion-tracking system; NA, not applicable; NIA, no information available; NRS, numeric rating scale; NS, non specific; OR, overhead reach; sf, short form; NWC, number of words chosen; PASS, pain anxiety symptoms scale;PCS, pain catastrophizing scale; PDI, pain disability index, PHM, treatment as usual; PRI, pain rating index; PSEQ, pain self-efficacy questionnaire; PSFS; Patient-specific functioning scale; RPE, rating of perceived exertion; VAS, visual analogue scale; WV, walking velocity.

Table 2. Methodological Description of Included RCTs

Author, Year (study design)	Population Group (n), % male	Mean Age (mean ± SD years*)	Type of env. (level of immersivity)	Input Device / Output Device (type of feedback)	Intervention (exercises involved)	Period (follow-up)	Pain and Motor Function Outcome	Main Findings
Cikajlo et al. [27] 2016 (RCT)	-EG: cLBP (6), NIA -CG: cLBP (5), NIA	-EG: NIA -CG: NIA	VR-based Gamma trainer exercise (moderate)	COG tracking system / 2D screen (visual)	To improve cLBP with physical therapy (hydrotherapy, IGE, FES, and balance training): -EG: balance training with the Gamma device. -CG: balance training with a wobble board.	14 sessions over 2 weeks (NA)	-Physical tests: postural perturbation response, reaching, leg standing	-CWG: slight improvement of postural response and significative improvement of functional reaching (P <.05) for both groups. -CBG: no significant difference between groups for all outcomes (P >.05).
Ji-Hyuk et al. [65] 2013 (RCT)	-EG1: cLBP (8), NIA -EG2: cLBP (8), NIA -CG: cLBP (8), NIA	-EG1: 44.1±5.5 -EG2: 43.4±5.4 -CG: 45.5±5.3	VR-based Nintendo Wii exercise (moderate)	Remote controllers with motion sensor / 2D screen and controllers (visual, acoustic, tactile)	To improve pain, back strength, and balance ability with physical therapy and: -EG1: Nintendo Wii exercise. -EG2: lumbar stabilization exercise. -CG: physical therapy only.	24 sessions of 30 min over 8 weeks (NA)	-Pain scale: VAS -Pain questionnaire: RAND-36 -Physical tests: leg standing, isometric lifting (strength) -Motor function questionnaire: RAND-36	-CWG: significant improvement of pain intensity for EG1 and EG2 (P <.05). Significant increase in back strength and RAND-36 pain section for all groups (P <.05). Significant improvement in balance for EG2 and CG (P <.05). Significant improvement of physical functioning section of RAND-36 for EG2 (P <.05).
Karahan et al. [70] 2016 (RCT)	-EG: ankylosing spondylitis (30), NIA -CG: ankylosing spondylitis (30), NIA	-EG: NIA -CG: NIA	VR-based Kinect games (moderate)	Kinect tracking system / 2D screen (visual, acoustic)	To improve pain intensity functional capacity with -EG: exergame using Kinect. -CG: no intervention, usual activities.	-EG: 40 sessions of 30 min over 8 weeks (NA). -CG: no exercise program (NA).	-Pain scale: VAS -Motor function questionnaires: BASFI, BASDAI	-CWG: significative improvement for all outcomes in the EG after intervention (P <.001). -CBG: significantly greater improvement for all outcomes in the EG compared to the CG (P <05).
Kim et al. [72] 2014 (RCT)	-EG: cLBP (15), 0% -CG: cLBP (15), 0%	-EG: 44.3±NIA -CG: 50.4±NIA	VR-based Nintendo Wii Fit yoga program (moderate)	Wii balance board and Wii motion tracking system / 2D screen (visual, acoustic)	To improve cLBP with trunk stabilizing exercises using: -EG: VR-based yoga program. -CG: Physical therapy program.	12 sessions of 30 min over 4 weeks (NA).	-Pain scale: VAS -QST: Pain pressure threshold	-CWG: significant improvement of VAS and significant decrease of pain pressure threshold for both group after the intervention (P <.05).
Kim et al. 2020 [73] (RCT)	-EG: NS cLBP (24), 68% -EC: NS cLBP (24), 42%	-EG: 26.0±3.82 -CG: 28.8±9.05	VR-based horse-riding simulator (moderate)	None / horse simulator and 2D screen (visual, motion-haptic)	To improve pain intensity and functional disabilities by comparing: -EG: horse-riding simulator (postural control training). -EC: physical therapy (stabilization exercises with suspension).	16 sessions of 40 min over 8 weeks (6 months after the last session)	-Pain scale: NRS	-CWG: significant improvement of NRS in both groups at 4 weeks, 8 weeks, and at the 6 months follow-up (P <.05).
Matheve et al. [84] 2020 (RCT)	-EG: NS cLBP (42), 36% -EC: NS cLBP (42), 36%	-EG: 42.1±11.5 -CG: 44.2±11.9	VR-based ValedoMotion exercise system (moderate)	Wireless motion sensors Valedo® Pro, / 2D screen (visual)	To influence pain with: -EG: VR-based exercise session. -CG: exercise session without VR games.	1 session (NA)	-Pain scales: NRS, PCS	-CBG: significative improvement of NRS for the EG compared to the CG during (P <.0001) and after (P <.003) the intervention. -CBG: patients with low PCS scores tend to have larger improvements in NRS compared to those with high PCS scores.

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Table 2. Continued

Author, Year (study design)	*Population Group (n), % male*	*Mean Age (mean ± SD years*)*	*Type of env. (level of immersivity)*	*Input Device / Output Device (type of feedback)*	*Intervention (exercises involved)*	*Period (follow-up)*	*Pain and Motor Function Outcome*	*Main Findings*
Mbada et al. [86] 2019 (RCT)	-EG: NS cLBP (24), NIA -CG: NS cLBP (32), NIA	-EG: NIA -CG: NIA	VR-based telerehabilitatio n McKenzie therapy (low)	None / mobile phone screen (visual)	To improve pain intensity and back muscles endurance with specific lumbosacral repeated movements using: -EG: Telerehabilitation-based McKenzie therapy. -EC: Clinic-based McKenzie Therapy.	24 sessions over 8 weeks (NA)	-Pain scale: QVAS -Motor function tests: modified BSME	-CWG: significative improvement of QVAS and BSME for all groups after the intervention (P <.001). -CBG: no significant difference between groups for all outcomes (P >.05).
Monteiro et al. [93] 2015 (RCT)	-EG: cLBP (17), 0% -CG: cLBP (17), 0%	-EG: NIA -CG: NIA	VR-based Nintendo Wii Fit program (moderate)	Wii balance board and Wii motion tracking system / 2D screen (visual, acoustic)	To improve pain and functional capacity with: -EG: strength exercises and core training and exercises with the Wii. -EC: strength exercises and core training.	24 sessions of 90 min overs 8 weeks (NA)	-Pain scale: NRS -Physical tests: balance, sit-to-stand test	-CWG: significative improvement of NRS for all groups after the intervention (p<.01) and significative improvement of functional capacity to sit for the EG (P =.04). -CBG: no significant difference between groups for all outcomes (P >.05).
Nambi et al. [96] 2020 (RCT)	-EG1: cLBP (15), 100% -EG2: cLBP (15), 100% -CG:cLBP (15), 100%	-EG1:21.3±1.2 -EG2: 20.2±1.6 -CG: 20.8±1.6	VR-based ProKin 252 balance training (moderate)	ProKin 252 balance board / 2D screen (visual)	To improve trunk muscle strength with: -EG1: VR-based balance training. -EG2: isokinetic training. -CG: conventional training exercises.	20 sessions over 4 weeks (8 weeks and 6 months after de last session)	-Pain scale: VAS -Physical tests: sprint performance, jump performance	-CWG: significative improvement of VAS and physical performances for all groups after the intervention (P ^.001). -CBG: significantly greater improvement of VAS and physical performance for EG1 compared to EG2 and CG (P <001).
Oh et al. [100] 2014 (RCT)	-EG1:LBP(10), 100% -EG2: LBP (9), 100% -EG3: LBP (9), 100% -CG: LBP (9), 100%	-EG1:20.6±0.7 -EG2: 20.3±0.5 -EG3: 20.4±0.3 -CG: 20.7±0.4	VR-based horse-riding simulator (moderate)	None / horse simulator and 2D screen (visual, motion-haptic)	To improve back pain, balance, and strength with: -EG1-2-3: horse simulator. -CG: no horse simulator.	-EG1: 24 sessions of 10 min over 8 weeks (NA). -EG2: 24 sessions of 20 min over 8 weeks (NA). -EG3: 24 sessions of 30 min over 8 weeks (NA). -CG: no intervention (NA)	-Pain scales: VAS (back pain, night pain) -Motor function scale: VAS (exercise) -Physical test: isokinetic trunk strength	-CWG: significative improvement of all VAS scores and overall isokinetic trunk strength measures for EG1-2-3 groups after the intervention (P <.05). -CBG: significantly greater improvement of all VAS scores and overall isokinetic trunk strength measures for EG2 compared to all other groups (P <.05).
Suh et al. [128] 2018 (RCT)	-EG: non-idiopathic cLBP (10), NIA -CG: non-idiopathic cLBP (10), NIA	-EG: 72.3±5.3 -CG: 66.7±3.1	VR-based Nintendo Wii Sports games (moderate)	Wii remotes and Wii motion tracking system / 2D screen (visual, acoustic)	To improve muscle rigidity, muscle tension and pain with: -EG: VR exercises (tennis, bowling, golf). -CG: no intervention, usual activities.	-EG: 12 sessions of 30 min over 4 weeks (NA) -CG: no intervention (NA)	-Physical test: BBS	-CWG: significative improvement of BBS for the EG after the intervention(P <.05) -CBG: no significant difference between groups after the intervention (P >.05).

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Table 2. Continued

Author, Year (study design)	*Population Group (n), % male*	*Mean Age (mean ± SD years*)*	*Type of env. (level of immersivity)*	*Input Device / Output Device (type of feedback)*	*Intervention (exercises involved)*	*Period (follow-up)*	*Pain and Motor Function Outcome*	*Main Findings*
Thomas et al. [130] 2016 (RCT)	-EG: cLBP (26), 54% -CG: cLBP (26),	-EG: 23.9±6.8 -CG: 26.7±8.5	VR-based dodgeball games (moderate)	Light-reflective marker clusters and Vicon Bonita system / 3D screen and Samsung 3D glasses (visual, acoustic)	To elicit graded increases in lumbar spine flexion using: -EG: VR-based dodgeball game. -CG: no intervention, usual activities.	-EG: 3 sessions of 15 min over 3 days (NA) -CG: no intervention (NA)	-Pain scales: MPQ-VAS, MPQ-PPI -Physical test: lumbar spine flexion	-CWG: significative improvement of pain outcomes for the EG after the intervention (P <.05), but no significant difference for the lumbar spine flexion after the intervention period (P >.05) for both groups. -CBG: no significant difference between groups for all outcomes after the intervention (P >.05).
Yelvar et al. [143] 2017 (RCT)	-EG: NS cLBP (22), 55% -CG: NS cLBP (22), 18%	-EG: 46.3±3.4 -CG: 52.8±11.5	VR-based motor imagery (moderate)	None / Wrap 920 glasses (visual, acoustic)	To improve pain and function using: -EG: traditional physiotherapy and VR walking motor imagery. -CG: traditional physiotherapy.	10 sessions over 2 weeks (NA)	-Pain scale: VAS -Pain questionnaire: HNP -Physical tests: TUG, 6MWT, single-leg balance test	-CBG: significative improvement of VAS, TUG, 6MWT for the EG compared to the CG (P <.031), no significative difference for the other outcomes (P >.05).
Yoo et al. [144] 2014 (RCT)	-EG: cLBP (24), 100% -CG: cLBP (23), 100%	-EG: 20.4±1.33 -CG: 20.7±1.45	VR-based horse-riding simulator (moderate)	None / horse simulator and 2D screen (visual, motion-haptic)	To stimulate posture enhancement and equilibrium on motor function and strength with: -EG: horse simulator riding group. -CG: no intervention, usual activities.	-EG: 24 sessions of 10-40 min over 8 weeks (NA) -CG: no intervention (NA)	-Pain scale: VAS (back pain, night pain) -Motor function scale: VAS (exercise) -Physical test: isokinetic trunk strength	-CWG: significative improvement of all VAS scores for both groups after the intervention period (P <.01). Significant improvement of overall isokinetic trunk muscles strength measures (P <.05). -CBG: significantly greater improvement for all pain VAS scores and overall trunk muscle strength measures in the EG compared to the CG (P <.01). No significant difference between groups for exercise VAS scores (P >.05).
Zadro et al. [146] 2019 (RCT)	-EG: cLBP (30), 40% -CG: cLBP (30), 57%	-EG: 68.8±5.5 -CG: 67.8±6.0	VR-based Nintendo Wii Fit U exercise (moderate)	Wii balance board and Wii motion tracking system / 2D screen (visual, acoustic)	To reduce pain with: -EG: the Wii Fit U (flexibility, strengthening, and aerobic exercises). -CG: no intervention, usual activities.	-EG: 24 session of 60 min over 8 weeks (3 and 6 months after the last session) -CG: no intervention (3 and 6 months after the last session)	-Pain scale: NRS -Pain questionnaire: PSEQ -Motor function scale: PSFS -Motor function questionnaire: RAPA	-CWG: significative improvement of all pain outcomes and PSFS after the intervention for the EG (P <.05). -CBG: significantly greater improvement of NRS and PSFS for the EG after intervention compared to the CG (P <.04). No significant between-group differences

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Table 2. Continued

Author, Year (study design)	Population Group (n), % male	Mean Age (mean ± SD years*)	Type of env. (level of immersivity)	Input Device / Output Device (type of feedback)	Intervention (exercises involved)	Period (follow-up)	Pain and Motor Function Outcome	Main Findings
								for the remaining outcomes ($P > .05$).
Zavarize et al [147]. 2016 (RCT)	-EG: cLBP (10), NIA -CG: cLBP (11), NIA	-EG: 68.8±5.5 -CG: 67.8±6.0	VR-based non- exercise video games (low)	Samsung tablet / Samsung tablet (visual, acoustic)	To provide gain and of lumbar flexibility with: -EG: physiotherapy program and non-exercise video games. -CG: physiotherapy program.	-EG: 5 session of 70 min over 1 wk (NA) - CG: 5 session of 50 min over 1 wk (NA)	-Pain scale: VAS -Pain questionnaire: MPQ	-CWG: significative improvement of VAS for all groups after the intervention ($P < .01$). Significative improvement of MPQ for the CG after the intervention ($P < .01$).

6MWT, 6 minute walking test; BASDAI, bath ankylosing spondylitis disease activity index; BASFI, bath ankylosing spondylitis functional index; BBS, Berg balance scale; BSME, Biering-Sørensen test of static muscular endurance; CBG, comparison between the groups (difference pre/post intervention of control group vs experimental group); CG, control group; cLBP, chronic low back pain; CNPq, Conselho Nacional de Desenvolvimento Científico e Tecnológico; COG; center of gravity; CWG, comparison within group (pre vs post intervention); EG, experimental group; Env., environment; FES, functional electrical stimulation; IGE, individual guided exercises; QST, quantitative sensory testing; MPQ, McGill pain questionnaire; NA, not applicable; NIA, no information available; NHP, Nottingham health profile; NRS, numeric rating scale; NS, non specific; PCS, pain catastrophizing scale; PPI, present pain intensity, PRI, pain rating index; PSEQ, pain self-efficacy questionnaire; PSFS; Patient specific functioning scale; RAND-36 RAPA, rapid assessment of physical activity questionnaire; RCT, randomized control trial; TUG, time-up-go test; VAS, visual analogue scale.

Outcome Measures

Pain

Among included studies, pain outcomes were evaluated with pain scales (92%), and/or pain questionnaires (38%), and/or quantitative sensory testing (4%). Pain scales included the VAS,[25,52,60,63-65,70,72,86,96,130,143,144,147] the NRS,[5,73,84,85,93,106,146] the pain catastrophizing scale,[60,84] the pain anxiety symptoms scale, [60] the present pain intensity scale,[130] the RAND-36, [65] the expected pain scale,[52] and the brief pain inventory.[5] Pain questionnaires included the McGill pain questionnaire,[5,60,147] the chronic pain acceptance questionnaire,[60] the pain disability index,[64] Nottingham health profile,[143] and the pain self-efficacy questionnaire,[106,146] while quantitative sensory testing included the evaluation of pain pressure threshold.[72]

A meta-analysis was performed on 16 controlled studies that met our inclusion criteria: RCTs and controlled before-and-after studies that quantified pain using VAS and NRS. These pain scales have previously been shown to be strongly correlated to each other in the measurement of low back pain intensity.[115] A statistically significant decrease in the average back pain intensity favoured VR intervention when experimental cohorts were compared to control groups (Mean difference (MD): -0.67; 95% CI: -1.12 to -0.23; $I^2 = 85\%$, Fig 3). Given the important heterogeneity observed in the main analysis, subgroup analyses were performed to investigate sources of heterogeneity. The subgroups were formed based on the sources of heterogeneity observed throughout the extraction of data (see the statistical analysis section for more information). The latter suggested that the potential beneficial effect of VR interventions was more important when more than 12 sessions were performed (MD: -0.89; 95% CI: -1.62 to −0.15, $I^2 = 89\%$, supplementary digital content Fig S1) and was limited to RCTs (supplementary digital content Fig S2). Moreover, the association between VR interventions and back pain intensity remained statistically significant only for VR exercises (supplemental digital content Fig S3) or when the control groups had traditional physical therapy instead of no intervention (supplementary digital content Fig S4). With slight differences, the average diminution of pain intensity following VR interventions was constant across outcome scales (VAS vs NRS, supplementary digital content Fig S5), but was only observed in studies at low risk of bias to deviations from the intended intervention (supplementary digital content Fig S6) and those in which there was no difference between groups in pain intensity scores at baseline (supplementary digital content Fig S7). Finally, results suggested that VR with low or moderate immersiveness had a beneficial impact on pain intensity whereas the only study with high immersiveness had a detrimental effect (supplementary digital content Fig S8). Visual inspection of the funnel plot suggested that studies with smaller standard errors were symmetrically distributed and that a publication bias was unlikely to alter our conclusions (supplemental digital content Fig S9). Taken individually, 63% of studies included in our meta-analysis (n = 10/16) reported a clinically significant improvement

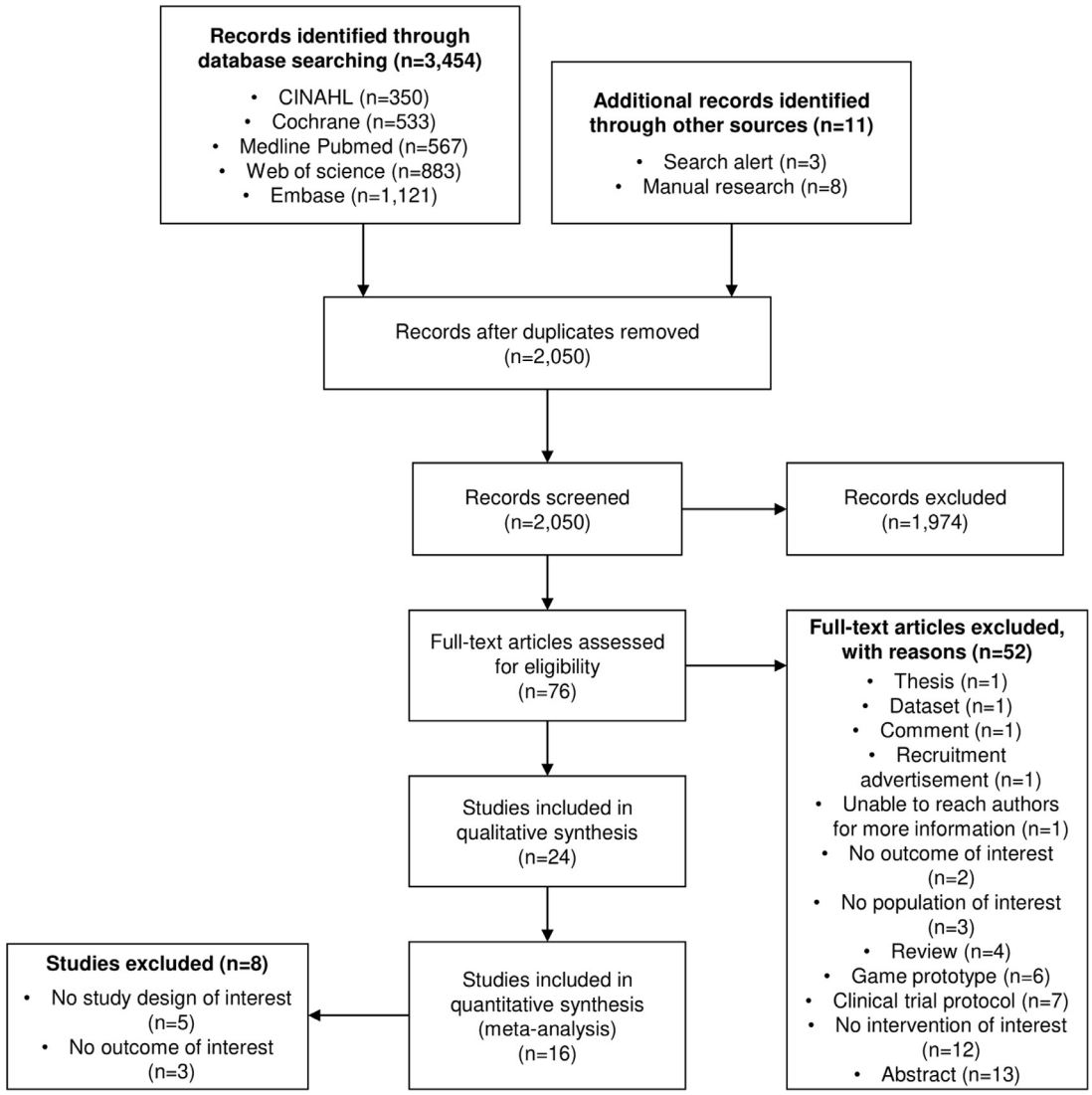

Figure 2. Flowchart of study selection according to PRISMA statement.

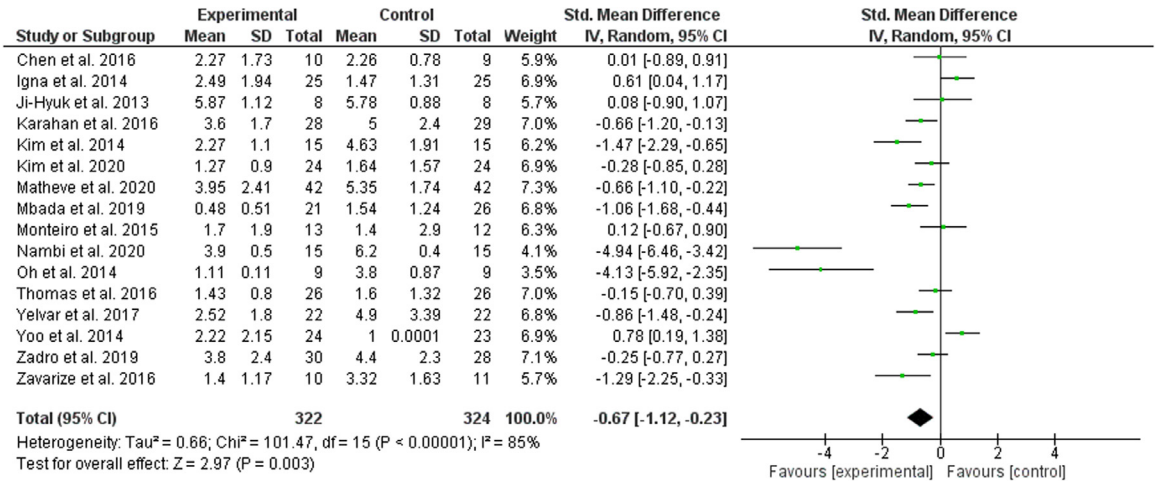

Figure 3. Forest plot showing means and standard deviations of pain intensity scores (on a 0 − 10 scale) in experimental compared with control group after interventions.

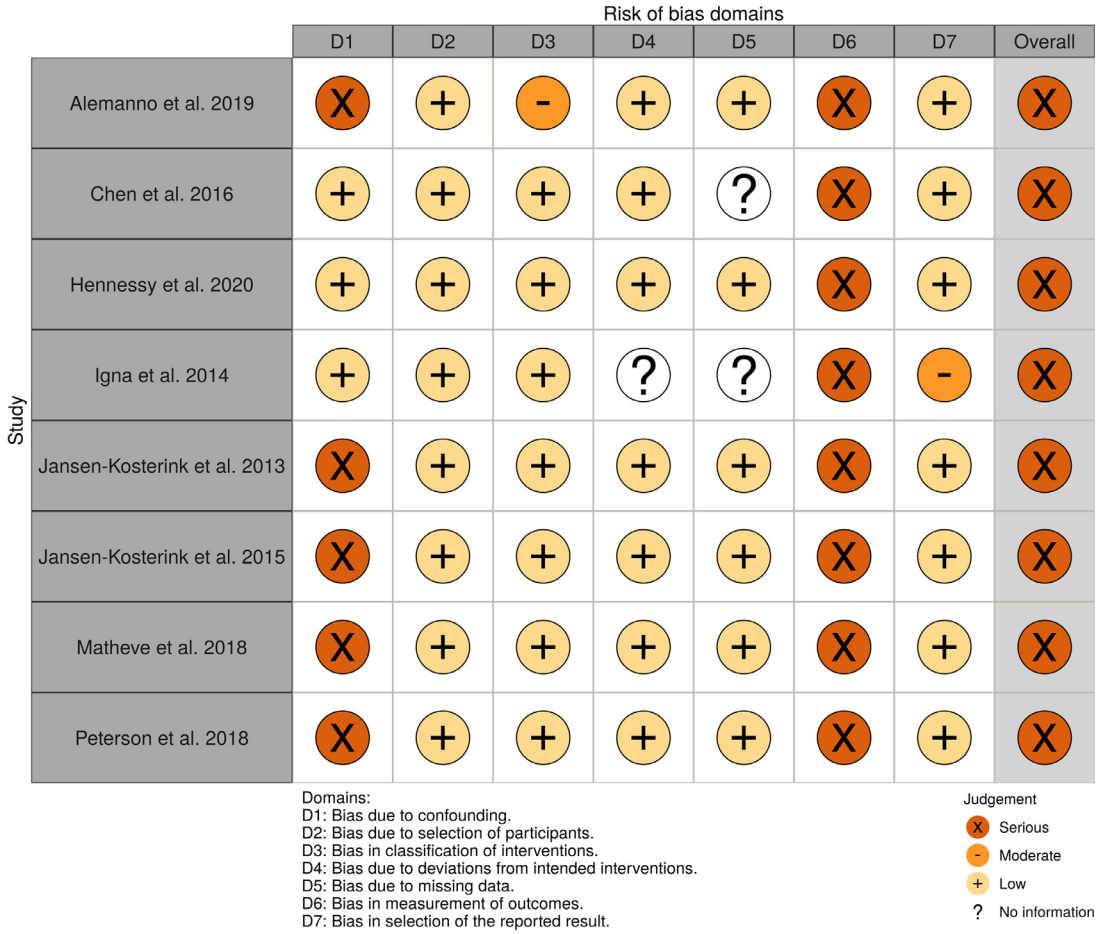

Figure 4. Risk of bias summary for non-RCTs evaluated with ROBINS-I.

in pain intensity of at least 2.5/10 points in their experimental group after the intervention[139] (supplementary digital content Table S3).

Motor Function

Motor function outcomes were evaluated with scales (21%), and/or questionnaires (17%), and/or physical tests (54%). Motor function scales included the rating of perceived exertion,[52] patient-specific functioning scales,[85,146] and VAS,[100,144] while motor function questionnaires included the RAND-36,[65] the bath ankylosing spondylitis disease activity index,[70] the bath ankylosing spondylitis functional index,[70] and the rapid assessment of physical activity questionnaire.[146] Physical test involved: maximal and average trunk's range of motion,[5] limit of stability,[25] 6 minute walking tests,[64,143] walking velocity,[64] overhead reach,[64] cervical range of motion,[64] Åstrand ergometer bicycle test, [63] postural perturbation response, [27] reaching/lumbar spine flexion,[27,130] leg standing,[27,65,143] isometric lifting,[65] isokinetic trunk strength,[100,144] modified Biering-Sørensen test of static muscular endurance,[86] sit-to-stand test,[93] balance test on Wii Balance Board,[93] sprint performance,[96] jump performance, [96] Berg balance scale,[128] and time-up-go test. [143] Due to the high heterogeneity across studies regarding motor function assessment procedures, study design, intervention duration, no meta-analysis could be carried out.

Safety

Adverse events were not reported in 67% of the studies.[25, 27,60,64, 65, 72, 84, 86,93, 96,100,106,128,143,144,147] Minor transient increase in pain during exercises[85] and unrelated to the intervention[63,85] were the only adverse events described. The remaining studies (n = 6/24, 25%) found no evidence of adverse events. [5, 52,70,73,130,146]

Risk of Bias

Detailed evaluations of the risk of bias of the included studies (non-RCTs using ROBINS-I, and RCTs using RoB 2) are presented in (Figs 4–7). All non-RCTs studies included (n = 8) presented serious risk of bias. Specifically, major limitations to study quality stemmed from bias due to confounding (ie, Domain 1), and bias in measurement of outcomes (ie, Domain 6). Only 3 studies controlled confounding bias through inclusion/exclusion criteria associated with the diagnosis of back pain and its severity to assess a more homogenous population. No non-RCT based studies blinded the outcome assessors (ie, the outcome was evaluated by assessors who were aware of the intervention received by study participants). Risk

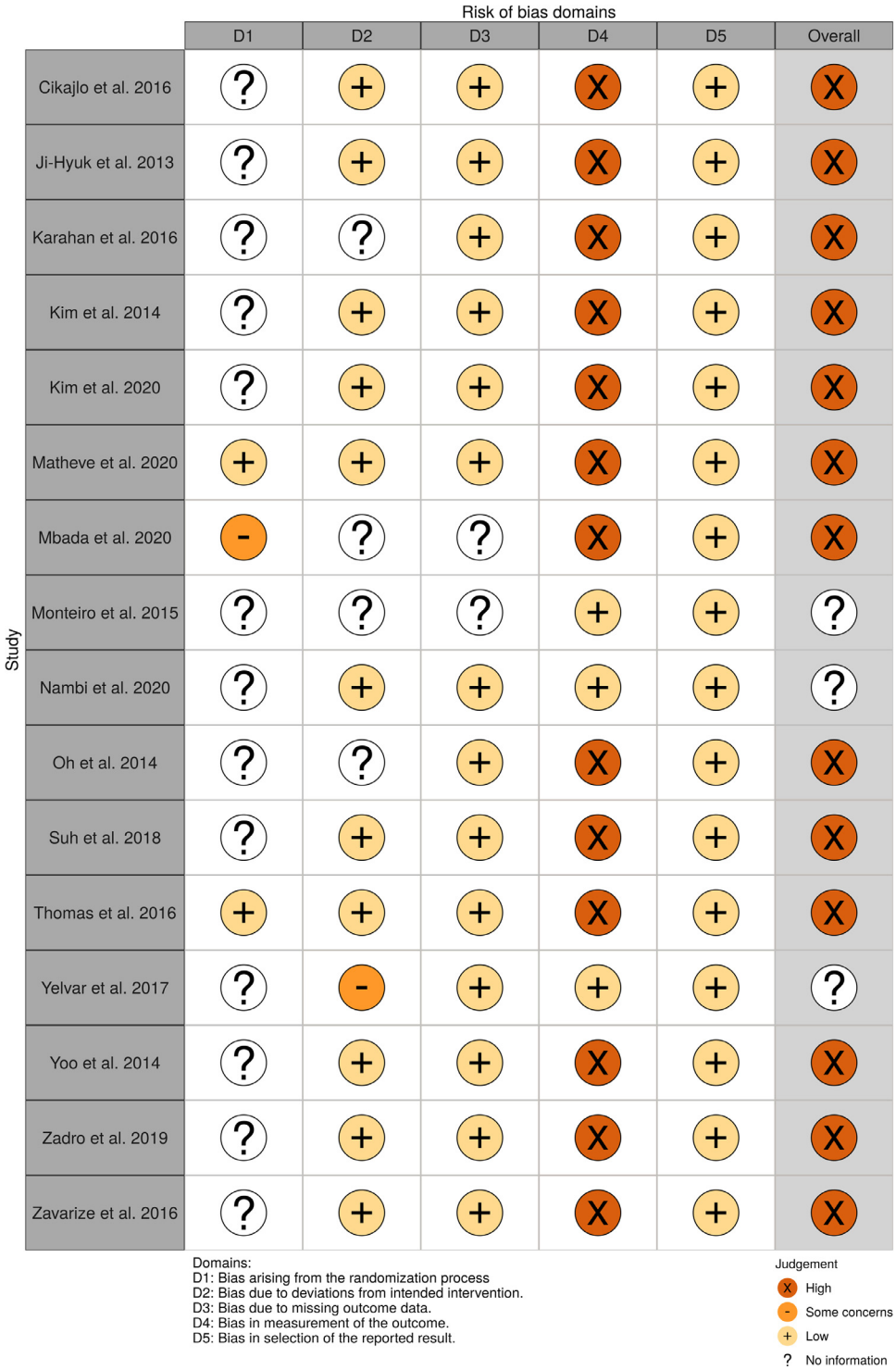

Figure 5. Risk of bias summary for RCTs evaluated with RoB 2.

of bias evaluation for RCTs (n = 16) showed that none were considered at low overall risk (low: 0%, some concerns: 0%, high: 81%, No information: 19%). Thirteen studies (80%) showed missing information regarding the randomization process (eg, allocation sequence, concealment method, adequate comparison of baseline characteristics). Additionally, most of studies presented a high risk of bias in the blinding components as 94% of them (n = 15/16) did not blind the participant (ie, Domain 2.1) or the care giver performing the intervention (ie, Domain 2.2), and only 18% of studies (n = 3/16) ensured that intervention status was blinded to the outcome assessors (ie, Domain 4).

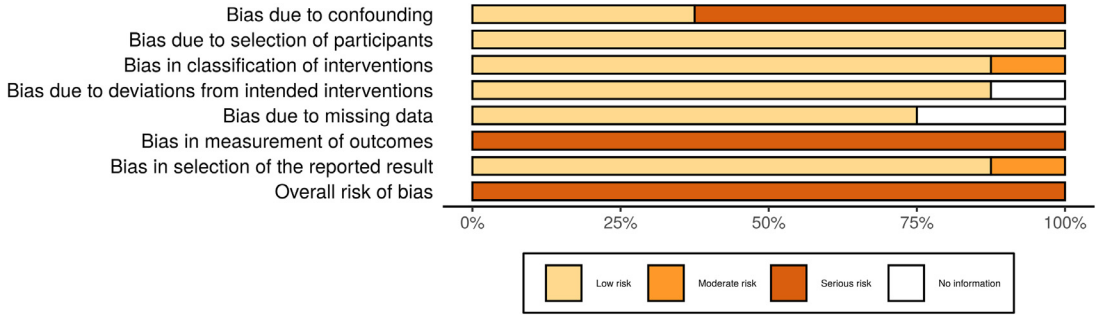

Figure 6. Risk of bias graph for non-RCTs evaluated with ROBINS-I.

Discussion

Overview

Considering the increased uptake of virtual-based rehabilitation for pain and motor function outcomes with back pain, this review sought to synthesize the evidence available to date for rehabilitation strategies applied across the XR spectrum. 24 peer reviewed articles reporting VR-based interventions involving physical exercises, hippotherapy, motor imagery, distraction, and cognitive behavioral therapy were included for systematic review. Of them, 16 were further assessed for their effectiveness on pain intensity using meta-analysis. A large proportion of the VR interventions included used moderate levels of immersion to influence back rehabilitation (75%). Generally, gamification of physiotherapy and rehabilitative interventions aimed to improve fear of movement (ie, kinesiophobia) through motor performance tasks (eg, reaching, bending, sustained trunk loading, trunk stabilisation exercises, pelvic tilts), often by incorporating sensory-based stimulations (eg, visual, acoustic, haptic, motional feedback). Other interventions providing low levels of immersion aimed to facilitate conventional therapies by allowing exercises to be undertaken at home by the patient and monitored remotely by the clinician (ie, via telemedicine) saving time and travel costs. 1 team used VR headsets in combination with a self-driven treadmill to deliver a VR walking experience in a interactive virtual environment to provide a highly immersive experience and reduce physical activity avoidance.[52] Together, these elements support the ability of immersive VR applications to fight back pain. With the availability of new affordable wireless VR headsets that provide high-quality immersive experiences (eg, Oculus Quest 2, Samsung Gear VR, VIVE Focus 3, etc.), the use of this type of technology with back pain patients will grow in popularity.[9,12,41,66,67,78,88,102,104,112,118]

Virtual Reality and Pain Intensity

Among included studies, the most common tools used were VAS and NRS pain scales. While included studies revealed significant variation across a variety of methodological aspects (eg, different interventions with varying degrees of effectiveness, various intervention periods involving different levels of immersivity, etc.), the meta-analysis highlighted that RCT studies using these scales whilst showing low-quality evidence tend to suggest that VR (and especially VR exercises) may provide a statistically and clinically significant improvement over conventional physiotherapy (or usual care without intervention) for pain intensity, immediately after the intervention period. The subgroup analysis also highlighted that the effect of VR interventions remains evident across different types of pain scales. Future studies are needed to evaluate extended follow-up periods to determine whether interventions remain effective over time.

Virtual Reality and Motion Function

In order to track motor activities, the studies included in this review used a great variety of methods which differed in their level of simplicity, precision, the type of information provided, and cost.

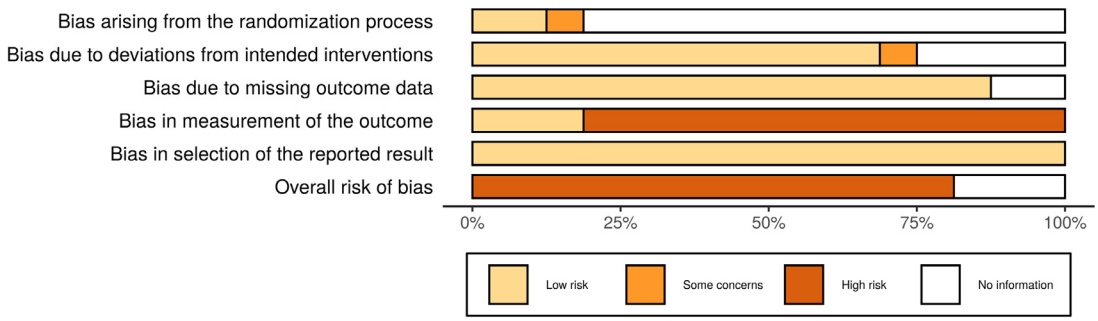

Figure 7. Risk of bias graph for RCTs evaluated with RoB 2.

They mostly involved physical tests, but also rating scales and self-reported questionnaires. Despite the advantages of self-reporting approaches (scales, questionnaires), subjective reporting can lead to over-and under-estimation of motor function.[108] On the other hand, direct motor activity evaluation methods are designed to enhance exercise volume and strength estimates, validate subjective reporting, and reduce human error in reporting and recall bias.[2,108] Some included studies used wearable sensors and tracking systems to directly measure changes over time associated with mechanical parameters that correspond to specific movements. All together, VR interventions showed a trend to have a positive effect in motion function. The mechanism underpinning this positive impact remains uncertain, however, the enhancement of motion function, across a number of different interventions and study designs, opens the door to greater uptake of VR technologies as VR technologies continue to progress.

Risk of Bias

Almost all included studies presented high risk of bias due to the inability to either blind participants, outcome assessors, or both. This challenge stems from the novelty of the equipment and methods used to apply XR interventions, with few attempting to incorporate this challenge of blinding into their experimental protocols/design. However, participant allocation blinding can be achieved by following different approaches. eg, participants can be informed that the study aim is to compare 2 different physical therapy interventions designed to reduce pain without receiving a complete description of the interventions. Participant blinding can also be achieved by exposing patients in both experimental and control groups to the same XR equipment but varying the intervention. eg, France et al.[45] have published a RCT protocol where they aim to evaluate the effects of VR games to encourage lumbar spine flexion among individuals with chronic low back pain. The study design includes two treatment groups which differ in the amount of lumbar flexion required to achieve the game objectives.[45] The control group lumbar flexion is minimized by manipulating the location of virtual targets to make it easier to reach compared to the locations presented to the experimental group. [45] In cases where blinding caregivers are not possible due, eg, to the comparison of highly different interventions (eg, the experimental group receiving Wii Fit exercising sessions and the control group receiving traditional physical therapy sessions [72]), the outcome assessors should at least be blinded to the allocation of patient groups to allow for an unbiased ascertainment of outcomes. [14] Moreover, participants should be instructed not to disclose to the outcome assessor their assigned group to maintain the blindness.[14] Measuring the perceived group assignment at the end of the study can also help to assess the success of blinding within the study.[14] The risk of bias risk analysis of the included studies also revealed problems arising from inadequate reporting of clinical trials. Authors should report their trial findings following standardized guidelines statements, such as the Consolidated Standards of Reporting Trials (CONSORT) [114] for RCTs, to describe, in a full and clear manner, the results yielded by their research.

Recommendations

As the use of therapeutic XR grows and offers greater mobility, affordability, immersive and engaging features, clear focus needs to be on developing guidelines that ensure scientific rigor in the development and evaluation of XR interventions.[14] To this end, the committee of Virtual Reality Clinical Outcomes Research Experts (VR-CORE) published a 3-part framework (VR1, VR2, and VR3) for best practices in developing and testing treatments inspired by experts inputs and recommendations on how to conduct high-quality VR clinical trials.[14] The VR1 studies concentrate on content development in collaboration with patients and end-users through human-centered design concepts.[14] The VR2 trials involved preliminary evaluation of the intervention on a small group of patients-users with an emphasis on feasibility, acceptability, tolerability, and initial clinical efficacy.[14] The VR3 studies are RCTs evaluating clinically important outcomes between experimental and control groups.[14] These recommendations are also applicable to any type of XR interventions and should be followed to facilitate the development of high-quality, relevant, and safe treatments for a broader spectrum of clinical applications.

Limitation

Our exhaustive search strategy did identify a number of preliminary works that we do not yet know the outcomes of. Indeed, we have identified a number of abstracts, [23, 33, 42, 75, 98, 133, 134] clinical trial protocols, [32, 98] and thesis [119] whose results have not yet been published in peer-reviewed scientific journals. **Table S2** (see supplemental digital content) compiles the preliminary results and the status of these studies. The same table include a description of qualitative studies [3, 4, 18, 95, 103] that have evaluated the game experience of different prototypes of VR gaming for back pain patients. Moreover, potential information bias due to a systematic difference in measurements of the intervention or outcomes across studies is also important to consider in this review. Such bias stem in part from the fact that several research teams cannot afford iterative VR development; hardware and software technologies grow faster than intervention testing, challenging methodological consistency and replication.[132] Furthermore, with the exception of distraction effects on pain intensity,[56] the expanding literature on VR has not been supplemented by significant developments in understanding how VR concretely influence on pain perception.[132] This may be explained by the relative youth of the domain, which poses theoretical and practical issues.[132] As a result, issues of gender and sexuality in VR interventions were not addressed in this review.

Conclusions

This systematic review is the first to address the impact of XR on pain and motor function outcomes in back pain patients. Despite broader XR search, all interventions were VR based (ie, no AR). While the specific set of studies showed high heterogeneity across a number of methodological factors, a tentative conclusion could be drawn that VR was effective at improving back pain intensity and tended to have a positive effect on improving other pain outcomes and function through motor function outcomes. The mechanism underlying these improvements remains elusive. However, the reduction in pain intensity and the improvement of pain and motor function outcomes regardless of intervention opens the door for greater uptake of XR technology as XR products and treatments continue to advance. International guidelines for best practices (eg, VR-CORE[14]) should be considered to facilitate the development and evaluation of high-quality, efficient, and safe XR applications. Futures studies should also use a standardized reporting tools (eg, CONSORT Statement for RCTs [114]) to describe, in a full and clear manner, the results yielded by their research, to facilitate article reading, quality assessment, and to be able to reproduce the intervention carefully.

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2021.08.001.

References

1. Ahern MM, Dean LV, Stoddard CC, Agrawal A, Kim K, Cook CE, Narciso Garcia A: The effectiveness of virtual reality in patients with spinal pain: A systematic review and meta-analysis. Pain Pract 20:656-675, 2020

2. Ainsworth B, Cahalin L, Buman M, Ross R: The current state of physical activity assessment tools. Prog Cardiovasc Dis 57:387-395, 2015

3. Alazba A, Al-Khalifa H, AlSobayel H: RabbitRun: An immersive virtual reality game for promoting physical activities among people with low back pain dagger. Technologies 7:17, 2018

4. Alazba A, Al-Khalifa H, AlSobayel H: Acm: Proposed Game for Promoting Physical Activities among People with Low Back Pain using Virtual Reality. New York, Assoc Computing Machinery, 2018

5. Alemanno F, Houdayer E, Emedoli D, Locatelli M, Mortini P, Mandelli C, Raggi A, Iannaccone S: Efficacy of virtual reality to reduce chronic low back pain: Proof-of-concept of a nonpharmacological approach on pain, quality of life, neuropsychological and functional outcome. PloS One 14: e0216858, 2019

6. Applegate ME, France CR, Russ DW, Leitkam ST, Thomas JS: Determining physiological and psychological predictors of time to task failure on a virtual reality Sorensen test in participants with and without recurrent low back pain: Exploratory Study. JMIR Serious Games 6: e10522, 2018

7. Aukstakalnis S, Blatner D: Silicon Mirage; the Art and Science of Virtual Reality. Peachpit Press, 1992

8. Bamodu O, Ye XM: Virtual reality and virtual reality system components. Advanced Materials Research. Trans Tech Publ, 2013, pp 1169-1172

9. Barsom EZ, Graafland M, Schijven MP: Systematic review on the effectiveness of augmented reality applications in medical training. Surg Endosc 30:4174-4183, 2016

10. Baus O, Bouchard S: Moving from virtual reality exposure-based therapy to augmented reality exposure-based therapy: A review. Front Hum Neurosci 8:112, 2014

11. Bekele MK, Pierdicca R, Frontoni E, Malinverni ES, Gain J: A survey of augmented, virtual, and mixed reality for cultural heritage. J Comput Cult Heritage (JOCCH) 11:1-36, 2018

12. Bekelis K, Calnan D, Simmons N, MacKenzie TA, Kakoulides G: Effect of an immersive preoperative virtual reality experience on patient reported outcomes: A randomized controlled trial. Ann Surg 265:1068-1073, 2017

13. Ben Mansouri K, Palazzo C, Dorner V, Poiradeau S, Ville I, Kadri A, Klingeri E: Ieee: How New Technologies can Support Patients Adherence to Home-Based Exercises? New York, Ieee, 2017

14. Birckhead B, Khalil C, Liu X, Conovitz S, Rizzo A, Danovitch I, Bullock K, Spiegel B: Recommendations for methodology of virtual reality clinical trials in health care by an International Working Group: Iterative Study. JMIR Mental Health 6:e11973, 2019

15. Bolte B, de Lussanet M, Lappe M: Virtual reality system for the enhancement of mobility in patients with chronic back pain. Int J Child Health Hum Dev 9:305-314, 2016

16. Bonnechére B, Jansen B, Omelina L, Da Silva L, Mouraux D, Rooze M, Van Sint JS: Patient follow-up using serious games. A feasibility study on low back pain patients. Games for Health. Springer, 2013, pp 185-195

17. Brodbeck D, Degen M, Stanimirov M, Kool J, Scheermesser M, Oesch P, Neuhaus C: BACKTRAINER Computer-Aided Therapy System with Augmented Feedback for the Lower Back. Setubal, Insticc-Inst Syst Technologies Information Control & Communication, 2009

18. Brodbeck D, Degen M, Stanimirov M, Kool J, Scheermesser M, Oesch P, Neuhaus C: Augmented feedback system to support physical therapy of non-specific low back pain, in Fred A, Filipe J, Gamboa H, (eds): Biomedical Engineering Systems and Technologies. Communications in

Computer and Information Science, Berlin, Springer-Verlag Berlin, 2010, pp 381-393

19. Brown L: The Use of Virtual Reality for Lumbar Pain Management in an Outpatient Spine Clinic. 2019. Available at: https://clinicaltrials.gov/show/nct03819907. Accessed September 9, 2021

20. Capecci M, Ceravolo MG, Ferracuti F, Iarlori S, Monteriu A, Romeo L, F Verdini: The KIMORE dataset: KInematic assessment of movement and clinical scores for remote monitoring of physical rehabilitation. IEEE Trans Neural Syst Rehabil Eng 27:1436-1448, 2019

21. Capecci M, Ciabattoni L, Ferracuti F, Monteriu A, Romeo L, Verdini F: Collaborative design of a telerehabilitation system enabling virtual second opinion based on fuzzy logic. IET Comput Vis 12:502-512, 2018

22. Caruso TJ, Madill M, Sidell D, Meister K, Wang E, Menendez M, Kist MN, Rodriguez S: Using augmented reality to reduce fear and promote cooperation during pediatric otolaryngologic procedures. Laryngoscope 131:E1342-e1344, 2021

23. Carvalho GF, Vergara-Diaz G, Scarton A, Adans-Dester C, Miranda JGV, Isaac Z, Bevilaqua-Grossi D, Zafonte R, Bonato P: Augmenting back pain exercise therapy using an interactive gaming-based intervention in the home setting...2016 ACRM /American Congress of Rehabilitation Medicine Annual Conference 30 October - 4 November 2016. Archf Phys Med Rehabil 97:e133, 2016

24. Castelnuovo G, Giusti EM, Manzoni GM, Saviola D, Gatti A, Gabrieli S, Lacerenza M, Pietrabissa G, Cattivelli R, Spatola CAM, Corti S, Novelli M, Villa V, Cottini A, Lai C, Pagnini F, Castelli L, Tavola M, Torta R, Arreghini M, Zanini L, Brunani A, Capodaglio P, D'Aniello GE, Scarpina F, Brioschi A, Priano L, Mauro A, Riva G, Repetto C, Regalia C, Molinari E, Notaro P, Paolucci S, Sandrini G, Simpson SG, Wiederhold B, Tamburin S: Italian consensus conference P. psychological treatments and psychotherapies in the neurorehabilitation of pain: Evidences and recommendations from the Italian consensus conference on pain in neurorehabilitation. Fronti Psychol 7:17, 2016

25. Chen S-Y, Kim S-K, Kim K-H, Lee I-S, HwangBo G: Effects of horse riding simulator on pain, oswestry disability index and balance in adults with nonspecific chronic low back pain. Korean Soc Phys Med 11:79-84, 2016

26. Chou R, Qaseem A, Snow V, Casey D, Cross JT Jr., Shekelle P, Owens DK: 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 147:478-491, 2007

27. Cikajlo I, Bajuk S: Response latencies to postural disturbances when using a virtual reality balance trainer or wobble board in persons with low back pain. Int J Child Health Hum Dev 9:323-331, 2016

28. Cipresso P, Giglioli IAC, Raya MA, Riva G: The past, present, and future of virtual and augmented reality research: a network and cluster analysis of the literature. Front Psychol 9:2086, 2018

29. Citrome L: Ride 'em cowboy! The therapeutics of virtual reality technology and simulation. Int J Clin Pract 68:931, 2014

30. 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 28:760-771, 2018

31. Cummings JJ, Bailenson JN: How immersive is enough? A meta-analysis of the effect of immersive technology on user presence. Media Psychol 19:272-309, 2016

32. Dar G: The Effectiveness of Telerehabilitation Modalities in Physical Therapy in the Management of Chronic Low Back Pain. 2018. Available at: https://clinicaltrials.gov/show/nct03756740. Accessed September 9, 2021

33. Daste C, Foissac F, Abdoul H, Rannou F, Poiraudeau S, Nguyen C: Patient acceptable symptom state for patient-reported outcomes in 2 populations of patients with non-specific chronic low back pain: a secondary analysis of 2 randomized trials. Ann Phys Rehabil Med:101451, 201846#. Available at: https://www.sciencedirect.com/science/article/abs/pii/S1877065720302001?via%3Dihub. Accessed September 9, 2021

34. de Araújo AVL, Neiva JFO, Monteiro CBM, Magalhães FH: Efficacy of virtual reality rehabilitation after spinal cord injury: A systematic review. BioMed Res Int 2019:7106951, 2019

35. De Miguel-Rubio A, Rubio MD, Alba-Rueda A, Salazar A, Moral-Munoz JA, Lucena-Anton D: Virtual reality systems for upper limb motor function recovery in patients with spinal cord injury: Systematic review and meta-analysis. JMIR Mhealth Uhealth 8:e22537, 2020

36. Deeks JJ, Higgins JP: Statistical Algorithms in Review Manager 5., 1 Statistical Methods Group of the Cochrane Collaboration, 2010

37. Diers M, Zieglgansberger W, Trojan J, Drevensek AM, Erhardt-Raum G, Flor H: Site-specific visual feedback reduces pain perception. Pain 154:890-896, 2013

38. Ding J, He Y, Chen L, Zhu B, Cai Q, Chen K, Liu G: Virtual reality distraction decreases pain during daily dressing changes following haemorrhoid surgery. J Int Med Res 47:4380-4388, 2019

39. Domínguez-Téllez P, Moral-Muñoz JA, Salazar A, Casado-Fernández E, Lucena-Antón D: Game-based virtual reality interventions to improve upper limb motor function and quality of life after stroke: Systematic review and meta-analysis. Games Health J 9:1-10, 2020

40. Dunn KM, Hestbaek L, Cassidy JD: Low back pain across the life course. Best PractRes Clin Rheumatol 27:591-600, 2013

41. Elor A, Kurniawan S: The ultimate display for physical rehabilitation: A bridging review on immersive virtual reality. Front Virtual Real 1:25, 2020

42. Evans R, Bronfort G, Keefe D, Taberko A, Hanson L, Haley A, Ma H, Jolton J, Yarosh L, Keefe F, Nam J: Virtual reality environments for supporting mindfulness based healing of low back pain. BMC Complement Altern Med 17 (Suppl 1):P48, 2017

43. Fatoye F, Gebrye T, Mbada C, Fatoye C, Ayanniyi O, Odole A, Makinde M, Dada O: Cost effectiveness of virtual reality game versus clinic based McKenzie extension therapy for chronic non specific low back pain. Value Health 23: S218, 2020

44. Ferreira ML, Ferreira P, Henschke N, Kamper S, Koes B, Hayden J, Maher C: Age does not modify the effects of treatment on pain in patients with low back pain: Secondary analyses of randomized clinical trials. Eur J Pain 18:932-938, 2014

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

46. Freburger JK, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, Castel LD, Kalsbeek WD, Carey TS: The rising prevalence of chronic low back pain. Arch Intern Med 169:251-258, 2009

47. Frey DP, Bauer ME, Bell CL, Low LK, Hassett AL, Cassidy RB, Boyer KD, Sharar SR: Virtual reality analgesia in labor: The VRAIL Pilot Study-A preliminary randomized controlled trial suggesting benefit of immersive virtual reality analgesia in unmedicated laboring women. Anesth Analg 128: e93-e96, 2019

48. George SZ, Lentz TA, Beneciuk JM, Bhavsar NA, Mundt JM, Boissoneault J: Framework for improving outcome prediction for acute to chronic low back pain transitions. PAIN Rep 5:e809, 2020

49. Georgescu R, Fodor LA, Dobrean A, Cristea IA: Psychological interventions using virtual reality for pain associated with medical procedures: A systematic review and meta-analysis. Psychol Med 50:1795-1807, 2020

50. Guarino D, La Paglia F, Daino M, Maiorca V, Zichichi S, Guccione F, Pintabona A, Wiederhold M, Riva G, Wiederhold B, La Barbera D: Chronic pain treatment through Virtual Reality. J Cyber Ther Rehabil 10:45, 2017

51. Hennessy R, Rumble D, Sprigner C, Uzochukwu J, Christian M, David B, Trost Z: Preliminary feasibility of a graded, locomotor-enabled, whole-body virtual reality intervention for individuals with chronic low back pain. J Pain 20, 2019. S69-S69

52. Hennessy RW, Rumble D, Christian M, Brown DA, Trost Z: A graded exposure, locomotion-enabled virtual reality app during walking and reaching for individuals with chronic low back pain: Cohort gaming design. JMIR Serious Games 8:e17799, 2020

53. Herrador Colmenero L, Perez Marmol JM, Martí-García C, Querol Zaldivar M, Tapia Haro RM, Castro Sánchez AM, Aguilar-Ferrándiz ME: Effectiveness of mirror therapy, motor imagery, and virtual feedback on phantom limb pain following amputation: A systematic review. Prosthet Orthot Int 42:288-298, 2018

54. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA: Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons, 2019

55. Higgins JP, Thompson SG, Deeks JJ, Altman DG: Measuring inconsistency in meta-analyses. BMJ (Clinical Research ed.) 327:557-560, 2003

56. Hoffman HG, Boe DA, Rombokas E, Khadra C, LeMay S, Meyer WJ, Patterson S, Ballesteros A, Pitt SW: Virtual reality hand therapy: A new tool for nonopioid analgesia for acute procedural pain, hand rehabilitation, and VR embodiment therapy for phantom limb pain. J Hand Ther 33:254-262, 2020

57. Hoffman HG, Richards TL, Van Oostrom T, Coda BA, Jensen MP, Blough DK, Sharar SR: The analgesic effects of opioids and immersive virtual reality distraction: evidence from subjective and functional brain imaging assessments. Anesth Analg 105:1776-1783, 2007

58. Hou J, Yang R, Yang Y, Tang Y, Deng H, Chen Z, Wu Y, Shen H: The effectiveness and safety of utilizing mobile phone-based programs for rehabilitation after lumbar spinal surgery: Multicenter, prospective randomized controlled trial. JMIR Mhealth Uhealth 7:e10201, 2019

59. Houdayer E, Alemanno F, Emedoli D, Locatelli M, Iannaccone S: Restoring "body image" in chronic pain: An innovative application of virtual reality. Neurorehabil Neural Repair 32:354, 2018

60. Igna R, Stefan S, Onac I, Onac I, Ungur RA, Szentagotai Tatar A: Mindfulness-based cognitive-behavior therapy (MCBT) versus virtual reality (VR) enhanced CBT, vs treatment as usual for chronic back pain. A Clinical Trial. J Evid-Based Psychother 14:229-247, 2014

61. JPT H, S G: Cochrane handbook for systematic reviews of interventions version 5.1. 0 [updated March 2011]. The Cochrane Collaboration 20011, 2011

62. JahaniShoorab N, Ebrahimzadeh Zagami S, Nahvi A, Mazluom SR, Golmakani N, Talebi M, Pabarja F: The effect of virtual reality on pain in primiparity women during episiotomy repair: A Randomize Clinical Trial. Iranian J Med Sci 40:219-224, 2015

63. Jansen-Kosterink S, Veld RH, Wever D, Hermens H, Vollenbroek-Hutten M: Introducing remote physical rehabilitation for patients with chronic disorders by means of telemedicine. Health Technol 5:83-90, 2015

64. Jansen-Kosterink SM, Huis In't Veld RM, Schonauer C, Kaufmann H, Hermens HJ, Vollenbroek-Hutten MM: A serious exergame for patients suffering from chronic musculoskeletal back and neck pain: A Pilot Study. Games Health J 2:299-307, 2013

65. Ji-Hyuk P, Sang-Heon L, Dae-Sik K: The effects of the Nintendo Wii exercise program on chronic work-related low back pain in industrial workers. J Phys Ther Sci 25:985-988, 2013

66. Jimenez YA, Cumming S, Wang W, Stuart K, Thwaites DI, Lewis SJ: Patient education using virtual reality increases knowledge and positive experience for breast cancer patients undergoing radiation therapy. Support Care Cancer 26:2879-2888, 2018

67. Jin C, Dai L, Wang T: The application of virtual reality in the training of laparoscopic surgery: A systematic review and meta-analysis. Int J Surg 87:105859, 2021

68. Jin W, Choo A, Gromala D, Shaw C: A virtual reality game for chronic pain management: a randomized, controlled clinical study. Postgraduate Med 128:31-32, 2016

69. Jin W, Choo A, Gromala D, Shaw C, Squire P: A virtual reality game for chronic pain management: A Randomized, Controlled Clinical Study. Stud Health Technol Inform 220:154-160, 2016

70. Karahan AY, Tok F, Yildirim P, Ordahan B, Turkoglu G, Sahin N: The effectiveness of exergames in patients with ankylosing spondylitis: A randomized controlled trial. Adv Clin Exp Med 25:931-936, 2016

71. Kardong-Edgren SS, Farra SL, Alinier G, Young HM: A call to unify definitions of virtual reality. Clin Simulation Nurs 31:28-34, 2019

72. Kim SS, Min WK, Kim JH, Lee BH: The effects of VR-based Wii fit yoga on physical function in middle-aged female LBP patients. J Phys TherSci 26:549-552, 2014

73. Kim T, Lee J, Oh S, Kim S, Yoon B: Effectiveness of simulated horseback riding for patients with chronic low back pain: A Randomized Controlled Trial. J Sport Rehabil 29:179-185, 2020

74. Kowatsch T, Lohse KM, Erb V, Schittenhelm L, Galliker H, Lehner R, Huang EM: Hybrid ubiquitous coaching with a novel combination of mobile and holographic conversational agents targeting adherence to home exercises: Four design and evaluation studies. J Med Internet Res 23: e23612, 2021

75. Lancere L, Wilken J: Use of real-time visual feedback to facilitate core muscle activation in individuals with low back pain. Arch Phys Med Rehabil 101:e153-e154, 2020

76. Lauwens Y, Rafaatpoor F, Corbeel K, Broekmans S, Toelen J, Allegaert K: Immersive virtual reality as analgesia during dressing changes of hospitalized children and adolescents with burns: A Systematic Review with Meta-Analysis. Children (Basel, Switzerland) 7:194, 2020

77. Li R, Wang N, Yan X, Wei K: Comparison of postural control between healthy subjects and individuals with non-specific low back pain during exposure to visual stimulus. Chinese Med J 127:1229-1234, 2014

78. Lin HT, Li YI, Hu WP, Huang CC, Du YC: A scoping review of the efficacy of virtual reality and exergaming on patients of musculoskeletal system disorder. J Clin Med 8:791, 2019

79. López-Valverde N, Muriel-Fernández J, López-Valverde A, Valero-Juan LF, Ramírez JM, Flores-Fraile J, Herrero-Payo J, Blanco-Antona LA, Macedo-de-Sousa B, Bravo M: Use of Virtual reality for the management of anxiety and pain in dental treatments: Systematic review and meta-analysis. J Clin Med 9:3086, 2020

80. Manogharan S, Kongsted A, Ferreira ML, Hancock MJ: Do older adults with chronic low back pain differ from younger adults in regards to baseline characteristics and prognosis? Eur J Pain 21:866-873, 2017

81. Martini M, Perez-Marcos D, Sanchez-Vives MV: Modulation of pain threshold by virtual body ownership. Eur J Pain 18:1040-1048, 2014

82. Matamala-Gomez M, Diaz Gonzalez AM, Slater M, Sanchez-Vives MV: Decreasing Pain ratings in chronic arm pain through changing a virtual body: Different strategies for different pain types. J Pain 20:685-697, 2019

83. Matheve T: Virtual Reality and Pain Perception During Exercises for Patients With Chronic Non-specific Low Back Pain. 2016. Available at: https://clinicaltrials.gov/show/nct02679300. Accessed September 9, 2021

84. Matheve T, Bogaerts K, Timmermans A: Virtual reality distraction induces hypoalgesia in patients with chronic low back pain: A randomized controlled trial. J Neuroengineering Rehabil 17:55, 2020

85. Matheve T, Claes G, Olivieri E, Timmermans A: Serious gaming to support exercise therapy for patients with chronic nonspecific low back pain: A Feasibility Study. Games Health J 7:262-270, 2018

86. Mbada CE, Olaoye MI, Dada OO, Ayanniyi O, Johnson OE, Odole AC, Ishaya GP, Omole OJ, Makinde MO: Comparative efficacy of clinic-based and telerehabilitation application of Mckenzie therapy in chronic low-back pain. Int J Telerehabil 11:41-58, 2019

87. McGuinness LA, Higgins JPT: Risk-of-bias visualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods n/a 12:55-61, 2020

88. McKnight RR, Pean CA, Buck JS, Hwang JS, Hsu JR, Pierrie SN: Virtual reality and augmented reality-translating surgical training into surgical technique. Curr Rev Musculoskelet Med 13:663-674, 2020

89. Mercier C, Roosink M, McFadyen BJ, Hébert LJ, Jackson PL, Bouyer LJ: Assessing the perception of movements in subjects with chronic pain using altered virtual feedback. Ann Phys Rehabil Med 58:e94, 2015

90. Milgram P, Kishino F: A taxonomy of mixed reality visual displays. IEICE Trans Inf Syst 77:1321-1329, 1994

91. Milgram P, Takemura H, Utsumi A, Kishino F: Augmented reality: A class of displays on the reality-virtuality continuum In. Telemanipulator and Telepresence Technologies. International Society for Optics and Photonics, 1995, pp 282-292

92. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 6:e1000097, 2009

93. Monteiro RS, de Souza CP, Lattari E, Rocha NBF, Mura G, Machado S, da Silva EB: Wii-workouts on chronic pain, physical capabilities and mood of older women: A Randomized Controlled Double Blind Trial. CNS Neurol Disord-Drug Targets 14:1157-1164, 2015

94. Morone G, Paolucci T, Luziatelli S, Iosa M, Piermattei C, Zangrando F, Paolucci S, Vulpiani MC, Saraceni VM, Baldari C, Guidetti L: Wii Fit is effective in women with bone loss condition associated with balance disorders: A randomized controlled trial. Aging Clin Exp Res 28:1187-1193, 2016

95. Nakad L, Rakel B: Attitudes of older adults with chronic musculoskeletal pain towards immersive virtual reality. J Pain 20:S42, 2019

96. Nambi G, Abdelbasset WK, Elsayed SH, Alrawaili SM, Abodonya AM, Saleh AK, Elnegamy TE: Comparative Effects of isokinetic training and virtual reality training on sports performances in university football players with chronic low back pain-randomized Controlled Study. Evidence-Based Complement Altern Med 2020:2981273, 2020

97. Nierula B, Martini M, Matamala-Gomez M, Slater M, Sanchez-Vives MV: Seeing an embodied virtual hand is analgesic contingent on colocation. J Pain 18:645-655, 2017

98. Niknam F: The Effect of Tele-Rehabilitation Technology on chronic non specific low back pain. 2016. Available at: http://www.who.int/trialsearch/trial2.aspx?Trialid=irct2016070528809n1. Accessed September 9, 2021

99. Nowlin L, Madi D, Guck A, Davis M, Trost Z: Examining virtual reality gaming for pain-related fear and disability in chronic low back pain. Ann Behav Med 49:S116, 2015

100. Oh H-W, Lee M-G, Jang J-Y, Jin J-J, Cha J-Y, Jin Y-Y, Jee Y-S: Time-effects of horse simulator exercise on

psychophysiological responses in men with chronic low back pain. Isokinetics Exerc Sci 22:153-163, 2014

101. Ong TL, Ruppert MM, Akbar M, Rashidi P, Ozrazgat-Baslanti T, Bihorac A, Suvajdzic M: Improving the intensive care patient experience with virtual reality-A Feasibility Study. Crit Care Explor 2:e0122, 2020

102. Pandrangi VC, Gaston B, Appelbaum NP, Albuquerque FC Jr., Levy MM, Larson RA: The application of virtual reality in patient education. Ann Vasc Surg 59:184-189, 2019

103. Penn T, Browning W, France C, Hardee G, Zielke M, Trost Z: Attitudes toward a virtual reality physical activity intervention among veterans with chronic low back pain. J Pain 18:S1, 2017

104. Pereira MF, Prahm C, Kolbenschlag J, Oliveira E, Rodrigues NF: Application of AR and VR in hand rehabilitation: A systematic review. J Biomed Inform 111:103584, 2020

105. Perrochon A, Borel B, Istrate D, Compagnat M, Daviet JC: Exercise-based games interventions at home in individuals with a neurological disease: A systematic review and meta-analysis. Ann Phys Rehabil Med 62:366-378, 2019

106. Peterson S: Telerehabilitation booster sessions and remote patient monitoring in the management of chronic low back pain: A case series. Physiother Theory Pract 34:393-402, 2018

107. Poiraudeau S: Analgesic Effect of a Prototype Device of Virtual Reality in a Population of Patients With Chronic Low Back Pain. 2011. Available at: https://clinicaltrials.gov/show/nct01407653. Accessed September 9, 2021

108. Prince SA, Adamo KB, Hamel ME, Hardt J, Connor Gorber S, Tremblay M: A comparison of direct versus self-report measures for assessing physical activity in adults: A systematic review. Int J Behav Nutr Phys Act 5:56, 2008

109. Rizzo AS, Koenig ST: Is clinical virtual reality ready for primetime? Neuropsychology 31:877-899, 2017

110. Roosink M, Robitaille N, McFadyen BJ, Hebert LJ, Jackson PL, Bouyer LJ, Mercier C: Real-time modulation of visual feedback on human full-body movements in a virtual mirror: development and proof-of-concept. J Neuroengineering Rehabil 12:2, 2015

111. Rothbaum BO, Tannenbaum L: (proposal summary) Emory begins NIH study using virtual reality therapy for back pain. Orthop Today 25:116, 2005

112. Scapin S, Echevarría-Guanilo ME, Boeira Fuculo Junior PR, Gonçalves N, Rocha PK, Coimbra R: Virtual Reality in the treatment of burn patients: A systematic review. Burns: J Int Soc Burn Injuries 44:1403-1416, 2018

113. Scapin S, Echevarria-Guanilo ME, Fuculo PRB, Goncalves N, Rocha PK, Coimbra R: Virtual Reality in the treatment of burn patients: A systematic review. Burns: J Int Soc Burn Injuries 44:1403-1416, 2018

114. Schulz KF, Altman DG, Moher D: CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Med 8:18, 2010

115. Shafshak TS, Elnemr R: The visual analogue scale vs numerical rating scale in measuring pain severity and predicting disability in low back pain. J Clin Rheumatol 1-4, 2020

116. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA: AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ (Clinical Research ed.) 358:j4008, 2017

117. Slater M, Wilbur S: A framework for immersive virtual environments (FIVE): Speculations on the role of presence in virtual environments. Presence: Teleoperators Virtual Environ 6:603-616, 1997

118. Smith V, Warty RR, Sursas JA, Payne O, Nair A, Krishnan S, da Silva Costa F, Wallace EM, Vollenhoven B: The effectiveness of virtual reality in managing acute pain and anxiety for medical inpatients: Systematic review. J Med Internet Res 22:e17980, 2020

119. Sobie TJ: Body schema acuity training and Feldenkrais RTM movements compared to core stabilization biofeedback and motor control exercises: Comparative effects on chronic non-specific low back pain in an outpatient clinical setting: A randomized controlled comparative efficacy study. Body schema acuity training & FeldenkraisRTM movements compared to core stabilization biofeedback & motor control exercises: Comparative effects on chronic non-specific low back pain in an outpatient clinical setting: A randomized controlled study.2016

120. VRx Spiegel B:: How Virtual Therapeutics Will Revolutionize Medicine. Basic Books, 2020

121. Springer KS, George SZ, Robinson ME: The development of a technology-based hierarchy to assess chronic low back pain and pain-related anxiety from a fear-avoidance model. J Pain 17:904-910, 2016

122. Stamm O, Dahms R, Muller-Werdan U: (abstract) "Virtual reality"-Pain therapy in geriatric patients with chronic back pain - A requirement analysis. Z Gerontol Geriatr 51:103-, 2018

123. Stamm O, Dahms R, Müller-Werdan U: Virtual reality in pain therapy: A requirements analysis for older adults with chronic back pain. 2020

124. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP: ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ (Clinical Research ed.) 355:i4919, 2016

125. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT: RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ (Clinical Research ed.) 366:l4898, 2019

126. Uahci 2015, Pt Iii. Lecture Notes in Computer Science. Su WC, Yeh SC, Lee SH, Huang HC: A virtual reality lower-back pain rehabilitation approach: System design and user acceptance analysis, in Antona M, Stephanidis C, (eds): Universal Access in Human-Computer Interaction: Access to Learning, Health and Well-Being, Berlin, Springer-Verlag Berlin, 2015, pp 374-382

127. Suh A, Prophet J: The state of immersive technology research: A literature analysis. Comput Hum Behav 86:77-90, 2018

128. Suh HR, Lee SY: 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 PublHealth Res Dev 9:1054-1059, 2018

129. Tack C: Virtual reality and chronic low back pain. Disabil Rehabil Assist Technol 16:637-645, 2019

130. Thomas JS, France CR, Applegate ME, Leitkam ST, Walkowski S: Feasibility and safety of a virtual reality dodgeball intervention for chronic low back pain: A randomized clinical trial. J Pain 17:1302-1317, 2016

131. Trost Z: Using virtual reality to treat chronic pain: Virtual graded exposure for chronic low back pain and virtual walking for persistent neuropathic pain in spinal cord injury. Psychosom Med 80:A142, 2018

132. Trost Z, France C, Anam M, Shum C: Virtual reality approaches to pain: toward a state of the science. Pain 162:325-331, 2021

133. Trost Z, France C, Zielke MA, Hardee GM: Development of a virtual reality graded exposure intervention for chronic low back pain: Initial findings and future directions. Spine J 18:S30, 2018

134. Trost Z, Nowlin L, Guck A, Madi D, Davis M: Exploring the role of pain-related fear and catastrophizing in response to a virtual reality gaming intervention for chronic low back pain. J Pain 16:S98, 2015

135. Trost Z, Parsons TD: Beyond distraction: Virtual reality graded exposure therapy as treatment for pain-related fear and disability in chronic pain. J Appl Biobehav Res 19:106-126, 2014

136. Trost Z, Zielke M, Guck A, Nowlin L, Zakhidov D, France CR, Keefe F: The promise and challenge of virtual gaming technologies for chronic pain: The case of graded exposure for low back pain. Pain Manage 5:197-206, 2015

137. Truter P, Russell T, Fary R: The validity of physical therapy assessment of low back pain via telerehabilitation in a clinical setting. Telemed J e-health 20:161-167, 2014

138. GBD 2019 Diseases and Injuries Collaborators: Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet (London, England 396:1204-1222, 2020

139. Wand BM, Tulloch VM, George PJ, Smith AJ, Goucke R, O'Connell NE, Moseley GL: Seeing it helps movement-related back pain is reduced by visualization of the back during movement. Clin J Pain 28:602-608, 2012

140. Wang X, Ferreira M, Hunter DJ, Vesentini G, Pozzobon D: (abstract) Digital disruptive technology for rehabilitation following elective surgery for low back pain, knee and hip osteoarthritis: A systematic review and meta-analysis. Arthritis Rheumatol 70:431-432, 2018

141. Wippert PM, Puschmann AK, Drießlein D, Banzer W, Beck H, Schiltenwolf M, Schneider C, Mayer F: Personalized Treatment suggestions: The validity and applicability of the risk-prevention-index social in low back pain exercise treatments. J Clin Med 9:1197, 2020

142. Wu A, March L, Zheng X, Huang J, Wang X, Zhao J, Blyth FM, Smith E, Buchbinder R, Hoy D: Global low back pain prevalence and years lived with disability from 1990 to 2017: Estimates from the Global Burden of Disease Study 2017. Ann Transl Med 8:299, 2020

143. Yelvar GDY, Cirak Y, Dalkilinc M, Demir YP, Guner Z, Boydak A: Is physiotherapy integrated virtual walking effective on pain, function, and kinesiophobia in patients with non-specific low-back pain? Randomised controlled trial. Eur Spine J 26:538-545, 2017

144. Yoo JH, Kim SE, Lee MG, Jin JJ, Hong J, Choi YT, Kim MH, Jee YS: The effect of horse simulator riding on visual analogue scale, body composition and trunk strength in the patients with chronic low back pain. Int J Clin Pract 68:941-949, 2014

145. Zadro JR, Shirley D, Simic M, Mousavi SJ, Ceprnja D, Maka K, Ferreira P: Video-game based exercises for older people with chronic low back pain: a protocol for a feasibility randomised controlled trial (the GAMEBACK trial). Physiotherapy 103:146-153, 2017

146. Zadro JR, Shirley D, Simic M, Mousavi SJ, Ceprnja D, Maka K, Sung J, Ferreira P: Video-game-based exercises for older people with chronic low back pain: A randomized controlledtable trial (GAMEBACK). Phys Ther 99:14-27, 2019

147. Zavarize SF, Paschoal MA, Muglia Wechsler S: Effects of physiotherapy associated to virtual games in pain perception and heart rate variability in cases of low back pain. Manual Ther Posturol Rehabil J 14:1-7, 2016