

Effects of immersive virtual reality-based exercise on quality of life, stress, anxiety, depression, and handgrip strength in fibromyalgia: A pilot study

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Abstract: **Background** Fibromyalgia (FM) is a chronic rheumatic disorder characterised by musculoskeletal pain, fatigue, and psychoemotional symptoms. Virtual reality (VR) has proven to be an innovative and motivating tool for managing FM, with several studies indicating that it can improve quality of life indices and reduce psychoemotional symptoms. However, studies on immersive VR-based exercise (iVRE) are limited. **Methods** The aim of this study was to evaluate the effects of iVRE on quality of life, stress, anxiety, depression, and handgrip strength in patients with FM. A single-arm pre-post-test pilot study was conducted. Individuals diagnosed with FM were recruited using convenience sampling. The iVRE protocol consisted of 12 sessions of 10 min warm-up and 15 min exercises applied with the Oculus Quest 2™ device. The impact on quality of life was assessed using the Revised Fibromyalgia Impact Questionnaire, and the effects on stress, anxiety, and depression were determined using the Depression Anxiety Stress Scale-21 questionnaire. Handgrip strength was evaluated using the Baseline® dynamometer. The normality assumption was evaluated, and the pre-post means were compared using Student's *t*-test ($p < 0.05$). **Results** Eleven individuals (40.6 ± 11.2 years) completed the protocol (10 women). There were significant differences in favour of iVRE in quality of life impact ($p < 0.001$, Cohen's *d*: 1.48), handgrip strength ($p < 0.05$, Cohen's *d*: 0.26), depression ($p < 0.05$, Cohen's *d*: 0.73), and anxiety ($p < 0.05$, Cohen's *d*: 0.73).

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Conclusions A six-week iVRE program significantly reduces the impact on quality of life, anxiety, and depression and improves handgrip strength in people with FM. Future studies should investigate the physiological effects using systemic biomarkers to explain the scope of this therapeutic modality.

Keywords: Human-computer interaction; Virtual environment; Fibromyalgia; Exercise

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1 Introduction

Fibromyalgia (FM) is a chronic rheumatic disorder characterised by widespread musculoskeletal pain, mood problems, and cognitive impairment^[1,2]. It has a global prevalence ranging from 2% to 4% and affects mainly women in a 9:1 ratio, with the age of most significant impact between 25 and 50 years^[3]. Patients with FM have impaired quality of life and frequently seek medical attention, which is reflected in significant healthcare costs. The annual number of medical consultations for FM is estimated to be almost double that for healthy individuals^[4]. Although the exact etiology of FM is not fully understood, individuals have been observed to exhibit a genetic predisposition that, in combination with physical and emotional factors, including the chronicity of a neuromusculoskeletal injury, may act as a trigger for the condition. In addition, central sensitisation and hormonal factors may play a key role in its onset and progression^[5].

The diverse symptomatology of FM makes its diagnosis challenging. Patients often report muscle weakness and fatigue, which can diminish their ability to maintain adequate strength for daily tasks^[6]. Similarly, sleep disturbances and irritable bowel syndrome may occur in 50% of individuals with fibromyalgia^[2]. The altered pain perception that characterises FM can make even simple tasks such as gripping difficult, as pain and discomfort tend to intensify with repetitive or prolonged use of the hand and forearm muscles. Several studies have reported a generalised decrease in muscle strength, noting that this decrease is inversely related to the symptom severity^[7,8]. Psychologically, FM is characterised by the presence of negative emotions associated with a state of generalised distress^[9]. This state of psychological distress may be accompanied by cognitive^[10] and emotional disturbances that can considerably affect the quality of life of patients and severity of the syndrome^[11]. Constant preoccupation with pain management and uncertainty regarding the future are both associated with additional symptoms, such as difficulty sleeping and fatigue. This creates a vicious circle in which stress contributes to physical discomfort, which favours stress^[12]. In this context, several authors have suggested reduced levels of resilience and effective coping strategies that may generate low self-efficacy and inefficient modulation of nociceptive stimuli, leading to a bidirectional relationship between the presence of pain and psychoemotional symptoms^[13–15]. In addition, these psycho-cognitive mechanisms may be influenced by nociplastic and inflammatory alterations, which could contribute to a reciprocal aetiopathogenesis between central and peripheral mechanisms, making treatment more difficult^[16].

The European Alliance of Rheumatology Associations recommends a multimodal therapeutic approach tailored to an individual patient's characteristics and contributes to reducing symptom severity and improving quality of life, allowing the person to learn to live as well as possible with their disease^[17]. This approach begins with non-pharmacological measures, such as health education, physical therapy, and psychotherapy, followed by pharmacological measures, such as the use of pain modulators, including

duloxetine or pregabalin, and medications for sleep disorders^[18]. Different studies have proposed that these approaches can be used simultaneously and that complementary strategies that could improve the therapeutic experience of the patient should also be considered^[19–22]. In this regard, virtual reality (VR) systems have proven to be a complementary therapeutic option with beneficial effects for treating various health conditions^[23–25]. One modality that presents a relevant multisensory experience is immersive VR-based exercise (iVRE), which offers a unique experience given the high level of immersion provided by VR, thereby providing a promising tool for the active treatment of FM^[26–29]. In iVRE, patients enter a controlled virtual environment that complements or improves conventional therapies. The efficacy of VR in chronic pain syndromes^[30–33], phantom limb pain, cancer, and central neurological injuries^[23,34], incorporating relaxation exercises, cognitive therapies, and adapted physical activities^[35,36], has been described. This interaction may improve cognitive function and reduce symptoms of anxiety and depression associated with their health condition^[37–40].

Although a growing body of evidence supports the positive effects of VR in physical activity and rehabilitation, its use as an immersive modality for treating FM remains in its early stages, especially when combined with exercise^[26,41,42]. A recent systematic review suggested that new studies should include the benefits of this intervention for physical capacity, quality of life, and psychoemotional variables in FM^[26]. In this context, the aim of this study was to assess the impact of a six-week pilot program of iVRE on quality of life (measured using the Revised Fibromyalgia Impact Questionnaire (FIQR)), as well as on stress, anxiety, and depression levels (evaluated using the Depression Anxiety Stress Scale-21 (DASS-21) questionnaire) and grip strength in individuals with FM. This pilot study will help to determine the feasibility of patient acceptance of this technology and provide insights for adjusting the type and difficulty of exercises before implementing the program in a larger group of participants.

2 Methods

2.1 Design and subjects

A single-arm pre-post-test pilot study was designed. The study was conducted at the Universidad San Sebastián, Bío-Bío Region, Republic of Chile, and originated from a collaborative community engagement project at the same University. The study was registered at www.clinicaltrials.gov under No. NCT06606132. The study sample was recruited by convenience after applying the following criteria: i) Inclusion: Adults over 18 years of age diagnosed with FM, with the diagnosis previously made by a medical professional under the updated FM diagnostic criteria^[43]. ii) Exclusion: Women in a state of pregnancy or breastfeeding, oncological pain, uncontrolled metabolic disorder, vertigo or a similar condition, or any physical or cognitive impairment that would hinder communication with the investigators and the ability to perform the intervention protocols. As this was a pilot study, a specific number of participants was selected instead of calculating the sample size based on formal statistical power, as the primary aim was to assess the feasibility of the intervention and evaluate participants' acceptance of the technology.

Clinical investigators performed a complete anamnesis and completed a structured clinical form to collect sociodemographic, health, and pharmacological treatment data. This study was approved by the Scientific Ethical Committee of the Universidad San Sebastián (No. 151-23). The study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent modifications^[44]. All patients signed an informed consent form prior to participation.

2.2 Intervention (iVRE)

The iVRE program consisted of twelve sessions (two per week for six weeks), each including 10 min of

warm-up followed by 15 min of exercise using the FitXR game (developed by FITAR LIMITED) on the Oculus Quest 2™ device (Figure 1). The exercise duration was based on recommendations to prevent adverse effects in individuals with chronic pain. Furthermore, several studies using immersive modality devices have demonstrated high satisfaction with protocols lasting between 10 and 20 min^[28,45]. The warm-up consisted of moderate-intensity aerobic exercise on a cycle ergometer. The BORG CR-10 perceived exertion scale was used to determine the intensity^[14]. Subsequently, the participants continued with the FitXR game (Figure 2). Before starting each virtual reality exercise session, the participants had the option to choose from various virtual environments, such as being on a beach or on a building's rooftop. They then selected the difficulty level with three options: beginner, intermediate, or advanced. The difference between these levels lay in the complexity and speed of the exercises.

Each virtual reality session was divided into three phases.

Phase 1: The first 3 min were dedicated to general mobility exercises for the upper and lower limbs and the spine. An avatar guided the participants through their movements and provided verbal cues to ensure proper execution.

Phase 2: This phase represented the primary activity of the game. While standing, the participants had to hit balls approaching them, simulating an aerobox workout. They were asked to strike a yellow ball with their right hand and a blue ball with their left hand. During this phase, the participants were instructed to vary their punches, incorporating movements such as uppercuts, hooks, jabs, and crosses. In addition, they had to avoid a bar that appeared either horizontally or diagonally. Each successful hit earned points.

Phase 3: The final phase was a 2-min cool-down, during which the participants performed general mobility exercises for the spine and limbs, complemented by breathing exercises. Finally, the participants were provided with their scores, congratulated for their performance, and encouraged to continue practising in future sessions.

2.3 Assessment of outcomes

The evaluations were performed at the Physical Therapy Center of the Universidad San Sebastián. Sociodemographic and clinical variables were identified by administering a questionnaire with previously coded closed questions in a personal interview, with information recorded in a clinical record. The handgrip strength questionnaires and evaluation were performed by physiotherapists specialising in musculoskeletal rehabilitation with more than 10 years of clinical experience. The tests were conducted before and after the sixth week of treatment.



Figure 1 The modality of the FitXR game corresponds to aerobox. The objective is to hit the approaching balls: the right hand must hit the yellow ball, and the left hand must hit the blue ball.

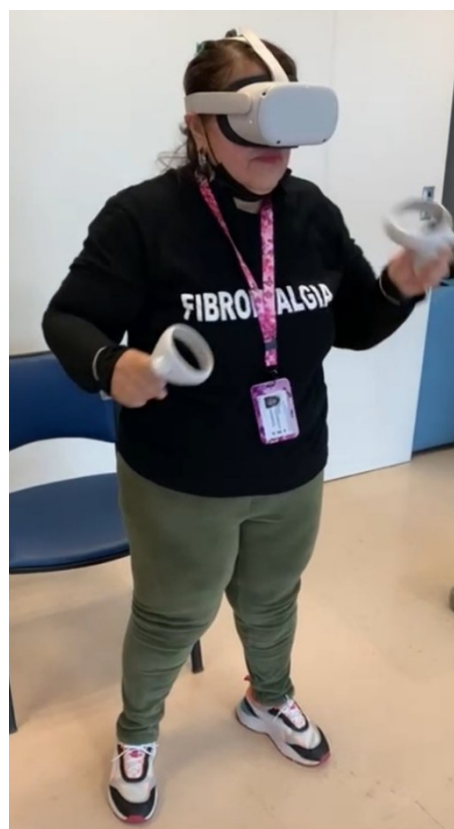


Figure 2 Participant using Oculus Quest 2 device.

2.3.1 Impact of FM on quality of life

The impact of FM on quality of life was assessed using the FIQR. This self-administered test measures the difficulty in performing activities of daily living, the overall influence of the disease, and the severity of symptoms during the previous week. The total scores range from 0 to 100, with higher scores indicating more severe symptoms and disability^[46].

2.3.2 Stress, anxiety and depression

Stress, anxiety and depression were assessed using the DASS-21 questionnaire. This self-administered dimensional test consists of 21 questions that evaluate three categories: stress, anxiety, and depression. It presents four response options for each category, evaluated on a scale from 0 to 3. The score obtained for each category is multiplied by 2, and the result is classified as normal, mild, moderate, severe, or extremely severe^[47].

2.3.3 Handgrip strength

The handgrip strength was measured using a Baseline hydraulic dynamometer (Fabrication Enterprises, Inc., White Plains, NY, USA). The dominant side was evaluated, and the average of three measurements in kilograms was obtained. Each measurement was performed with the subject seated, elbow flexed at 90°, and wrist in a neutral position, and the subject was instructed to squeeze the instrument as hard as possible^[48].

2.3.4 Adverse events

The occurrence of adverse events related to the use of IVR was monitored by a physiotherapist who oversaw the implementation of the intervention protocol. Specifically, the presence of dizziness, headaches, cervical pain, and general discomfort was assessed. The results were documented on a monitoring sheet with the options 'present' or 'absent'.

2.4 Statistical analysis

Participants who completed all intervention protocols were considered for the data analysis. The assumption of normality was evaluated using the Shapiro-Wilk test. Nominal categorical and ordinal variables were analysed and expressed as absolute frequencies and percentages. Discrete and continuous quantitative variables were expressed as means and standard deviations (SDs). Inferential analysis was performed using pre- and post-intervention mean analyses with Student's *t*-test for paired samples. To estimate the magnitude of the difference between the two conditions, the effect size was calculated for the main variables using Cohen's coefficient (*d*). Cohen's coefficients were interpreted as follows. Large effect sizes: $d > 0.8$, moderate effect sizes: $d = 0.5-0.79$, and small effect sizes: $d = 0.2-0.49$ ^[49]. All of these analyses were performed in the JASP® software (Version 0.18.3), considering a significance level of $n < 0.05$.

3 Results

A total of 26 individuals diagnosed with FM were evaluated, among which 20 met the inclusion criteria. Nine participants were excluded for personal reasons unrelated to the intervention protocol, including scheduling conflicts ($n = 1$), weather-related accessibility issues ($n = 3$), acute illnesses unrelated to FM ($n = 3$), unforeseen family obligations ($n = 1$), and scheduling delays that could not be accommodated ($n = 1$). Ultimately, 11 individuals (55%) completed the intervention protocols (10 women) and achieved a 100% adherence rate. The mean age was 40.6 ± 11.2 years. According to World Health Organization guidelines, 81.8% of the population was classified as having a low level of physical activity^[50]. The most commonly

used medications were NSAIDs (100%), antidepressants (81%), and GABAergics (81%). Table 1 presents the sociodemographic characteristics of the participants.

The intervention was adequately developed. No adverse events were reported during the execution of the study. After six weeks of intervention, significant differences were observed between the initial and final measurements for quality of life impact ($p < 0.001$, Cohen's d : 1.48), handgrip strength ($p = 0.043$, Cohen's d : 0.26), depression ($p = 0.034$, Cohen's d : 0.73), and anxiety ($p = 0.034$, Cohen's d : 0.73). However, there were no significant differences in stress ($p > 0.05$). The results are presented in Table 2.

4 Discussion and perspectives for research

The objective of this pilot study was to evaluate the effect of an iVRE program on quality of life, stress, anxiety, depression, and handgrip strength in people with FM. The results showed that a six-week program of exercises performed with immersive VR significantly decreased the impact on quality of life, anxiety levels, and depression. In addition, the results indicated a significant improvement in handgrip strength in people with FM.

Table 1 Sociodemographic characteristics of the sample

| Age (Years) | Mean | SD |
|-------------------|----------|------|
| | 40.6 | 11.2 |
| Sex | <i>n</i> | % |
| Women | 10 | 90.9 |
| Men | 1 | 9.1 |
| Occupation | <i>n</i> | % |
| Technician | 2 | 18.2 |
| Professional | 4 | 36.4 |
| Homeowner | 4 | 36.4 |
| Other | 1 | 9.1 |
| Physical activity | <i>n</i> | % |
| Low intensity | 9 | 81.8 |
| Mild intensity | 2 | 18.2 |
| Drugs | <i>n</i> | % |
| NSAIDs | 11 | 100 |
| Opioids | 3 | 27.3 |
| Cyclobenzaprine | 4 | 36.4 |
| GABAergics | 9 | 81.8 |
| Antidepressants | 9 | 81.8 |

SD: standard deviation, *n*: sample, %: percentage

Table 2 Effects of the iVRE program on FIQR, DASS-21 and handgrip

| Outcome | Pre-test media | SD | Post-test ¹ media | SD | <i>p</i> -value | Cohen's <i>d</i> |
|---------------------------|----------------|-------|------------------------------|-------|------------------|------------------|
| FIQR | 65.70 | 20.83 | 36.74 | 18.69 | <0.001 | 1.48 |
| DASS-21 depression | 8.54 | 6.54 | 5.27 | 4.45 | 0.03 | 0.73 |
| DASS-21 anxiety | 8.18 | 4.16 | 7.00 | 4.94 | 0.03 | 0.73 |
| DASS-21 stress | 11.36 | 5.18 | 9.54 | 4.61 | 0.11 | 0.51 |
| Handgrip Dynamometry (kg) | 16.99 | 6.41 | 20.62 | 6.65 | 0.04 | 0.26 |

¹Measurement after six weeks of iVRE.

FM is a chronic condition characterised by widespread pain, accompanied by a variety of additional symptoms such as fatigue, sleep disturbances, and cognitive problems, often referred to as 'fibrofog' [51]. Although FM is known for its physical manifestations, it also affects the psychological and emotional well-being of patients [52]. These effects can be observed in several conditions within this health dimension, including stress, anxiety, and depression, which intertwine and exacerbate one another, creating a complex cycle that can significantly affect quality of life [53].

In our study, the impact on the quality of life variable had the highest statistical significance and a large effect size. These results are similar to those obtained in a systematic review and meta-analysis that evaluated the effects of VR-based therapy in patients with FM. The review concluded that this approach may effectively reduce the impact on quality of life in patients with FM. These results could be explained by the multisensory stimulation provided by the iVRE and the positive impact of physical exercise, which contribute to improving overall well-being and reducing the perceived severity of symptoms [26]. Another study obtained equivalent results using an aerobic exercise protocol with a cycle ergometer and iVRE. The decrease in the impact on quality of life can mainly be explained by reduced fear of movement and greater self-regulation of symptoms [28]. Different studies have also shown that this improvement in quality of life

indicators is based on positive changes in mood, motivation, and self-efficacy in daily life tasks^[30,31,36].

Anxiety and depression are common problems among individuals with FM. Uncertainty regarding the course of the disease, constant worry about managing symptoms, and the limitations imposed by the condition can contribute significantly to feelings of anxiety. In contrast, depression may be a natural response to chronic pain and the impact it has on daily life. In our study, the anxiety and depression levels decreased significantly following the iVRE program. These results are similar to those obtained in a systematic review that concluded that VR interventions (immersive and non-immersive) of different durations (from 1 to 120 min) can significantly reduce anxiety and depression levels, suggesting that this distraction therapy generates fewer cognitive resources to process pain and associated symptoms in people with chronic pain; however, it suggests further research on mental health outcomes in this population^[54]. In any case, the different exercise programs in FM, either alone^[55] or in combination with VR, reduce levels of depression, improving the mood and sense of well-being^[26,56]. Furthermore, this approach can help to reduce repetitive and negative thoughts by engaging users in activities that require focused concentration. In addition, this type of therapy also allows participants to set achievable goals and receive immediate feedback, fostering a sense of accomplishment, progress, and success in their performance. Stress did not show a significant reduction in our study, partly due to the small sample size, which limited the ability to detect meaningful changes. However, this lack of a significant decrease could also be attributed to the complex nature of stress, which involves emotional factors and intense physiological responses, such as cortisol release and activation of the sympathetic nervous system. Although physical activity may help temporarily reduce cortisol levels, it does not necessarily target long-term modulation or adaptation to stressful situations. In contrast, anxiety and depression, which often have deeper cognitive foundations, can be more effectively addressed through distraction techniques or by altering emotional states^[57]. In contrast, people with FM have been found to present dysregulation of the neuroimmunoendocrine system, with elevated concentrations of cortisol, noradrenaline, and cytokines (IL6–IL8) and reduced serotonin and dopamine levels^[58–60]. These alterations could explain the difficulties in emotional regulation and pain processing^[61]. Although some studies have evaluated the physiological response to VR through biomarkers^[62–64], evidence is still incipient in investigating the biomolecular effects of immersive modalities for people with FM.

Handgrip strength is a reliable tool for measuring general physical capacity and predicting disability and impairment in rheumatic and neuromusculoskeletal conditions^[65,66]. Studies assessing handgrip strength in patients with FM have consistently found that these individuals tend to have decreased grip strength compared with healthy individuals^[7]. This handgrip weakness may result from the interaction between chronic pain, fatigue, and a decreased ability to integrate motor and sensory processing^[6,67]. Our study indicated a significant improvement in handgrip strength in individuals with FM, albeit with a small effect size. These results could be because this therapy generates a distraction status that influences pain processing, thereby reducing inhibition of the handgrip musculature^[68]. In addition, the small effect size could be because the intervention performed did not include strengthening exercises. This is in line with a recent narrative review that focused on the effectiveness of VR interventions for the management of musculoskeletal conditions, which reported that although improvements in grip strength were observed, these were mainly due to the focus on mental attention and not necessarily to an actual increase in strength^[69]. Several studies have suggested continuing to investigate the behaviour of this variable given its importance in the early detection of fall risk and deterioration of quality of life^[8,70,71].

The available literature does not clarify the relevance of sociodemographic characteristics such as the age, sex, or preferences of people with FM to the potential outcomes generated by VR interventions, including the influence of the level of technological literacy of users. In this regard, it would be interesting for future

research to investigate the specific parameters and dosages of such VR intervention programs in general and iVRE in particular that should be adapted to patients with FM. However, these protocols should include positive feedback through verbal stimuli or scoring mechanisms to affect motivation and adherence to treatment positively^[72,73].

The main limitations of this study are as follows: First, the small sample size and non-probabilistic sampling make the results not generalizable; second, the absence of a control group does not allow us to ensure that the results are exclusively attributable to the use of iVRE. In contrast, the strengths of this study lie in providing a proposed intervention protocol for future controlled trials, presenting promising results for the application of innovative exercise treatment in patients with FM, and determining the beneficial effects of iVRE on the study variables in this population.

5 Conclusion

A six-week iVRE program significantly reduced the impact on quality of life, anxiety, and depression levels and significantly improved handgrip strength in people with FM. However, there were no significant changes in stress levels. Thus, iVRE may be a potentially beneficial complementary therapeutic option for the treatment of FM. Future research should build on these results by conducting randomised clinical trials and incorporating systemic biomarkers to identify the potential extent of physiological responses to this therapeutic modality.

Declaration of competing interest

We declare that there are no competing interests.

CRediT authorship contributions statement

Gonzalo Arias-Álvarez: Conceptualisation, performance of the protocols, writing-original draft/review & editing. **Carla Guzmán-Pincheira:** Review & editing. **Claudio Carvajal-Parodi:** Conceptualisation, writing-original draft/review & editing. **Diego González-González:** Performance of the protocols. **Daniel Pecos-Martín:** Review & editing. **José Gómez-Pulido:** Review & editing.

Ethical approval

The study was approved by the Scientific Ethical Committee of the Universidad San Sebastián Republic of Chile (No. 151–23), and was conducted according to the guidelines of the Declaration of Helsinki and the Council for International Organizations of Medical Sciences (CIOMS). All participants voluntarily signed informed consent forms.

References

- 1 Giorgi V, Sirotti S, Romano M E, Marotto D, Ablin J N, Salaffi F, Sarzi-Puttini P. Fibromyalgia: One year in review 2022. *Clinical and Experimental Rheumatology*, 2022, 40(6): 1065–1072
DOI: 10.55563/clinexp Rheumatol/1f9gk2
- 2 Siracusa R, Paola R D, Cuzzocrea S, Impellizzeri D. Fibromyalgia: Pathogenesis, mechanisms, diagnosis and treatment options update. *International Journal of Molecular Sciences*, 2021, 22(8): 3891
DOI: 10.3390/ijms22083891
- 3 Maffei M E. Fibromyalgia: Recent advances in diagnosis, classification, pharmacotherapy and alternative remedies. *International Journal of Molecular Sciences*, 2020, 21(21): 7877
DOI: 10.3390/ijms21217877
- 4 Cabo-Meseguer A, Cerdá-Olmedo G, Trillo-Mata J L. Fibromialgia: Prevalencia, perfiles epidemiológicos y costes económicos. *Medicina Clínica*, 2017, 149(10): 441–448
DOI: 10.1016/j.medcli.2017.06.008
- 5 Bair M J, Krebs E E. Fibromyalgia. *Ann Intern Med*, 2020, 172(5): ITC33–ITC48
DOI: 10.7326/aitc202003030

- 6 da Cunha Melian N T, Branco J H L, Torres G, Andrade A, Matte D L. Relationship between handgrip strength, peripheral muscle strength, and respiratory muscle endurance in women with fibromyalgia: A cross-sectional study. *Acta Fisiátrica*, 2021, 28(2): 97–104
DOI: 10.11606/issn.2317-0190.v28i2a185921
- 7 Salaffi F, Farah S, Di Carlo M. Force-time curve features of handgrip strength in fibromyalgia syndrome. *Scientific Reports*, 2020, 10(1): 3372
DOI: 10.1038/s41598-020-60227-8
- 8 Cigarán-Méndez M, Úbeda-D'Ocasar E, Arias-Buría J L, Fernández-de-Las-Peñas C, Gallego-Sendarrubias G M, Valera-Calero J A. The hand grip force test as a measure of physical function in women with fibromyalgia. *Scientific Reports*, 2022, 12(1): 3414
DOI: 10.1038/s41598-022-07480-1
- 9 Paschali M, Lazaridou A, Paschalis T, Napadow V, Edwards R R. Modifiable psychological factors affecting functioning in fibromyalgia. *Journal of Clinical Medicine*, 2021, 10(4): 803
DOI: 10.3390/jcm10040803
- 10 Elgueta-Aguilera N, Guede-Rojas F, Mendoza C, Carvajal-Parodi C, Jerez-Mayorga D. Self-perceived cognitive function and neuropsychological performance in women with fibromyalgia. *Revista Médica de Chile*, 2022, 150(11): 1450–1457
DOI: 10.4067/s0034-98872022001101450
- 11 do Nascimento B, Franco K, Franco Y, Nunes Cabral C. Can psychological factors be associated with the severity of pain and disability in patients with fibromyalgia? A cross-sectional study. *Physiotherapy Theory and Practice*, 2022, 38(3): 431–440
DOI: 10.1080/09593985.2020.1765439
- 12 Fitzcharles M A, Rampakakis E, Ste-Marie P A, Sampalis J S, Shir Y. The association of socioeconomic status and symptom severity in persons with fibromyalgia. *The Journal of Rheumatology*, 2014, 41(7): 1398–1404
DOI: 10.3899/jrheum.131515
- 13 Lourenço S, Costa L, Rodrigues A M, Carnide F, Lucas R. Gender and psychosocial context as determinants of fibromyalgia symptoms (fibromyalgia research criteria) in young adults from the general population. *Rheumatology*, 2015, 54(10): 1806–1815
DOI: 10.1093/rheumatology/kev110
- 14 Soriano-Maldonado A, Estévez-López F, Segura-Jiménez V, Aparicio V A, Álvarez-Gallardo I C, Herrador-Colmenero M, Ruiz J R, Henriksen M, Amris K, Delgado-Fernández M, Project A Á. Association of physical fitness with depression in women with fibromyalgia. *Pain Medicine*, 2016, 17(8): 1542–1552
DOI: 10.1093/pm/pnv036
- 15 Pulido-Martos M, Luque-Reca O, Segura-Jiménez V, Inmaculada C Á G, Soriano-Maldonado A, Acosta-Manzano P, Gavilán-Carrera B, McVeigh J G, Geenen R, Delgado-Fernández M, Estévez-López F. Physical and psychological paths toward less severe fibromyalgia: A structural equation model. *Annals of Physical and Rehabilitation Medicine*, 2020, 63(1): 46–52
DOI: 10.1016/j.rehab.2019.06.017
- 16 Bidari A, Ghavidel-Parsa B. Nociceptive pain concept, a mechanistic basis for pragmatic approach to fibromyalgia. *Clinical Rheumatology*, 2022, 41(10): 2939–2947
DOI: 10.1007/s10067-022-06229-5
- 17 MacFarlane G J, Kronisch C, Dean L E, Atzeni F, Häuser W, Fluß E, Choy E, Kosek E, Amris K, Branco J, Dincer F, Leino-Arjas P, Longley K, McCarthy G M, Makri S, Perrot S, Sarzi-Putini P, Taylor A, Jones G T. EULAR revised recommendations for the management of fibromyalgia. *Annals of the Rheumatic Diseases*, 2017, 76(2): 318–328
DOI: 10.1136/annrheumdis-2016-209724
- 18 Sarzi-Putini P, Giorgi V, Marotto D, Atzeni F. Fibromyalgia: An update on clinical characteristics, aetiopathogenesis and treatment. *Nature Reviews. Rheumatology*, 2020, 16(11): 645–660
DOI: 10.1038/s41584-020-00506-w
- 19 Aratijo F M, DeSantana J M. Physical therapy modalities for treating fibromyalgia. *F1000Research*, 2019, 8: F1000 Faculty Rev–F1000 Faculty2030
DOI: 10.12688/f1000research.17176.1
- 20 Saracoglu I, Akin E, Aydin Dincer G B. Efficacy of adding pain neuroscience education to a multimodal treatment in fibromyalgia: A systematic review and meta-analysis. *International Journal of Rheumatic Diseases*, 2022, 25(4): 394–404
DOI: 10.1111/1756-185x.14293
- 21 Klemm P, Hudowenz O, Asendorf T, Dischereit G, Müller-Ladner U, Lange U, Tarner I H. Multimodal physical therapy for treating primary and secondary fibromyalgia—German multimodal rheumatologic complex treatment. *European Journal of Physiotherapy*, 2022, 24(3): 158–163
DOI: 10.1080/21679169.2020.1821767
- 22 Sarmiento-Hernández I, de Los Angeles Pérez-Marín M, Nunez-Nagy S, Pecos-Martín D, Gallego-Izquierdo T, Dolores Sosa-Reina M. Effectiveness of invasive techniques in patients with fibromyalgia: systematic review and meta-analysis. *Pain Medicine*, 2020, 21(12): 3499–3511
DOI: 10.1093/pm/pnaa321

- 23 Viderman D, Tapinova K, Dossov M, Seitenov S, Abdildin Y G. Virtual reality for pain management: An umbrella review. *Frontiers in Medicine*, 2023, 10: 1203670
DOI: 10.3389/fmed.2023.1203670
- 24 Xu W G, Liang H N, Baghaei N, Ma X Y, Yu K Y, Meng X R, Wen S Y. Effects of an immersive virtual reality exergame on university students' anxiety, depression, and perceived stress: Pilot feasibility and usability study. *JMIR Serious Games*, 2021, 9(4): e29330
DOI: 10.2196/29330
- 25 Wang L, Huang M J, Yang R, Liang H N, Han J, Sun Y. Survey of movement reproduction in immersive virtual rehabilitation. *IEEE Transactions on Visualization and Computer Graphics*, 2023, 29(4): 2184–2202
DOI: 10.1109/tvcg.2022.3142198
- 26 Cortés-Pérez I, Zagalaz-Anula N, Ibancos-Losada M D R, Nieto-Escámez F A, Obrero-Gaitán E, Osuna-Pérez M C. Virtual reality-based therapy reduces the disabling impact of fibromyalgia syndrome in women: Systematic review with meta-analysis of randomized controlled trials. *Journal of Personalized Medicine*, 2021, 11(11): 1167
DOI: 10.3390/jpm11111167
- 27 Polat M, Kahveci A, Muci B, Günendi Z, Kaymak Karataş G. The effect of virtual reality exercises on pain, functionality, cardiopulmonary capacity, and quality of life in fibromyalgia syndrome: A randomized controlled study. *Games for Health Journal*, 2021, 10(3): 165–173
DOI: 10.1089/g4h.2020.0162
- 28 Gulsen PT M, Soke PT P, Eldemir PT M, Apaydin PT M, Ozkul PT P, Guclu-Gunduz PT P, Akcali MD P. Effect of fully immersive virtual reality treatment combined with exercise in fibromyalgia patients: A randomized controlled trial. *Assistive Technology*, 2022, 34(3): 256–263
DOI: 10.1080/10400435.2020.1772900
- 29 Garcia-Palacios A, Herrero R, Vizcaino Y, Belmonte M A, Castilla D, Molinari G, Baños R M, Botella C. Integrating virtual reality with activity management for the treatment of fibromyalgia: acceptability and preliminary efficacy. *The Clinical Journal of Pain*, 2015, 31(6): 564–572
DOI: 10.1097/ajp.0000000000000196
- 30 Austin P D. The analgesic effects of virtual reality for people with chronic pain: A scoping review. *Pain Medicine*, 2022, 23(1): 105–121
DOI: 10.1093/pm/pnab217
- 31 Matheve T, Bogaerts K, Timmermans A. Virtual reality distraction induces hypoalgesia in patients with chronic low back pain: A randomized controlled trial. *Journal of Neuroengineering and Rehabilitation*, 2020, 17(1): 55
DOI: 10.1186/s12984-020-00688-0
- 32 Goudman L, Jansen J, Billot M, Vets N, De Smedt A, Roulaud M, Rigoard P, Moens M. Virtual reality applications in chronic pain management: Systematic review and meta-analysis. *JMIR Serious Games*, 2022, 10(2): e34402
DOI: 10.2196/34402
- 33 Guede-Rojas F, Andrades-Torres B, Aedo-Díaz N, González-Koppen C, Muñoz-Fuentes M, Enríquez-Enríquez D, Carvajal-Parodi C, Mendoza C, Alvarez C, Fuentes-Contreras J. Effects of exergames on rehabilitation outcomes in patients with osteoarthritis. A systematic review. *Disabil Rehabil*, 2025, 47(5): 1100–1113
DOI: 10.1080/09638288.2024.2368057
- 34 Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev*, 2017, 11: CD008349
DOI: 10.1002/14651858.cd008349.pub4
- 35 Morimoto T, Kobayashi T, Hirata H, Otani K, Sugimoto M, Tsukamoto M, Yoshihara T, Ueno M, Mawatari M. XR (extended reality: virtual reality, augmented reality, mixed reality) technology in spine medicine: Status quo and quo vadis. *Journal of Clinical Medicine*, 2022, 11(2): 470
DOI: 10.3390/jcm11020470
- 36 Abich J, Parker J, Murphy J S, Eudy M. A review of the evidence for training effectiveness with virtual reality technology. *Virtual Reality*, 2021, 25(4): 919–933
DOI: 10.1007/s10055-020-00498-8
- 37 Chen X M, Liu F, Lin S H, Yu L Q, Lin R H. Effects of virtual reality rehabilitation training on cognitive function and activities of daily living of patients with poststroke cognitive impairment: A systematic review and meta-analysis. *Archives of Physical Medicine and Rehabilitation*, 2022, 103(7): 1422–1435
DOI: 10.1016/j.apmr.2022.03.012
- 38 Torpil B, Şahin S, Pekçetin S, Uyanık M. The effectiveness of a virtual reality-based intervention on cognitive functions in older adults with mild cognitive impairment: A single-blind, randomized controlled trial. *Games for Health Journal*, 2021, 10(2): 109–114
DOI: 10.1089/g4h.2020.0086
- 39 Zhu K Y, Zhang Q Y, He B W, Huang M Z, Lin R, Li H. Immersive virtual reality-based cognitive intervention for the improvement of cognitive function, depression, and perceived stress in older adults with mild cognitive impairment and mild dementia: Pilot pre-post study. *JMIR Serious Games*, 2022, 10(1): e32117

DOI: 10.2196/32117

- 40 Christensen S W M, Heidi Almsborg M, Thomas Sogaard Vain M, Vaegter H B. The effect of virtual reality on cold pain sensitivity in patients with fibromyalgia and pain-free individuals: a randomized crossover study. *Games for Health Journal*, 2023, 12(4): 295–301
DOI: 10.1089/g4h.2022.0138
- 41 Mocco A, Valmaggia L, Bernardi L, Alfieri M, Tarricone I. Enhancing physical activity with immersive virtual reality: A systematic review. *Cyberpsychology, Behavior and Social Networking*, 2024, 27(5): 303–317
DOI: 10.1089/cyber.2023.0394
- 42 Baghaei N, Chitale V, Hlasnik A, Stemmet L, Liang H N, Porter R. Virtual reality for supporting the treatment of depression and anxiety: Scoping review. *JMIR Mental Health*, 2021, 8(9): e29681
DOI: 10.2196/29681
- 43 Wolfe F, Clauw D J, Fitzcharles M A, Goldenberg D L, Häuser W, Katz R L, Mease P J, Russell A S, Russell I J, Walitt B. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Seminars in Arthritis and Rheumatism*, 2016, 46(3): 319–329
DOI: 10.1016/j.semarthrit.2016.08.012
- 44 World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *The Journal of the American Medical Association*, 2013, 310(20): 2191–2194
DOI: 10.1001/jama.2013.281053
- 45 Darnall B D, Krishnamurthy P, Tsuei J, Minor J D. Self-administered skills-based virtual reality intervention for chronic pain: Randomized controlled pilot study. *JMIR Formative Research*, 2020, 4(7): e17293
DOI: 10.2196/17293
- 46 Bennett R M, Friend R, Jones K D, Ward R, Han B K, Ross R L. The revised fibromyalgia impact questionnaire (FIQR): Validation and psychometric properties. *Arthritis Research & Therapy*, 2009, 11(4): R120
DOI: 10.1186/ar2783
- 47 Vargas-Olano M O, Cárdenas-Ojeda S P, Herrera-Delgado C. Un recurso Para atención primaria de la salud mental. DASS-21, propiedades psicométricas. *Revista Peruana de Investigación En Salud*, 2022, 6(3): 141–148
DOI: 10.35839/repis.6.3.1481
- 48 Bohannon R W. Hand-grip dynamometry predicts future outcomes in aging adults. *Journal of Geriatric Physical Therapy*, 2008, 31(1): 3–10
DOI: 10.1519/00139143-200831010-00002
- 49 Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Frontiers in Psychology*, 2013, 4: 863
DOI: 10.3389/fpsyg.2013.00863
- 50 Bull F C, Al-Ansari S S, Biddle S, Borodulin K, Buman M P, Cardon G, Carty C, Chaput J P, Chastin S, Chou R, Dempsey P C, DiPietro L, Ekelund U, Firth J, Friedenreich C M, Garcia L, Gichu M, Jago R, Katzmarzyk P T, Lambert E, Leitzmann M, Milton K, Ortega F B, Ranasinghe C, Stamatakis E, Tiedemann A, Troiano R P, van der Ploeg H P, Wari V, Willumsen J F. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *British Journal of Sports Medicine*, 2020, 54(24): 1451–1462
DOI: 10.1136/bjsports-2020-102955
- 51 Kratz A L, Whibley D, Kim S, Sliwinski M, Clauw D, Williams D A. Fibrofog in daily life: An examination of ambulatory subjective and objective cognitive function in fibromyalgia. *Arthritis Care Res (Hoboken)*. 2020, 72(12):1669–1677
DOI: 10.1002/acr.24089
- 52 Wolfe F, Rasker J J, Ten Klooster P, Häuser W. Subjective cognitive dysfunction in patients with and without fibromyalgia: Prevalence, predictors, correlates, and consequences. *Cureus*, 2021, 13(12): e20351
DOI: 10.7759/cureus.20351
- 53 Cetingok S, Seker O, Cetingok H. The relationship between fibromyalgia and depression, anxiety, anxiety sensitivity, fear avoidance beliefs, and quality of life in female patients. *Medicine*, 2022, 101(39): e30868
DOI: 10.1097/md.00000000000030868
- 54 Wong K P, Tse M M Y, Qin J. Effectiveness of virtual reality-based interventions for managing chronic pain on pain reduction, anxiety, depression and mood: a systematic review. *Healthcare*, 2022, 10(10): 2047
DOI: 10.3390/healthcare10102047
- 55 Sosa-Reina M D, Nunez-Nagy S, Gallego-Izquierdo T, Pecos-Martin D, Monserrat J, Álvarez-Mon M. Effectiveness of therapeutic exercise in fibromyalgia syndrome: A systematic review and meta-analysis of randomized clinical trials. *BioMed Research International* , 2017, 2017: 2356346
DOI: 10.1155/2017/2356346
- 56 Villafaina S, Collado-Mateo D, Fuentes J P, Rohlfis-Domínguez P, Gusi N. Effects of exergames on brain dynamics in women with fibromyalgia: A randomized controlled trial. *Journal of Clinical Medicine*, 2019, 8(7): 1015
DOI: 10.3390/jcm8071015
- 57 Hinds J A, Sanchez E R. The role of the hypothalamus–pituitary–adrenal (HPA) axis in test-induced anxiety: Assessments, physiological

- responses, and molecular details. *Stresses*, 2022, 2(1): 146–155
DOI: 10.3390/stresses2010011
- 58 Otero E, Gálvez I, Ortega E, Hinchado M D. Influence of chronic fatigue syndrome codiagnosis on the relationship between perceived and objective psychoneuro-immunoendocrine disorders in women with fibromyalgia. *Biomedicines*, 2023, 11(5): 1488
DOI: 10.3390/biomedicines11051488
- 59 Favretti M, Iannuccelli C, Di Franco M. Pain biomarkers in fibromyalgia syndrome: Current understanding and future directions. *International Journal of Molecular Sciences*, 2023, 24(13): 10443
DOI: 10.3390/ijms241310443
- 60 Martins D F, Viseux F J F, Salm D C, Ribeiro A C A, da Silva H K L, Seim L A, Bittencourt E B, Bianco G, Moré A O O, Reed W R, Mazzardo-Martins L. The role of the vagus nerve in fibromyalgia syndrome. *Neuroscience and Biobehavioral Reviews*, 2021, 131: 1136–1149
DOI: 10.1016/j.neubiorev.2021.10.021
- 61 Montoro C I, Galvez-Sánchez C M. The mediating role of depression and pain catastrophizing in the relationship between functional capacity and pain intensity in patients with fibromyalgia. *Behavioural Neurology*, 2022, 2022: 9770047
DOI: 10.1155/2022/9770047
- 62 Rubio-Zarapuz A, Apolo-Arenas M D, Tomas-Carus P, Tornero-Aguilera J F, Clemente-Suárez V J, Parraca J A. Comparative analysis of psychophysiological responses in fibromyalgia patients: Evaluating neuromodulation alone, neuromodulation combined with virtual reality, and exercise interventions. *Medicina*, 2024, 60(3): 404
DOI: 10.3390/medicina60030404
- 63 Al-Sharman A, Ismaiel I A, Khalil H, El-Salem K. Exploring the relationship between sleep quality, sleep-related biomarkers, and motor skill acquisition using virtual reality in people with Parkinson's disease: A pilot study. *Frontiers in Neurology*, 2021, 12: 582611
DOI: 10.3389/fneur.2021.582611
- 64 Medina S, Clarke S, Hughes S. Virtual reality-based analgesia: Towards a novel framework for the biopsychosocial management of chronic pain. *British Journal of Anaesthesia*, 2024, 133(3): 486–490
DOI: 10.1016/j.bja.2024.06.005
- 65 Kulyk M, Dzhus M. Handgrip strength, physical activity, and body composition in young adults with juvenile idiopathic arthritis. *Pain, Joints, Spine*, 2023, 13(2): 101–107
DOI: 10.22141/pjs.13.2.2023.372
- 66 Kapuczinski A, Soyfoo M S, De Breucker S, Margaux J. Assessment of sarcopenia in patients with fibromyalgia. *Rheumatology International*, 2022, 42(2): 279–284
DOI: 10.1007/s00296-021-04973-6
- 67 Seo N J, Sindhu B S, Shechtman O. Influence of pain associated with musculoskeletal disorders on grip force timing. *Journal of Hand Therapy*, 2011, 24(4): 335–344
DOI: 10.1016/j.jht.2011.06.004
- 68 Tavares L F, Germano Maciel D, Pereira Barros da Silva T Y, de Brito Vieira W H. Comparison of functional and isokinetic performance between healthy women and women with fibromyalgia. *Journal of Bodywork and Movement Therapies*, 2020, 24(1): 248–252
DOI: 10.1016/j.jbmt.2019.05.024
- 69 Brady N, McVeigh J G, McCreesh K, Rio E, Dekkers T, Lewis J S. Exploring the effectiveness of immersive Virtual Reality interventions in the management of musculoskeletal pain: A state-of-the-art review. *Physical Therapy Reviews*, 2021, 26(4): 262–275
DOI: 10.1080/10833196.2021.1903209
- 70 Vaishya R, Misra A, Vaish A, Ursino N, D'Ambrosi R. Hand grip strength as a proposed new vital sign of health: A narrative review of evidences. *Journal of Health, Population, and Nutrition*, 2024, 43(1): 7
DOI: 10.1186/s41043-024-00500-y
- 71 Gerdle B, Dahlqvist Leinhard O, Lund E, Bengtsson A, Lundberg P, Ghafouri B, Forsgren M F. Fibromyalgia: Associations between fat infiltration, physical capacity, and clinical variables. *Journal of Pain Research*, 2022, 15: 2517–2535
DOI: 10.2147/jpr.s376590
- 72 Mouatt B, Smith A E, Mellow M L, Parfitt G, Smith R T, Stanton T R. The use of virtual reality to influence motivation, affect, enjoyment, and engagement during exercise: A scoping review. *Frontiers in Virtual Reality*, 2020, 1: 564664
DOI: 10.3389/frvir.2020.564664
- 73 Chan G, Arya A, Orji R, Zhao Z. Motivational strategies and approaches for single and multi-player exergames: A social perspective. *PeerJ. Computer Science*, 2019, 5: e230
DOI: 10.7717/peerj-cs.230