The influence of an at-home virtual reality intervention on the health-related quality of life of patients with chronic musculoskeletal pain awaiting pain treatment

A cluster randomised crossover trial

Diede Paarlberg, s2347229
Department of Health Sciences, Science and Technology, University of Twente
Master Health Sciences, Optimisation of Healthcare Processes

First supervisor: Dr. L. ter Weele - Nieuwenhuis
Second supervisor: Dr. L. Heesink
Third supervisor: Drs. E.S. Slatman
Date: 05-09-2024

Acknowledgements

This thesis, titled “The influence of an at-home virtual reality intervention on the health-related quality of life of patients with chronic musculoskeletal pain awaiting pain treatment”, marks the completion of my Master’s programme in Health Sciences at the University of Twente. The research was conducted between November 2023 and August 2024 as part of the Wait & Work research project.

I would like to thank my supervisors, Lisette ter Weele-Nieuwenhuis, Lieke Heesink and Syl Slatman, for their valuable guidance and feedback. Their support played a significant role in shaping both the direction and quality of this thesis. I am also grateful to the participants who took part in the study; their involvement was essential to the completion of this research.

My gratitude extends to my family and friends, whose constant support and encouragement have been incredibly important to me throughout this journey. Their belief in me has helped maintain my motivation and positivity, even during challenging times.

Thank you for taking the time to read this thesis.

Diede Paarlberg
Enschede, August 2024

Abstract

Background: Chronic musculoskeletal pain (CMP) affects approximately 20% of adults in the Netherlands, significantly impacting quality of life, daily functioning, and mental health. Current treatments often provide limited relief and carry risks such as addiction. Virtual reality (VR) technology has emerged as a potential (adjunctive) treatment modality for CMP, offering immersive experiences that may alter pain perception and improve psychological well-being. This study examined the influence of a four-week, home-based VR intervention, 'Reducept', compared to a standard waiting list period without VR intervention, on health-related quality of life (HRQoL) and pain-related outcomes in patients awaiting chronic pain treatment.

Methods: This pragmatic, open-label, randomised controlled trial utilised a cluster randomised, two-period, crossover design involving six clusters from four healthcare organisations. Participants in the intervention group used the at-home VR intervention 'Reducept' daily for 10-30 minutes, while the control group followed standard waiting list period procedures without an intervention. Both groups completed questionnaires at baseline and after four weeks, with the primary outcome being HRQoL. Secondary outcomes included pain intensity, pain catastrophising, pain self-efficacy and pain acceptance. Data analysis followed the intention-to-treat principle and utilised linear mixed-model analyses.

Results: The four healthcare organisations were randomised, resulting in 30 participants in the intervention group and 22 in the control group, making a total of 52 participants. Complete data fora six participants were missing and these participants were, therefore, excluded from the analysis. For nine participants with partial missing data, the Last Observation Carried Forward method was used. No significant baseline differences were found between groups. Analysis showed no significant differences in HRQoL or secondary outcomes between groups at baseline or after four weeks. Linear mixed-model analyses revealed no significant main effects of treatment, time, or interaction effects for any outcomes over the study period.

Conclusion: The four-week VR intervention did not lead to significant improvements in HRQoL or pain-related outcomes compared to standard waiting list procedures. These findings suggest that the short-term duration of the VR intervention may have been insufficient to achieve measurable benefits. Future research should explore the long-term effects of VR and its integration with other treatments to better understand its potential role in managing chronic pain.

Keywords: Chronic musculoskeletal pain, virtual reality, health-related quality of life, pain intensity, pain catastrophising, pain self-efficacy, pain acceptance, cluster randomised crossover design, pain management

Table of contents

List of abbreviations

ACT	Acceptance and Commitment Therapy
CBT	Cognitive Behavioural Therapy
CLBP	Chronic Low Back Pain
CMP	Chronic Musculoskeletal Pain
CPAQ	Chronic Pain Acceptance Questionnaire
CRXO	Cluster Randomised Crossover
DALY	Disability Adjusted Life Years
GP	General Practitioners
HMD	Head Mounted Display
HRQoL	Health-Related Quality of Life
LMM	Linear Mixed Model
LOCF	Last Observation Carried Forward
MCS	Mental Component Score
NPRS	Numeric Pain Rating Scale
NSAID	Non-Steroidal Anti-Inflammatory Drug
PCS	Pain Catastrophizing Scale
PNE	Pain Neuroscience Education
PSEQ	Pain Self-Efficacy Questionnaire
QoL	Quality of Life
RCT	Randomised Controlled Trial
SF-12	Short Form health survey
TENS	Transcutaneous Electrical Nerve Stimulation
VR	Virtual Reality

1. Introduction

1.1 Chronic musculoskeletal pain

Chronic musculoskeletal pain (CMP), characterized by a duration of pain exceeding three months or beyond the expected duration of tissue pathology healing [1], is a major health problem with a high prevalence [2]. A large European study has shown that one in five adults suffers from CMP, with 34% experiencing severe pain (scoring 8 or higher on a 10-point scale, where 1 means no pain and 10 means the worst pain imaginable) [3].

CMP has a large negative impact on the quality of life, activities of daily living and mental health for patients and their families [3,4]. According to a recent report on the 'Global Burden of Disease', which compared the Disability Adjusted Life Years (DALYs) of 291 diseases, two forms of CMP ranked high among Western European countries: back pain ranked number one and neck pain ranked number four [5]. Additionally, CMP results in high healthcare consumption and a great loss of work capacity. The total direct and indirect costs for the Netherlands are estimated at €20 billion per year [6].

CMP is a multidimensional condition involving an interplay of biological, social, and psychological factors [7]. Biological factors refer to physical aspects of the body that contribute to the experience of pain. These include, for example, tissue damage, inflammation, nerve sensitization and alterations in the functioning of the nervous system [8]. Biological factors can influence the intensity, duration, and location of pain, as well as the body's response to pain-relieving interventions [8]. Social factors encompass the broader social and environmental influences that impact an individual's experience of pain and access to treatment. These include aspects such as socioeconomic status, social support networks, cultural beliefs about pain, access to healthcare services, and the influence of work, family, and community dynamics [7]. Social factors can affect how pain is perceived, expressed, and managed, as well as the individual's ability to access appropriate treatment and support [7]. Psychological factors include how individuals think about pain (cognitive), their emotional responses to it, and their coping behaviours. These factors, including beliefs, mood, and coping strategies, greatly influence pain perception and overall well-being [9].

In addition to these three dimensions, psychosocial factors play a crucial role in the persistence of CMP. Unlike purely biological, social, or psychological factors, psychosocial aspects represent the interaction between psychological processes and social contexts in shaping pain experiences. Studies highlight that high levels of emotional distress, such as anxiety and depression, play a crucial role in exacerbating pain severity and disability [10–13]. Furthermore, pain catastrophising—a cognitive and emotional response to pain involving exaggerated negative beliefs and a sense of helplessness about pain—is associated with increased pain intensity and disability [10–13]. High levels of pain-related fear and fear of

movement are also common among individuals with CMP, contributing to avoidance behaviours and further disability [14]. The interplay of these psychosocial factors varies among patients and may fluctuate over time, influencing how individuals perceive pain and their ability to carry out everyday activities, which are crucial for their overall well-being and functional outcomes [15].

The biopsychosocial model provides a holistic framework for understanding CMP, emphasizing the interplay of biomedical, psychological, and social determinants in pain development and recovery [16]. This model acknowledges that cognitive processes, emotional responses, expectations, physical health, and behavioural patterns all contribute to the subjective experience of chronic pain [16]. Moreover, chronic pain can also impact psychological well-being and social interactions, highlighting the bidirectional relationship between pain and psychosocial factors [16]. The neuromatrix theory further supports this perspective by highlighting the role of psychosocial factors in pain perception, especially when there is no evident physical pathology [17]. Therefore, a holistic assessment that considers biomedical processes alongside cognitive, emotional, behavioural, and environmental factors is crucial for comprehending and managing chronic pain conditions [7,18].

1.2 Treatment of CMP

The current approach to treating CMP follows the stepped care principle [19], which means that primary care involves healthcare practitioners with direct-access, such as physiotherapists, general practitioners (GPs) and occupational therapists. Secondary care includes a range of services, mostly hospital-based and mental health interventions, where a referral from the GP or another medical practitioner is required. Lastly, tertiary care comprises highly specialized medical services provided by academic hospitals, involving complex interventions like interdisciplinary pain rehabilitation [16].

Pharmacological treatments play a central role in the management of pain, with a wide range of commonly prescribed analgesics: non-opioid analgesics (e.g., paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs) COX-2 selective inhibitors), opioids (e.g., morphine, fentanyl, oxycodone), and adjuvant analgesics (e.g., antidepressants, anticonvulsants, musculoskeletal agents, anxiolytics) [2]. Unfortunately, the use of opioids does not always result in sufficient pain control and is often associated with serious side effects such as breathing problems, confusion and depression [20]. Prolonged use of NSAIDs and opioids increases the risk of addiction and side effects such as gastrointestinal bleeding, arterial thrombosis, and mental dysfunction [21,22]. In addition to pharmacological treatments, there are also non-pharmacological treatments such as physical modalities (e.g., cryotherapy, heat therapy, transcutaneous electrical nerve stimulation therapy (TENS), acupuncture, therapeutic exercise) and (surgical) pain interventions (e.g., trigger point injection and intraspinal implants) [2].

However, treating CMP exclusively from a biomedical perspective contradicts the understanding of CMP as a multidimensional condition [23]. Hence, a multidisciplinary and holistic approach for managing CMP, incorporating a variety of treatment modalities, is deemed appropriate. A multidisciplinary approach involves integrating the diverse aspects of chronic pain conditions, including biopsychosocial effects on patients. Multidisciplinary pain services offer a variety of coherent treatment approaches that recognize pain as a complex problem requiring a multifaceted and continuous care approach. Typically, multidisciplinary treatment teams consist of physicians, physical and/or occupational therapists, and psychiatrists and/or clinical psychologists [2]. Several treatment modalities can be combined within a multidisciplinary approach, such as analgesics, mindfulness-based interventions, and cognitive-behavioural therapy (CBT). Pain education and self-management serve as foundational elements of a multidisciplinary and holistic approach, empowering patients to better understand their condition and enhance their beliefs and coping mechanisms related to pain [24].

1.3 Virtual Reality

Virtual reality (VR) has been introduced as a potential (adjunctive) non-pharmacological treatment modality for individuals coping with CMP, by means of pain education and management techniques [25]. Using computer-generated graphics, VR provides a simulated three-dimensional virtual world with immersive qualities when experienced through a head-mounted display (HMD) [25]. This immersive technology allows users to view the full panorama, creating a high sense of presence and immersion as if the individual is situated within the virtual environment [26]. Key features enhancing immersion in VR include: (1) the capability to block real-world visual and auditory stimuli, setting it apart from conventional television or computer screens, which do not block real-world sensory inputs, (2) high-fidelity and high-resolution graphics closely resembling reality, (3) directional audio and (4) a wide field of view mimicking normal vision [27].

In an immersive VR environment, which consumes finite attentional resources and blocks external stimuli, VR has the potential to influence pain perception [28]. Studies indicate that VR can increase pain tolerance and thresholds as a distraction intervention that works by competing for attention that would otherwise be directed towards painful stimuli [29,30]. This enables individuals to reduce their pain experience and engage higher cognitive and emotional centres of the nervous system [31]. Furthermore, research has shown reductions in pain intensity, anxiety levels, and time spent thinking about pain after VR distraction [32,33]. VR is considered more effective than conventional distraction techniques (e.g., pleasant imagining, rhythmic cognitive activities, external focus of attention, and neutral imagining) due to its immersive qualities, which engage individual's visual, auditory processing as well as physical actions, thereby demanding more attention [34,35]. Beyond distraction, prolonged use of VR is expected to lead to neuroplastic changes in both the sensory and motor brain regions [32].

With these strengths, VR can be utilised for diverse purposes, including exposure treatment [36], general activation of patients [37] and relaxation [38], potentially enhancing psychological therapies, such as mindfulness, Acceptance and Commitment Therapy (ACT) and CBT [39]. Additionally, VR offers several practical advantages, such as the feasibility for patients to use it within the comfort of their own homes, the accessibility without the need for the help of a healthcare provider and its supportive qualities for self-management [40]. Given these strengths, VR holds promise as an effective non-pharmacological intervention in the management of chronic pain.

1.4 Reducept

In this randomised controlled trial, participants in the intervention group used a recently developed VR intervention known as 'Reducept'. Reducept is grounded in the biopsychosocial model of pain and is designed as a tool for the management and treatment of CMP. It aims to enhance patients' understanding of their pain mechanisms and promote patient empowerment, education and self-management through evidence-based psychological treatment techniques [41].

Reducept is constructed as a game in which a relaxing voice guides the patient through a virtual journey within the body's nervous system. The patient is virtually situated in a spaceship, where pain mechanisms are visually explained and depicted. Reducept, hereby, utilises the 'explain pain theory', which allows the patient to reduce pain sensations by fostering understanding and influencing the cognitive, emotional, and behavioural processes related to pain [41]. During the virtual journey, the patient encounters five distinctive games incorporating exercises grounded in Pain Neuroscience Education (PNE) and various psychological therapies: ACT, CBT, hypnotherapy and mindfulness. Each game session lasts approximately ten minutes, with the various psychological therapies being alternated throughout the session.

ACT focuses on the acceptance of pain as a natural part of life and emphasizes mindfulness and values-based actions. In Reducept, ACT principles are integrated by guiding users to acknowledge and embrace pain in their daily lives. By fostering acceptance rather than avoidance, users learn to manage their pain more effectively and improve their overall well-being [42].

CBT aims to modify dysfunctional thoughts and behaviours that contribute to pain experiences. In Reducept, CBT principles are applied through interactive tasks where users engage in cognitive restructuring exercises. For example, in one game, users eliminate symbolic 'insects' representing their pain, which helps them reframe their perception and gain a sense of control over their pain experience [42].

Hypnotherapy involves using guided relaxation to help individuals achieve a heightened state of focus and awareness, which can alter their perception of pain. In Reducept, this is achieved through relaxation exercises and suggestive imagery. Mindfulness involves paying attention to the present moment and accepting it without judgment, including the experience of pain. In Reducept, mindfulness techniques are used to help users observe their pain in a non-judgmental way, fostering a more accepting and detached attitude [41].

These therapeutic principles collectively aim to reduce overall pain experiences for users and empower them to better manage their pain condition through a holistic approach combining education, psychological techniques and immersive virtual environments [41,42]. Reducept is collaboratively developed by researchers, patients, psychologists, and software developers and can be played on several VR headsets, including the CE-certified Pico G2 4K headset used in this study.

1.5 Current knowledge

To evaluate the influence of VR interventions on CMP, it is essential to review the existing literature. Previous research, including studies by De Vries et al. [23] and Groenveld et al. [24], has provided valuable insights, but these have also highlighted significant knowledge gaps that this study aims to address.

De Vries et al. [23] utilised a multiple baseline single-case experimental design to evaluate a VR-based intervention for patients with chronic low back pain (CLBP). Participants engaged in VR sessions focused on pain education and coping strategies, resulting in reductions in self-reported pain levels and improvements in functional abilities post-intervention. This study also reported enhanced pain self-efficacy and reduced pain catastrophising. However, the absence of an active control group complicates attributing these outcomes solely to the VR intervention, as factors such as personal attention or positive treatment expectations may have influenced the results.

Groenveld et al. [24] examined a behavioural therapy-based VR application designed at improving quality of life (QoL) for patients with CLBP. Using immersive environments and interactive scenarios, the VR application engaged patients in therapeutic exercises intended to reduce pain and enhance psychological well-being. This randomised controlled trial (RCT) found significant improvements in QoL metrics, reduced pain intensity and increased pain coping skills in the VR group compared to a control group receiving standard care. Nevertheless, the study did not include a sample size calculation and faced limitations related to small sample size and generalisability.

Both studies exclusively recruited patients with CLBP from (academic) hospitals. De Vries et al. [23] specifically focused on patients with long-standing CLPB who had no further medical treatment options

available, with most participants over 60 years old and a median age of 73 years. This narrow demographic and setting may limit the applicability of the findings to broader populations. Additionally, De Vries et al. [23] conducted a low frequency of VR sessions (three sessions per week over four weeks) in a hospital setting, whereas the developers of Reducept recommend more frequent, home-based sessions for optimal results [42].

To address these limitations and knowledge gaps, this study employs a RCT design with a control group following the standard waiting list protocol without additional treatment or VR intervention. This design aims to isolate the effect of the VR intervention more accurately. The study includes a larger and more diverse sample group, incorporating patients from both hospitals and rehabilitation centres, and includes different types of CMP conditions. By employing an a priori sample size calculation, this study seeks to enhance the reliability and generalisability of the findings. Furthermore, it incorporates daily home-based VR sessions for four weeks, aligning with recommended practices and addressing limitations related to session frequency and setting. Through this approach, this study aims to provide a more comprehensive evaluation of the VR program Reducept and its impact on pain management.

1.6 Objective

Building on previous research, this study aims to address knowledge gaps by exploring additional dimensions of the VR program Reducept.

The primary objective of this study is to examine the influence of a four-week, home-based VR intervention Reducept on patients with CMP who are on a waiting list for pain treatment. The study will evaluate the effect of Reducept on health-related quality of life (HRQoL) as the primary outcome. Secondary outcomes include pain-related outcomes such as pain intensity, pain catastrophising, pain self-efficacy, and pain acceptance. Therefore, the primary research question is formulated as follows:

> *To what extent does a four-week, home-based VR intervention, compared to the standard waiting list period without VR intervention, influence the health-related quality of life in patients with chronic musculoskeletal pain awaiting chronic pain treatment?*

The secondary research question is phrased as:

> *To what extent does a four-week, home-based VR intervention, compared to the standard waiting list period without VR intervention, influence pain-related outcomes (pain intensity, pain catastrophising, pain self-efficacy and pain acceptance) in patients with chronic musculoskeletal pain awaiting chronic pain treatment?*

2. Methods

2.1 Study design

This pragmatic, open-label, randomised controlled trial employed a cluster randomised, two-period, crossover design (CRXO) [43]. In this design, clusters alternated between treatment and control conditions over two periods, each lasting three months. The timing of these crossovers was critical, as it determined the treatment each participant received based on their cluster's allocation. The crossover design was chosen for its operational efficiency, allowing each cluster to administer only one type of intervention at a time, thereby reducing research complexity and associated costs. Additionally, the crossover feature enhanced statistical power and reduced the risk of chance imbalances [44].

This study involved six clusters, drawn from four participating healthcare organisations: Roessingh, Deventer Ziekenhuis, Nocepta and Revalidatie Friesland. To refine the design, Roessingh and Revalidatie Friesland were each divided into two separate clusters: Roessingh Pijnrevalidatie, Roessingh Centrum voor Revalidatie, Revalidatie Friesland Tjongerschans, and Revalidatie Friesland Emmeloord. These six clusters were randomised using the online program 'Sealed Envelope' (https://www.sealedenvelope.com/) prior to the inclusion of patients. Patients were assigned to either the intervention or control group based on the randomisation of their respective cluster. A schematic representation of the design is shown in Figure 1.

Ethical approval for this study was obtained from the University of Twente ethics committee (RP 2022-174) and the local ethics committees at the four participating healthcare organisations. The recruitment and study procedures took place between October 2023 and April 2024. This trial was retrospectively registered on ClinicalTrials.gov (identifier: NCT06312735).

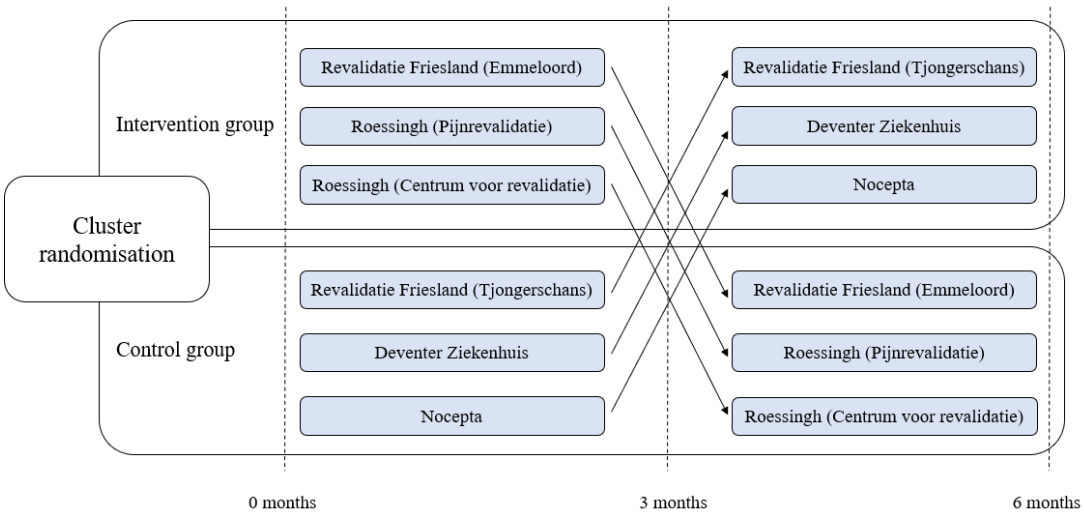

Figure 1. Schematic representation of the study design.

2.2 Study population

While awaiting pain treatment, patients with CMP were recruited from the four participating healthcare organisations. Patients were deemed eligible for participation if they: (1) were aged 18 years or older, (2) diagnosed with CMP (>3 months), (3) had finished biomedical diagnostics and treatment, (4) were open to a therapeutic intervention with biopsychosocial elements, and (5) were willing and capable of complying with the study procedures. Patients were excluded if they: (1) were not capable of finishing the intervention due to physical (e.g., facial wounds, severe visual impairment, vertigo, epilepsy, dementia, delirium), mental (e.g., sensitivity to VR stimuli), or practical challenges (e.g., insufficient comprehension of technology), (2) were enrolled in another study to evaluate alternative approaches to pain treatment, and/or (3) had no comprehension of the Dutch language.

The sample size was determined using *G*Power software version 3.1.9.7* (Heinrich-Heine-University, Dusseldorf, Germany) [45,46]. Since *G*Power software* does not have a direct option for linear mixed models, an a priori power analysis was conducted using the ANOVA with repeated measures, within-between interaction model. This analysis was set at an alpha level of 0.05 and a desired power of 80%. Based on the literature on virtual reality interventions for chronic pain, which suggests effects sizes around 0.20 [20], the estimated sample size required was 52 participants.

2.3 Intervention

Participants in the intervention group used the VR intervention Reducept daily at home. This CE-certified VR programme is specifically designed for individuals with CMP, who were on a waiting list for pain treatment. Each session, lasting between 10 and 30 minutes, was conducted independently by participants over a four-week period, either seated or lying down, without requiring physical movement. For further details on the intervention's design and theoretical background, see Section 1.4. The control group continued with the standard waiting list procedure and did not have access to the VR intervention.

2.4 Study procedure

Recruitment of patients took place at the four participating centres involved in this study. After their intake but before starting treatment, the healthcare providers screened the patients based on the inclusion and exclusion criteria and determined whether the patient was eligible for participation in this study. If eligible, the patient was contacted by their healthcare provider who provided a brief explanation (verbally and with an information letter) about the study. If interested in participating, the healthcare provider asked the patient for permission to forward their contact details to the researcher (through a fully secured app 'Siilo'; https://www.siilo.com). The researcher then contacted the patient and provided a more comprehensive and detailed explanation about the study and asked the patient to contemplate participating in the study. Before signing the informed consent, individuals in the intervention group had the opportunity to experience the VR intervention under the supervision of the researcher. All

patients were formally enrolled in the study by signing the informed consent, after which all participants (both in the control and intervention groups) received the first questionnaire (T0) as a baseline measurement. Participants in the intervention group received the VR headset to take home together with an instruction sheet. The participants in the intervention group carried out the intervention daily for 10-30 minutes over four weeks at home, while the participants in the control group followed the standard waiting list period procedure without VR intervention. Then, after four weeks, the participants in the intervention group were asked to return the used VR headset and all participants (both intervention and control groups) received the second questionnaire (T1). All participants were sent an email providing a hyperlink to access the questionnaires in Qualtrics software (Provo, USA) [47].

Participants were allowed to discontinue their participation in the study for any reason at any time without consequences. Additionally, the researcher could decide to terminate an individual's participation due to urgent medical considerations or if the VR intervention caused discomfort to any participants. In the case of withdrawal, participants were not included in further procedures.

2.5 Study outcomes

All outcome assessments were carried out at baseline (T0) and after four weeks (T1) in exactly the same manner across all healthcare organisations for all participants, using the Dutch translation of the original questionnaires.

The primary outcome, health-related quality of life, was assessed by the Short Form health survey (SF-12) [48], which has been validated in various chronic diseases and conditions [49–51]. The SF-12 consisted of 12 items that measured eight health domains to assess physical and mental health. The Physical Component Summary (PCS) included domains related to general health, physical functioning, role physical and bodily pain. The Mental Component Summary (MCS) included domains related to vitality, social functioning, role emotional and mental health. An example of an item in the PCS: '*In the past 4 weeks, how often have you had any of the following problems in your work or other daily activities, as a result of your physical health?'*. An example of an item in the MCS: '*During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?'*. For each participant, a norm-based score ranging from 0 to 100 points was calculated for both components using the method described by Ware et al. [52]. A higher score indicated a higher perceived health-related quality of life. However, data consistency issues were observed, with discrepancies between SF-12 scores provided by different data centres and the original data collected. For instance, scores from Revalidatie Friesland for the SF-12 at T1 often differed from the independently collected data. This inconsistency may affect the comparability of results across sources and should be considered when interpreting the findings.

Secondary study outcomes included pain-related outcomes, such as pain intensity, pain catastrophising, pain self-efficacy and pain acceptance.

- Pain intensity was assessed using the Numeric Pain Rating Scale (NPRS), specifically the 11-point version, which is widely preferred for its construct validity, acceptable responsiveness, and test-retest reliability [53–56]. Participants rated their pain intensity on a scale ranging from 0 (no pain at all) to 10 (worst pain imaginable). The NPRS consists of two items, with a maximum total score of 20, where higher scores indicate greater pain intensity. An example item was: *'How severe was your pain (on average) in the past week (7 days)?*'
- Pain catastrophising was assessed using the Pain Catastrophizing Scale (PCS), a validated instrument that was designed to evaluate patterns of negative cognition and emotion associated with existing or anticipated pain [57]. The PCS consisted of 13 items, each rated on a 5-point scale (0= not at all to 4= all the time), assessing feelings and beliefs related to painful experiences. Scores from these items were summed to generate a total score ranging from 0 to 52, with higher scores indicating a greater level of pain catastrophising. The scale included three subscales: rumination, magnification, and feelings of helplessness related to pain. An example item included: '*When I was in pain I constantly wondered if the pain would stop*'.
- Pain self-efficacy was assessed using the Pain Self-Efficacy Questionnaire (PSEQ), a validated instrument designed to evaluate an individual's confidence in their ability to perform daily activities despite experiencing pain [58–60]. The PSEQ measures how confident a person feels about their capacity to manage and continue functioning with pain. It consists of 10 items rated on a 7-point Likert scale, ranging from 0 (I am not sure) to 6 (I am entirely sure). The total score ranged from 0 to 60, with higher scores indicating greater self-efficacy or confidence in managing daily activities despite pain. An example item included: *'I can still perform my work duties, despite the experience of pain'*. This reflects how strongly a person believes they can persist in their usual activities despite their pain.
- Pain acceptance evaluated using the 8-item Chronic Pain Acceptance Questionnaire (CPAQ-8) short form, which measures an individual's ability to accept pain and continue engaging in meaningful activities despite its presence [61]. This instrument assesses how much a person has adjusted to living with chronic pain, focusing on their willingness to accept pain as a part of life rather than trying to control or avoid it. Participants rated each item on an 8-point scale from 0 (never true) to 7 (always true), with total scores ranging from 0 to 56. Higher scores indicate greater acceptance of pain and greater engagement in activities despite pain interference. The CPAQ-8 includes two subscales: pain willingness, which measures the degree to which individuals accept experiencing pain without avoidance, and activity engagement, which assesses the extent to which individuals persist in meaningful activities despite pain. An example item included: '*I continue to engage in activities that are important to me, even though I experience pain*'. Reflecting how well a person integrates pain into their life and maintains

involvement in valued activities despite it. It should be noted that some items in the CPAQ-8, as used in this study, were found to be incorrectly formulated. This issue may affect the accuracy and reliability of the pain acceptance measurements and warrants further review to ensure the validity of the responses.

The following patient characteristics were asked at baseline: gender, age, educational level, employment status, duration of CMP and pain medication usage (6 items in total).

2.6 Data analysis

The statistical analyses were performed using R version 4.2.1 (Vienna, Austria) [62], with a significance level set at 5% ($\alpha = 0.05$, $p \leq 0.05$, two-sided testing). Data analysis was conducted in accordance with the intention-to-treat principle [63], utilising all available data from each randomised participant who had completed baseline questionnaires. This approach was selected to evaluate the intervention's influence in a manner reflective of real-world conditions, where full protocol adherence is not always feasible. However, it is important to acknowledge that this approach could potentially lead to either an underestimation or overestimation of the true influence. Underestimation may have occurred if participants did not fully comply with the intervention, while overestimation could have arisen from biases such as differential dropout rates or other data anomalies.

Missing data at T1 were handled using the Last Observation Carried Forward (LOCF) method [64], where missing scores at T1 were substituted with the last observed scores from T0 for each participant. This method aimed to maximise sample size and maintain statistical power. Nonetheless, potential biases, such as under- or overestimation of effects, may have been introduced due to the imputation of missing data. To assess the robustness of the findings, a per-protocol analysis [65] was also performed, including only those participants who fully adhered to the intervention. This analysis indicated no significant differences compared to the intention-to-treat analysis, suggesting that the findings were robust regardless of the analytical approach.

Group-level comparisons (intervention group vs. control group) were conducted based on the differences in mean score changes across all study outcomes. Normality of the data was assessed using the Shapiro-Wilk test for each group and outcome measure, complemented by visual methods such as histograms, Q-Q plots and density plots.

Baseline characteristics of participants were described using descriptive statistics: means and standard deviations (SDs) or medians and interquartile ranges (IQRs) for continuous variables, and frequency counts and percentages for nominal variables. Group comparisons were conducted using independent t-

tests for continuous data and chi-square tests for categorical data, with Fisher's exact test used for categorical data where distributional assumptions were not met [66].

A linear mixed model (LMM) was used to evaluate the influence of the intervention. This model included the intervention group as an independent variable (a between-subjects factor) and time of measurement as a dependent variable (a within-subjects factor). This model assessed changes in SF-12 PCS and MSC scores over time between the intervention and control groups, accounting for within-person correlation (change from baseline) through a repeated measures design, incorporating subject-level random effects. The model included fixed effects for 'treatment (group)', 'time', and the interaction effect between 'treatment and time'. Satterthwaite's method for approximating degrees of freedom was used, implemented via the *lmerTest* package in R, to provide accurate p-values [67,68]. The primary focus was on comparing the VR intervention group with the control group across all time points (between-group comparison) and examining the interaction between time and group to assess the influence of the intervention on the trajectory of key variables (within-group comparison).

Similar analyses were performed for the secondary outcome measures, including pain intensity, pain catastrophising, pain self-efficacy and pain acceptance.

3. Results

3.1 Participants characteristics

Participants were recruited and enrolled between November 2023 and the end of March 2024. A total of 52 participants were randomised, with 30 allocated to the intervention group and 22 to the control group. Of these 52 participants, three from each group did not complete the questionnaires (both T0 and T1 data were missing) and were considered lost to follow-up.

Intention-to-treat analyses were conducted, resulting in a dataset that included 13 individuals with completely missing T1 data (four in the intervention group and nine in the control group) and nine individuals with partially missing T1 data (four in the intervention group and five in the control group). For these participants, the LOCF method was applied. Consequently, 27 participants in the intervention group and 19 participants in the control group were included in the final analysis. To the best of our knowledge, no participants withdrew due to adverse events related to the treatment. Figure 1 provides a summary of the study flow diagram.

The baseline demographic and clinical characteristics of the participants in both groups are summarized in Table 1. There were no statistically significant differences in demographic characteristics between the groups at baseline, indicating that randomisation was effective.

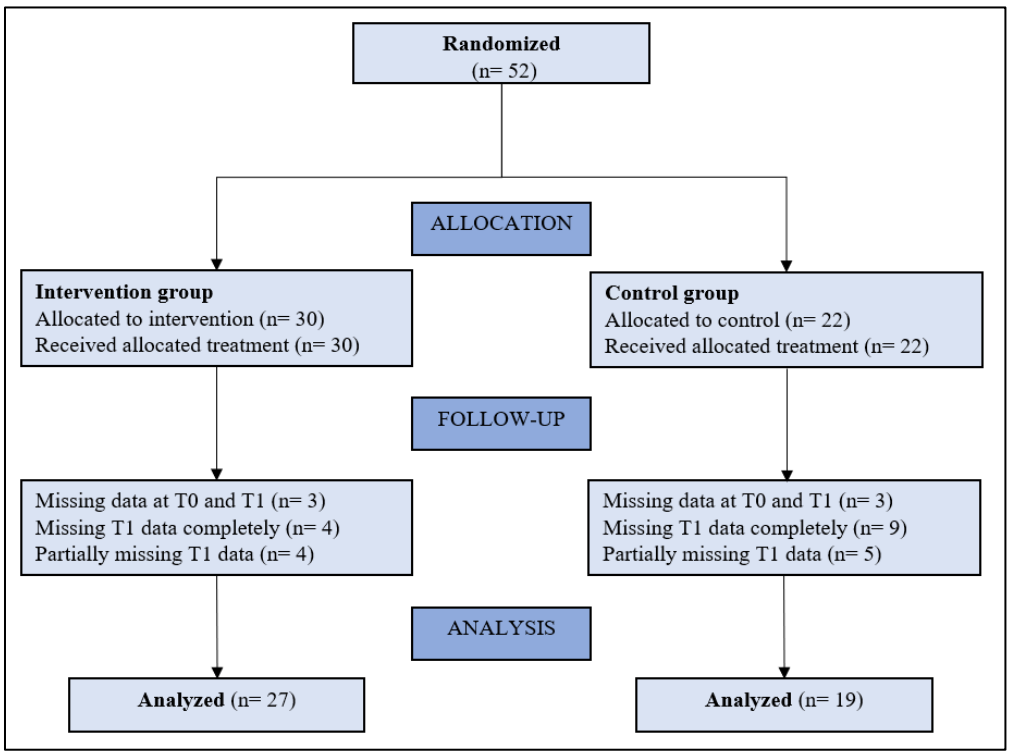

Figure 2. Flow diagram of the study.

Table 1. Baseline characteristics of participants.

	Intervention (n = 27)	Control (n = 19)	Statistical tests
Gender, n (%)			
Male	9 (33)	6 (32)	
Female	18 (67)	13 (68)	X^2 (1, N = 46) = 0.000, p = 1.000[a]
Age (years)			
Mean (SD)	54 (16.8)	57 (13.4)	t(44, N= 46) = 0.69, p = 0.494[c]
Range	21-78	25-74	
Educational level, n (%)			
Geen diploma	0 (0)	2 (11)	
Basisonderwijs	0 (0)	2 (11)	
VMBO, HAVO/VWO onderbouw, MBO1	10 (37)	5 (26)	X^2 (5, N = 46) = 8.89, p = 0.114[a]
HAVO, VWO, MBO2-4	9 (33)	8 (42)	
Bachelor (HBO/WO)	5 (19)	2 (11)	
Master (HBO/WO) of PhD	3 (11)	0 (0)	
Employment status, n (%)			
Fulltime werkzaam	4 (15)	5 (26)	
Parttime werkzaam	9 (33)	4 (21)	
Gepensioneerd	6 (22)	4 (21)	
Werkloos/-zoekend	0 (0)	0 (0)	Fisher's Exact Test: p = 0.766[b]
Vrijwilligerswerk	0 (0)	1 (5)	
Arbeidsongeschikt	5 (19)	5 (26)	
Student	1 (4)	1 (5)	
Overig	4 (15)	6 (32)	
Pain duration, n (%)			
Less than one year	5 (19)	0 (0)	X^2 (1, N = 46) = 2.27, p = 0.132[a]
More than one year	22 (81)	19 (100)	
Pain medication, n (%)			
Acetaminophen (paracetamol)	15 (56)	11 (58)	
NSAIDs	10 (37)	10 (37)	
Antidepressant medications	2 (7)	0 (0)	
Antiepileptic medications	1 (4)	2 (11)	Fisher's Exact Test: p = 0.921[b]
Local anaesthetics	0 (0)	0 (0)	
Opioid agents	4 (15)	2 (11)	
Other medications	2 (7)	2 (11)	
No medication	7 (26)	4 (21)	

[a]Chi-squared

[b]Fisher's exact test

[c]Independent t-test

Abbreviations: SD = Standard Deviation, VMBO = Voorbereidend Middelbaar Beroepsonderwijs, HAVO = Hoger Algemeen Voortgezet Onderwijs, VWO = Voorbereidend Wetenschappelijk Onderwijs, MBO = Middelbaar Beroepsonderwijs, HBO = Hoger Beroepsonderwijs, WO = Wetenschappelijk Onderwijs, PhD = Doctor of Philosophy, NSAIDs = Non-Steroidal Anti-Inflammatory Drugs

3.2 Primary study outcomes

Physical and mental scores of the SF-12 are shown in Figure 2 and 3. Estimated marginal means for SF-12 physical and mental component scores are reported in Table 2.

SF-12 PCS and MCS scores at baseline (T0) and 4 weeks (T1) did not show significant differences between the control and intervention group, as assessed using an LMM. For SF-12 PCS at baseline (T0), the mean difference between the control and intervention group was -1.81 (95% CI: -6.46 to 2.84; p = 0.44). At 4 weeks (T1), the mean difference was -4.07 (95% CI: -8.85 to 0.71; p = 0.09). For SF-12 MCS at baseline (T0), the mean difference was -2.06 (95% CI: -8.00 to 3.88; p = 0.49). At 4 weeks (T1), the mean difference was -4.37 (95% CI: -10.40 to 1.66; p = 0.15).

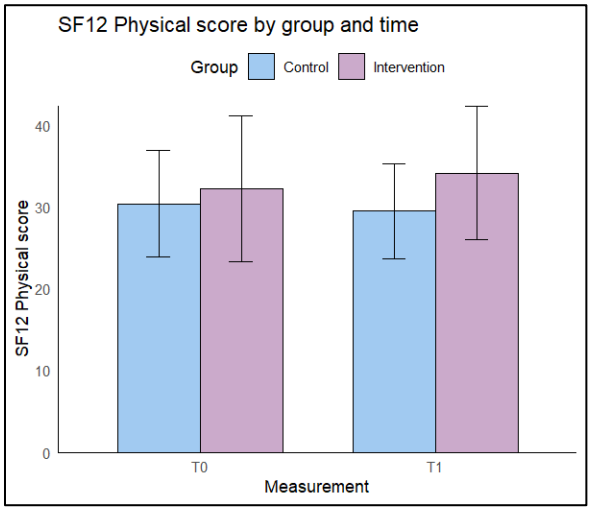

Figure 3. SF-12 physical scores, mean and SD.

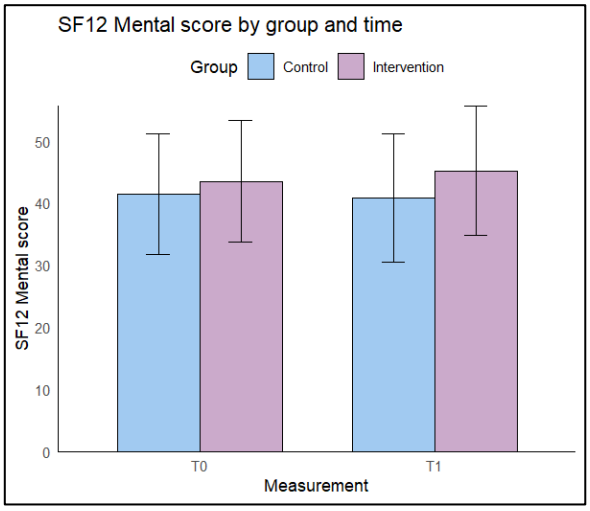

Figure 4. SF-12 mental scores, mean and SD.

Table 2. EMMs of SF-12 Physical and SF-12 Mental by group and time.

Group	Time	Mean	SE	95% CI	*p*-value
SF-12 Physical ↑					
Intervention	0 Weeks (Baseline)	32.4	1.50	(29.2, 35.3)	
	4 Weeks (Post-Intervention)	33.4	1.53	(30.4, 36.5)	
Control	0 Weeks (Baseline)	30.4	1.79	(26.8, 34.0)	
	4 Weeks (Post-Intervention)	29.4	1.84	(25.7, 33.1)	
Control - Intervention	0 Weeks (Baseline)	-1.81	2.34	(-6.51, 2.89)	0.443
	4 Weeks (Post-Intervention)	-4.07	2.39	(-8.87, 0.73)	0.095
SF-12 Mental ↑					
Intervention	0 Weeks (Baseline)	43.5	1.90	(39.7, 47.3)	
	4 Weeks (Post-Intervention)	45.3	1.93	(41.5, 49.2)	

Control	0 Weeks (Baseline)	41.4	2.27	(36.9, 46.0)	
	4 Weeks (Post-Intervention)	41.0	2.31	(36.3, 45.6)	
Control - Intervention	0 Weeks (Baseline)	-2.06	2.96	(-8.02, 3.89)	0.489
	4 Weeks (Post-Intervention)	-4.37	3.01	(-10.42, 1.67)	0.152

Abbreviations: EMMs = Estimated Marginal Means, SF-12 = Short Form 12 Health Survey, SE = Standard Error, CI = Confidence Interval

No significant main treatment effect was observed between the intervention and control group over time for the SF-12 Physical Component Score ($t(49.854) = 0.773$, $p = 0.443$) or the Mental Component Score ($t(48.679) = 0.697$, $p = 0.489$). Similarly, no statistically significant main time effects were observed for the SF-12 Physical Component Score ($t(38.527) = -1.000$, $p = 0.324$) or the Mental Component Score ($t(39.019) = -0.411$, $p = 0.683$). Additionally, no significant treatment-time interaction effect was found for the SF-12 Physical Component Score ($t(38.421) = 1.634$, $p = 0.111$) or the Mental Component Score ($t(38.943) = 1.565$, $p = 0.126$).

3.3 Secondary study outcomes

No statistically significant differences were observed between the estimated marginal means of the control and intervention groups across all secondary outcomes at both baseline (T0) and after 4 weeks (T1). For pain intensity (NPRS), the mean differences were 0.704 (95% CI: -0.86 to 2.27; $p = 0.371$) at baseline and 1.44 (95% CI: -0.26 to 3.08; $p = 0.096$) at 4 weeks. Pain catastrophising (PCS) differences were 2.09 (95% CI: -4.27 to 8.46; $p = 0.512$) at baseline and 4.83 (95% CI: -1.78 to 11.45; $p = 0.149$) at 4 weeks. Also, within the subscales of pain catastrophising, rumination, magnification, and helplessness differences remained non-significant. Pain self-efficacy (PSEQ) had mean differences of -3.87 (95% CI: -11.6 to 3.87; $p = 0.320$) at baseline and -5.35 (95% CI: -13.1 to -1.38; $p = 0.172$) at 4 weeks. Pain acceptance (CPAQ-8) and its subscales, pain willingness and activity engagement, also showed non-significant differences (Table 3).

No statistically significant main treatment effects, main time effects, or interaction effects were observed between the intervention and control groups over time for pain intensity (NPRS), pain catastrophising (PCS and its subscales of rumination, magnification, and helplessness), pain self-efficacy (PSEQ) and chronic pain acceptance (CPAQ and its subscales of pain willingness and activity engagement). Detailed statistical outputs for these analyses can be found in Appendix A.

Table 3. EMMs of pain intensity, pain catastrophising (rumination, magnification, helplessness), pain self-efficacy, and pain acceptance (pain willingness and activity engagement) by group and time.

Group	Time	Mean	SE	95% CI	*p*-value
Pain intensity (NPRS) ↓					
Intervention	0 Weeks (Baseline)	14.2	0.494	(13.2, 15.2)	
	4 Weeks (Post-Intervention)	13.3	0.509	(12.3, 14.4)	
Control	0 Weeks (Baseline)	14.9	0.605	(13.7, 16.1)	
	4 Weeks (Post-Intervention)	14.7	0.662	(13.4, 16.1)	
Control - Intervention	0 Weeks (Baseline)	0.704	0.780	(-0.86, 2.27)	0.371
	4 Weeks (Post-Intervention)	1.44	0.835	(-0.26, 3.08)	0.096
Pain catastrophising (PCS) ↓					
Intervention	0 Weeks (Baseline)	21.7	2.01	(17.7, 25.8)	
	4 Weeks (Post-Intervention)	17.9	2.05	(13.8, 22.0)	
Control	0 Weeks (Baseline)	23.8	2.46	(18.9, 28.8)	
	4 Weeks (Post-Intervention)	22.8	2.59	(17.6, 27.9)	
Control - Intervention	0 Weeks (Baseline)	2.09	3.17	(-4.27, 8.46)	0.512
	4 Weeks (Post-Intervention)	4.83	3.30	(-1.78, 11.45)	0.149
Pain catastrophising (PCS) – Rumination					
Intervention	0 Weeks (Baseline)	7.96	0.773	(6.49, 9.43)	
	4 Weeks (Post-Intervention)	6.24	0.754	(4.73, 7.75)	
Control	0 Weeks (Baseline)	8.72	0.898	(6.92, 10.52)	
	4 Weeks (Post-Intervention)	8.28	0.975	(6.33, 10.22)	
Control - Intervention	0 Weeks (Baseline)	0.759	1.16	(-1.57, 3.08)	0.515
	4 Weeks (Post-Intervention)	2.041	1.23	(-0.42, 4.51)	0.1023
Pain catastrophising (PCS) – Magnification					
Intervention	0 Weeks (Baseline)	4.02	0.540	(2.93, 5.10)	
	4 Weeks (Post-Intervention)	3.32	0.571	(2.17, 4.46)	
Control	0 Weeks (Baseline)	4.32	0.654	(3.02, 5.61)	
	4 Weeks (Post-Intervention)	3.86	0.685	(2.48, 5.23)	
Control - Intervention	0 Weeks (Baseline)	0.302	0.842	(-1.39, 1.99)	0.722
	4 Weeks (Post-Intervention)	0.539	0.892	(-1.25, 2.33)	0.548
Pain catastrophising (PCS) - Helplessness					
Intervention	0 Weeks (Baseline)	10.30	0.945	(8.40, 12.2)	
	4 Weeks (Post-Intervention)	9.19	0.980	(7.22, 11.1)	
Control	0 Weeks (Baseline)	11.28	1.158	(8.96, 13.6)	
	4 Weeks (Post-Intervention)	11.17	1.227	(7.22, 11.1)	
Control - Intervention	0 Weeks (Baseline)	0.981	1.49	(-2.02, 3.98)	0.514
	4 Weeks (Post-Intervention)	1.980	1.57	(-1.16, 5.12)	0.212
Pain self-efficacy (PSEQ) ↑					
Intervention	0 Weeks (Baseline)	41.5	2.44	(36.6, 46.4)	
	4 Weeks (Post-Intervention)	43.9	2.45	(39.0, 48.8)	

Control	0 Weeks (Baseline)	37.6	2.99	(31.6, 43.6)	
	4 Weeks (Post-Intervention)	38.6	2.99	(32.6, 44.6)	
Control - Intervention	0 Weeks (Baseline)	-3.87	3.86	(-11.6, 3.87)	0.320
	4 Weeks (Post-Intervention)	-5.35	3.87	(-13.1, -1.38)	0.172
Pain acceptance (CAPQ-8) ↑					
Intervention	0 Weeks (Baseline)	35.8	1.46	(32.9, 38.7)	
	4 Weeks (Post-Intervention)	38.0	1.47	(35.0, 40.9)	
Control	0 Weeks (Baseline)	35.5	1.78	(31.9, 39.1)	
	4 Weeks (Post-Intervention)	34.2	1.78	(30.6, 37.7)	
Control - Intervention	0 Weeks (Baseline)	-0.315	2.30	(-4.92, 4.29)	0.892
	4 Weeks (Post-Intervention)	-3.786	2.31	(-8.41, 0.84)	0.107
Pain acceptance (CAPQ-8) - Pain willingness					
Intervention	0 Weeks (Baseline)	17.3	1.03	(15.2, 19.3)	
	4 Weeks (Post-Intervention)	18.3	60.6	(16.3, 20.4)	
Control	0 Weeks (Baseline)	16.1	1.26	(13.6, 18.6)	
	4 Weeks (Post-Intervention)	15.8	1.26	(13.3, 18.3)	
Control - Intervention	0 Weeks (Baseline)	-1.19	1.62	(-4.43, 2.06)	0.468
	4 Weeks (Post-Intervention)	-2.51	1.63	(-5.76, 0.75)	0.129
Pain acceptance (CAPQ-8) - Activity engagement					
Intervention	0 Weeks (Baseline)	18.5	1.27	(16.0, 21.1)	
	4 Weeks (Post-Intervention)	19.6	1.28	(17.1, 22.2)	
Control	0 Weeks (Baseline)	19.4	1.55	(16.3, 22.5)	
	4 Weeks (Post-Intervention)	18.3	1.55	(15.2, 21.5)	
Control - Intervention	0 Weeks (Baseline)	0.87	2.00	(-3.15, 4.89)	0.666
	4 Weeks (Post-Intervention)	-1.29	2.01	(-5.32, 2.74)	0.523

Abbreviations: EMMs = Estimated Marginal Means, SE = Standard Error, CI = Confidence Interval

4. Discussion

4.1 Main findings

The primary aim of this study was to evaluate the influence of a four-week, home-based VR intervention, Reducept, in patients with CMP awaiting pain treatment. The study primarily assessed the influence of Reducept on health-related quality of life (HRQoL), as measured by the SF-12 (with physical and mental component scores) and included secondary outcomes such as pain intensity, pain catastrophising, pain self-efficacy and pain acceptance. No significant differences were observed between the intervention and the control groups for HRQoL or any secondary outcomes, consistent across both the intention-to-treat and per-protocol analyses.

An analysis of the SF-12 physical and mental health subscales revealed no significant improvements or declines between the intervention and control groups over the four-week period. This finding aligns with Groenveld et al. [24], who reported no significant differences in SF-12 scores between groups after four weeks. Similarly, De Vries et al. [23], using the SF-36/RAND 36-item Health Survey, found no significant changes in quality of life domains such as physical functioning, emotional well-being and pain. The absence of significant changes in either direction suggests that the intervention did not substantially influence HRQoL, which may indicate that it was either not robust enough or not sufficiently targeted to affect these outcomes within the short timeframe of four weeks. Further investigation could explore whether longer intervention periods or alternative methods might yield different results.

No significant reductions in pain catastrophising were observed between groups, consistent with Groenveld et al. [24]. Both studies used a home-based, self-administered VR intervention with daily sessions without continuous supervision. Groenveld et al. [24] included adherence monitoring through telephone interviews on days 7 and 14, potentially providing additional support and encouraging greater engagement. This study lacked such monitoring, potentially affecting adherence and cognitive changes. In contrast, De Vries et al. [23] reported significant reductions in catastrophising, which could be due to a more structured, supervised clinical setting. All treatment sessions were conducted in a hospital setting, with VR sessions held three times per week over a total of 9-12 sessions. Garcia et al. [69] also used a home-based intervention, instructing participants to complete one VR session daily for 56 days, with study staff monitoring the completion of twice-weekly surveys and device use. Despite these measures, Garcia et al. [69] still reported non-significant improvements in pain coping symptoms, including pain catastrophising. These findings suggest that while home-based interventions offer flexibility, improved monitoring strategies could enhance adherence and cognitive changes [70,71].

Regarding pain intensity, no significant reductions were observed between the intervention and control groups. This aligns with Eccleston et al.'s [72] findings, where a VR-based intervention aimed at reducing fear of movement and psychological barriers also reported no significant changes in pain intensity. Although De Vries et al. [23] used the same VR programme, they reported a modest yet statistically significant reduction in pain intensity. This discrepancy may be due to differences in study design and participant characteristics. De Vries et al.'s [23] study included participants with CLBP lasting more than six months and required a baseline mean pain intensity score of 4 on a 0-10 numeric rating scale. In contrast, this study included a broader range of CMP conditions with a minimum diagnosis duration of three months and did not require a specific baseline pain intensity score for inclusion. The absence of a baseline pain intensity score may have introduced variability in participant pain levels, potentially diminishing the intervention's effect. These findings suggest that the effectiveness of Reducept may be influenced by participant characteristics, including baseline pain levels and intervention design.

4.2 Strengths and limitations

This study has several strengths and limitations that are important to consider when evaluating the results.

4.2.1 Strengths

This study benefits from its inclusion of a diverse population across multiple healthcare organisations — Roessingh, Deventer Ziekenhuis, Nocepta, and Revalidatie Friesland —representing various geographical locations and healthcare settings (rehabilitation, specialised pain management, hospital care). This diversity enhances the generalisability of the findings to chronic pain patients from varied backgrounds and conditions. However, this diversity could also introduce variability in treatment protocols, healthcare practices and patient populations across the different sites, potentially influencing the consistency of the intervention's impact. Such variability might make it challenging to attribute observed effects solely to the intervention, as differences in healthcare delivery or patient management practices across sites could act as confounding factors.

The study utilised a cluster randomised two-period crossover (CRXO) design, chosen for its effectiveness in clinical research for reducing confounding factors within clusters. This design allowed each healthcare organisation to contribute data to both the intervention and control groups during designated periods, enhancing the study's ability to evaluate treatment effects across diverse settings. CRXO designs are particularly valuable in clinical research as they optimise resource use and minimise the impact of confounding variables, improving the reliability of treatment effect estimates [43,44,73].

4.2.2 Limitations

A significant limitation of this study is the relatively small sample size. Despite the initial aim for 52 participants based on a priori sample size calculation, the study ultimately included 46 participants (27 in the intervention group and 19 in the control group). While a smaller sample size does not inherently reduce the generalisability, in this case, it may have implications. A smaller sample size may limit diversity and affect statistical power, which could reduce the ability to detect significant effects or draw robust conclusions about the intervention's impact. Future research should aim for larger sample sizes to strengthen the evidence base and enable subgroup analyses.

Another notable limitation is the potential influence of the nocebo effect, which was not directly assessed. Research indicates that a waiting list setting can induce a nocebo effect, where patients experience worsening symptoms while awaiting treatment [74,75]. If such an effect was present, it could have either exaggerated or obscured any potential benefits of the VR intervention, making it difficult to accurately assess its true effectiveness. Future studies should consider explicitly measuring and accounting for this effect to better understand its impact.

To address these concerns, future research could incorporate sensitivity analyses and explore alternative methods for handling missing data, such as multiple imputation. Sensitivity analyses could assess how different assumptions about missing data (e.g., assuming uniformly positive or negative outcomes for participants with missing data) impact the outcomes [76]. Multiple imputation could provide a more robust approach to account for missing data, thereby enhancing the accuracy of findings [77]. Additionally, using an active control group — receiving a different but equally engaging intervention — could help isolate the specific effects of the VR intervention from other variables [78].

4.3 Practical implications and recommendations

Although the intervention did not reveal significant short-term effects, this does not rule out the potential of long-term effects. Short-term studies often capture only immediate responses, potentially missing delayed or gradual effects that could be significant over a longer duration. Pain management interventions, especially those incorporating cognitive and educational elements, often require more time to realise their full potential [79]. For instance, VR's immersive pain education can enhance patients' understanding and coping strategies, potentially leading to more durable benefits [7,20,80]. Evidence supports that such educational approaches provide lasting advantages by equipping patients with skills that extend beyond the immediate treatment period, thereby impacting long-term pain management [79,81–83]. Therefore, longitudinal studies are essential to determine whether sustained engagement with VR provides long-term effects not captured in short-term assessments.

Additionally, exploring the integration of VR into active treatment phases may offer potential advantages over its use as a standalone intervention. The literature suggests that VR may provide greater benefits when combined with traditional therapeutic approaches [84,85]. For instance, VR-mediated therapy significantly reduced pain intensity and disability in chronic neck pain patients compared to control conditions, and has also been successfully used alongside traditional pain management techniques, such as cognitive behavioural therapy and physical rehabilitation, to enhance patient outcomes and engagement [26,86]. Investigating how VR could be part of a comprehensive treatment plan may provide insights into its potential benefits.

Overall, future studies should emphasise both longitudinal research to evaluate extended VR use and its integration with other treatments, providing a more comprehensive understanding of VR's role in chronic pain management.

5. Conclusion

This study examined the influence of a four-week, home-based VR intervention, Reducept, in patients with chronic musculoskeletal pain awaiting pain treatment. The results indicated that the intervention did not yield significant improvements in health-related quality of life or secondary outcomes, including pain intensity, pain catastrophising, pain self-efficacy and pain acceptance, compared to standard waiting list procedures. Both the intervention and control groups showed no significant differences in these outcomes, suggesting that the four-week study period may have been insufficient to achieve measurable benefits.

These findings highlight the need for further research into long-term effects of VR interventions and their potential integration with other therapeutic approaches. Future studies should explore whether the extended use of VR and its combination with other treatments could lead to improved outcomes in chronic pain management and provide a more comprehensive understanding of VR's role in this context.

References

[1] Treede R-D, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. A classification of chronic pain for ICD-11. Pain 2015;156:1003–7. https://doi.org/10.1097/j.pain.0000000000000160.

[2] El-Tallawy SN, Nalamasu R, Salem GI, LeQuang JAK, Pergolizzi J V, Christo PJ. Management of Musculoskeletal Pain: An Update with Emphasis on Chronic Musculoskeletal Pain. Pain Ther 2021;10:181–209. https://doi.org/10.1007/s40122-021-00235-2.

[3] Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain 2006;10:287–333. https://doi.org/10.1016/j.ejpain.2005.06.009.

[4] Hadi MA, McHugh GA, Closs SJ. Impact of Chronic Pain on Patients' Quality of Life: A Comparative Mixed-Methods Study. J Patient Exp 2019;6:133–41. https://doi.org/10.1177/2374373518786013.

[5] Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2197–223. https://doi.org/10.1016/S0140-6736(12)61689-4.

[6] Boonen A, Heuvel R van den, Tubergen A van, Goossens M, Severens JL, Heijde D van der, et al. Large differences in cost of illness and wellbeing between patients with fibromyalgia, chronic low back pain, or ankylosing spondylitis. Ann Rheum Dis 2005;64:396 LP – 402. https://doi.org/10.1136/ard.2003.019711.

[7] Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. Psychol Bull 2007;133:581–624. https://doi.org/10.1037/0033-2909.133.4.581.

[8] Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain 2011;152:S2–15. https://doi.org/10.1016/j.pain.2010.09.030.

[9] Turk DC, Wilson HD. Fear of pain as a prognostic factor in chronic pain: conceptual models, assessment, and treatment implications. Curr Pain Headache Rep 2010;14:88–95. https://doi.org/10.1007/s11916-010-0094-x.

[10] Leeuw M, Goossens MEJB, Linton SJ, Crombez G, Boersma K, Vlaeyen JWS. The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. J Behav Med 2007;30:77–94. https://doi.org/10.1007/s10865-006-9085-0.

[11] Chou R, Shekelle P. Will this patient develop persistent disabling low back pain? JAMA 2010;303:1295–302. https://doi.org/10.1001/jama.2010.344.

[12] Traeger AC, Hübscher M, Henschke N, Moseley GL, Lee H, McAuley JH. Effect of Primary Care-Based Education on Reassurance in Patients With Acute Low Back Pain: Systematic Review and Meta-analysis. JAMA Intern Med 2015;175:733–43. https://doi.org/10.1001/jamainternmed.2015.0217.

[13] Martinez-Calderon J, Meeus M, Struyf F, Miguel Morales-Asencio J, Gijon-Nogueron G, Luque-Suarez A. The role of psychological factors in the perpetuation of pain intensity and disability in people with chronic shoulder pain: a systematic review. BMJ Open 2018;8:e020703. https://doi.org/10.1136/bmjopen-2017-020703.

[14] Vlaeyen JWS, Crombez G, Linton SJ. The fear-avoidance model of pain. Pain 2016;157:1588–9. https://doi.org/10.1097/j.pain.0000000000000574.

[15] Kongsted A, Kent P, Axen I, Downie AS, Dunn KM. What have we learned from ten years of trajectory research in low back pain? BMC Musculoskelet Disord 2016;17:220. https://doi.org/10.1186/s12891-016-1071-2.

[16] Jong L de, Janssen PGH, Keizer D, Köke AJA, Schiere S, Bommel M van, et al. NHG-Standaard Pijn. Huisarts Wet 2015;58:472–85.

[17] Melzack R. From the gate to the neuromatrix. Pain 1999;Suppl 6:S121–6. https://doi.org/10.1016/S0304-3959(99)00145-1.

[18] Gatchel RJ. Comorbidity of chronic pain and mental health disorders: the biopsychosocial perspective. Am Psychol 2004;59:795–805. https://doi.org/10.1037/0003-066X.59.8.795.

[19] Kroneman M, Boerma W, van den Berg M, Groenewegen P, de Jong J, van Ginneken E.

Netherlands: Health System Review. Health Syst Transit 2016;18:1–240.
[20] Mallari B, Spaeth EK, Goh H, Boyd BS. Virtual reality as an analgesic for acute and chronic pain in adults: a systematic review and meta-analysis. J Pain Res 2019;12:2053–85. https://doi.org/10.2147/JPR.S200498.
[21] Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet (London, England) 2013;382:769–79. https://doi.org/10.1016/S0140-6736(13)60900-9.
[22] Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. Pain Med 2008;9:444–59. https://doi.org/10.1111/j.1526-4637.2007.00370.x.
[23] de Vries FS, van Dongen RTM, Bertens D. Pain education and pain management skills in virtual reality in the treatment of chronic low back pain: A multiple baseline single-case experimental design. Behav Res Ther 2023;162:104257. https://doi.org/10.1016/j.brat.2023.104257.
[24] Groenveld TD, Smits MLM, Knoop J, Kallewaard JW, Staal JB, de Vries M, et al. Effect of a Behavioral Therapy-Based Virtual Reality Application on Quality of Life in Chronic Low Back Pain. Clin J Pain 2023;39:278–85. https://doi.org/10.1097/AJP.0000000000001110.
[25] Pourmand A, Davis S, Marchak A, Whiteside T, Sikka N. Virtual Reality as a Clinical Tool for Pain Management. Curr Pain Headache Rep 2018;22:53. https://doi.org/10.1007/s11916-018-0708-2.
[26] Goudman L, Jansen J, Billot M, Vets N, De Smedt A, Roulaud M, et al. Virtual Reality Applications in Chronic Pain Management: Systematic Review and Meta-analysis. JMIR Serious Games 2022;10:e34402. https://doi.org/10.2196/34402.
[27] Chuan A, Zhou JJ, Hou RM, Stevens CJ, Bogdanovych A. Virtual reality for acute and chronic pain management in adult patients: a narrative review. Anaesthesia 2021;76:695–704. https://doi.org/10.1111/anae.15202.
[28] Hoffman HG, Patterson DR, Carrougher GJ. Use of virtual reality for adjunctive treatment of adult burn pain during physical therapy: a controlled study. Clin J Pain 2000;16:244–50. https://doi.org/10.1097/00002508-200009000-00010.
[29] Hoffman HG, Patterson DR, Carrougher GJ, Nakamura D, Moore M, Garcia-Palacios A, et al. The effectiveness of virtual reality pain control with multiple treatments of longer durations: A case study. Int J Hum Comput Interact 2001;13:1–12.
[30] Wismeijer AAJ, Vingerhoets AJJM. The use of virtual reality and audiovisual eyeglass systems as adjunct analgesic techniques: a review of the literature. Ann Behav Med a Publ Soc Behav Med 2005;30:268–78. https://doi.org/10.1207/s15324796abm3003_11.
[31] Gold JI, Belmont KA, Thomas DA. The neurobiology of virtual reality pain attenuation. Cyberpsychology Behav Impact Internet, Multimed Virtual Real Behav Soc 2007;10:536–44. https://doi.org/10.1089/cpb.2007.9993.
[32] Rutter CE, Dahlquist LM, Weiss KE. Sustained efficacy of virtual reality distraction. J Pain 2009;10:391–7. https://doi.org/10.1016/j.jpain.2008.09.016.
[33] Malloy KM, Milling LS. The effectiveness of virtual reality distraction for pain reduction: A systematic review. Clin Psychol Rev 2010;30:1011–8. https://doi.org/https://doi.org/10.1016/j.cpr.2010.07.001.
[34] Johnson MH. How does distraction work in the management of pain? Curr Pain Headache Rep 2005;9:90–5. https://doi.org/10.1007/s11916-005-0044-1.
[35] Mahrer NE, Gold JI. The use of virtual reality for pain control: a review. Curr Pain Headache Rep 2009;13:100–9. https://doi.org/10.1007/s11916-009-0019-8.
[36] Trost Z, Parsons TD. Beyond Distraction: Virtual Reality Graded Exposure Therapy as Treatment for Pain-Related Fear and Disability in Chronic Pain. J Appl Biobehav Res 2014;19:106–26. https://doi.org/10.1111/jabr.12021.
[37] Tuck N, Pollard C, Good C, Williams C, Lewis G, Hames M, et al. Active Virtual Reality for Chronic Primary Pain: Mixed Methods Randomized Pilot Study. JMIR Form Res 2022;6:e38366. https://doi.org/10.2196/38366.

[38] Rothbaum AO, Tannenbaum LR, Zimand E, Rothbaum BO. A pilot randomized controlled trial of virtual reality delivered relaxation for chronic low back pain. Virtual Real 2023;27:3533–43. https://doi.org/10.1007/s10055-023-00760-9.
[39] Castelnuovo G, Giusti EM, Manzoni GM, Saviola D, Gatti A, Gabrielli S, et al. Psychological Treatments and Psychotherapies in the Neurorehabilitation of Pain: Evidences and Recommendations from the Italian Consensus Conference on Pain in Neurorehabilitation. Front Psychol 2016;7. https://doi.org/10.3389/fpsyg.2016.00115.
[40] Li A, Montaño Z, Chen VJ, Gold JI. Virtual reality and pain management: current trends and future directions. Pain Manag 2011;1:147–57. https://doi.org/10.2217/pmt.10.15.
[41] Reducept. Reducept Whitepaper 2019.
[42] Fennema M, Zantema L. Reducept manual for practitioners 2020.
[43] Arnup SJ, McKenzie JE, Hemming K, Pilcher D, Forbes AB. Understanding the cluster randomised crossover design: a graphical illustraton of the components of variation and a sample size tutorial. Trials 2017;18:381. https://doi.org/10.1186/s13063-017-2113-2.
[44] Hemming K, Taljaard M, Weijer C, Forbes AB. Use of multiple period, cluster randomised, crossover trial designs for comparative effectiveness research. BMJ 2020:m3800. https://doi.org/10.1136/bmj.m3800.
[45] Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39:175–91. https://doi.org/10.3758/bf03193146.
[46] Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009;41:1149–60. https://doi.org/10.3758/BRM.41.4.1149.
[47] No Title n.d.
[48] Ware JJ, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220–33. https://doi.org/10.1097/00005650-199603000-00003.
[49] Bohannon RW, Maljanian R, Landes M. Test-retest reliability of short form (SF)-12 component scores of patients with stroke. Int J Rehabil Res Int Zeitschrift Fur Rehabil Rev Int Rech Readapt 2004;27:149–50. https://doi.org/10.1097/01.mrr.0000127350.25287.08.
[50] Cheak-Zamora NC, Wyrwich KW, McBride TD. Reliability and validity of the SF-12v2 in the medical expenditure panel survey. Qual Life Res an Int J Qual Life Asp Treat Care Rehabil 2009;18:727–35. https://doi.org/10.1007/s11136-009-9483-1.
[51] Salyers MP, Bosworth HB, Swanson JW, Lamb-Pagone J, Osher FC. Reliability and validity of the SF-12 health survey among people with severe mental illness. Med Care 2000;38:1141–50. https://doi.org/10.1097/00005650-200011000-00008.
[52] Ware JE, Keller SD, Kosinski M. SF-12: How to score the SF-12 physical and mental health summary scales. Health Institute, New England Medical Center; 1995.
[53] Haefeli M, Elfering A. Pain assessment. Eur Spine J Off Publ Eur Spine Soc Eur Spinal Deform Soc Eur Sect Cerv Spine Res Soc 2006;15 Suppl 1:S17-24. https://doi.org/10.1007/s00586-005-1044-x.
[54] Abbott JH, Schmitt J. Minimum important differences for the patient-specific functional scale, 4 region-specific outcome measures, and the numeric pain rating scale. J Orthop Sports Phys Ther 2014;44:560–4. https://doi.org/10.2519/jospt.2014.5248.
[55] Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005;113:9–19. https://doi.org/10.1016/j.pain.2004.09.012.
[56] Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, et al. Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review. J Pain Symptom Manage 2011;41:1073–93. https://doi.org/10.1016/j.jpainsymman.2010.08.016.
[57] Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. Psychol Assess 1995;7:524.
[58] Nicholas MK. The pain self-efficacy questionnaire: Taking pain into account. Eur J Pain 2007;11:153–63. https://doi.org/10.1016/j.ejpain.2005.12.008.

[59] van der Maas LCC, de Vet HCW, Köke A, Bosscher RJ, Peters ML. Psychometric Properties of the Pain Self-Efficacy Questionnaire (PSEQ). Eur J Psychol Assess 2012;28:68–75. https://doi.org/10.1027/1015-5759/a000092.
[60] Dubé M-O, Langevin P, Roy J-S. Measurement properties of the Pain Self-Efficacy Questionnaire in populations with musculoskeletal disorders: a systematic review. Pain Reports 2021;6:e972. https://doi.org/10.1097/PR9.0000000000000972.
[61] Fish RA, McGuire B, Hogan M, Morrison TG, Stewart I. Validation of the chronic pain acceptance questionnaire (CPAQ) in an Internet sample and development and preliminary validation of the CPAQ-8. Pain 2010;149:435–43. https://doi.org/10.1016/j.pain.2009.12.016.
[62] No Title n.d. https://www.r-project.org/.
[63] Armijo-Olivo S, Warren S, Magee D. Intention to treat analysis, compliance, drop-outs and how to deal with missing data in clinical research: a review. Phys Ther Rev 2009;14:36–49. https://doi.org/10.1179/174328809X405928.
[64] Molenberghs G, Kenward M. Missing data in clinical studies. John Wiley & Sons; 2007.
[65] Tripepi G, Chesnaye NC, Dekker FW, Zoccali C, Jager KJ. Intention to treat and per protocol analysis in clinical trials. Nephrology 2020;25:513–7.
[66] Fisher RA. The Goodness of Fit of Regression Formulæ, and the Distribution of Regression Coefficients. J R Stat Soc 1922;85:597–612. https://doi.org/10.2307/2341124.
[67] Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4. J Stat Softw 2015;67:1–48. https://doi.org/10.18637/jss.v067.i01.
[68] Kuznetsova A, Brockhoff PB, Christensen RHB. lmerTest Package: Tests in Linear Mixed Effects Models. J Stat Softw 2017;82:1–26. https://doi.org/10.18637/jss.v082.i13.
[69] Garcia LM, Birckhead BJ, Krishnamurthy P, Sackman J, Mackey IG, Louis RG, et al. An 8-Week Self-Administered At-Home Behavioral Skills-Based Virtual Reality Program for Chronic Low Back Pain: Double-Blind, Randomized, Placebo-Controlled Trial Conducted During COVID-19. J Med Internet Res 2021;23:e26292. https://doi.org/10.2196/26292.
[70] Palazzo C, Klinger E, Dorner V, Kadri A, Thierry O, Boumenir Y, et al. Barriers to home-based exercise program adherence with chronic low back pain: Patient expectations regarding new technologies. Ann Phys Rehabil Med 2016;59:107–13. https://doi.org/10.1016/j.rehab.2016.01.009.
[71] Beinart NA, Goodchild CE, Weinman JA, Ayis S, Godfrey EL. Individual and intervention-related factors associated with adherence to home exercise in chronic low back pain: a systematic review. Spine J 2013;13:1940–50. https://doi.org/10.1016/j.spinee.2013.08.027.
[72] Eccleston C, Fisher E, Liikkanen S, Sarapohja T, Stenfors C, Jääskeläinen SK, et al. A prospective, double-blind, pilot, randomized, controlled trial of an "embodied" virtual reality intervention for adults with low back pain. Pain 2022;163:1700–15. https://doi.org/10.1097/j.pain.0000000000002617.
[73] Turner RM, White IR, Croudace T. Analysis of cluster randomized cross-over trial data: a comparison of methods. Stat Med 2007;26:274–89. https://doi.org/10.1002/sim.2537.
[74] Colloca L, Miller FG. The nocebo effect and its relevance for clinical practice. Psychosom Med 2011;73:598–603. https://doi.org/10.1097/PSY.0b013e3182294a50.
[75] Furukawa TA, Noma H, Caldwell DM, Honyashiki M, Shinohara K, Imai H, et al. Waiting list may be a nocebo condition in psychotherapy trials: a contribution from network meta-analysis. Acta Psychiatr Scand 2014;130:181–92. https://doi.org/10.1111/acps.12275.
[76] Little RJA, Rubin DB. Statistical Analysis with Missing Data. Wiley; 2002. https://doi.org/10.1002/9781119013563.
[77] Schafer JL. Analysis of Incomplete Multivariate Data. Chapman and Hall/CRC; 1997. https://doi.org/10.1201/9781439821862.
[78] Hróbjartsson A, Gøtzsche PC. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. N Engl J Med 2001;344:1594–602. https://doi.org/10.1056/NEJM200105243442106.
[79] Spiegel BM. Virtual medicine: how virtual reality is easing pain, calming nerves and improving health. Med J Aust 2018;209:245–7. https://doi.org/10.5694/mja17.00540.
[80] Keefe FJ, Porter L, Somers T, Shelby R, Wren A V. Psychosocial interventions for managing pain in older adults: outcomes and clinical implications. Br J Anaesth 2013;111:89–94.

https://doi.org/10.1093/bja/aet129.
[81] Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. Lancet (London, England) 2021;397:2082–97. https://doi.org/10.1016/S0140-6736(21)00393-7.
[82] Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, et al. Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. JAMA 2016;315:1240–9. https://doi.org/10.1001/jama.2016.2323.
[83] Winger JG, Nunez C, Kelleher SA, Ingle KK, Gandhi V, Keefe FJ, et al. Predictors of Intervention Session Completion in a Randomized Clinical Trial of a Behavioral Cancer Pain Intervention. J Pain Symptom Manage 2020;59:1268–77. https://doi.org/10.1016/j.jpainsymman.2020.01.020.
[84] Riva G, Baños RM, Botella C, Mantovani F, Gaggioli A. Transforming Experience: The Potential of Augmented Reality and Virtual Reality for Enhancing Personal and Clinical Change. Front Psychiatry 2016;7:164. https://doi.org/10.3389/fpsyt.2016.00164.
[85] Smits M, van Goor H, Kallewaard J-W, Verbeek P-P, Ludden GDS. Evaluating value mediation in patients with chronic low-back pain using virtual reality: contributions for empirical research in Value Sensitive Design. Health Technol (Berl) 2022;12:765–78. https://doi.org/10.1007/s12553-022-00671-w.
[86] Grassini S. Virtual Reality Assisted Non-Pharmacological Treatments in Chronic Pain Management: A Systematic Review and Quantitative Meta-Analysis. Int J Environ Res Public Health 2022;19:4071. https://doi.org/10.3390/ijerph19074071.

Appendix A

Table 4. Linear mixed model output for pain intensity, pain catastrophising (rumination, magnification, helplessness), pain self-efficacy, and pain acceptance (pain willingness and activity engagement).

Outcome	Effect type	Estimate	Std. Error	*t*-value	*p*-value
Pain intensity (NPRS) ↓	Main treatment effect	-0.70	0.78	-0.90	0.371
	Main time effect	-0.14	0.54	-0.27	0.790
	Interaction effect	-0.71	0.67	-1.06	0.296
Pain catastrophising (PCS) ↓	Main treatment effect	-2.09	3.17	-0.66	0.512
	Main time effect	-1.07	1.79	-0.60	0.551
	Interaction effect	-2.74	2.25	-1.22	0.231
Rumination	Main treatment effect	-0.76	1.16	-0.66	0.515
	Main time effect	-0.45	0.75	-0.59	0.556
	Interaction effect	-1.28	0.94	-1.37	0.179
Magnification	Main treatment effect	-0.30	0.84	-0.36	0.721
	Main time effect	-0.46	0.57	-0.81	0.426
	Interaction effect	-0.24	0.74	-0.32	0.752
Helplessness	Main treatment effect	-0.98	1.49	-0.66	0.514
	Main time effect	-0.11	0.90	-0.12	0.902
	Interaction effect	-0.99	1.14	-0.88	0.387
Pain self-efficacy (PSEQ) ↑	Main treatment effect	3.87	3.86	1.00	0.320
	Main time effect	0.94	1.77	0.53	0.597
	Interaction effect	1.48	2.30	0.64	0.523
Pain acceptance (CPAQ) ↑	Main treatment effect	0.31	2.30	0.14	0.892
	Main time effect	-1.33	1.47	-0.91	0.368
	Interaction effect	3.47	1.91	1.82	0.075
Pain Willingness	Main treatment effect	1.19	1.62	0.73	0.468
	Main time effect	-0.28	1.02	-0.27	0.787
	Interaction effect	1.32	1.33	1.00	0.326
Activity Engagement	Main treatment effect	-0.87	2.00	-0.43	0.666
	Main time effect	-1.06	0.90	-1.17	0.248
	Interaction effect	2.16	1.17	1.85	0.072