

Virtual Reality in Chronic Pain Rehabilitation: A Systematic Review

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Received date: December 11, 2024, **Accepted date:** February 25, 2025

Citation: Amorim P, Sousa MJ, Sousa JE, Martins H, Lee SH. Virtual Reality in Chronic Pain Rehabilitation: A Systematic Review. J Phys Med Rehabil. 2025;7(1):14-78.

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Abstract

Introduction: Approximately 19% of adults complain of chronic pain, which poses considerable physical, mental, and economic burdens. Conventional chronic pain management includes physical therapy, analgesic drugs, and the avoidance of pain triggers. Metaverse-related technologies such as virtual reality (VR) are promising complementary approaches. This review aimed to systematically analyse the applications of VR in chronic pain management in the context of rehabilitation.

Methods: Four electronic databases (MEDLINE, CENTRAL, PEDro, and IEEE Xplore) were searched following the PRISMA guidelines, and data were collected until October 2023.

Results: A total of 56 articles were included in the qualitative synthesis. VR was used in several conditions: musculoskeletal disorders (40/56, 71%), fibromyalgia (5/56, 9%), burns (4/56, 7%), phantom pain after limb amputation (1/56, 2%), upper-limb pain after stroke (1/56, 2%), mastectomy with axillary lymph nodes (2/56, 4%), vestibular rehabilitation (1/56, 2%), active ageing (1/56, 2%), and pain during cardiac rehabilitation after cardiac surgery (1/56, 2%). VR was useful in increasing treatment adherence and pain tolerance and facilitating the achievement of other endpoints such as functional measures, range of motion, and functional performance. No significant side effects were reported aside from occasional episodes of nausea and headaches with immersive VR.

Discussion: The included studies were heterogeneous, limiting comparative analysis.

Conclusion: VR interventions are efficacious complementary methods for managing chronic pain, increasing the quality of care, and potentially reducing drug intake in chronic pain management.

Keywords: Chronic pain, Virtual reality, Pain management, Rehabilitation, Quality of care, Development of new rehabilitative technologies

List of Abbreviations: AR: Augmented Reality; DASH: Disabilities of the Arm, Shoulder and Hand; PICOS: Population, Intervention, Comparison, Outcomes, Study Design; PLP: Phantom Limb Pain; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QoL: Quality of Life; ROM: Range of Motion; RCTs: Randomised Controlled Trials; SCI: Spinal Cord Injury; VAS: Visual Analogue Scale; VR: Virtual Reality; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Article Summary

- VR interventions are safe and effective for chronic pain management in rehabilitation settings.
- Immersive and non-immersive techniques are used in VR interventions.
- Although VR interventions are heterogeneous, they reduce chronic pain intensity in several conditions.

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- VR interventions increase treatment adherence and pain tolerance, facilitating the achievement of other endpoints such as increased ROM and functional performance.
 - Quality of care in chronic pain rehabilitation benefits from VR as a complementary approach.
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Introduction

Pain is a global health priority because of its high prevalence worldwide [1], and physical and rehabilitation medicine is one of the specialties in which publication-based academic interest in pain management is most intensive [2]. Based on the 2020 revised definition of *pain* by the International Association for the Study of Pain, *chronic pain* is defined as pain in one or more anatomical regions that (1) persists or recurs for >3 months and (2) is associated with significant emotional distress (e.g., anxiety, anger, frustration, or depressed mood) or functional disability (i.e., interference in activities of daily life and participation in social roles) [3]. Approximately 19–20% of adults complain of chronic pain [4,5], which poses considerable physical and mental burden and has significant economic and social consequences [6]. Depression is three-fold higher in patients with chronic pain than in those without chronic pain [7]. Chronic pain also limits participation in work through sickness absence and affects productivity; the cost of productivity loss greatly exceeds the cost of absenteeism and medical care combined [8].

Chronic pain management often entails a multidisciplinary or interdisciplinary pain management program relying on a biopsychosocial approach, including physical therapy, analgesic and antidepressant drugs, and the avoidance of pain triggers [9,10].

Opioid use has consistently increased over time, and global opioid use has doubled to 7.35 billion daily doses per year from 2001–2003 to 2011–2013 [11]. Chronic pain treatment may improve some problems associated with opioid intake, such as overdose, dependency, and mortality. However, the financial cost of pain management is estimated to be greater than the annual costs of heart disease, cancer, and diabetes [12]. Thus, identifying effective, safe, and affordable tools to treat and prevent chronic pain may improve the quality of care and quality of life (QoL) of millions of people by reducing drug intake as well as the physical, mental, and economic burden.

Quality of care is one of the most quoted principles of health policy and is currently high on the agenda of policy-makers [13-15]. As defined by the World Health Organization, quality of care refers to the degree to which health services for individuals and populations increase the likelihood of desired health outcomes [16]. Quality health services across the world should be effective, provide substation-grounded healthcare services, and maximise the benefits of available coffers while avoiding waste [17].

The metaverse can be considered a new tool to improve the quality of the healthcare system in terms of intervention,

education, and standardised training and to help create world databases. Considering the time spent by the young population in front of a screen, the metaverse could also be a place where they can start to practice sports and learn something [18].

Although healthcare has traditionally been thought of as a human-to-human relationship, modern society has been revolutionised by the rise of big data and artificial intelligence technology [19]. Moreover, the pandemic has helped in accelerating innovations in the digital age. We are now moving rapidly towards the age of the metaverse, a graphically rich virtual space, leaning towards verisimilitude where people can do everything that they do in real life, such as shopping, playing, socialising, and partying [20]. This includes the Internet of Things, high-speed communication networks, augmented reality (AR), virtual reality (VR), cloud computing, edge computing, blockchain, artificial intelligence, and other technologies [20].

The metaverse encompasses AR, VR, lifelogging, and mirror world. VR and AR are more common concepts: VR is defined as an entirely computer-generated virtual environment [21] without means to connect with the real world or see it [22]. AR aims to augment users' perception and comprehension of reality by overlaying virtual content within the real-world view [22]. Lifelogging refers to technologies that allow users to record or monitor their internal states to augment their lives (e.g., smartwatch to monitor the heart rate during physical activity). A mirror world captures and creates a virtual simulation of a person's external reality (e.g., Google Street View) [23]. Among these technologies, VR has gained greater popularity as a valuable tool for treating various conditions in rehabilitation care [24].

Research related to the applications of the metaverse to health has been sparse [25], and even more so in rehabilitation. VR is classified into non-immersive and immersive: immersive 360° surroundings allow users to feel as though they are inside the terrain, whereas non-immersive surroundings only allow users to see the contents grounded on how the device in use—personal computer, smartphone, or tablet—is held and moved [26]. VR has been used in several areas of physiotherapy, occupational therapy, and speech therapy to improve the upper-limb function in stroke survivors, including hand therapy, pain management, rehabilitation from COVID-19, lower back pain and balance treatment, cognition, communication, and acquired brain injury rehabilitation [27-29].

This review aimed to analyse the scientific evidence on the use of VR in chronic pain management in the field of rehabilitation

and to explore how VR could improve the quality of care. This review focused on VR, irrespective of the level of immersion, as it is the most studied domain of the metaverse. The research question for this systematic review, which conformed to the Population, Intervention, Comparison, Outcomes, Study Design (PICOS) components [30], was as follows: in people with chronic pain who need rehabilitation care (P), what is the utility of VR (I) compared with standard care (C) in pain relief (O), and how many randomised controlled trials (RCTs) were published with results (S)?

This systematic review was registered in the PROSPERO database (reference no. CRD42024506055).

Methods

Search strategy

This review was based on research material obtained from

MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Physiotherapy Evidence Database (PEDro), and IEEE Xplore; data were collected until October 2023. Articles were selected manually, and no automatic limits were applied. The search terms were those found in the controlled vocabulary of the U.S. National Library of Medicine (Medical Subject Headings [MeSH]). A search in PROSPERO was conducted to exclude revisions that had already been initiated. The same search terms were used for all databases to ensure comparisons of the obtained results. The search strings and Boolean operators used were as follows: (virtual reality) AND (rehabilitation OR physiotherapy OR exercises) AND (pain). This review was conducted and reported in accordance with the PRISMA statement [31] (**Figure 1**). Additional searches included visually scanning reference lists from relevant studies; manually searching key journals and conference proceedings; contacting study authors, experts, and other organisations; searching Internet resources; and searching for citations.

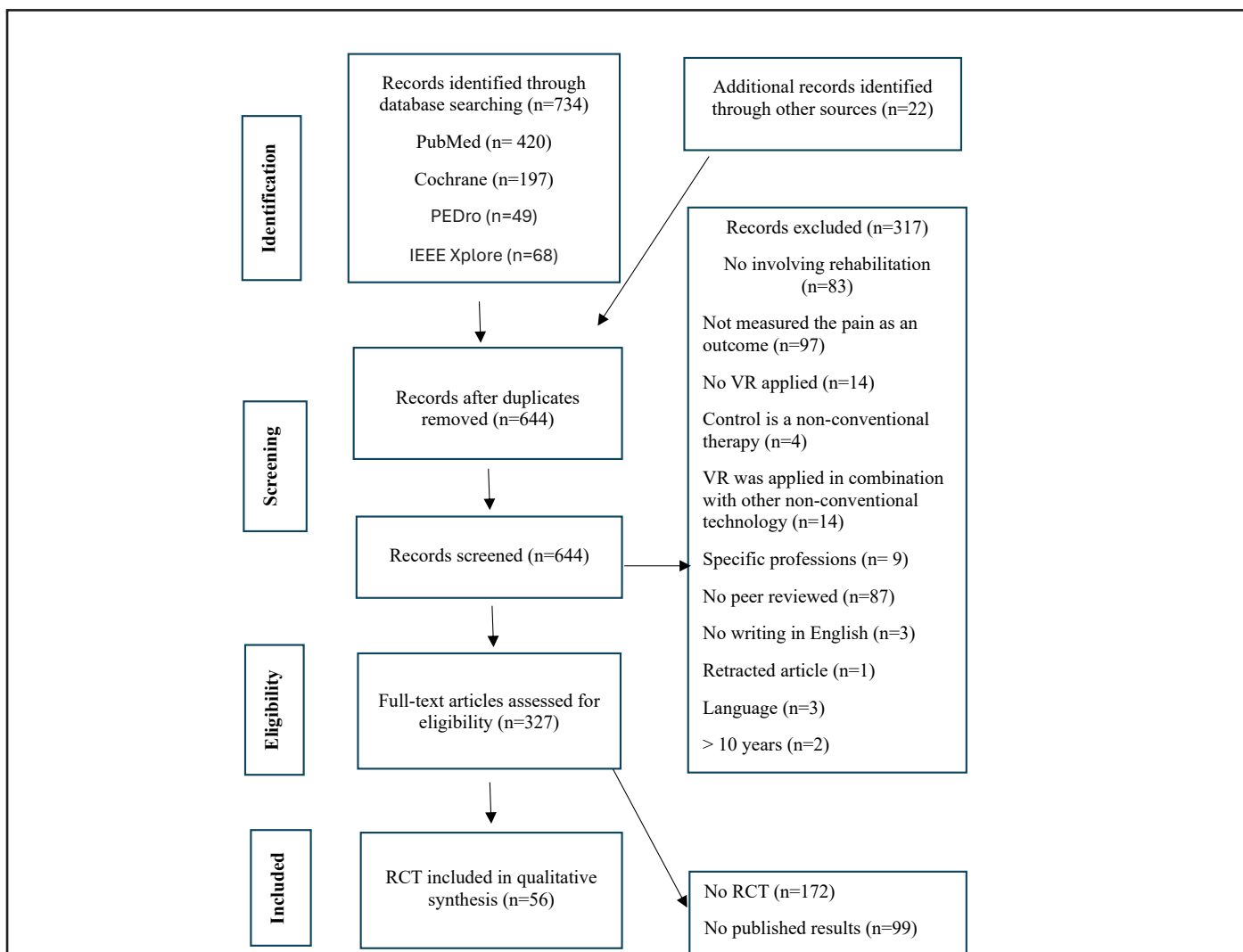


Figure 1. Flow diagram adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA), showing the process for identifying and screening of the articles for inclusion and exclusion.

Study selection

After removing duplicates, two authors independently screened the records based on the titles and abstracts of papers. The inclusion criteria were as follows: (1) medical conditions involving chronic pain that required rehabilitation; (2) rehabilitation using VR as a target intervention; (3) conventional rehabilitation treatment or no treatment as control intervention to deal with chronic pain; (4) pain as an outcome; (5) RCTs; (6) full-text articles published in English; and (7) publications in the last 10 years. No restrictions were imposed on race, sex, or age. The exclusion criteria were as follows: (1) target population for specific professions; (2) non-original articles and non-peer-reviewed articles (letters, comments, and conference abstracts); (3) combination of VR and other non-conventional therapies as the intervention group; (4) non-conventional treatment as the control group; (5) inability to secure full-text; (6) trial protocols without published results; and (7) retracted articles. Records were excluded if they were marked by two authors. The full text of all remaining articles was further examined to exclude irrelevant studies. Disagreements were resolved through a team discussion.

Data extraction

Two authors independently extracted data on each included study using a table designed for this review. Discrepancies were resolved through consensus with a third author. Extracted data included (1) the cause of pain; (2) study author name, country, and publication year; (3) number, age, and sex of patients and controls included in the analysis; (4) type of VR (immersive or non-immersive); (5) intervention; (6) follow-up; (7) outcomes (pain and others); (8) main findings; (9) effect on pain; and (10) side effects.

Risk of bias and methodological quality of the included RCTs

Two authors independently assessed the risk of bias in the included articles. In the event of a disagreement, a third author was consulted. The included RCTs were examined using the PEDRo scale [32], which is one of the most frequently used scales for assessing the methodological quality of RCTs in systematic reviews of interventions in physiotherapy. The PEDRo scale evaluated 11 items related to the study's internal validity and statistical reporting, except for eligibility criteria, which were not computed in the total score. Each item was scored as either present (1) or absent (0), with a maximum score of 10. A trial was considered to have moderate-to-high quality if it scored at least 6/10, although other criteria have been suggested thereafter [33].

The internal validity of each item was assessed by calculating the internal validity score (IVS). Criteria 2, 3, 5, 6, 7, 8, and 9 from the PEDro scale were selected to calculate the IVS.

Methodological quality was scored and interpreted as follows: (1) studies with an IVS of 6–7 were considered to have high methodological quality, (2) those with an IVS of 4–5 were considered to exhibit moderate methodological quality, and (3) those with an IVS of 0–3 were deemed to have limited methodological quality.

To reduce inter-examiner bias, the quality of studies was evaluated by three independent reviewers. Consensus was reached by discussing and resolving discrepancies between the PEDro scale scores (included in the **Results** section). Because it was not possible to group the extracted and analysed data and the overall effect size could not be calculated, qualitative methods were employed to analyse the data.

Statistical analysis

A narrative synthesis of findings derived from the included studies was conducted and structured around the study setting, study population, intervention characteristics (immersive/non-immersive VR, duration, and follow-up), type of outcome, and main results. RCTs that used pain scales (numeric rating scale or visual analogue scale [VAS]) to measure pain intensity immediately after the intervention period were included.

Results

Table 1 summarises the main characteristics of the 56 included studies. A total of 2,993 participants were included, with a sample size ranging from 17–287 participants. The measurement outcomes, such as pain, physical function, joint range of motion (ROM), self-efficacy, and QoL, and the measurement tools used varied among the studies.

Most studies focused on musculoskeletal disorders (40/56, 71%) (**Table 2**). Other conditions (**Table 3**) included fibromyalgia (5/56, 9%), burns (4/56, 7%), phantom pain after limb amputation (1/56, 2%), upper-limb pain after stroke (1/56, 2%), mastectomy with axillary lymph nodes (2/56, 4%), vestibular rehabilitation (1/56, 2%), active ageing (1/56, 2%), and pain during cardiac rehabilitation after cardiac surgery (1/56, 2%). Among musculoskeletal disorders, degenerative causes were the most frequent condition in the included studies (30/40, 75%), with lower back pain being the most frequent (15/30, 50%), followed by chronic neck pain (8/30, 27%).

Eighteen studies used immersive VR techniques, whereas 37 used non-immersive techniques; one study [34] did not specify the level of immersion. Within the immersive technique category, VR games (10/56, 56%), mindfulness-based and behavioural interventions (3/18, 17%), practical exercises (3/18, 17%), and visual illusions (3/18, 17%) were used. In the non-immersive technique category, an avatar or exoskeleton in front of a television or computer screen was used in exergames. The use of VR as a distraction in these

Musculoskeletal disorders									
Table 1. Studies included in the systematic review.									
Study identification		Participants		Intervention and Comparator		Outcomes		Results	
Pathology	Authors/ Publication year/ Country	Number of participants, age, sex	Type of VR	Intervention in each Group	Intervention duration and Follow-up	Outcomes (including pain measurement)	Main findings	Effect on pain	Side effects
Degenerative									
1. Chronic neck pain	Sarig Bahat <i>et al.</i> [36] Australia, Israel	32 VR group (kinematic training + VR) =16 Control group (Kinematic training)=16 Age (years) VR group = 40.63 ± 14.18 Control group = 41.13 ± 12.59 Gender: females, males VR group = 11,6 Control group = 11,5	Immersive (head- mounted display) VR game	Both groups completed four to six training sessions comprising of similar kinematic training (KT) activities. The head pursuit task was conducted with the VR game in the VR group and with a laser pointer and poster in the control (laser) group.	5 weeks	Neck disability index (NDI), cervical range of motion (ROM), head movement velocity and accuracy. Kinematic measures were collected using the VR system that was also used for training, pain intensity (visual analogic scale- VAS), TAMPA scale of kinesiophobia, static and dynamic balance, global perceived effect and participant satisfaction	Significant improvements in NDI, ROM (rotation), velocity, and the step test in both groups postintervention. At 3-month post- intervention, these improvements were mostly sustained; however, there was no control group, which limits the interpretation of this. Between-group analysis showed a few specific differences including global perceived change that was greater in the VR group	At post- intervention only the VR group improved significantly in VAS: Pre-intervention (Mean ± SD): 35.72 ± 17.7 Post- intervention (Mean ± SD) 22.10 ± 24.1 (P < 0.05) Cohen's d : 0.65 2 Three- month post- intervention (Mean ± SD) 6.95 ± 16.5 Cohen's d : 0.65 2 0.51	4 participants experienced motion sickness with the use of the VR device during assessment.

2. Chronic neck pain	Sarig Bahat <i>et al.</i> [37] Australia, Israel	90 VR training group=30 Laser training group =30 Control group=30 Age median (Q1, Q3) VR=48 (38.5, 57.5) Laser=48 (35.5, 59) Control=48 (35, 59) Gender (F, M): VR= 19 (63%); 11 (37%) Laser= 21 (70%); 9 (30%) Control= 23 (77%); 7 (23%)	Immersive (head-mounted display) VR game	A head-laser beam and poster, or VR hardware and software was provided for home use while control group waited. The laser beam provided visual feedback relating to head motion, but unlike the VR, laser training velocity was not controlled.	12 weeks	Neck disability index (NDI), global perceived effect (GPE), and cervical motion velocity (mean and peak). Secondary outcome measures included pain intensity (VAS), health status (EQ5D), kinesiophobia (TSK), range, smoothness, and accuracy of neck motion as measured by the neck VR system	Significant improvements were demonstrated in NDI and velocity with good effect sizes in intervention groups compared to control. Velocity significantly improved at both time points in both groups. NDI, VAS, EQ5D, TSK and accuracy significantly improved at both time points in VR and in laser at 3 months evaluation in all but TSK. GPE scores showed 74-84% of participants perceived improvement and/or were satisfied. Significant advantages to the VR group compared to laser were found in velocity, pain intensity, health status and accuracy at both time points.	Pain intensity (VAS 0-100 mm) Pre-intervention VR group= Mean 47.11 SD 21.1 Laser group= Mean=45.54 SD=22.35 Post-intervention VR group: Mean= 25.83** SD=21.1 Laser group: Mean=39.92 SD=22.4 3 months VR group: Mean=25.43** SD=23.1 Laser group= Mean=35.26** SD=24.1	Information not available
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3. Neck pain	Rezaei et al [41] Iran	44 VR group=22 Control group=22 Age between 20 and 55 years. Mean age in VR group=36.19 (9.80) Mean age in control group 31.23 (9.49) Sex (female %) VR group: 42.90 Control group: 52.4	Non-immersive (Video game) PC screen	A video game was placed above the laptop computer monitor screen. The head mouse was aimed on reflective marker, which represented head movements to control pointer movement on the laptop computer. The control group received eye-follow, gaze stability, eye-head coordination and position movement sense training.	4 weeks	Visual analogue scale score, neck disability index and Y-balance test	There were significant improvements in all variables in both groups immediately after and 5 weeks after the intervention. Greater improvements were observed in the visual analogue scale and neck disability index scores in VRT group, and the results for all directions in Y-balance test were similar in both groups. No side effects were reported.	VAS: There were significant main effects for time (F2,80=167.16, P<0.001) but not group (F1,40=2.46, P=0.124) and the interaction between time and group was significant (F2,80=17.21, P<0.001). After the intervention, VAS score improved by a mean of 36.36 mm in the VRT group and 19.32 mm in the CPT group. At the 5-week follow-up appointment, the improvements were 37.54 mm and 18.78 mm, respectively.	There were no reports of discomfort, motion sickness or pain exacerbation during or after playing the VR game.
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4. Cervical Spondylosis	Mukherjee <i>et al.</i> [35] India	44 VR group= 22 Control group=22 Age 30 and above Conventional group: 13 female and 9 male. Mean age: 54.81 ± 13 years. VRT group: 8 female and 14 male. Mean age: 55.81 ± 15 years.	Immersive (head-mounted display) VR game	Both groups were given a hot pack before every session for 3 consecutive days. The conventional group included active cervical exercises and stretching. VR group required active cervical ROM to play the game.	Pain and ROM were assessed on the immediate (day 1) and short-term (day 3) basis while kinesiophobia was assessed only on day 3.	Pain (Numeric Pain Rating Scale), ROM, Tampa Scale of kinesiophobia (TSK)	VRT is more effective than conventional treatment alone in the reduction of pain immediately (day 1) and in short term (day 3). VRT also demonstrated improvements in ranges of bilateral cervical rotations and lateral flexion on the short-term basis (day 3) while there was no improvement observed immediate posttreatment (day 1). Both the treatment methods were equally effective in reducing kinesiophobia.	Mean and SD Pain level (VAS): Conventional group: Pre: 5.72 ± 1.07 Immediate: 3.94 ± 1.67 Short-term: 2.71 ± 1.45 VR group: Pre: 5.77 ± 5.05 Immediate: 4.65 ± 1.08 Short term: 1.5 ± 0.80	Information not available
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5. Chronic neck pain	Sarig Bahat <i>et al.</i> [79] Israel	52 VR group=27 Laser group= 25 Age: Mean 48.3; SD 13.5 Sex, female, n (%) Mean 52; SD 65.8	Immersive (head-mounted display) VR game	Participants were taught how to train by a qualified physiotherapist during a 20-minute session at baseline. A head-laser beam and poster or a VR system was provided for 4 weeks of home training. Individuals were instructed to train for short sessions up to 5 minutes continuously to avoid side effects.	4 weeks of KT using laser or virtual reality, with baseline, post-intervention, and 3-month follow-up measures	Pain intensity (VAS), Neck Disability Index (NDI), Global perceived effect (GPE), Global mean velocity (°/s) of cervical motion (Vmean), Global Peak velocity (°/s) of cervical motion (Vmean), Tampa Scale of Kinesophobia (TSK), Home exercise (number of exercise sessions performed in the 4 weeks of training), Global accuracy error (°) was measured during the VR accuracy module (difference between the target's and the player's position in degrees).	Self-reported response was 71% to 73% and kinematic response was 41% to 46%. Prediction models indicated an immediate increase in self-reported measures in men with NDI 20% slower (65°/s), and less accurate (16° error) cervical motion at baseline. In the longer term, older patients with higher NDI seemed to benefit more. In the second model, no factors significantly predicted improvement in kinematic measures at either time point.	At post intervention 55 (69.6) reported pain intensity VAS reduced by over 50%. At 3 months' follow-up 38 (73.1) of participants reported pain intensity reduced by over 50%	Information not available
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6. Chronic neck pain	Tejera <i>et al.</i> [38] Spain	44 VR group=22 Control group=22 Age (years) VR group (mean ± SD): 32.72 ± 11.63 (27.56–37.88) Control group:26.68 ÷ 9.21 (22.59–30.76) p = 0.063 Male VR group: 11 (50%) Control group 10 (45.5%) p = 0.763 Female VR group: 11 (50%) Control group 12 (54.5%)	Immersive (Head-mounted display) VR game	Two VR mobile applications were installed: in the first one the participants performed only lateral flexion movements and the second includes flexion, extension and rotation movements. The control group performed neck exercises (flexion, extension, rotation and tilt exercises)	4 weeks	Visual Analog Scale (VAS), Conditioned Pain Modulation (CPM), Temporal Summation (TS), active cervical range of movement (CROM), Neck Disability Index (NDI), Pain Catastrophizing Scale, Pain-Related Fear of Movement/ (Re)Injury, fear-avoidance beliefs questionnaire (FABQ), pain pressure threshold (PPT), Pain Anxiety Symptoms Scale (PASS-20),	Statistically significant differences were revealed for time factor and group*time interaction for kinesiophobia showing post-hoc differences in favor of the VR group at 3 months. Significant effects were shown for time factor but not for the group*time interaction for pain intensity, rotation range of motion (ROM), Neck Disability Index, pain catastrophizing, fear-avoidance beliefs, left side pressure pain threshold (PPT) and anxiety. Statistically significant differences were not found for time factor and neither in group*time interaction for CPM, TS, right side PPT, flexo-extension and lateral-flexion ROM.	There was a large effect size for the VR group post-treatment (p=0.01, d=0.1.21), 1 month follow-up (p<0.01, d=1.12) and 3 month follow-up (p<0.01, d=1.44). There was a large effect size for control group post-treatment (p<0.01, d=0.82), 1 month follow-up (p<0.01, d=1.53) and 3 months follow-up (p<0.01, d=1.44)	Information not available
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7. Chronic neck pain	Nusser <i>et al.</i> [39] Germany	51 control group (CG) =20; sensorimotor group (SMG) =18; virtual reality group (VR) =17. Age, year, mean (SD) CG: 49.8 (8.1) SMG:53.1 (5.7) VR: 51.2 (8.8) Number of women, <i>n</i> (%) CG: 12 (66) SMG: 11 (69) VR: 9 (53)	Immersive (head-mounted display) VR game	The CG underwent a "standard rehabilitation programme"; patients also received special lectures about chronic pain. The SMG received the "standard rehabilitation programme" plus a "general sensorimotor training". In addition to the "standard rehabilitation programme", patients in the VR completed "neck-specific sensorimotor training".	3 weeks	Neck pain, headaches, active cervical range of motion, and Neck Disability Index	Compared with the control group, the virtual reality group showed significant advantages in relief of headaches, and active cervical range of motion in flexion and extension. Compared with the sensorimotor group, the virtual reality group showed significant improvements in cervical extension.	Within-group analysis showed a statistically significant improvement in the VRG across all pain categories. For the SMG, significant improvements were seen in reducing headaches while at rest. The CG saw significantly reduced neck pain during motion. Between group analysis showed that the VRG improved significantly more than the CG in reducing headaches at rest (VRG vs CG $p=0.008$) and headaches during motion (VRG vs CG $p=0.023$), each with large effect sizes.	Besides the weight of the helmet, which some patients found unpleasant, no other negative side-effects were reported regarding the VR device or in general.
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8. Chronic neck pain	Cetin <i>et al.</i> [40] Turkey	41 VR group=21 Control group=20 Age (years) Mean \pm SD: VR group: 40.0 \pm 11.88 Control group: 41.94 \pm 10.76 Gender Female VR group: 12 (70.5); Control group: 11 (64.7) Male VR group: 5 (29.5); Control group: 6 (35.3)	Immersive (Head-mounted display) Practical exercises	The VR group first performed exercises and then VR. The control group performed only exercises.	6 weeks	Pain intensity (visual analogue scale), pain pressure thresholds (PPTs), joint position sense error (JPSE), and muscle performance, Profile Fitness Mapping Questionnaire (ProFitMap-Neck), Hospital Anxiety-Depression Scale (HADS), and quality of life (SF-36).	VR was advantageous in terms of PPTs of the C1/C2 and C5/C6 articular pillar bilaterally and large effect size. VR was more effective in decreasing JPSE and functional limitation. Neither intervention was superior in terms of pain intensity, muscle performance, symptoms	Pain intensity decreased similarly in the two groups. There were no differences in the deltas of VAS between groups	Information not available
9. LBP	Kim <i>et al.</i> [45] South Korea	30 middle-aged female patients VR group=15 Control group=15 Age VR group mean age of 44.33 years Control group: 50.46 years Sex: all females	Non-immersive (Wii Fit games)	In the experimental group, a virtual reality-based yoga program using Wii Fit activities. The CG performed trunk stabilizing exercise during the same time and same frequency.	The virtual reality-based yoga programs were performed in a total of 12 sessions over the course of four weeks, with each session lasting 30 minutes	VAS, algometer, Oswestry low-back pain disability index (ODI), Roland Morris disability questionnaire (RMDQ), and fear avoidance beliefs questionnaire (FBQ) scores	The experimental group showed a significant increase in VAS, algometer, ODI, RMDQ and FBQ scores. The control group showed a significant increase in VAS, algometer, ODI, RMDQ and FBQ scores.	VR group: significant decrease in VAS (from 7.00 \pm 0.89 points to 2.27 \pm 1.10 points). Control Group: significant decrease in VAS (from 6.95 \pm 0.79 points to 4.63 \pm 1.91 points),	Information not available

10. LBP	Yoo <i>et al.</i> [46] South Korea	47 VR group=24 Control group=23 Age (mean; SD): Control: 20,70 ± 1.45 VR group: 20,44 ±1.33 Sex: all men	Non-immersive Exergame Avatar	The VR group performed horse simulator riding. The control group did any exercise.	8 weeks	VAS, body composition, isokinetic torque	Horse simulator exercise significantly reduced pain scores and enhanced torques of trunk. There was no significant increase in muscle mass and decreased fat mass in horse simulator riding group.	Back pain CG Baseline: 1.50 ± 0.51 8 weeks: 1.00 ± 0.00 HG Baseline: 4.37 ± 2.13 8 weeks: 2.22 ± 2.15 Night pain Baseline: CG 1.10 ± 0.31 HG: 0.90 ± 0.31	Information not available
11. LBP	Monteiro <i>et al.</i> [47] Brazil	30 VR group=16 Control group=14 Thirty older women (68 ± 4 years; 68 ± 12 kg; 154 ± 5 cm	Non-immersive Exergame Avatar	The control group was submitted to an exercise program with core and strength training. The VR group received the same intervention plus VR training using Nintendo Wii and Wii Balance Board. To minimize bias, control group performed balance tests on Wii Balance Board weekly.	8 weeks	-Pain scale: NRS -Physical tests: balance, sitto-stand test	Significative improvement of NRS for all groups after the intervention and functional capacity for sit only in VR group. It was not identified significant differences within or between groups for balance	Both groups showed similar perceived pain post-training (1,4 ± 2,9 and 1,7 ± 1,9, respectively). For this comparison ANOVA 2 x 2 showed F=0.08 and P=0.79 for interaction.	Information not available

12. LBP	Chen <i>et al.</i> [48] South Korea	19 VR group=10 Control group=9 Age between 19 and 30	Non-immersive (Indoor riding machine simulating riding a real horse through the visual information that appeared on the front screen by diving the virtual environment.)	Each group carried out for 30 minutes exercise three times a week for 4 weeks. Horse riding simulator exercise group carried out 15 minutes horse riding simulator exercise and 15 minutes lumbar strengthening exercise. Lumbar strengthening exercise group carried out 30 minutes lumbar strengthening exercise.	4 weeks	Visual analogue scale (VAS) was measured for evaluation back pain. Korean Oswestry disability index (KODI) was measured for dysfunction. Limits of stability (LOS) were measured for dynamic balance.	VR group and Control group showed significant differences after the intervention in VAS, KODI, and LOS. Comparison between the groups revealed no significant difference between the groups in VAS, KODI, and LOS before and after the intervention.	VAS (Mean \pm SD): Exercise 49.10 \pm 18.89 22.70 \pm 17.25 Control 43.66 \pm 8.23 22.55 \pm 7.77	Information not available
13. LBP	Yilmaz <i>et al.</i> [42] Turkey	44 VR group=22 Control group=22 subjects Age, years Mean (SD) VR group: 46.3 (3.4) Control group: 52.8 (11.5) Gender, n (%) Male 12 (54.5) Female 10 (45.5) 18 (81.8)	Immersive (head-mounted display) Mindfulness-based intervention	In each group, physical therapy was performed using physical agent modalities and therapeutic exercises. The experimental group was asked to passively watch the same virtual walking video clip in a sitting position with video glasses at each therapy session during hotpack application. For the virtual walking task, a video clip was taken by a cameraman who was naturally walking down Ireland forest.	3 weeks intervention	Visual Analog Scale (VAS), TAMPA Kinesiophobia Scale (TKS), Oswestry Disability Index (ODI), Nottingham Health Profile (NHP), Timed-up and go Test (TUG), 6-Minute Walk Test (6MWT), and Single-Leg Balance Test	Participants in the experimental group reported a significant improvement in the TUG score as compared with those in the control group. The effect size of the pre-post comparison in the experimental group was large. With regard to pain intensity, there was a significant interaction effect. The effect size of the pre-post comparison in the experimental was small. There was no significant interaction effect regarding kinesiophobia, disability, quality of life, balance, and 6MWT, respectively	Activity Pain (VAS) Mean (SD) Pre intervention VR: 6 (1.06) Control: 5.63 (2.36) Group difference: 0.514 Post intervention VR: 2.52 (1.80) Control: 4.90 (3.39) Group difference: 0.031 (p<0.05)	Information not available

14. LBP	Thomas <i>et al.</i> [49] USA	52 VR group=26 Control group=26 Age (mean (SD)) VR group: 23.9 (6.8) Control group: 26.7 (8.5) Sex (% female) VR group: 46.2 Control group: 50.0	Non-immersive 3-D shutter glasses which are required to produce the 3-D effect on television screen Avatar	All participants completed a pregame baseline and a follow-up assessment (4–6 days later) of lumbar spine motion and expectations of pain and harm during standardized reaches to high (easier), middle, and low (hardest to reach) targets. The game environment was a basketball arena in which the participant played dodgeball against 4 virtual opponents.	For 3 consecutive days, participants in the game group played virtual dodgeball between baseline and follow-up.	(Roland-Morris Disability Questionnaire), pain (McGill Pain Questionnaire; MPQ), fear of movement (Tampa Scale of Kinesiophobia), and anxiety (State-Trait Anxiety Inventory)	For the standardized reaching tests, there were no significant effects of group on changes in lumbar spine flexion, expected pain, or expected harm. However, virtual dodgeball was effective at increasing lumbar flexion within and across gameplay sessions. Participants reported strong positive endorsement of the game, no increases in medication use, pain, or disability, and no adverse events.	The 2 Time (session 1, session 5) – 2 Group (game, control) repeated measures ANOVAs revealed significant main effects of time for the Visual Analog Scale, $F_{1,50}=24.82$, $P<0.001$, $hp_2=0.33$, and Present Pain Intensity scale, $F_{1,50}=10.30$, $P<0.01$, $hp_2=0.17$, and a marginal effect for the overall Pain Rating Index, $F_{1,50}=3.74$, $P=0.06$, $hp_2=0.07$.	No reported adverse events related to gameplay.
15. LBP	Zavarize <i>et al.</i> [50] Brazil	21 VR=10 Control group=11 Average age of the sample: 46.81 years (46.36 for Control Group and 47.30 for VR Group). Both sexes	Non-immersive (video games)	Control group participated in a physical therapy program to provide gain and of lumbar flexibility and VR group participated in the same physical therapy program plus joint sessions with virtual games	1 week	VAS, Mc Gill's pain questionnaire (MPQ), heart rate monitor	Significative improvement of VAS for all groups after the intervention, being higher in VR group	VAS (Mean, SD) Control Group: Pre-test: 7.18, 0.6 Post test: 3.32, 1.63 VR Group: Pre-test: 6.7, 1.06 Post test: 1.4, 1.17	Information not available

16. LBP	Zadro <i>et al.</i> [51] Australia	60 VR group=30 Control group=30 Age (Mean, SD) VR group:68.8 (5.5) Control Group: 67.8 (6.0) Sex Men VR group: 29 (48.3) Control group: 12 (20) Women VR group: 31 (51.7) Control group: 18 (30)	Non-immersive Exergames	Participants in the video-game exercise group engaged in an unsupervised home-based exercise program using a Nintendo Wii U console. In the control group the participants continued their usual activities.	8 weeks	Pain self-efficacy and care-seeking (primary outcomes), and physical activity, pain, function, disability, fear of movement/reinjury, falls efficacy, recruitment and response rates, adherence, experience with the intervention, and adverse events (secondary outcomes).	Adherence to the total recommended exercise time was 70.8%, and no adverse events were reported. Participants completing Wii Fit U exercises had significantly higher pain self efficacy at 6 months, but not immediately post-intervention or at 3 months; there were no between-group differences in care-seeking. Compared with the control group, participants completing Wii Fit U exercises demonstrated significantly greater improvements in pain and function at 8 weeks and were more likely to engage in flexibility exercises at 6 months. There were no significant between-group differences for the remaining outcomes.	Wii Fit U exercises demonstrated significantly greater improvements in pain ($\beta = -1.07$, 95% CI $= -2.11$ to -0.03 , $P=0.04$) immediately post-intervention compared with the control group.	Information not available
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17. LBP	Kim <i>et al.</i> [56] South Korea	48 VR group=24 Control group=24 Age (Mean (SD)) VR: 26.0 (3.82) Control: 28.79 (9.05) Sex: VR group: Female (%): 7 (31.8%); Male: 15 (68.2%) Control: VR: 15 (57.7%) Control: 11 (42.3%)	Non-immersive (VR-based horse-riding simulator 2D screen visual, motion-haptic feedback)	The VR group performed similar patterns of exercise similar to a real horse riding. Control group performed exercises based on the same manual, focused on the exact motion and posture. The repetition of exercises and time required were dependent on the individual participant.	8 weeks of intervention, 6 month follow-up	Pain scale: NRS Functional disabilities: Oswestry Disability Index (ODI), Roland-Morris Disability Questionnaire (RMD) Fear-avoidance belief questionnaire (FABQ)	Both groups demonstrated significant differences in ODI and RMD and NRS at 4 weeks, 8 weeks, and at the 6 months follow-up. The VR group was more effective for reducing work related FABQ compared to control group at 6 month follow-up.	No significant differences in the NRS (F=1.696; p=0.211), In within-group comparisons, both groups presented significant differences in NRS (both VR and Control groups after 4 weeks)	Information not available
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18. LBP	Matheve <i>et al.</i> [52] Belgium	84 VR group=42 Control group=42 Age (Mean (SD)) Control: 44.2 (11.9) VR: 42.1 (11.5) Sex (n female, %) Control: 27 (64%) VR: 27 (64%)	Non-immersive (Exergames) Television screen	The VR group played games with pelvic tilts in the sagittal plane. A wireless motion sensor was placed on the sacrum and the sensor-signals were sent to a laptop connected to a TV screen on which the games were displayed. During the control intervention, participants stood in exactly the same spot as those in the VR group, but with the TV screen switched off and performed pelvic tilts in the sagittal plane according to a beep tone.	A single-session intervention	Numeric pain rating scale (NPRS) Roland Morris disability questionnaire (RMDQ) Pain Catastrophizing scale (PCS) Tampa scale for Kinesiophobia (TSK)	VR distraction had a hypoalgesic effect during and immediately after the exercises, and it also reduced the time spent thinking of pain. Preliminary exploratory analyses showed that pain-related fear, pain catastrophizing and baseline pain intensity did not moderate the effects of VR distraction.	Compared to the control group, the VR-group had a significantly larger reduction in pain intensity during the exercises (VR group M=1.66, SE=0.25; Control group M=-0.55, SE=0.26; Difference=2.20, SE=0.36, t80.9=6.11, p<0.0001, d=1.29 (95% CI=0.82-1.76)) and after the exercises (VR group M=0.81, SE=0.25; Control group M=-0.50, SE=0.26; Difference=1.31, SE=0.36, t80.9=3.64, p<0.003, d=0.85 (95% CI=0.40-1.29)).	Information not available
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19. LBP	Park et al. [53] South Korea	80 elderly woman (61–84 years) VR group=40 Control group=40 Age (y) Control: 72.05 ± 6.82 VR: 71.50 ± 6.34 All women	Non-immersive (VR Horse simulator)	While the VR group participants were exercising on the horse, the control group participants sat on the horse and watched video from the monitor.	12 weeks	Oswestry Disability Index, visual analogue scale, body composition and spinal alignment measured using bioelectrical impedance and raster stereography. The isokinetic moments of trunk extensor and flexor were measured before and after the training period.	The VR group showed a significant decrease in back pain compared to the control group. No differences were shown in terms of muscle mass. There was an increased basal metabolic rate (BMR) in the VR group. Spinal alignment in the VR group significantly improved. The peak torques of the trunk extensor in the VR group were also significantly increased.	VAS (Mean ± SD) Pre Control: 7.27 ± 1.52 VR: 7.35 ± 1.63 Post Control: 7.64 ± 1.31 VR: 2.10 ± 2.54	Information not available
20. LBP	Tomruk et al. [54] Turkey	42 VR group=21 Control group=21 Age (year) VR: 46.00 (40.05–50.50) Control: 45.00 (44.00–48.00) Sex not indicated	Non-immersive	Computer-based stability training (postural limits of stability training, weight shift training, and maze control training) was applied to study group by help of computer-based device while in control group the training was applied in the same manner but without computer-based system.	12 weeks	Numeric Pain Scale, Oswestry Disability Index, limits of stability (LoS) and postural stability (PS) tests were used to evaluate postural control	Significant improvements occurred in LoS and PS scores in both groups after interventions. Physical activity scores for both groups did not significantly change. There was superiority of computer-based stability training over the traditional training in improving LoS.	NRS scores decreased significantly in both groups with 2.0 points median change (p<0.05). NRS score Pre-intervention VR: 7.00 (4.00–9.00) Control: 6.00 (3.00–9.00) Post-intervention Control: 3.00 (2.00–5.00) Control: 4.00 (2.00–7.00)	Information not available

21. LBP	Yalfani <i>et al.</i> [43] Iran	25 elderly women VR group=13, control group=12 Age VR: 68 ±2.94 Control: 67.08 ±2.9 All women	Immersive (Head-mounted display) VR game	The VR group involved weekly sessions of exercises that were carried out using the Xbox Kinect headset. The control group carried on the daily live routines, without any special treatments during this period.	8 weeks	Pain intensity, fall risk, and QoL were assessed via the Visual Analog Scale, the Biodex Balance System, and the 36-Item Short Form Health Survey, respectively	pain intensity score of the intervention group significantly decreased after participation in the VRT program. The intervention group also showed reduced fall risk and elevated QoL.	VAS VR: Pre test: 6.73 ± 2.42 Post test: 2.19 ± 1.49 Control: Pre-test: 6.79 ± 1.99 Post-test: 7.54 ± 1.9	Information not available
22. LBP	Afzal <i>et al.</i> [55] Pakistan	84 VR group= 42 Control group=42	Non-immersive Practical exercises Television screen The mean age in group A was 37.5 ± 12.5 years and in group B it was 38.2 ± 11.8 years 28 (33%) males and 56 (66.6%) females.	CG received routine physical therapy, while VRG received Virtual Reality exercises with routine physical therapy. In the VR group, the patients were subjected to trunk slide flexion, sitting to avoid obstacles, jumping and combined movement of arms, as displayed on the screen.	4 weeks	Visual Analogue Scale and Modified Oswestry Disability Index	VR group showed significantly better results than group A. Significant intra-group improvement in terms of pain and disability with VR showing significant more improvement than routine physical therapy.	Pain score at baseline was 6.62 ± 1.04 in group A and 6.50 ± 1.24 in group B which decreased to 3.32 ± 0.81 and 1.00 ± 0.60 respectively after the 12th session ($p<0.05$).	Information not available

23.LBP	Groenveld <i>et al.</i> [44] Netherlands	41 VR group=21 Control group=20 Age (y) VR: Mean (SD) 51 (2.9) Range 27-71 Control: Mean 52 (2.5) Range: 30-73 Sex Females VR: 17 (85) Control: 16 (80)	Immersive (Head-mounted display) Behavioural therapy-based VR games	The VR and the control group were both on the waiting list for a follow-up visit to discuss advanced pain treatment, but the control group received no additional treatment or VR intervention. Vr games included psychological treatment principles based on the biopsychosocial model of pain.	4 weeks	Quality of life (SF-12), visual analogue scale (VAS), analgesics used daily, Pain Catastrophizing Scale Pain, Oswestry Low Back Pain Disability Index Nottingham Extended Activities of Daily Living questionnaire (NEADL), Positive Health Questionnaire Hospital anxiety and depression scale (HADS)	No significant treatment effect was found for the short form-12 physical score and mental score 4 weeks. VR seemed to positively affect daily "worst pain score" and "least pain score". Opioid use in the VR group was halved. VR had good treatment adherence and minimal and mild side effects.	A significant main treatment effect of VR was seen on the daily worst experienced pain score (F (1, 91.425)=33.3, P<0.001)	Three patients reported mild and temporary dizziness.
24. Subacromial impingement syndrome and scapular dyskinesis	Pekyavas <i>et al.</i> [57] Turkey	30 VR Group=15 Control Group= 15 Control group: mean age: 40.6 ± 11.7 years VR Group: mean age: 40.33 ± 13.2 years Sex not specified	Non-immersive Exergames	All the subjects were included in a home exercise program. The VR group received supervised virtual reality exergaming program for shoulder movements with Nintendo Wii. This was parallel to the given home exercise program in control group.	6 weeks	Visual Analogue Scale (based on rest, activity and night pain), Neer and Hawkins Tests, Scapular Retraction Test (SRT), Scapular Assistance Test (SAT), Lateral Scapular Slide Test (LSST) and shoulder disability (Shoulder Pain and Disability Index (SPADI)).	Intensity of pain was significantly decreased in both groups with the treatment. The VR Group had significantly better results for all Neer test, SRT and SAT than the Control Group.	Intensity of pain was significantly decreased in both groups between time factors (p<0.05).	Information not available

25. Frozen shoulder	Donny Gunawan <i>et al.</i> [34] Indonesia	75 (Not specified how many participants in each group) 35-65 years (Age and sex not specified)	Non-immersive	CG received ultrasound diathermy modal therapy on painful shoulder for 10 minutes and shoulder stretching exercise Over Head Pulley (OHP). VR group received ultrasound diathermy at shoulder pain area for 10 minutes and shoulder stretching exercises using VR games	3 to 9 times a week	Pain and Functional Ability (DASH), shoulder joint motion range (JMR)	Stretching exercises compared with VG group exercises provided the same benefits of stretching with the OHP on improvement.	No significant difference between the VR and the control groups	Information not available
26. Rotator cuff rupture	Menek <i>et al.</i> [58] Turkey	45 CEG=16 CKCEG=16 VGEG=16 Age (years), mean (SD) CEG=52 (6.3) CKCEG=50 (5.5) VGEG=47 (7.1) 0.56 Gender, n (%) Male CEG=7 (47) CKCEG=8(53) VGEG=6 (40) Female CEG=8 (53) CKCEG=7 (47) VGEG=9 (60) 0.54	Non-immersive Exergames	Three arms: conventional exercise group (CEG), a structured closed kinetic chain exercise group (CKCEG), and a video-based game exercise group (VGEG).	6 weeks	Pain severity; pain threshold; disabilities of the arm, shoulder, and hand questionnaire (DASH); rotator cuff quality of life index (RCQOL); range of motion (ROM); and joint position sense and approximation force of all individuals were evaluated pre- and post-treatment.	Statistically significant difference in all values of the pre- and post-treatment of the groups. When the differences between the groups were compared, CKCEG and VGEG values were more significant than CEG in all parameters. Improvements in pain threshold, ROM in shoulder flexion and abduction, DASH score, and all parameters of the RCQOL questionnaire in VGEG were statistically more significant than CKCEG.	CKCEG and VGEG values were more significant than CEG in all parameters (P<0.017). Improvements in pain threshold, in VGEG were statistically more significant than CKCEG (P<0.017).	Information not available

27. Shoulder pain	Rizzato <i>et al.</i> [59] Italy	22 VR group=11 Control group=11 Age Control: 62 ± 10.20 VR: 59.91 ± 10.93	Non-immersive Exergames	All the subjects were treated manually by the physiotherapist, while for the last 20 min, they performed active exercises to improve shoulder strength and mobility, which had the same goals but differed in the exercising modality that was non-digital for Control group and digital for VR group.	10 consecutive sessions	VAS, shoulder mobility measured with a wireless inertial sensor, maximal isometric strength (Fmax) of the injured shoulder, PENN shoulder Score, Physical Activity Enjoyment Scale (PACES-short), Self-efficacy questionnaire, Attitudes to train at home questionnaire, Intention to train at home, and System usability scale (SUS).	Significant improvements in pain, strength, and PENN Shoulder Score in both groups. Patients' engagement improved, with significant increments in Self-efficacy and attitude scores in both groups after the rehabilitation. Pearson correlation showed significant correlations of the Δ scores ($T_1 - T_0$) between PACES and Self-efficacy and between PACES and Intention to train at home only in the VR group. SUS score after the rehabilitation overcame the cutoff value of 68, representative of good usability of a device.	VAS Control: Pre: 4.30 ± 2.52 Post: 2.70 ± 2.02 VR: Pre: 4.04 ± 2.19 Post: 3.17 ± 2.49 (p<0.01)	Information not available
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28. Patellofemoral pain	Ebrahimi <i>et al.</i> [127] Iran	26 women VR group=13 Control group=13 Age (years) VR group: 29.69 ± 5.69 19 40 Control group: 31.76 ± 5.52 25 40 All women	Non-immersive Avatar	In the VR group the participants could move their whole body in the space with Kinect, in addition to educations provided to the control group, who continued their usual and normal lifestyle without any intervention	24 sessions within 8 weeks	Balance was evaluated by modified star excursion balance test (mSEBT) Other measures were pain, QOL, function, and brain activity, which were assessed using VAS, SF-36 questionnaire, Kujala questionnaire and step-down test, and quantitative EEG	Balance score, function, and quality of life improved significantly at post-intervention and 1 month follow-up in the VR group compared with the control group. VRT group showed a significantly decreased pain score. Alpha and theta power activity also increased in the brain of the VR group.	VR group showed a significantly decreased pain score ($P=0.004$).	Information not available
29. Knee Osteoarthritis	Özliü <i>et al.</i> [61] Turkey	73 VR group=35 Control group=38 Age (X ± SD) VR: 53.28 ± 10.42 Control: 53.71 ± 9.65 Gender Female VR: 17 (48.6) Control: 26 (68.4) 0.069 Male VR: 18 (51.4) Control: 12 (31.6)	Immersive (head-mounted display) VR game	In the experimental group, plus the conservative treatment, a total of 15 sessions of a disease-specific gamification through VR glasses were applied	3 weeks Assessment before treatment, after treatment (3th weeks), and 4 weeks after treatment (7th weeks).	Pain (visual analogue scale [VAS]), functionality (Lysholm functional knee score [LFKS], 6 minutes walking test [6MWT]), disability (Western Ontario and McMaster Universities Arthritis Index [WOMAC]), and balance (Berg Balance Scale [BBS])	VAS and WOMAC scores of the experimental group were lower at the 3rd and 7th weeks than those of the control group. LFKS of the experimental group was higher at the 3rd and 7th weeks than that of the control group. No difference was found between the groups in terms of 6MWTs. BBS score of the experimental group was higher in the 7th week than that of the control group.	VAS Week 0: VR: 5.57 – 0.88 Control: 5.78 – 0.74 ≠ between groups: 0.299 Week 3: VR: 4.11 – 1.34 Control: 5.05 – 1.43 ≠ between groups: 0.005 Week 7 VR: 4.05 – 0.72 Control: 5.36 – 0.99 ≠ between groups: 0.000	Side effects such as mild nausea, headache that did not last long, require additional treatment.

Traumatic injury with conservative treatment									
30. Post-traumatic osteoarthritis	Nambi <i>et al.</i> [62] Saudi Arabia	60 VRgroup=20 Sensoriomotor training (SMT) group=20, and control groups=20.	Non-immersive VR games	The participants of both groups underwent 4 weeks of rehabilitation. The VR group received proprioceptive-stabilometric machine with screen. The SMT group received sensorimotor training exercises. The control group received supervised conventional exercise programs for the knee muscles.	4 weeks of intervention. 3 months of follow-up	Clinical (pain intensity and functional disability) and biochemical (bone morphogenic proteins and inflammatory biomarkers) values were measured at baseline, after 4 weeks, 8 weeks and 3 months follow up.	Four weeks following training, the VRT group shows more significant changes in pain intensity and functional disability than SMT and control groups. Bone morphogenic protein (BMP) measures such as BMP 2, 4, 6, and 7 don't show any significant changes between the groups. But at the same time, the VRT group shows positive improvement in inflammatory biomarkers (CRP, TNF- α , IL-2, IL-4, IL-6) analysis than the other two groups.	Pain intensity (VAS) Base line VR: 7.2 \pm 0.5 SMT: 7.4 \pm 0.4 Control: 7.3 \pm 0.4 p-value: 0.355 4 weeks VR: 3.3 \pm 0.4 SMT: 5.8 \pm 0.5 Control: 6.5 \pm 0.5 p-value: 0.001* 8 weeks VR: 2.5 \pm 0.4 SMT: 3.5 \pm 0.5 Control: 4.2 \pm 0.5 p-value: 0.001* 3 months VR: 0.5 \pm 0.3 SMT: 1.5 \pm 0.4 Control: 3.8 \pm 0.4 p-value: 0.001*	Information not available

31. Ankle sprains	Punt <i>et al.</i> [63] Switzerland	90 VR group=30 Physical therapy (PT)=30 No treatment group (NT)=30 Age (years): VR group: 34.7 ± 10.7 PT group: 34.7 ± 11.3 NT group: 33.5 ± 9.5 Sex: M/F 1VR group: 9/11 PT group: 20/10 NT group: 12/18	Non-immersive (Exergames)	The participants in the VR group received a Wii balance board, the Wii Fit™ software, and detailed instructions so as to independently carry out their rehabilitation program at the difficulty level preferred. Patients allocated to conventional physical therapy received treatment in order to guarantee homogenous treatment modalities. The control group did not receive any exercise therapy.	6 weeks	Foot and Ankle Ability Measure, pain during rest and walking, delay before return to sport, patient satisfaction, and effectiveness of the allocated treatment	Six weeks after the baseline measures, foot and ankle ability scores had improved in all groups, and pain had decreased during walking. VR was not more effective than only physical therapy, or no exercise therapy at all.	VAS during rest VR group: Baseline: 1.3 ± 2.2 6 weeks: 0.6 ± 1.8 P value: 0.045 PT group: Baseline: 1.3 ± 2.1* 6 weeks: 0.9 ± 1.7* P value: 0.163 NT group: Baseline: 1.1 ± 1.4 6 weeks: 0.7 ± 1.2 P value: 0.091 VAS during walking: VR group: Baseline: 2.6 ± 2.6 6 weeks: 0.9 ± 1.9 P value < 0.001 PT group: Baseline: 2.6 ± 2.5* 6 weeks: 1.7 ± 2.5* P value = 0.018 NT group: Baseline: 2.6 ± 2.1 6 weeks: 1.7 ± 2.1 P value = 0.005	Information not available
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Orthopaedic surgery									
32. Distal radius fracture	Naqvi <i>et al.</i> [60] India	20 VR group=10 Control group=10 VR group: 20% 18-25 years, 10% 26-35 years, 50% 36-45 years, 20% 56-65 years 80% males; 20% females. Control group: 30% 18-25 years, 10% 26-35 years, 30% 36-45 years, 30% 56-65 years 50% male-female distribution	Immersive (Head-mounted display) VR game	VR patients played on Oculus Quest head-mounted display (HMD), while control group patients received a conventional rehabilitation program.	4 weeks	Visual analogue scale (VAS), universal goniometer, Jamar dynamometer, and Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire	There were significant improvements in pain, range of motion (ROM), grip strength, and functional independence in both groups. However, improvements in hand function and functional independence were significantly greater in the gamification group than in the conventional physiotherapy rehabilitation group.	The improvement in pain intensity between the groups was statistically analyzed with an unpaired t-test and found to be statistically insignificant at t0 - baseline (p=0.08) but significant at t2 (end of the second week) and t4 (end of the treatment) (p<0.001).	Information not available
33. Total Hip Arthroplasty	Fascio <i>et al.</i> [64] Italy	43 VR group=21 Control group=22 Age (years) Control group: 60.9 ± 7.52 VR group: 61.5 ± 6.21 Men—n. (%) Control group: 13 (56.5%) VR group: 12 (57.1%)	Non-immersive Practical exercises	All participants were invited to perform a daily home exercise program for rehabilitation after THA with different administration methods—an illustrated booklet for the control group and a tablet with wearable sensors for the VR group	2 weeks of intervention. Outcomes were measured before surgery and at the 4th, 7th, and 15th day after surgery.	BARTHEL: Modified Barthel Index; FIM: Functional Independence Measure; HOOS JR: Hip Dysfunction and Osteoarthritis Outcome Score for Joint Replacement and the degree of global perceived effect of the rehabilitation program (GPE).	Virtual-reality-based home rehabilitation resulted in similar improvements in functional outcomes with a better GPE compared to the traditional rehabilitation program following THA.	No difference was found in the HOOS JR between VR and control at T0 (p=0.99), T1 (p=0.99), T2 (p=0.95), or T3 (p=0.855).	Information not available

34. Total hip arthroplasty	Zavala <i>et al.</i> [65] Chile	73 VR group=36 Control group=37 Age (yr), mean (SD) VR group: 69.6 (8.8) Control group: 69.9 (8.8) Gender, number (%) VR group: 18 (50) female 18 (50) male Control group: 20 (54) female 17 (46) male	Non-immersive Exergames	The control group received 6 weeks of physiotherapy treatment; the VR group received the same treatment plus virtual reality exercises with the Nintendo Wii console.	6 weeks	WOMAC questionnaire, Berg Balance Scale, distance covered with the six-minute walk test, and difference in weight load on the lower extremities.	The VR group showed statistically significant differences in the function of patients with total hip replacement, but these differences were not minimally clinically important	The difference between groups for the total WOMAC score was -10.4 points (p=0.00) in favour of the intervention group.	Information not available
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35. Total knee arthroplasty (TKA)	Jin <i>et al.</i> [66] China	66 VR group=33 Control group=33 Age (years): VR group: 66.4 ± 3.49 Control group: 66.30 ± 4.41 Gender (n/percentage) VR group: 15/45.45 male 18/54.55 female Control group: 13/39.39 male 20/60.61 female	Immersive Practical exercises	All recruited patients exercised by performing foot dorsiflexion and plantar flexion beginning the first day after TKA. Exercises targeting quadriceps muscle strength occurred from the second day after TKA. Passive exercises on knee flexion began after the drainage tube was removed. Exercises were assisted with psychological intervention and pain management education. In VR group the patients were asked to row a boat using knee flexion, beginning the second day after TKA. Patients in the control group were asked to flex their knees passively using their arms until pain tolerance was reached.	Variable depending on the number of Days needed for knee ROM to reach 60° and 90°	Western Ontario and McMaster University osteoarthritis index (WOMAC) measured before TKA and 1, 3, 6 months after TKA; Hospital for Special Surgery knee score (HSS) measured before TKA and 1, 3, and 6 months after TKA; Visual analogue scale (VAS) for pain measured at 1, 3, 5, and 7 days after TKA; Range of motion (ROM) measured before TKA and at 3, 7, and 14 days after TKA. Days needed for knee ROM to reach 60° and 90° were also recorded.	No significant differences were found in preoperative WOMAC index, HSS score, and knee ROM between control and experimental groups. WOMAC indexes were significantly lower and HSS scores were significantly higher in the experimental group than in the control group at 1, 3, and 6 months after TKA, respectively. VAS scales were significantly lower in experimental group than the control group at 3, 5, and 7 days after TKA.	No significant difference was observed in VAS scales between the two groups 1 day after TKA (P>0.05). VAS scales were significantly lower in VR group than control group at 3, 5, and 7 days after TKA (P<0.05). WOMAC indexes were significantly lower in both groups after TKA as rehabilitation continued (P<0.05). Also, WOMAC indexes were significantly lower in the experimental group than the control group at 1, 3, and 6 months after TKA (P<0.05)	Information not available
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36. Primary total knee arthroplasty (TKA)	Gianola <i>et al.</i> [67] Italy	85 VR group=44 Control group=41 subjects Age (years) VR group: 66.6 ± 8.7 Control group: 70.7 ± 8.5 Gender Men – no. (%) VR group: 24 (54.5) Control group: 13 (31.7)	Non-immersive Avatar Screen	Subjects were randomly allocated 3 to 4 days after TKA to one of two rehabilitation groups: experimental (VR rehabilitation) or control (traditional rehabilitation).	Baseline: 3–4 days after TKA; discharge: 10 days after surgery.	VAS, Western Ontario and McMaster Universities osteoarthritis index (WOMAC); health-related quality was measured by EuroQol five-dimensional (EQ-5D) questionnaire; global perceived effect (GPE) score; the functional independent measure (FIM); the frequency of medication assumption; the isometric strength of the quadriceps and hamstring muscles as assessed using a dynamometer, the knee active range of movement (ROM) and the proprioception assessed using the stabilometric platform of the VRRS.	VR-based and traditional rehabilitation shown no statistically significant reduction between groups as well as in all other outcomes, whereas a statistically significant improvement was present in the global proprioception, in favor of the VR-based rehabilitation group.	VAS pain score Before TKA VR group: 47.65 ± 21.29 ~ Control group: 60.20 ± 21.71 After TKA VR group: 24.62 ± 16.80 3Control group: 1.23 ± 19.59 Change VR group: -23.03 (95% CI -30.26 to -15.79) P value 0.26 Control group: -28.97 (95% CI -36.82 to -21.12) WOMAC-total score Before TKA VR group: 1519.85 ± 170.39 Control group: 1670.25 ± 199.03 After TKA VR group: 729.57 ± 175.73 Control group: 904.48 ± 229.14 Change VR group: -790.28 (95% CI -870.79 to -709.78) Control group: -765.77 (95% CI -829.66 to -701.87) p value 0.62	Information not available
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37. Total Knee Arthroplasty	Prvu <i>et al.</i> [68] USA	287 VR group=143 Control group=144 Age VR group: 65.4 ± 7.7 Control group: 65.1 ± 9.2 Sex VR group: 59.6% female Control group: 65.4% female	Non-immersive Avatar	After discharge, the VR group used a virtual telehealth system that functions with use of 3-dimensional (3D) tracking technology to quantify pose and motion, an avatar (digitally simulated coach) to demonstrate and guide activity, visual and audible instructions and immediate feedback on exercise quality, and a virtual video connection for synchronous telehealth visits with an assigned intervention telehealth physical therapist. Patients in the conventional group followed their care team's recommendations for all preoperative and postoperative medical and rehabilitative care.	12 weeks	The primary outcome was total health-care costs for the 12-week post-hospital period. Secondary (noninferiority) outcomes included 6 and 12-week Knee injury and Osteoarthritis Outcome Score (KOOS); 6-week knee extension, knee flexion, and gait speed; and 12-week safety measures (patient-reported falls, pain, and hospital readmissions).	VR patients had fewer rehospitalizations than the usual care group. VR was noninferior to usual physiotherapy in terms of the KOOS at 6 and 12 weeks. VR was also noninferior to usual care at 6 weeks in terms of knee extension, knee flexion, and gait speed and at 12 weeks in terms of pain and hospital readmissions. Falls were reported by 19.4% of VR patients and 14.6% of usual care patients.	Pain (points) VR group: 3.6 ± 2.0 Control group: 3.2 ± 2.0 p value 0.120 KOOS (points) VR group: 61.0 ± 11.5 Control group: 61.8 ± 13.5 P value 0.604 Pain VR group: 66.6 ± 15.6 Control group: 68.7 ± 17.1 P value 0.286	Information not available
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38. Total knee arthroplasty (TKA)	Fuchs <i>et al.</i> [69] Israel	<p>55 VR group=30 Control group=25</p> <p>Age (mean (SD)) VR group: 70 (7) Control group: 70 (7)</p> <p>Sex (n (%)) VR group: 19 (63.3%) female 11 (36.7%) male</p> <p>Control group: 13 (52%) female 12 (48%) male</p>	Immersive (Head mounted display) Virtual illusion	Both groups were treated with conventional physiotherapy and CPM equipment (Continuous passive motion device), the VR group received additional VR modality. The VR intervention included a movie that was picked by the patient from several options, either a nature film or a music film. The patient watched the VR film during the CPM physiotherapy.	The intervention was performed in day 1 and day 2 post-operatively. Reevaluation after 6 months	State-Trait Anxiety Inventory (STAI) questionnaire (used to diagnose anxiety), Visual analog scale (VAS) for pain and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) (knee function score).	Both groups showed a decrease in pain and anxiety following the intervention but there was no difference between the groups. The was no difference in the WOMAC scores in the six-month postoperative examination between groups.	There was no difference in the amount of decreased pain between the study and the control groups (delta VAS Day 1 p-value=0.141; delta VAS Day 2 p-value=0.365).	Information not available
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Rheumatological diseases	
39. Ankylosing spondylitis	<p>Karahan <i>et al.</i> [70] Turkey</p> <p>57 VR group=28 Control group=29</p> <p>Age in years (mean ± SD) VR group: 36.1 ± 12.4 Control Group: 36.6 ± 11.3</p> <p>Sex (m/f) VR group: 24/6 Control group: 23/7</p> <p>Non-immersive Exergames</p> <p>The VR patients engaged in exergaming, and Control patients did not engage in any exercises.</p> <p>8 weeks</p> <p>Visual analogue scale (VAS), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Quality of Life (ASQOL) questionnaire.</p> <p>In the exergame group, VAS, BASFI, BASDAI and ASQoL scores improved significantly after eight weeks of the program. The intergroup comparison after the eighth week showed significant differences between the two groups in VAS, BASFI, BASDAI and ASQoL, with the VR patients showing considerable improvement). No strain, injury or other musculoskeletal complications were recorded during the exergame workouts.</p> <p>VAS VR group: Baseline: 4.9 ± 2.0 After 8 weeks: 3.6 ± 1.7*a (*p < 0.001 within groups; a p < 0.05 between groups.) P value < 0.001</p> <p>Control group: Baseline: 5.1 ± 2.2 After 8 weeks: 5.0 ± 2.4 P value = 0.241</p> <p>No strain, injury or other musculo-skeletal complications were recorded during the exergame workouts.</p>

40. Juvenile Idiopathic Arthritis	Arman <i>et al.</i> [71] Turkey	50 VR group=25 Control group=25 Age, yr (Mean) Control group=13.16 (3.35) VR group=12.36 (2.98) Sex (Female/male) Control group=21/4 VR group=21/4	Non-immersive Exergames	In control group, activities of daily living were practiced using real materials from daily life, and in VR group, activities of daily living were practiced using video-based games	8 weeks	Numeric Rating Scale Muscle strength Grips strength Childhood Health Assessment Questionnaire Canadian Occupational Performance Measure Duruoz Hand Index	After treatment in both groups, significant changes were found in the Numeric Rating Scale, muscle strength, grips strength, Childhood Health Assessment, Canadian Occupational Performance Measure, and Duruoz Hand Index. VR group was statistically superior to Control group in changes of almost all upper limb muscle strengths, palmar pinch strength, Canadian Occupational Performance Measure satisfaction, and Duruoz Hand Index scores.	CHAQ-Pain (Mean) Before Control group: 43.60 (28.52) VR group=31.00 (28.68) P=0.12 After Control group=9.20 (17.54) VR group=8.68 (15.60) P=0.00 Difference between groups (Mean): Control group=34.40 (24.03) VR group=22.32 (21.41) P=0.06	Information not available
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Chronic Pain Generalization										
41.	Fibromyalgia	Collado-Mateo <i>et al.</i> [72] Spain	83 VR group=42 Control group=41 Mean age \pm SD: VR group=52.52 \pm 9.73 Control group=52.47 \pm 8.75 Sex: all women	Non-immersive Exergame	The VRG completed an 8-week training program, while the CG continued their normal daily life.	8 weeks	Fibromyalgia Impact Questionnaire (FIQ), EuroQoL-5 Dimensions-5 Levels (EQ-5D-5L)	97.62% of participants in the exercise group completed the 8-week intervention. The exercise group showed a significant improvement in the EQ-5D-5L utility index, and in 3 of 5 dimensions. For the FIQ, significant improvements were observed in the dimensions of pain, stiffness, anxiety, and feel good. The FIQ score was also reduced. The mean between-group improvement was 8.25 (95% confidence interval, 2.85-13.65).	VAS Health score Mean (SD) VR group: Before= 50.12 (14.50) After= 58.41 (17.12) Control group: Before= 51.22 (18.86) After=49.62 (17.20) Mean difference (95% CI)= -9.89 (-18.28 to -1.50) P=0.021 Effect size= 0.064	Information not available
42.	Fibromyalgia	Villafaina <i>et al.</i> [73] Spain	50 VR group=25 Control group=25 Age Mean (SD) VR group= 54.04 (8.45) Control group= 52.72 (9.98) Sex: all women	Non-immersive Exergame	VR participants completed 24 weeks of exercise intervention, whereas the control group continued with their usual daily life, including medication for those who were taking.	24 weeks	Euroqol-5 Dimensions-5 Levels (EQ-5D-5L), visual analogue scale (VAS).	89.29% of adherence in VR group. Significant effects on the perceived health status and pain intensity were found. The respond group obtained significant effects of the exergame intervention in EQ-5D-5L, pain VAS, and VAS-EQ, compared with those who did not respond.	VAS Mean (SD) VR group Before: 64.80 (17.83) After: 60.20 (16.74) P=0.029 Control Before: 59.20 (19.13) After: 67.20 (17.44)	Information not available

43. Fibromyalgia	Carvalho et al. [74] Brazil	35 VR group=16 Control group=19 Age, years Mean (SD) Control group=47.70 (15.46) VR group=55.64 (9.16)>0.05 Sex: all women	Non-immersive Wii Exergames	Six subgames of Wii Fit Plus were chosen for the VR group; the exergames group performed the program thrice per week with each session lasting 1 hour. The control group performed the chain muscle stretching technique thrice per week with each session lasting 1 hour.	7 weeks of intervention with three 1-hour sessions weekly and reevaluation after the 10th and the 20th sessions.	Fibromyalgia impact questionnaire (FIQ), algometry, step tests, cardiopulmonary parameters, and fatigue in the lower limbs	The exergames group showed significant reduction of their fibromyalgia symptoms, as demonstrated by lower FIQ scores in the key domains on questions regarding missed work, pain, fatigue, problems resting, stiffness, anxiety, and depression. Significant improvements were observed in mean algometric values in the cervical region, the second chondrocostal junction, the lateral epicondyle, left medial knee border, left occipital region, trapezius, supraspinatus, gluteal muscles, and the greater trochanter. Improved cardiovascular adaptation was reflected by decreased systolic blood pressure, reduction in fatigue of the lower limbs assessed by the CR10 Borg scale, and improved exercise capacity assessed by a step test.	Pain, (cm) Control group E0=8.40 (1.50)A E1=7.00 (2.53)A E2=5.16 (1.96)B VR group E0=7.36 (2.36)A E1=4.45 (1.57)B E2=4.44 (1.30)B ANOVA—P Time- group=0.214 Time<0.001 Group=0.030 effect size (f2)=0.753 Bonferroni test: WG versus CG and A versus B P < 0.05; effect size (f2). E0 Baseline E1: after 10 sessions E2: after 20 sessions.	Information not available
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44. Fibromyalgia	Gulsen <i>et al.</i> [75] Turkey	20 VR group=10 Control group=10 Age (years) Control group=38.50 (29.50–50.00) VR group= 46.50 (36.50–49.50) Sex: all women	Immersive (Head-mounted display) Practical exercises	The control group had combined exercise training consisted of 30 minutes of aerobic training and 30 minutes of Pilates training and VR group had the same protocol with EG plus 20 minutes of IVR, twice a week for 8 weeks	8 weeks	Visual analogue scale for pain, Modified Sensory Organization Test for balance, Tampa Scale of Kinesiophobia for kinesiophobia, Fibromyalgia Impact Questionnaire for impact of fibromyalgia, Fatigue Severity Scale for fatigue, International Physical Activity Questionnaire for level of physical activity, six-minute walk test for functional capacity, and Short-Form 36 Health Survey for quality of life were used for evaluation	Pain, balance, kinesiophobia, impact of fibromyalgia, fatigue, level of physical activity, functional exercise capacity and quality of life scores improved significantly in both groups. VR group showed significant improvement compared to the EG regarding pain, kinesiophobia, fatigue, level of physical activity, and mental component of quality of life.	VAS, cm Control group: Before=7.40 (5.92–8.35) After=4.50 (3.47–5.72) Within group Comparison ^a : p=0.012* Between group comparison the baseline ^b : p= 0.225 VR group: Before=8.00 (7.55–8.95) After=3.95 (3.32–4.5) Within group Comparison ^a : P=0.012* Between group comparison the baseline ^b : p=0.225 *p<0.05 aWilcoxon test bMann-Whitney U test	Information not available
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45. Fibromyalgia	Polat et al [76] Turkey	42 VR group=21 Control group=21 Age VR group= 46.00 (40.05-50.50) Control group=45.00 (44.00-48.00)	Non-immersive Biodex Balance System (BBS)	Computer-based stability training was applied to study group by help of computer-based device two times a week for 12 weeks while traditional training was done to another group.	12 weeks	Pain and disability were assessed by Numeric Pain Scale and Oswestry Disability Index, respectively. Limits of stability (LoS) and postural stability (PS) tests were used to evaluate postural control by Biodex Balance System and SenseWear Armband was used for physical activity assessment. All measurements were applied before and after the training.	Significant improvements occurred in LoS and PS scores in both groups after interventions (p<0.05). However, physical activity scores for both groups did not significantly change (p<0.05). Statistical analyses of between-group mean differences showed that there was superiority of computer-based stability training over the traditional training in improving LoS (p=0.023).	NRS score VR group: Before=7.00 (4.00-9.00) After=3.00 (2.00 -5.00) P=0.021 Control group: Before=6.00 (3.00-9.00) After= 4.00 (2.00 - 7.00) P=0.038 Difference between groups Before: p=268 After=0.041 *p<0.05	Information not available
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46. Paediatric burn patients	Parry et al. [83] USA	17 VR group=9 Control group=8 Age Mean (SD) Control group=12.3 (± 4.4) VR group=10.6 (± 4.5)	Non-immersive (Videogames)	The participants performed exercises using either standard therapy range of movement activities (Control group) or interactive videogame therapy (VR group).	6 months	Planar and functional ROM was measured using goniometry and motion analysis. Pain, enjoyment, engagement, and perceived "fun" that they experienced during the treatment session using a 0 to 10 rating scale	Patients in both groups showed significant improvement in shoulder flexion, shoulder abduction, shoulder external rotation, and elbow flexion ROM from baseline to 6 months as measured with goniometry. There was no difference in ROM gains between the groups. Control subjects showed an increase in pain during the intervention, whereas VR subjects did not.	For the rating of "worst pain" during therapy session, control group subjects demonstrated a slight increase over time ($r=0.18$; $P < 0.01$) but the VR group did not ($r=0.047$). A significant difference was found between these correlation coefficient ($P=0.015$). The difference between correlation coefficients was also significant for lower pain before stretching (VR group: $r=-0.05$, Control group: $r=0.176$; $P=0.02$) and after stretching (VR group: $r=-0.133$, Control group: $r=0.119$; $P=0.009$).	Information not available

47. Adolescent burned	Waked <i>et al.</i> [80] Egypt	56 VR group=28 Control group=28 Age (Mean \pm SD) VR group=13.96 \pm 2.05 Control group=13.61 \pm 1.97 Sex VR group: 18(64.3%) male; 10(35.7%) female Control group: 13(46.4%) male; 15(53.6%) female	Immersive (Head-mounted display) Visual illusion	VR group received VR during physiotherapy session while control group received physiotherapy without VR.	2 weeks	Adolescent Paediatric Pain Tool (APPT) Range of Motion measurement (ROM)	Highly significant and substantial declines in all pain outcomes (mean total painful areas, pain intensity, sensory, affective, evaluative and temporal dimensions of pain) and improvement in ROM of Hip extension, hip abduction, dorsiflexion and knee extension in VR group compared to control group.	Marked decrease in mean total number of descriptive words of sensory F (1.79, 48.52)=259.32, p<0.001, affective F (1.37, 75.66)=122.72, p<0.001, evaluative F (2.22, 59.92)=219.51, p<0.001, and temporal dimensions F (2.52, 68.29)=414.88, p<0.001 in VR group with the time from first session to sixth session. For control group, there is decrease mean total number of descriptive words of sensory F (1.29, 35.02)=13.76, p<0.001, affective F (2.91, 78.49)=41.27, p<0.001, evaluative F (3.06, 82.56)=21.15 p<0.001 and temporal dimension F (3.02, 81.63)=42.57, p<0.001 with	Information not available
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48. Burned Hands	Joo <i>et al.</i> [82] South Korea	<p>57 VR group=28 Control group=29</p> <p>Age (years) VR group= 48.07 ± 8.14 Control group= 41.69 ± 14.05</p> <p>Sex Male: Female VR group=28:0 Control group=26:3</p>	Non-immersive (Exoskeleton type glove combined with the VR system)	<p>All patients received a four-week intervention. The VR group received 30-min standard therapy and 30-min VR-based rehabilitation. The Control group received 60-min standard therapy. An effort was made to match the exercise rehabilitation in both groups and to adapt the level of difficulty to each patient's performance. The intervention frequency and duration did not differ between the VR and Control groups.</p>	4-week	<p>Hand function was evaluated before intervention and four weeks after intervention using the Jebsen-Taylor hand function test (JTT), Grasp and Pinch Power Test, Purdue Pegboard test (PPT), and Michigan Hand Outcomes Questionnaire (MHQ).</p>	<p>The JTT scores for picking up small objects and the MHQ scores for hand function, functional ADL, work, pain, aesthetics, and patient satisfaction were significantly higher in the VR group than in the Control group</p>	<p>Pain (changes of pre-intervention and post-intervention) VR group=-23.21 ± 24.62 Control group=-13.62 ± 21.25 p=0.12</p>	Information not available
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49. Paediatric burns	Ali <i>et al.</i> [81] Egypt	<p>22 VR group=11 Control group=11</p> <p>Age (years) VR group= 13.82 ± 1.4 Control group=12.55 ± 2.06</p> <p>Sex (Boys/Girls) VR group=7/4 Control group=6/5</p>	Immersive (Head mounted display) Visual illusion	The control group received physical therapy session. The subjects in the VR group were treated by the same exercises program while using VR oculus as a distraction method. Children look into VR oculus which blocks their view of the hospital room. Earphones block sounds and substitute more calming music and sound effects.	Before-after 20 min treatment assessment	VAS before and immediately after the treatment session. Maximum available range of motion of the treated joints was measured before the physical therapy session and immediately after the session, using an electronic digital goniometer	There was a significant decrease in pain intensity and increase of ROM after application of VR in the study group and a significant difference between groups after treatment for pain and ROM.	<p>Pain VR group: Before: 7.27 ± 0.9 After: 3.1 ± 1.04 p=0.001</p> <p>Control group: Before: 7.6 ± 1.02 After: 7.72 ± 1.3 p=0.739</p> <p>Between groups p<0.001</p>	Information not available
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Neurological disorders									
50. Phantom pain (PLP)	Rothgangel <i>et al.</i> [84] Netherlands	75 Group A (n=25): mirror therapy (MT) followed by tele-treatment using augmented reality MT Group B (n=26): traditional MT followed by self-delivered MT (group B) Group C (n=24): sensorimotor exercises to the intact limb followed by self-delivered exercises. Age, mean (SD) Group A=59.7 (16.1) Group B=62.5 (11.4) Group C= 61.0 (15.2) Gender, male Group A=80.8 (21) Group B=56.0 (14) Gender, male Group A=80.8 (21) Group B=56.0 (14) Group C=70.8 (17) Group c=70.8 (17)	Non-immersive (Augmented virtual reality using the tablet-integrated camera)	Four weeks of traditional mirror therapy (MT) followed by six weeks of tele-treatment using augmented reality MT (group A), four weeks of traditional MT followed by six weeks of self-delivered MT (group B) and four weeks of sensorimotor exercises to the intact limb followed by six weeks of self-delivered exercises (group C).	Intervention for 6 weeks. Measurements at baseline and follow-up measurements at 4 weeks, 10 weeks and 6 months	Numeric Rating Scale Neuropathic Pain Symptom Inventory German version of the Patient-Specific Functional Scale Pain-related disturbances in sleep and mood were measured using an 11-point NRS. German version of the 5-dimensional EuroQol questionnaire Visual Analogue Scale to score overall health Global Perceived Effect scale German version of the Pain Self-Efficacy Questionnaire	Effects of MT at four weeks on PLP were not significant. MT significantly reduced the duration of PLP at six months compared to the tele-treatment and control group. The tele-treatment had no additional effects compared to self-delivered MT at 10 weeks and 6 months	The frequency of PLP showed a positive change in all groups, with 22 patients (47%) in the MT group and 6 patients (32%) in the control group reporting improvement. Two patients in the MT group showed complete recovery of PLP. The duration of PLP improved in 17 patients (35%) in the MT group and in 3 patients (16%) in the control group. Patients who suffered from constant pain profiting most.	Information not available

51. Joint pain in stroke* (*'joint pain in stroke is a musculo-skeletal disorder integrated in a neurological condition)	Anwar <i>et al.</i> [85] Pakistan	68 VR group=34 Control group=34 Age VR group=51.56 Control group=51.35	Non-immersive (Exergames)	The VR group received a 1-hour session of VR training for 3 weekdays over 6 weeks, and the routine physical therapy group received different stretching and strengthening exercises.	6 weeks	Berg Balance Scale for balance and the Fugl-Meyer Assessment (upper extremity) scale for sensorimotor, joint pain, and range assessment. The assessment was done at the start of treatment and after the 6 weeks of intervention	Significant difference between the two groups was found in the Berg Balance Scale score, Fugl-Meyer Assessment for motor function, and Fugl-Meyer Assessment for joint pain and joint range suggesting a clinically meaningful increase in the VR training community relative to the routine physical therapy group.; no significant difference in the Fugl-Meyer Assessment for upper extremity sensation.	Fugl-Meyer Assessment for joint pain Mean (SD) VR group: Before=12.47 (3.79) After=19.62 (2.86) Control group: Before=11.65 (3.16) After=14.62 (4.00) P<0.01	Information not available
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Cancer	
52. Mastectomy with axillary lymph node dissection	<p>Feyzioglu <i>et al.</i> [86] Turkey</p> <p>All participants were women</p> <p>40 VR group=20 Control group=20</p> <p>Age (years) Mean (SD) VR group=50.84 (8.53) Control group=51.00 (7.06)</p> <p>Non immersive (Exergames)</p> <p>The Kinect-based rehabilitation group and the physical therapy group received standard physiotherapy.</p> <p>6 weeks of intervention. Assessment at baseline and after the 6-week treatment.</p> <p>Pain (visual analogue scale), grip strength (dynamometer), functionality (disabilities of the arm shoulder and hand questionnaire), muscle strength (handheld dynamometer), ROM (digital goniometer), and fear of movement (Tampa kinesiophobia scale (TKS)).</p> <p>Both groups detected significant changes in pain, ROM, muscle strength, grip strength, functionality, and TKS scores after the treatment. Fear of movement was significantly improved in the VR and the Control group displayed more improvement in functionality. There were no differences in ROM, muscle strength, grip strength, and pain between the groups after the treatment.</p> <p>Pre-post treatment VR group: P=0.001** Control group P=0.001*** 0.065</p> <p>**p values obtained from the paired t test for the VR group ***p values obtained from the paired t test for the Control group</p> <p># p overall values obtained from the linear model, repetitive measures= 0.065</p> <p>VAS for pain (0-10) VR group: Before treatment=6.53 (1.65) After=1.53 (1.35) Control group: Before treatment=6.53 (2.07) After=2.56 (1.82)</p> <p>No complications occurred during Xbox Kinect VR training performed early in the postoperative period after breast cancer surgery</p>

53. Breast cancer-related lymphedema	Basha <i>et al.</i> [87] Saudi Arabia	60 VR group=30 Control group=30 Age Mean (SD) VR group=48.83 ± 7.0 Control group=52.07 ± 7.48 All participants were women	Non immersive (Exergames)	The Xbox Kinect group received VR Kinect-based games and Control group received resistance training. In addition, both groups received complex decongestive physiotherapy (manual lymphatic drainage, compression bandages, skin care, and exercises).	8 weeks	Excessive limb volume visual analogue scale (VAS) Disability of the Arm, Shoulder, and Hand (DASH) questionnaire shoulder range of motion (ROM) shoulder muscles strength, hand grip strength Study Short-Form (SF-36).	Statistically significant differences were recorded in VAS (pain intensity), DASH, shoulder ROM, bodily pain, general health, and vitality in favour of the VR group. However, there were statistically significant differences in shoulder flexion strength, external rotation strength, and abduction strength and handgrip strength in favour of the Control group	Change from baseline to 8 weeks MD (95% CI) VR group: VAS pain= 31.0 (28.85, 33.15), p<0.0001 VAS-heaviness= 21.67 (19.58, 23.75), p<0.0001 VAS-tightness= 15.67 (12.98, 18.35), p<0.0001 Control group: VAS pain=15.67 (13.52, 17.82), p<0.0001 VAS-heaviness= 19.0 (16.92, 21.08), p<0.0001 VAS-tightness= 12.67 (9.98, 15.35), p<0.0001	Information not available
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		Other							
54. Cardiac Rehabilitation	Cacau et al. [88] Brazil	60 VR group=30 Control group=30 Age (Mean ± SD) VR group= 49.2 ± 2.6 Control group= 52 ± 2.4 Sex (male/female) VR group= 13/17 Control group= 16/14	Non-immersive (exergames)	Patients allocated in control group performed conventional physical therapy treatment twice a day. The treatment protocol included: breathing exercises, airway clearance techniques, metabolic exercise and motor exercise. Patients allocated in virtual reality group were treated twice a day performing the same techniques than conventional treatment however the motor exercise was performed using virtual reality.	All patients had their functional performance reassessed on the first, third, postoperative day (PO) and at the discharge day	Six-minute walk test (6MWT) and Nottingham Health Profile (NHP) reassessed on the first, third, postoperative day (PO) and at the discharge day	On the first day after surgery, patients in both groups showed decreased functional performance. However, the VR group showed lower reduction when compared to Control group in first postoperative day, and no significant difference in performance on discharge day. In evaluating the NHP field, we observed a significant decrease in pain score at third assessment. There were no differences with statistical significance for emotional reactions, physical ability, and social interaction. The length of stay was significantly shorter in patients of VR group, who also had a higher 6MWD.	Post surgical pain in the field of NHP (Nottingham Health Profile): Lower score (P<0.05) among deltas 1, 2 and 3 as well as the type of treatment, with a significant statistical improvement in the VR group in delta 3 (P<0.05). Delta 1 (difference of pre-operative score for first postoperative day); Delta 2 (difference of pre-operative score for third postoperative day) and Delta 3 (difference of preoperative score for the discharge day). Data were analysed using two-way ANOVA (Delta 3 *VR x CG, P<0.05)	Information not available

55. Vestibular disorders	Alahmari <i>et al.</i> [89] USA	48 VR group=20 Control group=18 Age (Mean±SD) VR group=53 ± 2 Control group=61 ± 3 Sex (female/male) VR group=15/5 Control group=16/2	Immersive (CAVE) VR game	For the PT intervention, subjects were treated for 6 treatment sessions (one session per week) by a physical therapist. For the VRBT intervention, subjects were treated for 6 treatment sessions (one session per week) using a virtual grocery store displayed in an immersive environment. Both interventions also included prescription of home exercises, consisting of gaze stabilization or static balance sensory integration tasks.	6 weeks of intervention. Subjects were examined one week before, one week after, and six months after the intervention	Activities-specific Balance Confidence scale Dizziness Handicap Inventory Situational Characteristics Questionnaire Dynamic Gait Index Functional Gait Assessment Timed Up and Go test Sensory Organization Test nausea, headache, dizziness, and visual blurring using a visual analogue scale (VAS) Simulator Sickness Questionnaire	In both groups, significant improvements were noted on the majority of self-report measures one week after the intervention. Subjects maintained improvements on self-report and performance measures at 6 months follow up. There were not between group differences. Nausea, headache, dizziness and visual blurring increased significantly during the VR sessions, but overall symptoms were reduced at the end of the six-week intervention.	Headache VAS significantly increased during the session but decrease at the end of the six-week intervention Pre and post VAS headache ratings (mean ± SEM) : Before VR= 0.5 ± 0.2 After VR= 0.8 ± 0.3 Time p value=0.034 VAS Headache After session 1=0.4 ± 0.1 After session 2=0.7 ± 0.2 After session 3=0.5 ± 0.2 After session 4=0.4 ± 0.1 After session 5=0.6 ± 0.3 After session 6=0.2 ± 0.1 Session p value=0.34	Nausea, headache, dizziness and visual blurring increased significantly during the VRBT sessions, but overall symptoms were reduced at the end of the six-week intervention.
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56. Active aging	Lee <i>et al.</i> [90] South Korea	54 VR group=26 Control group=28 Age, mean (SD) VR group=68.77 (4.62) Control group=67.71 (4.31)	Non-immersive (Xbox games + KINECT to capture the movement)	Both groups received a 60-min intervention three times a week for eight weeks. The VR and the non-VR exercise plan were similar.	8 weeks	Short-Form Health Survey (SF-36) 30-Second Chair Stand Test (30SCST) 8-Foot Up-and-Go Test (8FUGT) 2-Minute Step Test (2MST)	VR group showed greater improvement in mental health and lower body strength, compared to GG. Within-group analysis for HRQoL revealed that VR group showed an increase in role-physical, bodily pain, general health, vitality, role-emotional, and mental health, whereas control group showed an increase in role-physical, general health, and social functioning. Both groups showed an increase in 30SCST, 2MST and 8FUGT.	Bodily pain VR group: Baseline=65.65 (21.38) Follow-up=76.31 (19.27)* Change=10.65 (21.28) Control group: Baseline=54.36 (24.70) Follow-up=64.43 (24.77) Change=10.07 (28.43) Adjusted between-group mean difference (95% CI) b=7.71 (-4.00 to 19.42) p<0.192	Information not available
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Table 2. Musculoskeletal disorders included in the studies.

Musculoskeletal disorders		
Condition	Anatomic region	Number of studies
Degenerative	Chronic low back pain	15
	Chronic neck pain	8
	Sholder pain	4
	Knee pain	2
Traumatic injury treated with conservative treatments	Ankle sprains	1
	Post-traumatic knee osteoarthritis	1
Orthopaedic surgery	Distal radius fracture	1
	Total hip arthroplasty	2
	Total knee arthroplasty	4
Rheumatological diseases	LBP in ankylosing spondylitis	1
	Juvenile idiopathic arthritis	1

Table 3. Conditions included in the studies other than musculoskeletal disorders.

Aetiology	Condition	Number of studies
Musculoskeletal disorders		40
Generalised chronic pain	Fibromyalgia	5
Burn	Pain during rehabilitation treatments in burned patients	4
Neurological disorders	Phantom pain after limb amputation	1
	Upper limb pain after stroke	1
Cancer	Mastectomy with axillary lymph node dissection	2
Other	Vestibular rehabilitation (headaches)	1
	Active aging (pain during exercises)	1
	Pain during cardiac rehabilitation after cardiac surgery	1

patients was effective in reducing pain compared to the control group, showing that it can be used as a bonus therapy tool for pain management.

According to the PEDro scale (**Table 4**), the methodological quality of the studies included in this systematic review was generally moderate, with an IVS of 4–5 (37/56 studies, 66%). Only two studies had high methodological quality (IVS of 6–7). Out of 56 studies, 17 (30%) showed limited methodological quality.

Many studies did not provide information about the blinding of the research team members or outcome-measuring assessors. The heterogeneity of the intervention protocols and outcome measures also promoted bias in the comparisons between studies.

Results According to the Conditions

Musculoskeletal disorders and degenerative aetiologies

Neck pain: Only one study [35] had a specific diagnosis of spondylosis, whereas other studies evaluated patients with non-specific chronic neck pain. Six studies [35-40] used immersive VR, whereas only one study [41] used non-immersive VR. Study designs varied with different treatment durations (3 days to 12 weeks) and control groups: comparison of VR with a no exercise program [37,41], training with neck exercises [35-38,40], or rehabilitation programs [39]. Sarig Bahat *et al.* [37] compared VR with training and a no exercise program, and Nusser *et al.* [39] compared it with a standard rehabilitation program and sensorimotor training. Tejera *et al.* [38] evaluated conditioned pain modulation (a psychophysical experimental

Table 4. PEDRo classification (Y: Yes; N: No; NA: Information Not Available).

Pain condition	Study	PEDRo scale											Total	IVS		
		1 Eligibility	2 Randomization	3 Allocation Concealed	4 Groups Similar	5 Blinding Subjects	6 Blinding Assessors	7 Outcome Measures	8 Outcome Measures	9 Intention to treat	10 Statistical comparison	11 Variability measures				
1. Chronic neck pain	Sarig Bahat <i>et al.</i> 2015 [36]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	9	7
2. Chronic neck pain	Sarig Bahat <i>et al.</i> 2018 [37]	Y	Y	Y	Y	N	N	NA	N	N	N	Y	Y	Y	6	2
3. Neck pain	Razae <i>et al.</i> 2019 [41]	Y	Y	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y	8	4
4. Cervical Spondylosis	Mukherjee <i>et al.</i> 2020 [35]	Y	Y	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y	9	5
5. Chronic neck pain	Sarig Bahat 2020 <i>et al.</i> [79]	Y	Y	NA	NA	N	N	NA	N	N	N	Y	Y	Y	4	1
6. Chronic neck pain	Tejera <i>et al.</i> 2020 [38]	Y	Y	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y	9	5
7. Chronic neck pain	Nusser <i>et al.</i> 2021 [39]	Y	Y	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y	8	4
8. Chronic neck pain	Cetin <i>et al.</i> 2022 [40]	Y	Y	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y	8	4
9. LBP	Kim <i>et al.</i> 2014 [45]	Y	Y	NA	Y	N	NA	NA	N	NA	Y	Y	Y	Y	7	3
10. LBP	Yoo <i>et al.</i> 2014 [46]	Y	Y	NA	Y	N	N	NA	N	NA	Y	Y	Y	Y	6	2
11. LBP	Monteiro <i>et al.</i> 2015 [47]	Y	Y	Y	Y	N	NA	Y	N	NA	Y	Y	Y	Y	8	4
12. LBP	Chen <i>et al.</i> 2016 [48]	Y	Y	NA	Y	N	NA	NA	N	NA	Y	NA	Y	Y	6	2
13. LBP	Yilmaz <i>et al.</i> 2016 [42]	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	Y	Y	9	5
14. LBP	Thomas <i>et al.</i> 2016 [49]	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	Y	Y	9	5
15. LBP	Zavarize <i>et al.</i> 2016 [50]	Y	Y	Y	Y	N	N	NA	N	NA	Y	Y	Y	Y	8	4

48. Burned Hands	Joo <i>et al.</i> 2020 [82]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	5
49. Pediatric Burn	Ali <i>et al.</i> 2022 [81]	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	8	4
50. Phantom pain (PLP)	Rothgangel <i>et al.</i> 2018 [84]	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	8	4
51. Joint pain in stroke	Anwar <i>et al.</i> 2022 [85]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	5
52. Mastectomy with axillary lymph node dissection	Feyzioğlu <i>et al.</i> 2020 [86]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	5
53. Breast cancer related lymphedema	Basha <i>et al.</i> 2022 [87]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	5	1
54. Cardiac rehabilitation	Cacau <i>et al.</i> 2013 [88]	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	8	4
55. Vestibular rehabilitation	Alahmari <i>et al.</i> 2014 [89]	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	7	3
56. Active aging	Lee <i>et al.</i> 2015 [90]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	5

measure of the endogenous pain inhibitory pathway), temporal summation, and functional and somatosensory outcomes in patients with nonspecific chronic neck pain and compared the effects of VR and exercise treatment on pain intensity. The median patient age was 26–55 years. In all studies, >50% of patients in each group were women. Almost all studies [35-37,39-41] reported a significant improvement in the Neck Disability Index and ROM in both groups. VR showed better results in terms of global perceived change and pain reduction, as assessed with the VAS. Cetin *et al.* [40] reported that the VR group demonstrated the best results with respect to pain pressure thresholds, proprioception, and functional limitations.

Only three studies [36,39,41] reported the presence or absence of side effects, two of which being immersive studies [36,39]. One study [36] described motion sickness with the use of a VR device, whereas the other study [39] just described some discomfort due to the weight of the helmet. The non-immersive study [41] referred no discomfort, motion sickness, or pain exacerbation.

Low back pain: With respect to the evaluation of VR for lower back pain, immersive VR was employed in three studies [42-44], whereas non-immersive VR was used in other selected studies [45-55]. Demographically, the studies were different: some trials only evaluated female patients [43,45,47,53], one study assessed only male participants [46], whereas other studies had similar proportions of men and women. Chen *et al.* [48] and Tomruk *et al.* [54] did not mention about sex. The mean age was 20–72 years, indicating a large diversity of participants.

The programs varied; some used VR yoga, whereas others used a horse-riding simulator, balance board, or pelvic sensor. In the studies by Yoo *et al.* [46], Zadro *et al.* [51], Park *et al.* [53], and Yalfani *et al.* [43], the control group performed any exercise, just their usual activities, whereas the other study participants performed a trunk-stabilising exercise program. Yilmaz *et al.* [42], Zavarize *et al.* [50], and Afzal *et al.* [55] used physical therapy. The duration of studies varied from a single-session intervention to 12 weeks.

Most studies [43-45,47,48,50,54,56] reported significant improvements in pain scale scores, disability index, stability, and kinesiophobia in both groups, although they were better in the VR group. Yoo *et al.* [46] reported reduced pain and enhanced trunk torque; however, the control group did not do anything. Yilmaz *et al.* [42] demonstrated a significant improvement in Timed Up and Go Test results. In the study by Thomas *et al.* [49], all participants completed a pre-study baseline program, and the control group did not do anything more; their results indicated an effective increase in lumbar flexion within and across the gameplay sessions in the VR group. Zadro *et al.* implemented an unsupervised home-based exercise program and reported improvements in pain

and function [51]. Matheve *et al.* [52], who provided the intervention in just a single session, demonstrated that VR distraction had a hypoalgesic effect during and immediately after the exercise.

Park *et al.* [53] included only elderly women in their study, in which the control group watched a video while sitting on a horse simulator. As expected, the VR group exhibited a significant reduction in back pain compared to the control group, as well as significantly improved spinal alignment and peak torque of the trunk extensors.

Yalfani *et al.* [43] showed a significant decrease in pain intensity and fall risk with VR; the control group had a normal daily life without any special treatment.

Only Thomas *et al.* [49], Zadro *et al.* [51] and Groenveld *et al.* [51] referred to the presence or absence of side effects. The immersive study by Groenveld *et al.* reported mild temporary dizziness, whereas Thomas *et al.* and Zadro *et al.* reported no adverse effects.

Subacromial impingement syndrome and subscapular dyskinesia: Pekyavas *et al.* [57] investigated the short-term effects of a home exercise program and a VR exergaming program on scapular dyskinesia in participants with subacromial impingement syndrome. They concluded that the VR exergaming program improved symptoms more effectively than the same program without VR (control group). However, the data indicated a significant reduction in pain intensity in both groups. The results showed a significant difference in the Neer test between the VR and control groups, but no difference in the Hawkins test. Shoulder pain and disability index results suggested significant differences in the VR group. The population was not well defined (sex was not specified), and it was not possible to determine whether the participants performed the exercises at home regularly.

Frozen shoulder: Gunawan *et al.* [34] compared the effects of stretching exercises using VR games and stretching using an overhead pulley. Both groups received ultrasound diathermy in the shoulder pain area and were stretched 3–9 times per week. The number of participants included in this study was not mentioned, and the complete protocol used in this study was not explained. No significant differences were observed between the two groups.

Rotator cuff rupture: Menek *et al.* [58] evaluated the effectiveness of video-based game exercises, structured closed kinetic chain exercises, and conventional exercises in patients with pain and partial supraspinatus tendon rupture. The exercises for both groups were meticulously described, and the results indicated significant differences in the pre- and post-treatment values for all parameters among the three groups. The video game exercises were found to be more effective. The games were task-oriented and allowed the shoulder to be exercised at different angles.

Shoulder pain: Rizzato *et al.* [59] investigated whether a gaming rehabilitation program was effective in improving patient engagement (perceived enjoyment and self-efficacy during therapy, as well as attitude and intention to train at home) compared with a control non-gaming rehabilitation program. The study was well-described, with well-defined inclusion criteria, device used to measure maximal strength, and duration of daily rehabilitation in both groups. However, the sample size was small (n = 22).

The main findings were that the rehabilitation carried out with gaming rehabilitation was as effective as the equivalent non-digital rehabilitation and that both effectively enhanced shoulder rehabilitation, improved strength, reduced pain, and globally increased the participants' self-perceived satisfaction and functionality. The questionnaires confirmed that the device favoured greater engagement of participants, potentially leading to a greater predisposition to exercise at home.

Distal radius fracture: Naqvi *et al.* [60] described cases of distal radial fractures managed with closed reduction and K-wire internal fixation. The study sample comprised 20 patients. They used immersive VR with an Oculus head-mounted display; however, the methods were not completely clarified.

Both groups displayed significant improvements in pain, ROM, grip strength, and functional independence; nevertheless, improvements in hand function and functional independence were significantly greater in the gamification group.

Patellofemoral pain in women: Rizzato et al. [59] reported sustained improvement in balance and pain, potentially due to neurodynamic modulation at the cerebral level, which enhanced the patients' capacity for distraction and relaxation. Limitations include a small sample size, exclusive focus on females, lack of data on the duration of VR effects after one month, and use of only non-immersive VR. The primary goal was to improve balance.

Traumatic injury treated with conservative treatments

Post-traumatic knee osteoarthritis: Özlü *et al.* [61] applied immersive VR, whereas Nambi *et al.* [62] applied non-immersive VR. Both studies demonstrated early improvements in functionality (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]) and pain (VAS) compared with conventional programs. For knee osteoarthritis following anterior cruciate ligament injury, there appears to be an improvement in inflammatory biomarkers with the VR programs, which could explain these results. These improvements appeared to be sustained for up to three months.

Ankle sprain: Punt et al. [63] included a heterogeneous

population with different prognoses for grade I and II sprains, affecting the relevance of rehabilitation. Their study did not include patients with total ligament rupture (grade III) or chronic instability and did not consider the implications of recurrence risk, focusing on younger patients who were more frequently affected.

Orthopaedic surgery

Total hip arthroplasty: In total hip of [64,65] only non-immersive VR was used. The studies did not include the type of surgery (cemented or non-cemented arthroplasty) or presence of other osteoarthritis pathologies (hip or knee). Functional measures varied across studies (Hip Disability and Osteoarthritis Outcome Score-Joint Replacement, WOMAC, Functional Independence Measure, and Barthel scale), showing no significant clinical relevance compared with conventional rehabilitation. There was no control group without a directed rehabilitation program for comparison of measures.

Total knee arthroplasty: These studies [66-69] included various types of immersive and non-immersive VR. Functional measures were similar, focusing on WOMAC and VAS scores, suggesting that immersive VR provides at least comparable functional results for up to six months [66,69]. Initial pain control was apparent and less time was required to achieve 90° knee flexion [66]. Other studies did not show significant pain control differences but highlighted VR's role of VR in proprioceptive reinforcement, reflected in fewer falls in the VR group [68]. Limitations include inconsistent postoperative pain control medication/blockage and a lack of universal application. Notable were the results of lower healthcare costs and rehospitalizations with VR programs [68].

Rheumatological diseases

Ankylosing spondylitis: Only one RCT [70] with non-immersive VR was found to be related to ankylosing spondylitis. The results were promising on important scales, such as the Bath Ankylosing Spondylitis Disease Activity Index, compared to conventional rehabilitation, suggesting that VR could be an extra stimulus for regular physical activity. The limitations of this study include the lack of patient stratification by disease progression and disease-modifying antirheumatic drug use, with insufficient information on allocation and assessor blinding.

Juvenile idiopathic arthritis: Only one study [71] on non-immersive VR was found in this pathology. Patients with monoarticular or polyarticular involvement and significant clinical heterogeneity were included. This study focused on the upper-limb functionality and muscular strength endpoints, which might bias the results owing to the small sample size and high dropout rates. Comparing VR with a physical therapy program could be interesting, as previous studies have focused on comparisons with occupational therapy techniques.

Generalised chronic pain: fibromyalgia

Four studies [72-76] used non-immersive VR and one used immersive VR [75]. Study designs varied with different treatment durations (7–24 weeks) and control groups, comparing VR with no exercise program [72,77] or rehabilitation programs [74,76] with aerobic exercise and clinical pilates [78]. Regardless of the control group, VR showed superiority in crucial endpoints, such as multifocal pain control, particularly lumbar pain [76] (Oswestry Disability Index), fatigue, anxiety, depression, kinesiophobia, and reconditioning.

Burns

Two studies [80,81] used immersive VR, and another two studies [82,83] utilized non-immersive VR. Despite clinical heterogeneity (different burn degrees, locations, and ages, including paediatric and adult patients), VR was superior with respect to pain control and ROM gains [80-82] with faster improvements [83].

Neurological disorders

Phantom limb pain (PLP): Rothgangel et al. [84] compared conventional physiotherapy with VR-enhanced mirror therapy and conventional mirror therapy. Contrary to the literature, their RCT demonstrated no benefit of VR for a PLP duration of >6 months. Longer treatment (>1 month) with conventional mirror therapy benefitted women and patients with motor changes associated with PLP, such as cramping and unnatural positioning, indicating the impact of VR on maladaptive neuroplasticity in PLP pathophysiology. Future studies should include less-heterogeneous groups with similar amputation levels, causes, and PLP descriptors.

Stroke: Only one RCT [85] **involving** the use of non-immersive VR reported improvements in ROM and joint pain in the upper limb after stroke, as well as marked functional improvement on the Fugl-Meyer motor and Berg scales, compared to conventional physiotherapy.

Cancer

Mastectomy and axillary dissection: Basha et al. [86-87] reported similar designs and homogeneous groups using non-immersive VR along with manual techniques for oedema drainage and scar retraction prevention. VR was not inferior in pain control or ROM, showing superiority over conventional physiotherapy in terms of upper-limb functionality (Disabilities of the Arm, Shoulder and Hand [DASH] questionnaire). Despite noting reduced kinesiophobia with VR, they reported poorer functional results on the DASH questionnaire with a shorter follow-up period.

Other conditions

Pain during cardiac rehabilitation after cardiac surgery:

Only one RCT [88] with potential bias due to high dropout rates in the subgroups showed the benefits of complementing conventional cardiac rehabilitation programs with non-immersive VR in phase 1, improving pain control, functionality (Functional Independence Measure), and endurance (6-Minute Walk Test), resulting in shorter hospitalisation times. The limitations include the inclusion of only post-valve replacement or bypass surgery patients in phase 1, suggesting that future studies should broaden the scope to include interventions with established evidence in other phases of cardiac rehabilitation programs.

Vestibular rehabilitation: Only one RCT [89] with immersive VR showed non-inferiority in balance improvement and fall risk reduction compared to conventional physiotherapy. Increased reports of nausea and dizziness did not interfere with the VR programs after six weeks. The study included patients with central and peripheral nervous system disorders, indicating the need for stratification by pathology to identify conditions benefiting most from VR compared with conventional programs.

Active aging (pain during exercises): Good adherence to non-immersive VR programs has been noted in the geriatric population, with benefits in mental health and lower-limb muscle strength, presenting VR as an additional therapeutic modality for fall risk prevention and reduced caregiver supervision needs [90]. The results were similar to those of conventional programs, contributing to active aging and improved QoL.

Discussion

Efficacy of VR in chronic pain management

The analysis of the results of this systematic review concluded that VR seems to have positive effects on chronic pain management in several rehabilitation settings, which agrees with the conclusions of other systematic reviews [9,91,92].

The use of VR in psychological and physical rehabilitation can reduce stress, emotional tension, total Hospital Anxiety and Depression Scale score, anxiety, depression, pain, systolic blood pressure, and length of hospitalisation [93]. VR can also aid patients in complementing their rehabilitation programmes and performing some exercises at home, either without supervision or through remote supervision (telerehabilitation) [94].

Studies have applied VR to several painful conditions, including degenerative, traumatic, rheumatological, and neurological conditions.

Musculoskeletal pain, particularly neck and lower back pain, is the most common type.

The distraction generated by VR programs may explain increased pain tolerance because pain is largely controlled by cognition. This may lead to better adherence and outcomes in rehabilitation programs with VR, facilitating the achievement of other endpoints such as functional measures, ROM, and functional performance, which become more attainable with pain control. Distraction is a simple nonpharmacological technique that reduces pain perception by altering nociceptive responses [95,96]. Regarding lower-limb rehabilitation, VR seems to play a significant role in improving proprioception and balance [59,67], potentially because of the neuromodulation occurring at the central nervous system level.

In addition to the distraction effect, serious games with VR can activate the *nucleus accumbens* with the release of dopamine, which is associated with reward-based learning and feelings of pleasure and motivation to perform specific behaviour [97]. Evidence from both animal and human studies suggests that chronic pain results in a hypodopaminergic tone that impairs motivated behaviour [98].

Pain duration is more difficult to classify in certain situations such as postoperative pain. In post operative period after cardiac surgery, patients can develop complications such as pain, respiratory complications, functional loss, neurocognitive decline, depression and increased anxiety [99-102]. These complications are the main causes of morbidity and mortality after surgery [103], contributing to an increase in the length of hospital stay and its cost [104,105]. The benefits of inserting a postoperative patient into a rehabilitation program are well established [106]. However, treatment faces some restrictions owing to pain, fear, insecurity, and post-operative unwillingness [107]. The use of VR as a support for physiotherapeutic treatment brings several benefits, including less pain after painful procedures [108] and greater motivation during treatment [109]. In addition, after breast cancer surgery, VR therapy is comparable to standard physiotherapy, promoting task-oriented programs that are superior to exercises involving multiple repetitive movement patterns [86]. These principles are also applicable to other types of surgeries that benefit from postoperative rehabilitation.

In neurological conditions, such as post-stroke pain, neuropathic and nociceptive pain occur in up to 30% of stroke survivors; the most common is musculoskeletal pain, affecting up to 72% of stroke patients, with shoulder pain being the most frequent cause. Other pain syndromes include central poststroke pain, pain secondary to spasticity, complex regional pain syndrome, and headache [110].

In addition, most amputees report PLP at some point after limb amputation, and lifetime prevalence estimates are between 50 and 80% [111]. Pain is typically neuropathic in origin, usually reported within the first week after amputation, and generally decreases in severity and frequency over time in most individuals [112].

Given the chronic nature of PLP, non-pharmacological approaches which address central malplasticity are potentially effective in reducing PLP, including mental imagery and mirror therapy [113,114]. VR involves placing an individual in a virtual world, whereas AR adds digital elements, such as the missing limb, to a real environment. These interventions represent a 'high-tech' alternative to conventional mirror therapy, as they allow amputees to move their intact and phantom limbs independently while seeing their phantom limb integrated into, and interacting with, the surrounding setting.

Although this systematic review did not find any RCT comparing VR alone (without other techniques) with conventional therapy in spinal cord injury (SCI), chronic pain is a common secondary complication post-SCI, with an estimated prevalence of 61% [115].

Immersive VR could be a helpful adjunct to current pharmacotherapy to provide neuropathic pain relief for patients with SCI [116].

Pain is one of the most common chronic symptoms experienced by cancer survivors, with prevalence rates of 55.0% during anticancer treatment, 39.3% after curative treatment, and 66.4% in advanced, metastatic, or terminal diseases [117].

Cancer pain is complex and has multidimensional behavioural, emotional, cognitive, and sensory components [118]. Cancer pain requires multimodal, targeted, dynamic, and personalised management, including, in addition to pharmaceutical and/or interventional therapies, the use of non-pharmacologic, non-invasive approaches, called complementary integrative therapies [119]. VR has been successfully used in rehabilitation systems to treat cancer survivors coping with chronic pain [119-121].

VR acts as a nonpharmacologic type of analgesia through a collection of emotional-affective, emotion-based cognitive, and attentional processes in the body-involved pain modulation system [108,122]. A recent systematic review and meta-analysis [123] included 17 studies involving 799 cancer patients. Within-group pooled analysis indicated that the patients demonstrated significant improvements in pain ($P<0.001$), fatigue ($P<0.001$), anxiety ($P<0.001$), upper-extremity function ($P<0.001$), and QoL ($P=0.008$) after the VR intervention. Between-group pooled analysis indicated significant improvements in pain ($P=0.004$), anxiety ($P<0.001$), and upper-extremity function ($P<0.001$) compared with controls. Three studies reported the positive effects of VR on cognition.

The most important benefits and opportunities of using VR from a mental perspective in this group of patients were that it reduced anxiety and pain, and led patients to underestimate the time spent using VR technology compared to the duration of treatment without this technology [124].

To determine whether immersive VR is an effective adjuvant of morphine alone in relieving pain and anxiety, Bani Mohammad *et al.* [125] performed an RCT involving 80 women with breast cancer, in which the VR session started exactly at the peak time effect of morphine for 15 min (i.e., reassessment was performed at 15 min from the peak time effect). The comparison group was assessed just before morphine administration and at 15 min after the peak time effect. The study findings showed that one session of immersive VR plus morphine resulted in a significant reduction in self-reported pain and anxiety scores compared to morphine alone in patients with breast cancer.

The use of VR in other situations, such as vestibular rehabilitation or pain during exercise in the elderly, has multiple possibilities, as the use of VR does not appear to have deleterious side effects, aside from occasional episodes of nausea and headaches with immersive VR.

Adverse Effects and Challenges

VR appears to be a secure approach to pain management, with cybersickness symptoms reported in some studies. The weight of headsets and helmets, quality of the visual image, and cost of equipment are other challenges of using this technology [124].

Strengths and Limitations

This systematic review focused on chronic pain, which is a highly prevalent problem, and on the use of new technologies to complement conventional approaches. The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The major strengths of this review are its rigorous assessment of the prior literature and the focus on an emerging area of patient care in the rehabilitation field.

An important limitation of this study was related to the search strategy. The focus of this review was chronic pain; however, most studies did not mention the duration or recurrence of pain. Furthermore, the authors included conditions that accompanied pain for >3 months, and conditions in which obvious pain was acute, such as pain associated with needle interventions, were excluded.

There was a lack of comparison between immersive and non-immersive VR across different pathologies in this review; nonetheless, simulation sickness appears to negatively affect spatial ability in more immersive conditions [126]. Although the results were positive in terms of efficacy, safety, and patient adherence, several methodological problems arose in most studies. Several studies did not provide sufficient information about the methodology. With the available information, a high percentage of studies had limited methodological quality. The heterogeneity of intervention protocols and outcome

measurements made comparisons between studies difficult. Furthermore, the included studies did not measure the long-term benefits of VR in chronic pain management. Future studies should be aware of these limitations to develop more robust protocols in terms of methodologies and evaluate the long-term benefits of VR.

Conclusion

VR is an enjoyable, safe, and well-tolerated nonpharmacological approach that may reduce the need for opioids and other analgesic drugs, offering multiple possibilities in terms of scenarios and tasks according to patients' needs and preferences in the rehabilitation field. As a complementary intervention, VR may improve the quality of conventional rehabilitation care.

Declaration of Interests

The authors declare no conflicts of interest.

Funding

This research received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions

P.A., M.J.S., J.E.S., and H.M. contributed to the study design and implementation, data analysis, and manuscript writing. All authors were involved in reviewing the manuscript and its final version.

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