Cristiano Martins

Patient-centred education and exercise versus exercise alone for patients with fibromyalgia: a randomized controlled trial

Dissertação de Mestrado em Fisioterapia

Relatório de Projeto de Investigação

Professora Doutora Carmen Caeiro

Setembro de 2021

Relatório do Projeto de Investigação apresentado para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Fisioterapia, área de especialização em Fisioterapia em Condições Músculo-Esqueléticas realizada sob orientação científica da Professora Doutora Carmen Caeiro

Declaração

Declaro que este Relatório de Projeto de Investigação é o resultado da minha investigação pessoal e independente. O seu conteúdo é original e todas as fontes consultadas estão devidamente mencionadas no texto, nas notas e na bibliografia.

O Candidato,

_____

(Cristiano Gonçalves Martins)

Setúbal, 6 de setembro de 2021

Declaro que este Relatório de Projeto de Investigação se encontra em condições de ser apresentada a provas públicas.

A orientadora,

_____

(Professora Doutora Carmen Caeiro)

Setúbal, 6 de setembro de 2021

“Fibromyalgia is not an illness where you can walk into a doctor’s office and…he will have a ready-made prescription for you…it needs to be very much a team experience. He needs to learn as much, if not more, from you as he can share with you (…)”

Este trabalho é financiado por fundos nacionais através da FCT - Fundação para a Ciência e Tecnologia, I.P., no âmbito do projeto PTDC/LLT-OUT/29231/2017

AGRADECIMENTOS

Durante os últimos anos, tive o privilégio de estar envolvido num projeto desafiante, que em muito contribuiu para o meu desenvolvimento pessoal e profissional, mas a sua conclusão não teria sido possível sem o apoio e a contribuição de diversas pessoas.

Agradeço à Professora Doutora Carmen Caeiro, maestrina deste projeto, pela confiança depositada no meu trabalho, mesmo sabendo que a distância poderia ocasionar algumas contrariedades. Foram dois anos de circunstâncias inesperadas. O seu compromisso com a excelência, a sua capacidade de (re)organização e de resolução de adversidades constituem para mim uma referência profissional.

Obrigado à Patrícia Falcão, fisioterapeuta que implementou as intervenções e a parte operacional deste projeto. Foste exemplar durante todo o processo Patrícia, desde a divulgação até à implementação e organização da recolha de dados – os resultados que obtivemos foram sobretudo graças a ti, muito obrigado pelo teu trabalho!

Agradeço às participantes do programa por, voluntariamente, terem aceitado fazer parte desta investigação. É por vocês e graças a vocês que aprendemos e nos reinventamos todos os dias. A vossa capacidade de resiliência, boa disposição e disponibilidade marcaram o meu espírito e aguçaram a minha sensibilidade.

Agradeço igualmente à Berta Antunes, colega com quem tive oportunidade de discutir e trocar conhecimentos ao longo desta jornada.

Não perco a oportunidade de agradecer a todos os professores envolvidos não só no mestrado como também na licenciatura. O humanismo e espírito crítico desenvolvidos são atributos preciosos que levo para a vida. A ESS-IPS será sempre a minha casa.

Agradeço à minha esposa e companheira de aventuras, Nina, pela presença e pelo constante apoio. Tornaste este desafio muito mais leve e agradável, repleto de amor, carinho e sabedoria. Há quatro anos atrás estávamos na estrada a sonhar com isto. Agora que concretizámos este sonho, é tempo de voltar à estrada.

Agradeço aos meus pais, por me terem proporcionado as condições para estudar no ensino superior e por me terem dado o livre-arbítrio na escolha do meu caminho profissional. A vossa persistência, coragem e espírito trabalhador são uma inspiração para mim. Agradeço à minha irmã por desde cedo ter estado na retaguarda a zelar por mim, participando ativamente na minha formação e educação enquanto homem.

RESUMO

Educação centrada no utente e exercício *versus* exercício em indivíduos com fibromialgia – estudo randomizado controlado

Cristiano Martins e Carmen Caeiro

Introdução: O exercício e a educação constituem o tratamento não-farmacológico de primeira linha recomendado para a fibromialgia. **Objetivo**: O objetivo deste estudo foi investigar os efeitos de um programa de 8 semanas que combina educação centrada no utente e exercício *versus* exercício na intensidade da dor, incapacidade funcional e impacto da fibromialgia e perceção global de mudança na dor e funcionalidade. **Metodologia**: Sessenta indivíduos com fibromialgia foram aleatoriamente distribuídos pelo grupo experimental (exercício e educação) ou pelo grupo controlo (exercício). A medida de avaliação primária foi a intensidade da dor, avaliada pela Escala Numérica da Dor e a secundária foi a incapacidade, avaliada pela versão portuguesa da *Revised Fibromyalgia Impact Questionnaire*, assim como a perceção global de mudança, avaliada pela versão Portuguesa da *The Patient Global Impression of Change*. Os participantes foram avaliados antes da intervenção, 4 semanas após o início e no final das 8 semanas de intervenção. A significância da efetividade das intervenções para a dor e para a incapacidade foi avaliada com uma *two-way mixed-model ANOVA*, enquanto o *chi-square tests of independence* foi utilizado para avaliar a relevância clínica dos resultados. **Resultados**: Trinta participantes em cada grupo foram analisados no final da intervenção. Não se verificou efeito de interação entre grupo e tempo para a intensidade da dor (p=.488) nem para a incapacidade (p=.370). Verificou-se que o efeito do tempo foi estatisticamente significativo para a intensidade da dor (p<.001) e para a incapacidade (p<.001). O efeito de grupo foi estatisticamente significativo para a intensidade da dor em favor do grupo de controlo (p=.003). A análise da relevância clínica revelou que não houve diferenças estatisticamente significativas entre os grupos para a intensidade da dor (p=.432), incapacidade (p=.405) e perceção global de mudança da dor (p=.071) e da incapacidade (p=.100). A análise do risco relativo demonstrou que o grupo experimental apresentou 1.3 mais probabilidade de atingir resultados com relevância clínica na intensidade da dor. **Conclusão**: Ambos os tratamentos foram efetivos na redução da dor e da incapacidade. Um programa de exercício combinado com educação não é mais efetivo do que um programa de exercício isolado para a diminuição da dor e incapacidade em indivíduos com fibromialgia. Proporções semelhantes de indivíduos em ambos os grupos alcançaram melhorias clinicamente significativas para ambas as medidas de resultados, mas o grupo experimental apresentou mais probabilidade de atingir resultados com relevância clínica na intensidade da dor.

Palavras-chave: Fibromialgia; estudo randomizado controlado; exercício; educação centrada no utente.

ABSTRACT

Patient-centred education and exercise versus exercise alone for patients with fibromyalgia: a randomized controlled trial

Cristiano Martins and Carmen Caeiro

Background: Non-pharmacological therapeutic interventions are highly recommended for treating fibromyalgia. **Objectives:** To compare the effectiveness of an 8-week intervention programme who combine patient-centred education and exercise versus exercise alone on pain intensity, disability and patient's global impression of change for pain and function. **Methods**: Sixty fibromyalgia patients were randomly allocated to the experimental group (education and exercise programme) or control group (exercise alone). The primary outcome was pain intensity, assessed by the Numeric Pain Scale and the secondary outcome was disability, assessed by the Portuguese Revised Fibromyalgia Impact Questionnaire and the patient's global impression of change, assessed by the Portuguese version of the Patient Global Impression of Change. The participants were assessed at baseline, week 4 and week 8. Two-way mixed-model Anova was used for pain intensity and disability while the clinical relevance was examined using chi-square tests of independence. **Results**: Thirty patients each group were analysed at the end of the interventions. No significant group-by-time interactions were found neither for pain intensity (p=.488) nor for disability (p=.370). Significant effects of time were found for pain intensity (p<.001) and disability (p<.001). Significant effects of group were found for the control group on pain intensity (p=.003). Clinical relevance showed no significant differences between groups at the end of the interventions for pain intensity (p=.432), disability (p=.405), and patient global impression of change for pain (p=.071) and function (p=.100). Risk Relative revealed that the experimental group have 1.3 more probability to achieve clinically relevant outcomes for pain intensity. **Conclusion**: Both treatments were effective for decreasing pain intensity and disability. A combined exercise and education program seems not superior to exercise alone in reducing pain intensity and disability for individuals with fibromyalgia. Similar proportions of patients achieved clinically meaningful improvements for both outcomes, but the experimental group have more probability to achieve clinically relevant outcomes in terms of pain intensity.

Keywords: Fibromyalgia; randomized controlled trial; exercise; patient-centred education.

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LIST OF ABBREVIATIONS

FM - Fibromyalgia

MSK - Musculoskeletal

IASP - International Association for the Study of Pain

CS - Central sensitization

HRQOL - Health-related quality of life

BMI - Body Mass Index

AE - Aerobic

STG - Strength

STR - Stretching

BPS - Biopsychosocial

CLBP - Chronic low back pain

PNE - Neuroscience Education

RCT - Randomized control trials

ESS/IPS - Escola Superior de Saúde do Instituto Politécnico de Setúbal

CEDOC - Chronic Diseases Research Centre

EXP - Experimental group

CONT - Control group

WPI - Widespread Pain Index

SSS - Severity Symptoms Scale

NRPS - Numeric Rating Scale for Pain

MCID - Minimal clinically important change

FIQr - Revised Fibromyalgia Impact Questionnaire

FIQ - Fibromyalgia Impact Questionnaire

PGIC - Patient Global Improvement of Change Scale

1RM - One-repetition maximum

HRR - Heart rate reserve

RR - Relative Risk

NNT - Number needed to treat

MI - Multiple imputation

MCAR - Missing completely at random

MAR - Missing at random

MNAR - Missing not at random

SD - Standard deviation

CCA - Complete cases analysis

HeiQ - The Health Education Impact Questionnaire

TEM - Treatment effect modifiers

PASS - Patient acceptable symptomatic state

EULAR - European League Against Rheumatism

INTRODUCTION

Fibromyalgia (FM) is a chronic musculoskeletal (MSK) pain disorder with an unclear and multifactorial pathophysiology, classified as a chronic primary pain syndrome by the International Association for the Study of Pain (IASP) (Treede et al., 2019; Álvarez-Gallardo et al., 2018; Cheng, Wong, Hui, Chung, & Wong, 2018). It is characterised clinically by chronic widespread pain, sleep disturbances, cognitive dysfunction, fatigue and functional symptoms (Wolfe et al., 2011).

Some hypotheses can be proposed with respect to the pathogenic mechanisms of this condition. Studies have demonstrated peripheral mechanisms alterations in patients with FM, such as joints low-grade chronic inflammation (Andrade et al., 2017)and the presence of small fibre neuropathy (Grayston et al., 2019). Other researchers defend that the development of the disease is characterized by central sensitization (CS) due to widespread musculoskeletal pain, amplifying peripheral input and/or generating the perception of pain in the absence of a noxious stimulus (Cheng et al., 2018; Häuser, Ablin, Perrot, & Fitzcharles, 2017; Sluka & Clauw, 2016). However, researchers argue that the evidence for explaining CS in widespread pain is limited, and no definitive method of diagnosing is currently proposed (Arendt-Nielsen et al., 2018).

Abnormalities in central pain processing are generally accepted as both peripheral and central components seem to play an important role in the establishment and maintenance of FM (Eller-Smith, Nicol, & Christianson, 2018; Lee, Nassikas & Clauw, 2011). Studies have demonstrated differences in pain perception through quantitative sensory testing methods and functional magnetic resonance imaging. FM patients present lower pressure pain thresholds, enhanced temporal summation and cortical augmentation of pain processing when compared to healthy controls (Geisser et al., 2003; Staud et al., 2003; Gracely, Petzke, Wolf, & Clauw, 2002).

Although the etiology of FM is still unknown, evidence suggests that factors known to contribute to the development of this syndrome includes abnormal neuroendocrine system and autonomic nervous system functioning, as well as environmental triggers such as psychosocial/life stressors and trauma (Häuser & Jones, 2019; Cheng et al., 2018; Dougados & Perrot, 2017). It is also widely

accepted that cognitive, affective, and behavioural variables are related to the development and maintenance of this syndrome (Lami, Martínez, Miró, Sánchez, & Guzmán, 2018).

The global mean prevalence of FM spreads from .5 to 12%, with a higher prevalence reported in females, with an increased prevalence in middle age (50−59 years), dropping off in the oldest age groups (80+ years) (Arnold et al., 2019; Queiroz, 2013; Wolfe, Brähler, Hinz, & Häuser, 2013; Branco et al., 2010). In Portugal, fibromyalgia prevalence is 1.7% (1.1;2.1%), which seems to correspond to approximately 200.000 individuals (Branco et al., 2016), although the condition is still considered underdiagnosed by many researchers (Arnold et al., 2019; Hadker et al., 2011; Choy et al., 2010). The suggested annual incremental costs are up to approximately 12 billion euros for a population of 80 million, for every year these patients are not treated (Spaeth, 2009). FM patients take more medication, make six more yearly medical visits, and show a higher average number of work days missed or early retirement due to disability (Sicras-Mainar et al., 2009).

FM has a negative impact on individuals' health-related quality of life (HRQOL) (Rowe et al., 2019; Campos & Vázquez, 2012; Arnold et al., 2008). The most frequently experienced physical symptoms are pain, stiff joints, diffuse tenderness at multiple tender points and loss of strength (Glattacker, Opitz, & Jäckel, 2010; Wolfe et al., 1990). Patients often suffer from multiple cognitive impairments, such as recurrent headaches, fatigue, disturbances of sleep, memory and concentration (Galvez-Sánchez, Duschek & Reyes, 2019; Choy, 2015; English, 2014). Mood disorders are also frequently encountered in patients with FM including depression, anxiety, panic disorder and difficulty to cope with stressful situations (Eller-Smith et al., 2018). In Portugal, FM is the third rheumatic disease with worse quality of life and disability, the second rheumatic disease most associated with depression and the most associated with the presence of anxiety (Branco et al., 2016).

Physical inactivity, sedentary lifestyles and higher Body Mass Index (BMI) have also been suggested as factors associated with FM (Galvez-Sánchez et al., 2019; Kim, Luedtke, Vincent, Thompson & Oh, 2012). Moreover, fear of movement, avoidance behaviours towards physical activity and pain catastrophizing were correlated with

higher levels of pain, emotional distress, and disability (Lami et al., 2018; Nijs et al., 2013). These factors can lead to an enhanced state of self-awareness of pain sensations, a reduction in the threshold of pain and a prevalence of fear of pain and activity (English, 2014; Turk, Robinson & Burkwinkle, 2004).

Exercise is the most recommended non-pharmacological therapeutic interventions (Thieme, Mathys & Turk, 2017; Macfarlane et al., 2017). Several studies have demonstrated that individuals with fibromyalgia can perform without any harm different types of exercise, such as aerobic (AE), strength (STG) and stretching (STR) exercises (Andrade, Dominski & Sieczkowska, 2020; Andrade et al., 2018; Bidonde et al., 2017; Geneen et al., 2017; Gavi et al., 2014; Mannerkorpi, Nordeman, Ericsson, & Arndorw, 2009). AE and STG exercises seem to have a positive impact on reducing pain and improving quality of life while STR can improve the physical and mental component of HRQOL in people with FM (Andrade et al. 2020; Sosa-Reina et al., 2017). Still, there is insufficient evidence to suggest superiority of one over the other (Häuser et al., 2017; Macfarlane et al., 2017). In their umbrella review, Andrade et al. (2020) found that a poor description of the exercise protocols in terms of the type of exercise, intervention time, volume and intensity of training, was the most important limitation among clinical trials. Another limitation that emerged was the heterogeneity of the effect size found in those studies.

International recommendations suggest an optimal management beginning with patient education regarding the current knowledge of FM, the biopsychosocial (BPS) model and the biological and psychosocial aspects that contributes to the development and maintenance of this syndrome (Macfarlane et al., 2017; Häuser et al., 2017). Patients with diffuse chronic MSK pain who are poorly informed about their pain have less tolerance to it, present greater catastrophic thoughts and maladaptive coping strategies (Garcia-Rios et al., 2019; Malfliet et al., 2017). Moreover, education should ensure that patients have an active participation in applying healthy lifestyle practices, be able to self-manage their symptoms and engage in regular exercise (Häuser et al., 2017; Fitzcharles et al., 2013).

In the field of physiotherapy, two different educational interventions have been investigated for the treatment of various chronic MSK pain disorders, including FM, chronic low back pain (CLBP), chronic Whiplash, and chronic fatigue syndrome. These are Pain Neuroscience Education (PNE) and Self-Management Programs.

PNE is an educational intervention that aims to guide patients through the reconceptualization of their pain from a biomedical model towards a BPS understanding of this phenomenon. It requires to educate patients about the neurophysiology, neurobiology, processing and representation of pain, with the purpose to decrease pain and disability (King et al., 2018; Butler & Moseley, 2003). Moseley (2007) has identified four key points to explore during this process: pain is not a measure of the state of the tissues; pain is modulated by many factors such as somatic, psychological and social; the relationship between pain and the state of the tissues becomes less predictable as pain persists; and that pain can be conceptualised with the implicit perception that tissue is in danger. In their systematic review of randomized control trials (RCT), Louw, Zimney, Puentedura and Diener (2016) found that PNE is an effective intervention for improving pain, disability, psychosocial variables such as pain catastrophizing, fear-avoidance and behaviours towards movement in chronic MSK pain disorders.

Self-management interventions are patient education programmes that intend to increase patients' ability to self-manage their symptoms, treatment as well as physical and psychosocial consequences of living with chronic pain (Banerjee, Hendrick, Bhattacharjee & Blake, 2017). During this process, the patients are encouraged to create person-centred goals and achievable plans, through an interactive and collaborative care with the healthcare professionals, promoting patients' empowerment. The intervention is not focused on symptoms treatment but to improve pain management and support patients during the rehabilitation process (Pearson et al., 2020; Du et al., 2017; Mehlsen, Heegaard, & Frostholm, 2015). In their systematic review of RCT, Du et al. (2017) have investigated the effectiveness of self-management programs on CLBP. The authors found that self-management programs are a safe strategy, with moderate effect on pain intensity and small to moderate effects on disability.

To promote greater effects on outcomes, literature suggests longer duration of the educational components (Watson et al., 2019). Amer-Cuenca et al. (2020) have searched for the effectiveness of different PNE dosages on central nociceptive processing, pain intensity, disability, and psychological variables in patients with FM. In a four-arms RCT, the authors compared a high PNE dose (6 sessions of 45 minutes each, one session per week) with a low concentrated PNE dose (2 sessions of 45 minutes each, one session per week), a dilute low dose (6 sessions of 15 minutes each, one session per week) and a control group who received 2 sessions of biomedical education (45minutes, one session per week). The authors found that regardless of its dosage, PNE and biomedical education seemed to produce similar improvements on central nociceptive processing, pain catastrophizing and pain anxiety. Yet, from baseline to three months follow-up, a higher dosage of PNE (six sessions of 45 minutes) appeared to present superior effects on pain intensity than lower dosages of PNE (two sessions of 45 minutes or six sessions of 15 minutes) and biomedical education. To improve long-term outcomes, Bernardy, Klose, Welsch and Hauser (2018) suggest up to 75h of educative interventions in patients with FM.

Some limitations should be considered when educating patients with FM. Patient education alone has not proved to be effective for pain, disability or HRQOL (Bernardy et al., 2018; Elizagaray-Garcia, Muriente-Gonzalez & Gil-Martinez, 2016). Nevertheless, there is evidence of the effectiveness when combining patient education with exercise for decreasing pain, disability, fatigue and improving HRQOL in the short, medium and long term (Giannotti et al., 2014; Martín et al., 2014; Häuser, Bernardy, Arnold, Offenbächer & Schiltenwolf, 2009; Mannerkorpi, Nordeman, Ericsson, & Arndorw, 2009; King, Wessel, Bhambhani, Sholter, & Maksymowych, 2002). However, the results of a RCT in FM combining exercise and education showed small to moderate effect sizes and the quality was low to moderate (Garcia-Rios et al., 2019).

Previous research has emphasised the need for a personalized treatment approach and an effective method for educating patients living with FM (Fitzcharles et al., 2017). Complex theoretical biomedical explanations seem to work poorly on the majority of patients (Hyland et al., 2016), given that the disease can impact the

patients' capacity of concentration, the ability of remembering basic aspects of daily life and the accomplishment of cognitive tasks (Pearson et al., 2020; Pires, Costa, Martins & Cruz, 2018). Evidence also demonstrates that people with FM do not feel heard or believed during their encounters with health care providers (McMahon, Murray, Sanderson & Daiches 2012). Similar conclusions were reported by Allvin, Fjordkvist and Blomberg (2019) with other chronic MSK pain such as CLBP. The author's pointed out that persons with CLBP feel stigmatized, do not perceive to be seen and understood as a person and have a desire to be taken care and listened. Such unfavourable encounters with the healthcare providers might affect the adjustment process of the disease, delay the access to appropriate treatment as well as threaten the identity and integrity of the patient (Sallinen, Mengshoel & Solbrække, 2019).

The results of a research study conducted recently in Portugal with individuals with non-specific CLBP underline the importance on focusing the educational approaches on the patient's needs and expectations (Caeiro, Moore & Price, 2021). The author highlighted the patients need for an explanatory model that assimilated their personal experience with their clinical narratives (Caeiro et al., 2021). Although there was no FM patients included in this study, similar pathophysiologic mechanisms such as CS can be found in both conditions (Henry, Chiodo, & Yang, 2011; Branco, 2010) and the fact that these populations present similar cultural background and shared the same National Health System, allows us to transfer, with some limitations, these results to the Portuguese population with FM.

Current recommendations for the treatment of chronic MSK pain advocates a BPS and patient-centred approach to communicate and educate patients to guide a non-pharmacological treatment (Foster et al., 2018). The patient-centred approach when educating patients is closely related to the BPS model. Communication is used to share information and responsibility during the treatment process, incorporating the needs and perspectives of individual patients. Within a patient-centred approach, healthcare providers demonstrate respect on behalf of the patient's knowledge and experience (Hiller & Delany, 2018).

Clinical narratives are considered a useful tool to collect, interpret and share clinical information, consenting patients to express their feelings, worries and doubts about the disease (Fioretti et al., 2016). Telling a narrative is a cognitive process that requires the reorganisation of a lived experience in a culturally accepted form (Sallinen, Leena & Peltokallio, 2011). Such process allows critical reflexion and dialectical discourse to emerge – which can lead to a change in beliefs, feelings, knowledge, behaviours and values linked to the illness experience (Barclay-Goddard, King, Dubouloz & Schwartz, 2012; Mezirow, 2003). The main goal of this approach is to enable a shift on the patient´s meaning perspectives and behaviours, promoting a reconstruction of an identity that incorporates the disease (Dubouloz et al., 2010; Glattacker et al., 2010).

The integration of the clinical narratives into an educational program combined with exercise have been barely explored in individuals with FM. It might be a promising form of tailored treatment approach to reduce pain and disability and empower the patients through the self-management of their conditions.

Considering previous information, the main purpose of this study was to investigate the effectiveness of combining exercise with a patient-centred education approach compared to exercise alone in individuals with fibromyalgia on pain intensity, disability and patient's global impression of change.

METHODS

Study design

This study design was a prospective, parallel, double-bind, multi-centre, randomised controlled trial that evaluated the clinical effectiveness of a treatment that combines exercise and education (CEE) with exercise alone (EXE) in patients with fibromyalgia, with assessments at baseline, week 4 and at the end of intervention at week 8. This trial followed the recommendations of CONSORT guidelines (Moher et al., 2010). The study was approved by the local ethics committee of Escola Superior de Saúde do Instituto Politécnico de Setúbal (ESS-IPS), Centro Hospitalar de Setúbal and Centro Hospitalar Lisboa Ocidental - Hospital Egas Moniz (Appendix I).

Participants

Participants and recruitment

Participants were recruited through medical referral from the Unidade Multidisciplinar de Terapêutica da Dor – Centro Hospitalar de Setúbal and Serviço de Reumatologia - Hospital Egas Moniz and via self-inscription through dissemination of the study in Setúbal Municipality and Myos – Associação Nacional Contra a Fibromialgia e Síndrome de Fadiga Crónica.

The inclusion criteria were: (1) to have been diagnosed with FM, according to the latest American College of Rheumatology criteria (Wolfe et al., 2016); (2) to be aged from 18 to 65 years old (Bourgault et al., 2015; Hooten et al., 2012).

Exclusion criteria included: (1) other cardiovascular/ pulmonary/ metabolic/ neurological/ and renal condition untreated (Giannotti et al., 2014; American College of Sports Medicine, 2014 ; McBeth et al., 2012); (2) ongoing oncologic pathology (until 5 years) under treatment; (3) other rheumatic diseases beyond fibromyalgia; (4) severe osteoporosis and osteoarthritis (grade IV using Kellgren-Lawrence Classification of Osteoarthritis) (Kohn, Sassoon, & Fernando, 2016); (5) orthopaedic surgery, such as spine or hip/knee surgery in the previous year (Giannotti et al., 2014) or thoracic surgery (American College of Sports Medicine, 2014); (6) individuals who were unable to perform the exercise protocol or for whom moderate-

level exercise was contraindicated (McBeth et al., 2012; Rooks et al., 2007); (7) pregnancy (American College of Sports Medicine, 2014); (8) individuals who had attended physical therapy treatments including exercise in the previous 3 months (Giannotti et al., 2014); (9) individuals who were unable to read and write informed consent and questionnaires (Häuser et al., 2009).

Patient eligibility took place during a face-to-face interview at ESS/IPS in Setúbal and Chronic Diseases Research Centre (CEDOC) in Lisbon. The participants who met the criteria proceeded to the assessment protocol and were referred to physiotherapy treatment. Eligible patients gave their written informed consent, statement of responsibility and completed a pre-exercise questionnaire for cardiovascular screening, after receiving oral and written information about the study (Appendix II).

Randomisation and Blinding procedures

Participants who met the inclusion criteria were coded and assessed by a blind evaluator. The identification and code of each participant was sent to another researcher for randomization procedures. A computer-generated randomization list with blocks of six participants each was used, allocating participants to the experimental group (EXP) or the control group (CONT). The researcher responsible for the randomization was not involved in the recruitment and assessment of participants.

Participants were not informed about the study hypothesis or allocation (double-blind design). Both control and experimental interventions took place at ESS/IPS in Setúbal and CEDOC in Lisbon with the same physiotherapist, who made sure that participants from different groups did not interact with each other, to avoid group contamination. The physiotherapist who delivered both the control and the experimental interventions was blinded to the outcomes of the measurements but aware of the study hypothesis.

Sample Size

Sample size was calculated for each group with the follow equation $n = \frac{(\sigma_1^2+\sigma_2^2)(Z_{1-\alpha/2}+Z_{1-\beta})^2}{\Delta^2}$, proposed by Rosner (2016) and based on our previous pilot

study (Fernandes & Caeiro, 2019). An expected change of 2.0 points on NRS as a clinically meaningful difference in pain intensity was considered (Fioravanti et al., 2018; Farrar et al., 2001), with a type 1 error of .05, type 2 error of .20 and a desired statistical power of .80 (Charles & Giraudeau, 2009). Assuming a maximum dropout rate of 35% and a standard deviation of 2.363 (Parreira & Caeiro, 2019), a sample size of 30 patients in each group was required.

Outcome measures

Assessment protocol

The participants were assessed by a researcher blinded to the participant's group. During the initial assessment, the evaluator completed a questionnaire with sociodemographic and clinical data. Sociodemographic information such as age, height, weight, gender, marital status, educational level and employment was collected. Clinical data included years since diagnosis, medication, absence from work, paid leave, Widespread Pain Index (WPI), Severity Symptoms Scale (SSS), expectations towards pain, fatigue and disability. The outcomes measures pain intensity and disability were assessed through the numeric rating pain scale and the revisited fibromyalgia impact questionnaire, respectively. The neuropathic pain screening tool Pain*DETECT* questionnaire was also applied. After the initial assessment, the participants were re-evaluated in two different moments in time (during and after the intervention) by phone call and were instructed to not reveal the content of their programme during the evaluations. The blindness of the evaluators was also maintained in these two assessments.

Outcome measures selection was based on OMERACT recommendations for fibromyalgia (Mease et al., 2011). The outcomes were collected at the baseline, at week 4 and at the conclusion of the 8-weeks intervention, except for the Pain*DETECT* questionnaire and sociodemographic data, which were only assessed at baseline. The Patient Global Improvement of Change Scale was assessed only at week 4 and 8 (figure 1) (Appendix III).

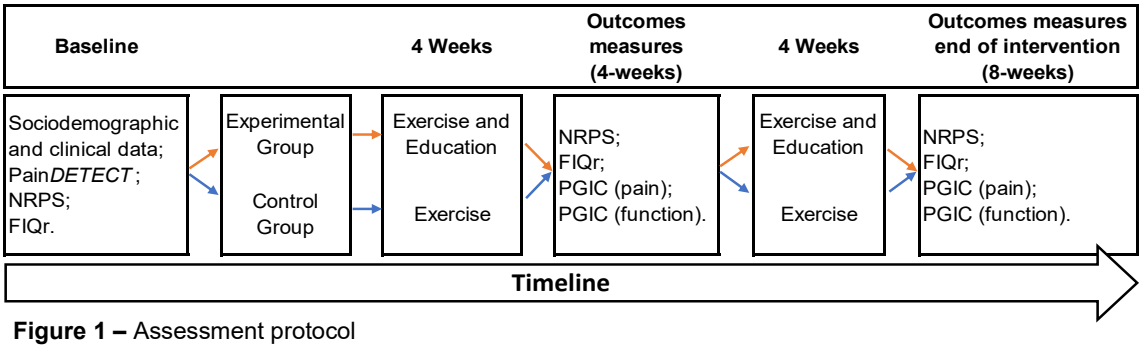

Figure 1 – Assessment protocol

Primary outcome measure

The pain intensity was assessed through the Numeric Rating Scale for Pain (NRSP). The NRPS is a unidimensional measure of pain intensity in adults, including those with chronic pain, with good psychometric properties (Hawker, Mian, Kendzerska & French, 2011). It has a common format of a horizontal line with 11-points (0 to 10) that reflects the pain intensity "in the last 24 hours", with 0 representing one pain extreme (e.g., "no pain") and 10 representing the other pain extreme (e.g., "worst pain imaginable"). Higher scores indicate greater pain intensity. At least 30% reduction (or 2 points) on the NRS is considered a benchmark for a minimal clinically important change (MCID) in pain intensity for individuals with chronic pain (Mease et al., 2011; Moore et al., 2010; Farrar, Young, Lamoreaux, Werth, & Poole, 2001).

Secondary outcome measures

The disability was assessed through the Portuguese version of Revised Fibromyalgia Impact Questionnaire (FIQr). FIQr is a disease-specific self-reported questionnaire composed of 21 items, divided into three domains (function, overall impact and symptoms) that measure disease severity. The total FIQr score ranges between 0 and 100 with higher scores indicating more impact of FM on individual's daily life. This questionnaire is considered to have good psychometric properties, justifying its use in clinical practice and research (Costa et al., 2016; Bennett et al., 2009a). Recent literature suggests 27.04 points or 45.5% improvement in the FIQr score as a MCID (Surendran & Mithun, 2018) but this score was not being used in recent clinical trials and there is no official article published, although an abstract was published in a peer-reviewed journal. Also, this score is much higher than the 14% score reduction obtained for the older Fibromyalgia Impact Questionnaire (FIQ)

by Bennet et al. (2009a). In their FIQr validation and psychometric properties analysis, Bennet et al. (2009b) have demonstrated a strong correlation between the FIQ and the FIQr total scores ($r=0.88$, $p<0.001$). This information allowed the authors to the conclusion that patients' relative standings on the two scales are very similar.

Considering previous information and to reduce the risks of underestimate our results, a conservative approach was chosen by using the 14% score reduction of the FIQ as a MCID. FIQ has been validated for the Portuguese population by Rosado, Pereira, da Fonseca and Branco (2006) and seems to be a reliable and valid instrument to measure health status and physical function in Portuguese patients with FM.

Patients' perception of overall change was assessed through the Portuguese version of Patient Global Impression of Change (Domingues & Cruz, 2010). The PGIC scale is a 7-point scale, ranging from 1 ('no change') to 7 ('a considerable improvement that has made all the difference'). Scores ≥5 were considered indicative of moderate to considerable changes in the patients perceived status (Dworkin et al., 2008; Hurst & Bolton, 2004).

Pain*DETECT* questionnaire is a neuropathic pain screening tool developed and validated in patients with low back pain (Freynhagen, Baron, Gockel, & Tölle, 2006). It was validated for Portuguese population by Santos and Cruz (2017) and showed good psychometric properties. The questionnaire consists of nine items: seven questions that address the quality of neuropathic pain symptoms and two questions related to the spatial and temporal characteristics of the individual's pain pattern. The final score varies between –1 and 38, indicating the likelihood of a neuropathic pain component. A cut-off score of ≤ 12 means that pain is unlikely to have a neuropathic component, while a score of ≥ 19 indicates that a neuropathic component is likely to be present at > 90%.

There has been some debate about the use of the Pain*DETECT* questionnaire as a diagnostic tool (Bouhassira & Attal, 2011). Gauffin, Hankama, Kautiainen, Hannonen & Haanpää (2013b) found that the instrument cannot distinguish neuropathic pain from non-neuropathic pain in FM patients and do not recommend

it as the principal diagnostic tool. Nevertheless, in their cross-sectional survey of 3035 patients with FM, Rehm et al. (2010) have identified subgroups of patients with different sensory profiles using the Pain*DETECT* questionnaire. Differences in pathophysiological mechanisms of pain generation were found, with a variety of pain qualities and sensory abnormalities.

In this study, this questionnaire was not used with a diagnostic purpose or to evaluate treatment effects but rather as a clinical instrument to characterize and discriminate between various pain mechanisms, such as neuropathic and/or nociceptive components. For such reasons, Pain*DETECT* questionnaire was used only at the baseline.

Intervention Protocol

Exercise Program

Both control and experimental groups received an exercise programme based on ACSM's Guidelines for exercise testing and prescription (American College of Sports Medicine, 2017). The protocol included aerobic, strength and stretching components with a duration of 50 to 90 minutes in group sessions twice a week, plus one session of autonomous aerobic training, for 8 weeks. Participants were instructed to begin the exercise at a level that was comfortable to them. The intensity and the duration of the exercises were monitored, gradually increasing.

Strength training included muscular strength and endurance of six major muscle groups (quadriceps femoris, hamstrings, gluteus, pectoral, deltoid, and latissimus dorsi), in supine position, using elastic bands if necessary, from week 5. Each participant began with 1 set of 8 repetitions at a resistance level they could perform easily with proper technique and progressed to 3 sets of 10 repetitions at 50-80% of 1-RM (American College of Sports Medicine, 2017; Gavi et al., 2014; Rooks, 2007). Stretching exercises were recommended for all muscle tendon groups in the pain-free range, holding the stretch for 15-20 seconds, repeated 3 times. Aerobic exercise had an initial duration of 6 minutes, progressing to 20 minutes on the last session at 50% of heart rate reserve (HRR), which corresponds to light to moderate intensity on Borg CR-10 scale (Andrade, Zamunér, Forti, França & Silva 2017). The

type of exercise was low impact, such as walking on flat ground. Detailed information about the exercise program can be found in the Appendix IV.

Education Program

The experimental group received additional educative sessions through a patient-centred and narrative-based approach. Participants were encouraged to share the experiences and strategies they had developed to manage their condition, being the audience for the narratives of each other. The physiotherapist acted as a facilitator for the narrative process as well as health literacy educator, according to the main goals of each session. 9 group sessions of 45 minutes each were planned over 8 weeks. One session per week was planned - except for the first week when it happened twice. The educative sessions occurred in association with exercise: first the participants had education sessions followed by exercise.

The main purpose of the first sessions was to listen and understand patients` illness narratives, the response behaviours towards pain and set individual goals. The contribution of psychosocial factors was also explored, and the neurophysiology of pain was explained, to challenge patient's beliefs and cognitions about pain. From week 5, participants were encouraged to formulate and share strategies to manage pain and fatigue while increasing their levels of activity. One of the sessions was dedicated to understanding the role of the context in persistent pain and participants were invited to present the program to a guest or family member, so they could summarise the main learnings and involve those who are close to them in the process of rehabilitation. Finally, in the last session, participants reviewed their participation along the programme and assessed their individual goals while exploring future ambitions. Detailed information about the education program can be found in the Appendix IV.

Statistical analysis

Statistical analyses procedures were performed by non-blinded researchers using the Statistical Package for the Social Sciences Version 21.0 (IBM Corporation, Chicago, IL). A level of significance of $p \leqslant 0.05$ was set for this study.

Sociodemographic data included age, sex, height, weight, body mass index, marital status, educational level and employment status. Baseline clinical characteristics comprised Widespread Pain Index (WPI), Symptom Severity Scale (SSS), Pain*DETECT* total score, pain intensity (NRPS), disability (FIQ-R), and intervention expectations towards pain, fatigue and disability. Time since diagnosis, medication use, absence from work and paid leave were also included.

For the nominal and ordinal variables, frequency distributions were performed while numerical variables were analysed using measures of central tendency and dispersion (means; standard deviation). Clinical and sociodemographic baseline variables, including pain intensity and disability were compared between groups using the independent t tests or Mann-Witney for continuous data and chi-square tests of independence for categorical data.

Data was assessed for outliers, normality, homogeneity of variances and covariances. The changes in NRPS and FIQr scores were explored using a two-way mixed-model ANOVA with treatment condition (experimental or control) as between subjects' factor and time as within subjects' factor.

Patients' perception of overall change (PGIC) was analysed using chi-square tests of independence, after the dichotomisation of the results in "clinically stable" and "clinical improvement", according to the MCID defined in the literature (Dworkin et al., 2008).

Effect sizes of clinically relevant benefits were reported by calculating Cohen's *d*, Relative Risk (RR) and Number Needed to Treat (NNT). Cohen's *d* was calculated to assess the magnitude of effects. A *d* value of 0.20 is described as small, 0.50 as medium, 0.80 as large and 1.30 as very large (Maher, Markey & Ebert-May, 2013).

The RR is the ratio of patients improving in a treatment group (experimental group) divided by the probability of patients improving in a different treatment (control

group). RR is interpreted in the context of the actual probability of this event occurring. RR ratios can range from zero to infinity. In a study of two treatments, an RR of 1 indicates that outcomes did not differ in the two groups, while an RR of 3 indicates that the treatment group had a threefold greater probability than the control group of showing improvement (McGough & Faraone, 2009).

The NNT is defined as the number of subjects one would expect to treat with an intervention to have more success than if the same number were treated with another intervention. NNT is a measure related to absolute risk reduction and may be most useful in assessing relevance of treatment effects (McGough & Faraone, 2009). In this study, RR and NNT were calculated through the dichotomization of the outcomes pain intensity (NRPS) and disability (FIQr).

In all the cases data was analysed according to the intention to treat-analysis principle using multiple imputation methods of missing values. The Multiple Imputation (MI) method was used to consider the missing data of our outcomes of NRPS, FIQr and PGIC for the drop-out participants. This procedure allowed us to handle missing data by creating several different plausible imputed data sets and appropriately combining results obtained from each of them, based on the distribution and correlation with other sample variables (Hughes, Heron, Sterne & Tilling, 2019; Pedersen et al., 2017).

Missing data are categorized into the following three types of mechanisms: missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR). When data are MCAR, “there are no systematic differences between the observed and missing data” (Huges et al., 2019), that is, missing data arises due to random events occurred during the study. When data are MAR, “any systematic differences between the observed and missing data can be explained by associations with the observed data” (Huges et al., 2019), that is, MAR occurs when the missingness can be explained by information already observed. Finally, when the missingness mechanism is MNAR, missing data may not be random, but cannot be explained by measurable variables already observed and “case associations with observed data cannot justify all systematic differences between the observed and missing data” (Huges et al., 2019). Considering that our missing data was due to

the dropout rate occurred by different reasons non-related to intervention such as personal, professional and other health problems, we assumed that the missing data mechanism was “missing at random - MAR”. In such circumstances, missing data can be explained by associations with the observed data (Pedersen et al., 2017).

Regarding the choice of our imputed variables, continuous variables were selected for the process: pain (NRPS), disability (FIQ-R) and patient perception of improvement (PGIC). Missing data was imputed using the set of baseline characteristics as well as the 4 and 8-weeks outcomes. The number of imputed datasets was created depending on the percentage of missing values and a desired relative efficiency of 99%. The relative efficiency is measured against a situation of perfect efficiency (100%), that is, the truth (Newgard & Haukoos, 2007). Considering that one can never know the trues values of the missing data, this imputation method maximizes statistical efficiency and validity of the results and generates less biased estimates than other methods of handling the same missing values (Newgard & Haukoos, 2007).

RESULTS

Participants

Between January 2020 and January 2021, a total of 70 individuals were recruited according to the established eligibility criteria. During this period, the study was interrupted for six months, due to restrictions related to COVID19 pandemic. From the total of 70 individuals, 7 were excluded for not meeting the inclusion/exclusion criteria and 3 for not accepting to integrate the study. The final sample was established with 60 participants diagnosed with FM and after randomisation, 30 integrated the control group and 30 the experimental group. The flow diagram of the study is presented in figure 2.

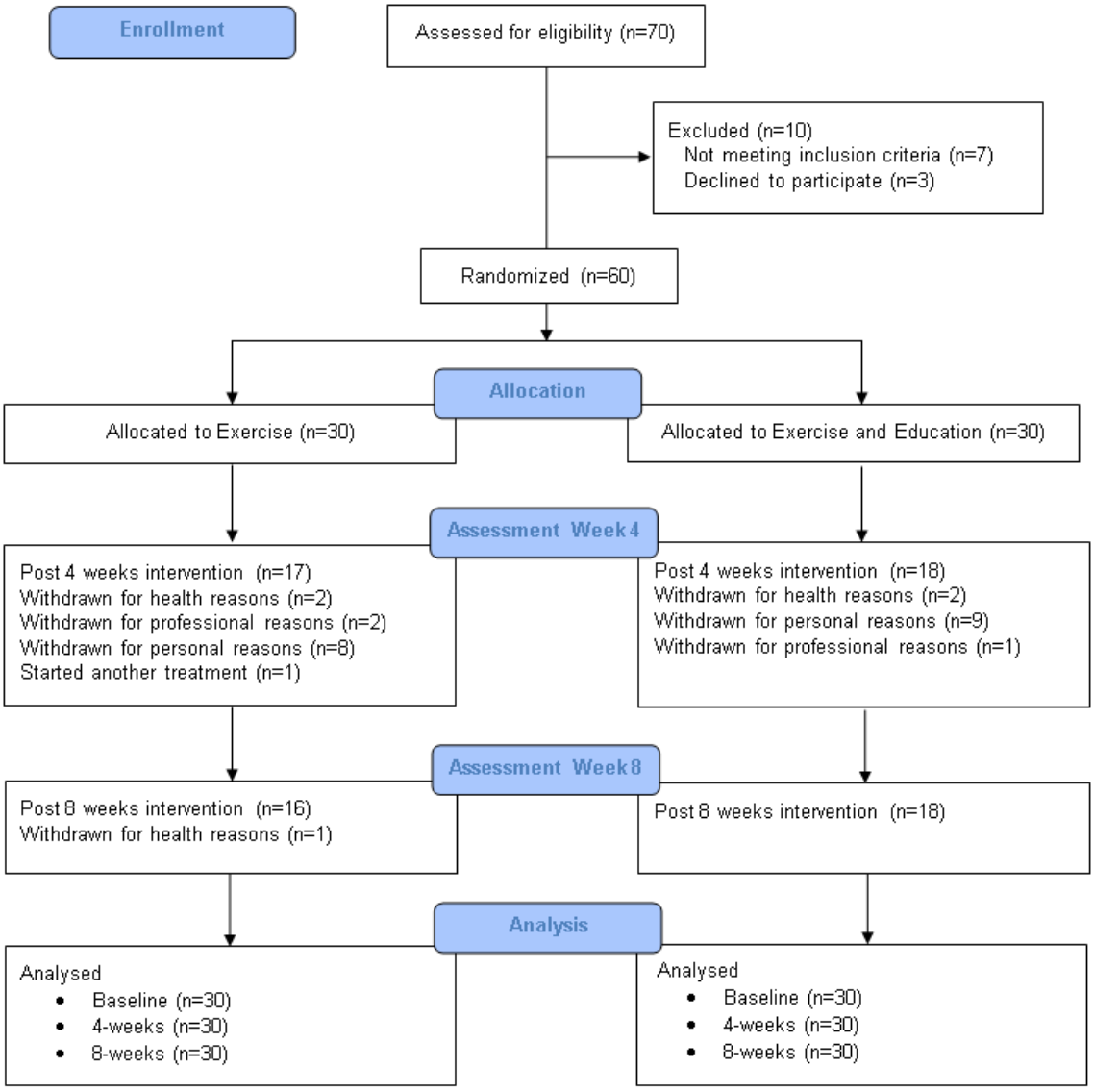

Figure 2 – Flow diagram of the study

Baseline sociodemographic and clinical characteristics of the 60 participants included in the study are presented in Table 1 and 2, respectively. The sample was composed exclusively by women, with a mean age of 50.83 in the CONT group and 46.20 in the EXP group (p=.060) and a Body Mass Index (BMI) of 26.83 in the CONT group and 26.99 in the EXP group (p=.876), indicating an overweight range (NCD Risk Factor Collaboration [NCDRisC], 2016). In terms of educational level, 33.3% attended the elementary and middle school, 30% high school and 36.7% college/higher education in the CONT group versus 36.7% in the elementary and middle school, 23.3% high school and 40% college/higher education in the EXP group (p=.843). During this study, 63.3% of the participants in the CONT and EXP were working. There were no significant differences between groups in any of the demographic or clinical variables.

Table 1. Baseline sociodemographic data

Variables	**CONT n= 30**	**EXP n=30**	
	Mean (SD)	**Mean (SD)**	***p-value***
Age, years	50.83 ± 9.21	46.20 ± 10.42	0.060[c]
BMI	26.83 ± 3.88	26.99 ± 4.58	0.876[a]
	n (%)	**n (%)**	
Gender			
Male	0 (0%)	0 (0%)	
Female	30 (100%)	30 (100%)	
Marital status			
Single	6 (20%)	6 (20%)	0.817[b]
Married or living with significant other	16 (53%)	18 (60%)	
Widowed, Divorced or separated	8 (27%)	6 (20%)	
Educational level			
Elementary and middle school	10 (33.3%)	11 (36.7%)	0.843[b]
High school	9 (30%)	7 (23.3%)	
College	11 (36.7%)	12 (40%)	
Employment			
Working	19 (63.3%)	19 (63.3%)	1.000[b]
Not working	9 (36.7%)	9 (36.7%)	

[a]Analysed by student t test; [b] Analysed by chi-square test; [c]Analysed by Mann-Whitney test. **Abbreviations**: CONT: Control Group; EXP: Experimental Group; SD: Standard Deviation; BMI: Body Mass Index.

Table 2. Baseline clinical data			
Variables	**CONT n= 30**	**EXP n=30**	***p-value***
	n (%)	**n (%)**	
Years since diagnosis			
≤ 24 months	9 (30%)	8 (26.7%)	0.774[b]
>24 months or dont know	21 (70%)	22 (73.3%)	
Medication			
Yes	20 (67%)	22 (73%)	0.573[b]
No	10 (33%)	8 (27%)	
Absence from work			
Yes	18 (60%)	16 (53%)	0.602[b]
No	12 (40%)	14 (47%)	
Paid Leave			
Yes	9 (30%)	8 (27%)	0.774[b]
No	21 (70%)	22 (73%)	
	Mean (SD)	**Mean (SD)**	
WPI (0-19)	12.10 ± 3.37	12.53 ± 3.37	0.620[a]
SSS (0-12)	8.39 ± 1.96	9.00 ± 1.7	0.231[c]
NRSP (0-10)	5.80 ± 2.58	7.00 ± 1.80	0.069[c]
FIQr total (0-100)	63.93 ± 15.38	67.47 ± 15.70	0.382[a]
Pain*DETECT* total score (-1-38)	20.27 ± 6.77	20.27 ± 5.30	1.000[a]
Expectations towards pain (1-5)	4.07 ± 0.25	3.90 ± 0.40	0.062[c]
Expectations towards fatigue (1-5)	4.07 ± 0.36	3.97 ± 0.56	0.599[c]
Expectations towards disability (1-5)	4.10 ± 0.40	4.10 ± 0.55	0.895[c]

[a]Analysed by student t test; [b]Analysed by chi-square test; [c]Analysed by Mann-Whitney test. **Abbreviations:** CONT: Control Group; EXP: Experimental Group; SD: Standard Deviation; WPI: Widespread Pain Index; SSS: Severity Symptom Scale; NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited.

The dropout rate was higher than the 35% expected, with a total of 43% withdrawals at the end of the interventions. This may have been related to the COVID19 pandemic because most of the interventions occurred during the pandemic year of 2020. Before the pandemic, the drop-out rate was 25% while during the pandemic it was above 50%.

There was no adverse effect associated with the interventions. The CONT group presented a slightly higher dropout rate with 47% (n=14), against EXP group with 40% (n=12). The largest dropout rate happened in the first 4 weeks, with 43% (n=13) in the CONT group and 40% (n=12) in the EXP group.

The participants reported that the withdrawals occurred due to personal reasons, such as schedule incompatibility, lack of transportation or unspecified personal problems, specifically 62% (n=8) in the CONT group and 75% (n=9) in the EXP group. Less significant dropout occurred for health reasons (not associated with the intervention), 15% (n=2) in the control group and 17% (n=2) in the experimental group. Finally, 15% (n=2) withdrew for professional reasons in the control group and 8% (n=1) in the experimental group. Dropout causes and frequencies were similar in both groups.

Participants' adherence to the intervention was registered to ensure a minimum of 75% of the treatment programme, considering group and autonomous sessions. None of the participants were excluded from the analysis for not attending the minimum established. The minimum attendance was similar in the EXP and CONT groups (76.2% vs 72.4%, respectively). Participants in the EXP group attended a mean of 18.28 (± 3.79) out of 24 planned sessions, while CONT group attended a mean of 17.38 (± 3.67).

Baseline characteristics of the participants who completed the study and those who dropped out were compared using the independent t tests or Mann-Witney for continuous data and chi-square tests of independence for categorical data. When more than 20% of cells had expected frequencies <5, Fisher’s exact test was used. There were no statistically significant results, except for marital status. Results are presented in table 3.

Drop-out participants showed a slightly lower mean age (47.04 ± 11.06 vs 49.65 ± 9.16, p=.322). Age was dichotomized according to the study of Garcia-Campayo et al. (2008). No differences were found among age groups (p=.822). BMI mean was similar and above 25 in both groups (p=.623), BMI was dichotomized according to the conventional World Health Organisation classification (NCD Risk Factor Collaboration [NCDRisC], 2016). No differences were found between groups (p=.911).

Widespread Pain Index (WPI) and Severity Symptom Scale (SSS) were dichotomized in low severity (WPI 0-6 and SSS 0-8) and high severity (WPI ≥7 and SSS ≥9) according to Wolfe, Egloff and Häuser (2016). Average scores were similar

in both groups for WPI (12.44 ± 3.10 vs 12.15 ± 3.66, p=.745) and for SSS (8.41 ± 1.81 vs 9.08 ± 1.83, p=.130). In terms of groups severity, high severity of WPI was found in both groups (97% vs 96%, p=.683). For the SSS, a higher proportion of individuals with high score severity was found among participants who dropped out, although it was not statically significant (73% vs 56%, p=.171).

Table 3. Baseline characteristics of the participants who completed the study and those who dropped out

Observed data	**Completed the study (n=34)**	**Dropped out (n=26)**	***p-value***
Age, mean	**49.65 ± 9.16**	**47.04 ± 11.06**	0.322[a]
≤ 39	4/34 (12%)	4/26 (16%)	
40-49	13/34 (38%)	11/26 (42%)	0.821[c]
≥ 50	17/34 (50%)	11/26 (42%)	
BMI, mean	**26.67 ± 4.54**	**27.22 ± 3.80**	0.623[a]
< 25	13/34 (38%)	10/26 (38%)	
25.0 - 29.9	12/34 (35%)	8/26 (31%)	0.911[b]
≥ 30	9/34 (27%)	8/26 (31%)	
WPI, mean (0-19)	**12.44 ± 3.10**	**12.15 ± 3.66**	0.745[a]
Low severity 0-6	1/34 (3%)	1/26 (4%)	0.683[c]
High severity ≥ 7	33/34 (97%)	25/26 (96%)	
SSS, mean (0-12)	**8.41 ± 1.81**	**9.08 ± 1.83**	0.130[d]
Low to moderate severity 0-8	15/34 (44%)	7/26 (27%)	0.171[b]
High severity ≥ 9	19/34 (56%)	19/26 (73%)	
Pain intensity, mean (NRPS 0-10)	**6.47 ± 2.09**	**6.31 ± 2.56**	0.447[a]
Mild to moderate pain < 6	12/34 (35%)	5/26 (19%)	0.171[b]
Severe pain ≥ 6	22/34 (65%)	21/26 (81%)	
Disability, (FIQr 0-100)	**63.00 ± 16.60**	**69.20 ± 13.46**	0.124[a]
Mild disability (34-41)	5/34 (15%)	0/26 (0%)	
Moderate disability (41-50)	2/34 (6%)	2/26 (8%)	0.134[c]
Severe disability (> 50)	27/34 (79%)	24/26 (92%)	
	n (%)	**n (%)**	
Educational level			
Elementary/middle school	4/34 (12%)	4/26 (15%)	
High school	15/34 (44%)	13/26 (50%)	0.767[c]
College	15/34 (44%)	9/26 (35%)	
Employment			
Working	23/34 (67.7%)	15/26 (57.7%)	0.428[b]
Not working	11/34 (32.3%)	11/26 (42.3%)	
Marital status			
Married or living with significant other	26/34 (77%)	8/26 (31%)	**<0.001[b]***
Single, widowed, divorced or separated	8/34 (23%)	18/26 (69%)	
Medication			
Yes	24/34 (71%)	18/26 (69%)	0.909[b]
No	10/34 (29%)	8/26 (31%)	

[a]Analysed by student t test; [b] Analysed by chi-square test; [c]Analysed by fischer's test; [d]Analysed by Mann-Whitney test. *statistically significant. **Abbreviations**: BMI: Body Mass Index; NRPS: Numeric Rating Pain Scale (Higher score indicates greater pain intensity); WPI: Widespread Pain Index; SSS: Severity Symptoms Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited (Higher scores indicate greater disability)

Pain intensity (NRPS 0-10) was dichotomized in mild to moderate pain (< 6/10) and severe pain (≥ 6/10), according to the study of Moore, Straube and Aldington (2013). Pain average was similar in both groups (6.47 ± 2.09 vs 6.31 ± 2.56, p=.447) and a high proportion of individuals suffering from severe pain was found in both groups, especially in those who dropped out (65% and 81%, respectively), although it was not statistically significant (p=.171).

Disability (FIQr 0-100) was also dichotomised in mild disability (34-41), moderate disability (41-50) and severe disability (>50), according to the study of Rivera, Vallejo and Offenbächer (2014). Although this cut-off scores were based on the original FIQ, the instruments are considered very similar and the author pointed out a strong correlation between FIQ and FIQr (Benett et al., 2009a). This study's results showed a higher proportion of severe disability in the participants who dropped out compared to those who completed the study (92% vs 79%, p=.134, respectively). Drop-out participants presented also a higher FIQr score average at the baseline (69.20 ± 13.46 vs 63.00 ± 16.60, p=.124), but none of these results were statistically significant.

Educational level seemed to not have an influence on the accomplishment of this study interventions (p=.746). A higher proportion of individuals who were working during the intervention was found in the participants who completed the study compared to those who dropped out (67.7% vs 57.7%, p=.428).

Marital status seemed to have an important influence on the accomplishment of this study interventions. We observed that there was a higher and significant proportion of married (or living with a significant other) participants among those who have completed our intervention programme (77% vs 31%, p<.001). On the contrary, for those who dropped out, there was a higher and significant proportion of participants who were single, widowed or divorced (23% vs 69%, p<.001).

Finally, medication intake seemed to be equal in both groups, considering that both groups showed a high proportion of individual taking medication (71% of those who completed the study vs 69% of those who dropped out, p=.909).

Continuous data were also compared between the drop-out participants and those who completed the study in the CONT group and compared between the drop-out

participants and those who completed the study in the EXP group, using independent t tests or Mann-Whitney U test, according to the data normality. Results are presented in table 4. There was no statistical difference for any variable neither in the CONT nor the EXP group. For the CONT group, the participants who dropped-out during the study showed similar characteristics to those completing the study, except for age variable. The dropout participants showed a slightly lower mean age (47.93 ± 10.68 vs. 53.38 ± 7.10, p=.107). Interestingly, for the EXP group, the dropout participants presented slightly higher Body Mass Index (28.09 ± 3.86 vs. 26.27 ± 4.99, p=.297), higher pain intensity (7.50 ± 1.57 vs. 6.67 ± 1.91, p=.220) and higher disability (73.42 ± 13.80 vs. 63.50 ± 15.99, p=.090), although none of these results were statistically significant.

Table 4. Comparison between the drop-out participants and those who completed the study in the CONT and EXP groups

Variables	**CONT n= 30**			**EXP n=30**		
	Completed the study (n=16)	**Dropped out (n=14)**	***p-value***	**Completed the study (n=18)**	**Dropped out (n=12)**	***p-value***
	Mean (SD)	**Mean (SD)**		**Mean (SD)**	**Mean (SD)**	
Age, years	53.38 ± 7.10	47.93 ± 10.68	0.107[a]	46.33 ± 9.68	46.00 ± 11.87	0.933[a]
BMI	27.13 ± 4.10	26.48 ± 3.75	0.657[a]	26.27 ± 4.99	28.09 ± 3.86	0.297[a]
WPI (0-19)	12.63 ± 3.44	11.50 ± 3.30	0.370[a]	12.28 ± 2.93	12.92 ± 4.06	0.509[b]
SSS (0-12)	7.94 ± 1.81	8.93 ± 2.06	0.171[a]	8.83 ±1.76	9.25 ± 1.60	0.516[a]
NRSP (0-10)	6.13 ± 2.39	6.21 ± 1.76	0.909[a]	6.67 ± 1.91	7.50 ±1.57	0.220[a]
FIQr total (0-100)	62.44 ± 17.78	65.64 ± 12.55	0.578[a]	63.50 ± 15.99	73.42 ± 13.80	0.090[a]
Pain*DETECT* total score (-1-38)	20.38 ± 6.30	20.14 ± 7.50	0.927[a]	21.28 ± 5.29	18.75 ± 5.17	0.206[a]

[a]Analysed by student t test; [b]Analysed by Mann-Whitney test. **Abbreviations**: SD: Standard Deviation; BMI: Body Mass Index; NRPS: Numeric Rating Pain Scale (Higher score indicates greater pain intensity); WPI: Widespread Pain Index; SSS: Severity Symptoms Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited (Higher scores indicate greater disability).

Considering our missing data, for a maximum of 1140 observations for the 4 outcomes (END, FIQr, PGIC pain and PGIC function) measured along the 3 assessment points (baseline, 4-weeks and 8-weeks), 357 values were missing, which correspond to a 31.3% of missingness. To improve the statistical power and precision of our estimations, 20 imputed datasets were created for the imputation process, with a desired efficiency of 99%, based on the recommendations of Newgard and Haukoos (2007) (Appendix V).

Clinical course of main outcomes

Pain intensity (NRPS) and disability (FIQr) clinical course were monitored through the 8-weeks intervention programme using scores mean. Results are presented in figure 3 and 4, respectively.

An average decrease in pain intensity over time (week 4 and 8) was observed in both groups. The CONT group had a slightly lower average score at the baseline (5.87±2;43 vs 7.00±1.80, p=.069). The evolution of both groups was similar during all the intervention periods. From baseline to 8-weeks, a total reduction of 1.81 points was achieved by the CONT group against 1.82 in the EXP group.

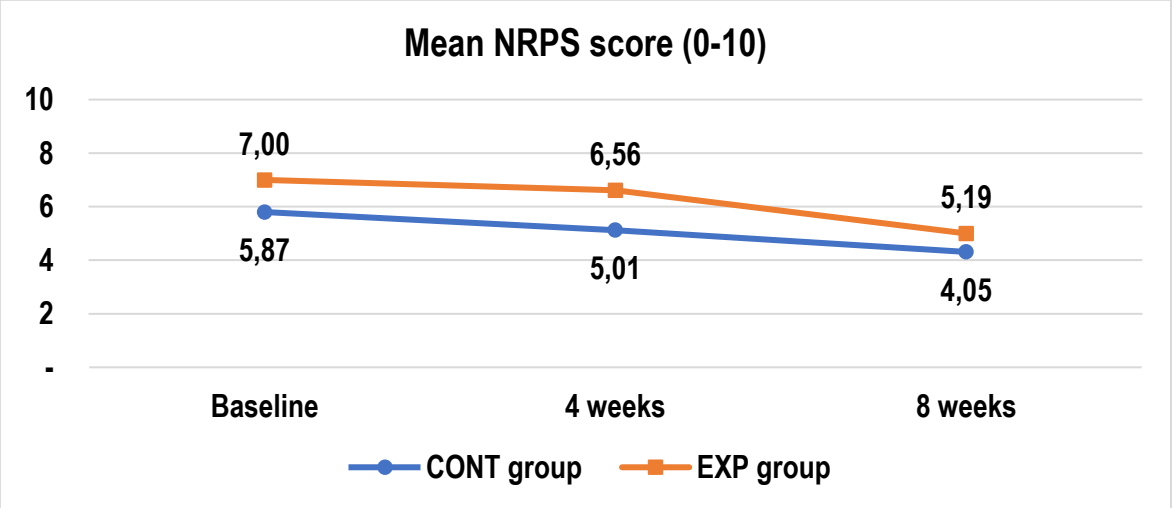

Figure 3 – The time course of mean pain intensity (NRPS 0-10) score in the CONT (control) and EXP (experimental) group through de 8-weeks intervention. Higher scores indicate greater pain intensity.

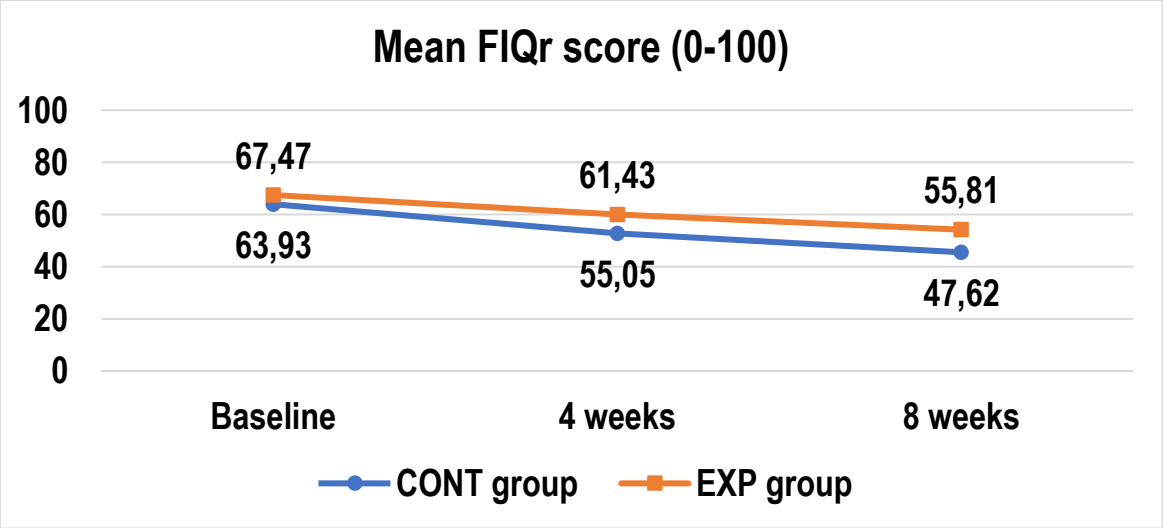

Figure 4 – The time course of mean disability (FIQ-R 0-100) score in the CONT (control) and EXP (experimental) group through de 8-weeks intervention. Higher scores indicate greater disability.

Concerning the disability (FIQr), the CONT group had a slightly lower average score at the baseline (63.93±15.39 vs 67.47±15.70, p=.382). For both groups there was a decrease in disability score over time (4-weeks and 8-weeks). From baseline to 8-weeks, a total reduction of 16.31 points was achieved by the CONT group against 11.66 in the EXP group.

ANOVA assumptions assessment

To ensure the applicability of Two-way mixed-model ANOVA, data was assessed for normality, outliers, homogeneity of variances and covariances and sphericity for the main outcomes pain intensity (NRPS) and disability (FIQr) at three different moments: baseline (T0), 4-weeks (T1), 8-week (T2). Results are presented in table 5 (Appendix VI).

The normality was tested using the Shapiro-Wilk test. There was one violation of normality for the NRPS in the EXP group at T1 (p=.030). There was no violation of normality for the FIQr at any moment. Outliers were analysed using histograms and boxplots. For the NRPS, 2 extreme outliers were found at T0 and 1 extreme at T1 for the CONT group and 2 moderate outliers at T1 for the EXP group. For FIQr, there was 1 moderate outlier for the CONT group at T0 and 1 moderate outlier in the EXP group at T1 and T2

Considering that data normality was violated at T1 in the EXP group for the NRPS and 2 outliers were found for the same group at T1, the substitution of such values were conducted by replacing the closest and less extreme value. The data normality after this transformation was not statistically significant (p=.291). The same procedure was adopted for the extreme outliers present in the CONT group for the NRPS. After the substitution of the values, there was no more outliers for the NRPS. For the FIQr and considering that normality was not violated neither extreme outliers were found, no modification of the values was executed. As there are no clear recommendations in the literature about the most appropriate procedures when outliers are detected but rather a set of possibilities, the option of removing the values was not considered to not discard important information.

Table 5. ANOVA assumptions assessment

		Normality Shapiro–Wilk test ***p-value***			**Outliers**			**Homogeneity of variance** Levene's test ***p-value***			**Equality of variance-covariance** Box's M test ***p-value***	**Sphericity** Mauchly's test ***p-value***
		T0	**T1**	**T2**	**T0**	**T1**	**T2**	**T0**	**T1**	**T2**		
NRPS	**CONT**	0.086	0.214	0.492	**2²**	**1²**	0	0.149	0.068	0.742	0.031	**0.013*³**
	EXP	0.255	**0.030*¹**	0.437	0	**2²**	0					
FIQr	**CONT**	0.153	0.994	0.226	**1**	0	0	0.575	0.735	0.306	0.647	**0.015*³**
	EXP	0.365	0.971	0.508	0	1	**1**					

* Statistically significant; ¹ after the substitution of the outliers, p=.291; ² 0 outliers after the substitution of the values; ³ Huynh-feldt correction. **Abbreviations**: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; CONT: Control Group (exercise); EXP: Experimental group (exercise & education).

Homogeneity of variance was obtained with Levene's test and the results showed a p-value >.005 for both NRPS and FIQr at the baseline, 4-weeks and 8-weeks.

Equality of variance-covariance was tested using Box's test. A significance level of p<0.001 was considered for this test (Maxwell, Delaney & Kelley, 2018). Results presented a p-value of 0.031 and 0.647 for NRPS and FIQr, respectively.

The assumption of sphericity was tested using the Mauchly's test, considering a significance level of p<0.05. Mauchly's test of sphericity indicated that the assumption of sphericity was violated for the two-way interaction for the NRPS ($\chi2(2) = 8.612$, p=0.013) and the FIQr ($\chi2(2) = 8.374$, p=0.015). Since ANOVA is sensitive to the violation of sphericity, Field (2013) and Maroco (2007) suggests Huynh–Feldt correction when estimates of sphericity are greater than .75.

Considering the results mentioned above, a two-way mixed-model ANOVA with treatment condition as between subjects' factor and time as within subjects' factor was used to evaluate our hypothesis (Appendix VII). As the assumption of sphericity was not met, Huynh-Feldt correction was used when analysing data. All pairwise comparisons were run where reported 95% confidence intervals and p-values are Bonferroni-adjusted. Principal results are presented in table 6.

Two-way interaction (group*time)

Pain intensity

The results show no statistically significant interaction between the intervention and time on pain intensity (*F* (1,836, 106,462) = .698, p=.488, partial η^2=.012).

Disability

The results show no statistically significant interaction between the intervention and time on disability (*F* (1,842, 102,057) = .989, p=.370, partial η^2=.017).

If there is no evidence for the group-by-time interaction effects, the analysis is usually followed up with the main effects of time and groups (Leppink, O'Sullivan & Winston, 2017).

Table 6. Two-way mixed-model ANOVA - results

Primary Outcome	***df***	***F***	***p***	***η2***
Pain Intensity (NRPS 0-10)				
Group-by-time interaction effect	1.836, 106.462	0.698	0.488	0.012
Time effect	1.836, 106.462	42.486	**<0.001***	0.423
Group effect	1, 58	9.981	**0.003***	0.147
Secondary Outcome				
Disability (FIQr 0-100)				
Group-by-time interaction effect	1.842, 102.057	0.989	0.370	0.017
Time effect	1.842, 106.816	35.062	**<0.001***	0.377
Group effect	1,58	3.256	0.076	0.053

Abbreviations: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; df: degrees of freedom; η^2: effect size. *Statistically significant.

Main effect of time

Pain intensity

The main effect of time showed a statistically significant difference in pain intensity at the different time points (*F* (1,836, 106,462) = 42.486, p<.001, partial η^2 = .423). It suggests that there was a definite reduction in pain intensity scores across the three time points (baseline, week 4 and week 8) in our CONT and EXP groups, with a medium effect size of 0.439 (Maher et al., 2013).

Post-Hoc analysis using Bonferroni adjustments revealed that pain intensity was statistically significantly decreased from baseline to 4-weeks (T1) (0.65 (95% CI, 0.71 to 1.22), p=.023), from 4-weeks to 8-weeks (1.17 (95% CI, 0.71 to 1.61), p<.001) and from baseline to 8-weeks (1.81 (95% CI, 1.38 to 2.25), p<.001). Results are presented in table 7.

Table 7. Pairwise comparisons - Within-Subjects effects

Pain Intensity (NRPS 0-10)	**Mean Dif.**	**95% CI**	**p-value[a]**
Baseline (T0) - 4 weeks (T1)	0.65	(0.71; 1.22)	**0.023***
4 weeks (T1) - 8 weeks (T2)	1.17	(0.71; 1.61)	**<0.001***
Baseline (T0) - 8 weeks (T2)	1.81	(1.38; 2.25)	**<0.001***
Disability (FIQr 0-100)			
Baseline (T0) - 4 weeks (T1)	7.46	(3.11; 11.81)	**<0.001***
4 weeks (T1) - 8 weeks (T2)	6.52	(3.23; 9.82)	**<0.001***
Baseline (T0) - 8 weeks (T2)	13.99	(9.39; 18.59)	**<0.001***

Abbreviations: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; Dif: difference; CI: Confidence Interval. [a]Bonferroni adjustment; * Statistically significant, p< 0.005

Disability

The main effect of time showed a statistically significant difference in disability at the different time points (*F* (1,842, 106,816) = 35.062, p<.001, partial η^2 = .377). It suggests that there was a definite reduction in disability scores across the three time points (baseline, week 4 and week 8) in our CONT and EXP groups, with a medium effect size of 0.377 (Maher et al., 2013).

Post-Hoc analysis using Bonferroni adjustments revealed that disability was statistically significantly decreased from baseline to 4-weeks (T1) (7.46 (95% CI, 3.11 to 11.81), p<.001), from 4-weeks to 8-weeks (6.52 (95% CI, 3.23 to 9.82), p<.001) and from baseline to 8-weeks (13.99 (95% CI, 9.39 to 18.59), p<.001). Results are presented in table 7.

Main effect of group

Pain intensity

The main effect of group showed that there was a statistically significant difference in mean pain intensity between intervention groups (*F* (1, 58) = 9.981, p=.003, partial η^2=.147). It suggests that there was a definite difference between groups in terms of pain intensity mean scores, with a small effect size of 0.147 (Maher et al., 2013).

Post-Hoc analysis using Bonferroni adjustments revealed a statistically significant mean score difference in terms of pain intensity (NRPS) between the CONT and EXP groups (-1.28 (95% CI, -2.08 to -0.47), p=.003). It suggests that the mean pain intensity of the three timepoints (baseline, 4-weeks and 8-weeks) is 1.28 point lower for those who are in the CONT group. Results are presented in table 8.

Table 8. Pairwise comparisons - Between-Subjects effects

Pain Intensity (NRPS 0-10)	**Mean Dif.**	**95% CI**	**p-value[a]**
Control - Experimental	-1.28	(-2.08; -0.47)	**0.003***
Disability (FIQr 0-100)			
Control - Experimental	-6.04	(-12.74; 0.66)	0.076

Abbreviations: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; Dif: difference; CI: Confidence Interveal. [a]Bonferroni adjustment; * Statistically significant, p< 0.005

Disability

The main effect of group showed that there was no statistically significant difference in mean disability between intervention groups (F (1, 58) = 3.256, p=.076, partial η^2=.053. It suggests that there was no definite difference between groups in terms of disability scores.

Post-Hoc analysis using Bonferroni adjustments revealed no statistically significant mean score difference in terms of disability (FIQr) between the EXP and CONT groups (6.04 (95% CI, -0.66 to 12.74), p=.076). Results are presented in table 8.

Comparison between Intention-to-treat and Per-protocol analysis

Literature suggests comparing results of imputed values and complete cases analysis (CCA) if there is a large fraction of missing data (Hughes, Heron, Sterne & Tilling, 2019; Sterne et al., 2009). Detailed information about the results can be found in the (Appendix VIII).

In the primary outcome pain intensity (NRPS), there was no group-by-time interaction neither in the MI nor in the CCA (p=.488 vs p=.273, respectively).

Regarding the secondary outcome disability (FIQr), no group-by-time interaction difference was found neither in the MI nor in the CCA (p=.370 vs p=.341, respectively).

The main effect of time showed similar results in both methods for pain intensity (MI p<.001 vs CCA p<.001). Post-Hoc analysis using Bonferroni adjustments revealed similar results from 4-weeks to 8-weeks (MI p<.001 vs CCA p=.001) and from baseline to 8-weeks (MI p<.001 vs CCA p<.001) but slightly different from baseline to 4-weeks, favouring the MI process (MI p=.023 vs CCA p=.380).

The main effect of time for disability showed also similar results in both methods (MI p<.001 vs CCA p<.001). Post-Hoc analysis using Bonferroni adjustments revealed similar results from baseline to 4-weeks (MI p<.001 vs CCA p<.001), from 4-weeks to 8-weeks (MI p<.001 vs CCA p=.017) and from baseline to 8-weeks (MI p<.001 vs CCA p<.001).

The main effect of group showed different results between the methods for pain intensity (MI p=.003 vs CCA p=.064). Those differences where confirmed by the post-Hoc analysis using Bonferroni adjustments (MI p=.003 vs CCA p=.149).

The main effect of group for disability showed similar results between the methods (MI p=.076 vs CCA p=.273). Post-Hoc analysis using Bonferroni adjustments revealed also similar results (MI p=.076 vs p=.273).

Clinical significance

To evaluate the impact of our findings on clinical outcomes, descriptive statistics were made for pain intensity (NRPS), disability (FIQr) and Patient's global impression of change – PGIC (pain and function). Participants were dichotomized in two groups: "clinically stable" and "clinical improvement", according to the minimum clinically important difference (MCID) defined in the literature. Frequencies of clinical improvement were compared between treatment groups using chi-square tests of independence (table 9). Detailed information about the results can be found in the (Appendix IX).

For the NRPS, “clinically stable” was defined as those patients having a score inferior to 2 points, meanwhile “clinical improvement” was set for those who had a score equal or superior to 2 points (Mease et al., 2011). For FIQr and considering that there is no MCID consensus defined in the literature, we used the findings from Bennett et al. (2009a) for the FIQ, who estimate an MCID of 14% score reduction. For the PGIC, “clinically stable” was defined as a score inferior to 5 and “clinical improvement” equal or superior to 5 (Dworkin et al., 2008; Hurst & Bolton, 2004).

Table 9. Clinical significance of the outcomes

	4-weeks			8-weeks		
	CONT	EXP	p-value[a]	CONT	EXP	p-value[a]
NRPS (0-10)						
Stable (<2)	22/30 (73.3%)	20/30 (66.7%)	.573	14/30 (46.7%)	11/30 (36,7%)	.432
Improvement (≥2)	8/30 (26.7%)	10/30 (33.3%)		16/30 (53.3%)	19/30 (63.3%)	
FIQr (0-100)						
Stable (<14%)	16/30 (53.3%)	16/30 (53.3%)	1.000	8/30 (26.7%)	11/30 (36.7%)	.405
Improvement (≥14%)	14/30 (46.7%)	14/30 (46.7%)		22/30 (73.3%)	19/30 (63.3%)	
PGIC Pain (0-7)						
Stable (<5)	21/30 (70.0%)	25/30 (83.3%)	.222	11/30 (36.7%)	18/30 (60.0%)	.071
Improvement (≥5)	9/20 (30.0%)	5/30 (16.7%)		19/30 (63.3%)	12/30 (40.0%)	
PGIC Function (0-7)						
Stable (<5)	17/30 (56.7%)	19/30 (63.3%)	.598	7/30 (23.3%)	13/30 (43.3%)	.100
Improvement (≥5)	13/30 (43.3%)	11/30 (36.7%)		23/30 (76.7%)	17/30 (56.7%)	

[a]Analysed by chi-square independent test. **Abbreviation**s: CON: Control Group; EXP: Experimental group; NRPS: Numeric Rating Pain Scale; FIQ-R: Fibromyalgia Impact Questionnaire Revisited; PGIC: Patient’s Global Impression of Change.

Globally, the percentages of clinical improvement almost duplicated for each outcome at the end of interventions (8-weeks) when compared to the results at 4-weeks (figure 5 and 6). However, there is still no statistical differences between groups at 4- and 8-weeks for any outcomes measure (table 9).

Concerning the NRPS at 4-weeks, the results were similar, slightly superior for the EXP group (26.7% vs 33.3%). On the contrary, for the PGIC (pain), CONT group presented a higher percentage of clinical improvement (30.0% vs 16.7%). When comparing the NRPS and PGIC (Pain), the results are similar for the CONT group (26.7% and 30.0%) but little different for EXP group (33,3% and 16,7%) (figure 5).

Regarding the FIQr, percentages of improvement at 4-weeks in the CONT and EXP group were identical (46.7%). PGIC (function) also showed similar results between CONT and EXP groups (43.3% vs 36.7%). When comparing the FIQr and PGIC

(function) between groups, results are alike, although the difference was more pronounced in the EXP group (46.7% and 36.7%).

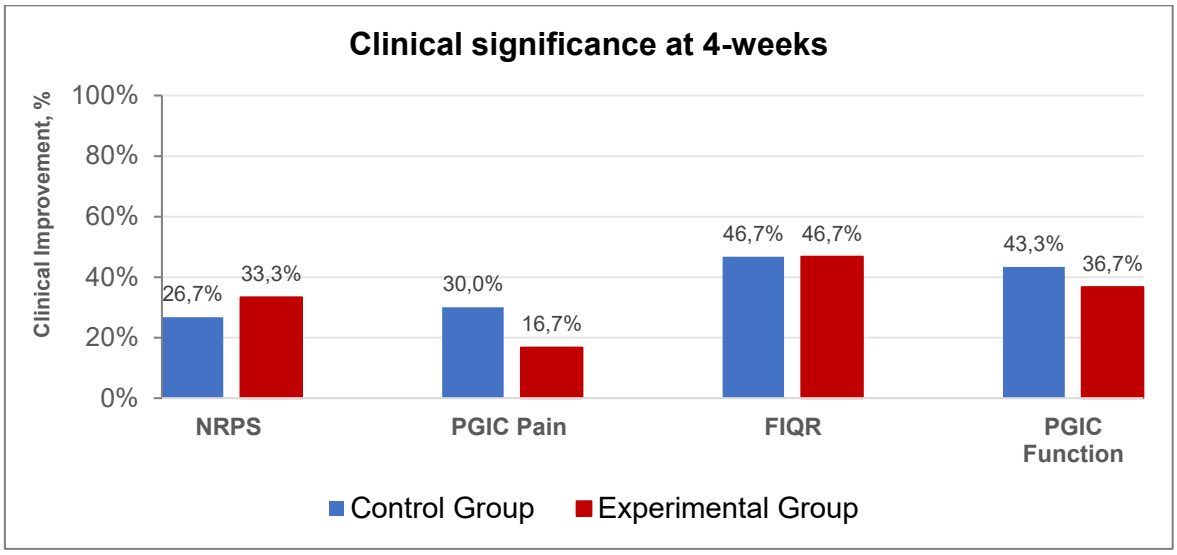

Figure 5– Clinical significance of the outcomes at 4-weeks. Clinical improvement of the participants are expressed in percentages. **Abbreviations:** NRPS: Numeric Rating Pain Scale; PGIC: Patient's Global Impression of Change; FIQ-R: Fibromyalgia Impact Questionnaire Revisited.

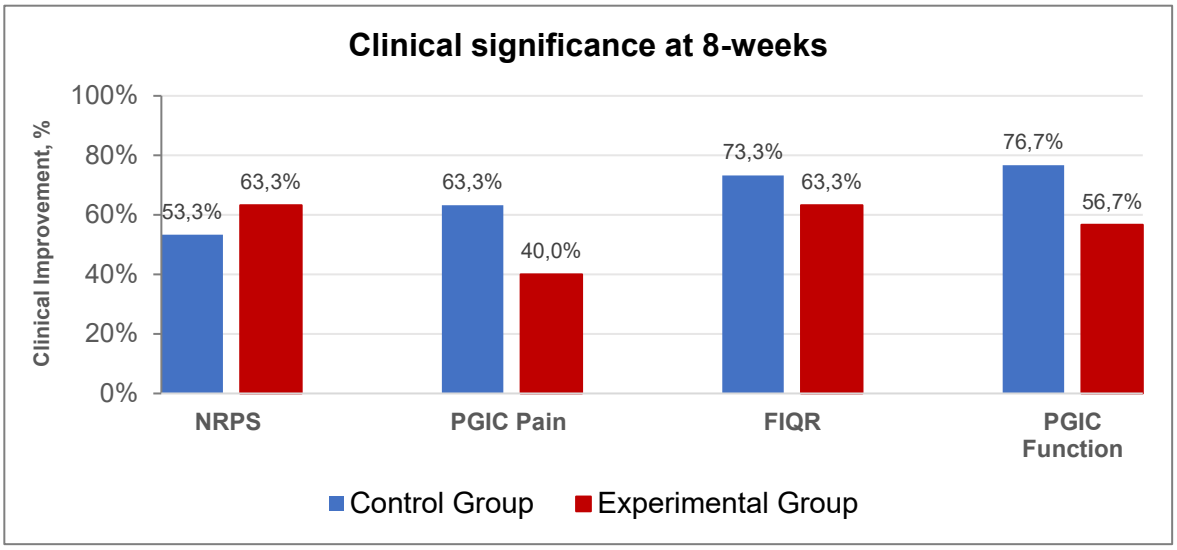

Figure 6 – Clinical significance of the outcomes at 8-weeks. Clinical improvement of the participants are expressed in percentages. **Abbreviations:** NRPS: Numeric Rating Pain Scale; PGIC: Patient's Global Impression of Change; FIQ-R: Fibromyalgia Impact Questionnaire Revisited.

Concerning the NRPS at 8-weeks, the percentage of improvement in both groups duplicated, and the differences between groups were like those found at 4-weeks, also favouring the EXP group (53.3% vs 63.3%). For the PGIC (pain), the percentage of improvement in both groups also duplicated, and like at 4-weeks, the

CONT group presented a higher percentage of clinical improvement comparing to the EXP group (63.3% vs 40.0%).

Regarding the FIQ-R and PGIC (function), the percentages of improvement increased largely in the CONT and EXP group comparing to 4-weeks. At the end of intervention, the results between groups were similar, favouring the CONT group for FIQ-R (73.3% vs 63.3%) and PGIC (76.7% vs 56.7%).

To assess relevance of treatment effects, Relative Risk (RR) and Number needed to treat (NNT) were calculated for pain intensity and disability (NRPS - table 10, FIQr – table 11).

Table 10. Relative Risk and Number Needed to Treat for pain intensity outcome

	4-weeks	8-weeks
Relative Risk (RR)	1.3 (CI 95% 0.57 - 2.73)	1.2 (CI 95% 0.77 - 1.83)
Number Needed to treat (NNT)	15 (CI 95% -4 - 6)	10 (CI 95% -3 - 7)

Herbert R. Confidence Interval Calculator (2013). http://www.pedro.org.au/english/downloads/confidence-interval-calculator/. Accessed on [30-08-2021)

At 4-weeks, 33.3% of patients in the EXP group versus 26.7% in the CONT group achieved a MCID in the NRPS, suggesting that the participants in the EXP group have 1.3 more probability to attain the MCID than the CONT group. The NNT suggests that for every 15 patients treated with exercise and education (EXP group), at least one will have a better outcome than if treated with exercise alone (CONT group).

At the end of the interventions (8-weeks), 63.3% of patients in the EXP group versus 53.3% in the CONT group achieved a MCID in the NRPS, suggesting an RR of 1.2 for the benefit of the EXP group. The NNT suggests that for every 10 patients treated with exercise and education (EXP group), at least one will have a better outcome than if treated with exercise alone (CONT group).

Table 11. Relative Risk and Number Needed to Treat for disability outcome		
	4-weeks	8-weeks
Relative Risk (RR)	1.0 (CI 95% 0.36 - 2.76)	0.9 (CI 95% 0.61 - 1.22)
Number Needed to treat (NNT)	0 (CI 95% -4 - 4)	10 (CI 95% -8 - 3)

Herbert R. Confidence Interval Calculator (2013). http://www.pedro.org.au/english/downloads/confidence-interval-calculator/. Accessed on [30-08-2021)

Concerning disability, at 4-weeks, 46.7% of patients in the EXP group versus 46.7% in the CONT group achieved a MCID on FIQr, suggesting that the participants in the EXP group have the same probability (1.0) to attain the MCID than the CONT group. The NNT suggests that patients treated with exercise and education, or exercise alone at 4 weeks will have the same outcome.

At the end of the interventions (8-weeks), 63.3% of patients in the EXP group versus 73.3% in the CONT group achieved a MCID on FIQr, suggesting that the participants in the EXP have less probability (0.9) to attain the MCID than the CONT group. The NNT suggests that for every 10 patients treated with exercise and education (EXP group), at least one will have a better outcome than if treated with exercise alone (CONT group).

DISCUSSION

Overall discussion

This RCT aimed to compare the effectiveness of an 8-week intervention program combining exercise with a patient-centred education approach that integrated the participants clinical narratives compared to exercise alone on pain and disability.

The present study found no significant interaction between our interventions and time, for pain intensity or disability. The main effect of time analysis showed a statistically significant difference in terms of pain intensity reduction from the baseline to the end of the interventions, with a medium effect size. Also for disability, there was a statistically significant difference from the baseline to the end of the interventions, with a medium effect size. For the main effect of group, there was a statistically significant difference between intervention groups on pain intensity, favouring the CONT group, with a small effect size. There was no statistically significant differences between intervention groups for disability.

In terms of clinical significance for pain intensity, a higher proportion of participants in the EXP group achieve the MCID at 4- and 8-weeks, although these results were not statistically significant. RR suggest that the participants in the EXP group have 1.3 more probability to attain the MCID than the CONT group at 4-weeks, and 1.2 more probability to attain the MCID than the CONT group at the end of the interventions. The NNT at 4-weeks suggest that for every 15 patients treated with exercise and education, at least one will have a better outcome than if treated with exercise alone. At 8-weeks, the NNT suggests that for every 10 patients treated with exercise and education, at least one will have a better outcome than if treated with exercise alone.

The clinical significance for disability showed identical proportions of participants achieving the MCID in both groups at 4-weeks, and slightly superior for CONT group at 8-weeks, without any statistical significance. The RR analysis demonstrated that both groups have the same probability (1.0) to attain the MCID on the FIQr at 4-weeks and the EXP group has 0.9 less probability to attain the MCID at 8-weeks. The NNT suggests that patients treated with exercise and education, or exercise alone will have the same outcome at 4-weeks, and for every 10 patients treated with

exercise and education, at least one will have a better outcome than if treated with exercise alone at 8-weeks.

The clinical significance for PGIC (pain and disability) showed that the proportion of participants attaining the MCID was slightly superior for the CONT group at 4- and 8-weeks, without statistically significant result.

There are several potential explanations for the findings of no significant interaction between the interventions and time. First, this study results lead us to speculate that the exercise program has been the responsible for the improvement of pain intensity, disability and PGIC in both CONT and EXP groups. By doing exercise regularly, participants may have improved their physical capacities and enhanced their ability to perform physical tasks as well as decreased FM impact and symptoms.

Second, the choice of the outcomes measures to assess the clinical effect of the education programmes must be questioned. It is well established that changes in the patients' capacity to self-manage chronic MSK pain are still measured with outcomes measures such as pain, disability, physical functioning, psychosocial variables and quality of life (Banerjee et al., 2018). Since the objective of this study was to compare the effectiveness of an 8-week intervention program combining exercise with a patient-centred education approach, it is possible that the outcomes measures selected for this purpose were not able to perceive the clinical effect of the education programme.

Furthermore, pain intensity seems to not be an important indicator to assess improvement in patients submitted to a program that combines exercise and education (Parreira and Caeiro, 2019; Bourgault et al., 2015). According to the study of Parreira and Caeiro (2019), patients reported the capacity to self-manage the clinical condition as a critical aspect to assess their improvements rather than pain intensity. Bourgault et al., (2015) did not found neither significant changes on 0-10 pain intensity scale between their control and experimental group. Instead, they found, in their qualitative analysis, that a combined education and exercise program might be successful in helping patients to improve the self-management of the disease and achieve improvements towards pain coping strategies.

The Health Education Impact Questionnaire (heiQ) is a reliable outcome measure specifically design for the assessment of patient education programs. It has proved to be an acceptable multidimensional instrument to assess different self-management related constructs, with good psychometric properties (Banerjee et al., 2018). The heiQ provides a broad profile of the potential impacts of patient education programs, covering 8 scales that assess constructs like positive engagement in life, health directed behaviours, skill and technique acquisition, constructive attitudes, self-monitoring, health service navigation, social support and emotional wellbeing (Osborne, Elsworth & Whitfield, 2007). A recent RCT in patients with FM compared two education programs using the heiQ as a primary outcome measure (Musekamp et al., 2019). The authors found some promising results at the short term in terms of subjective knowledge, pain related control, self-monitoring and insight, communication about disease, action planning for physical activity and treatment satisfaction (all $p < 0.05$). Plus, the effect of knowledge persisted for 6 or 12 months (Musekamp et al., 2019). However, this study did not include any exercise component.

Another valid argument that has been used to explain the limited effects of non-pharmacological interventions, is the heterogeneity of patients suffering from FM. In other words, there may be subgroups of patients who are most likely to benefit from a specific treatment than others and measuring the average treatment effectiveness may lead to misleading results and conclusions (Sarzi-Puttini et al., 2020; Rehm et al., 2010; Van Koulil et al., 2007). This could have been the case in our study since, the average pain reduction favours the CONT group at 4-weeks, but a higher percentage of participants in the EXP group achieve the MCID in pain intensity. Yet, the PGIC (pain) still favours the CONT group. These results lead us to conclude that average scores, MCID and PGIC are three different forms of clinical outcome measurements that varies considerably among individuals with FM.

One promising form of subgroup analysis is the treatment effect modifiers (TEM). TEM represent information contained at the baseline which indicate an interaction with treatment to change outcomes. It allows to identify subgroups of patients who have a better response or not to an intervention (Pincus et al., 2011). Such information can be obtained through a secondary analysis of an RCT and are

considered a cost-effective form of subgroup analysis (Steenstra et al., 2009). This is particularly important in conditions such as fibromyalgia, that are considered heterogeneous. Possible TEM might include sex, age, socioeconomic class, initial severity of symptoms and other potential baseline characteristics (Kraemer, Frank & Kupfer, 2006). These findings could inform future researchers and clinicians about characteristics of patients who respond better to a specific intervention such as exercise and education, therefore tailoring treatment in fibromyalgia. To our current knowledge, there is no study which has explored the TEM in individuals with FM.

The beliefs and attitudes about health and illness held by the healthcare professionals may affect patient's beliefs, attitudes and behaviours, influencing the health outcomes. Recent literature in CLBP found that a biomedical model placing importance on the severity of tissue damage may lead to high levels of fear avoidance beliefs and reinforcement of a cautionary and passive approach from physiotherapists. This could result in long-term passivity by patients, as well as fear avoidance beliefs about activity, and disengagement from a self-management approach (Gardner et al., 2017). Concerning the physiotherapist in charge in this study, we could not control her beliefs and attitudes towards participants and interventions. A BPS approach was expected from the physiotherapist to handle the combined exercise and education programme. It is possible that this approach could have also influenced positively the results in the group submitted to an exercise program alone (control group).

Finally, a non-statistically significant interaction between intervention and time does not necessarily translate into a clinically relevant difference. For that reason, the frequencies of participants achieving the MCID in pain intensity and disability were analysed, identified as a treatment responder to our interventions. It is important to note that the percentages almost duplicated in both groups from 4 weeks to the end of the interventions.

At the end of this study interventions, statistically significant results were observed in terms of time effect for pain intensity and disability with medium effects sizes. That means that this study interventions were effective for decreasing pain intensity and disability.

We unexpectedly found statistical differences for the main group effect favouring the CONT group (p=0.003) regarding the primary outcome pain intensity. We attribute several reasons to these results. First, it is important to note that the mean difference for the overall timepoints (baseline, T0, T1 and T2) was just -1.28 points (95% CI 0.47, -2.1) and the effect size was small (0.15). Plus, the group effect analysis ignore the time factor, which is an important aspect of the interventions. Second, a statistically significant difference between two groups does not necessarily translate into a clinically relevant difference. For instance, to determine the clinical relevance of our results, the individual response to our interventions must be looked, that is, the MCID in each outcome measure. Our results showed at 4- and 8-weeks a higher proportion of participants in the EXP group achieving the MCID on the NRPS. Finally, an interesting result was observed when comparing the CCA with the MI analysis. In the CCA, there was no statistical differences for the main effect of group for pain intensity (p=.064). This may indicate that there was no statistical difference between groups for those who completed both interventions. However, this results must be interpreted with caution because CCA have less statistical power than MI and a type II error could be at the origin of this result.

Hudson et al., (2009) observed that changes in clinical variables such as pain, physical functioning and fatigue were moderately to highly correlated with PGIC outcomes. Our results were consistent with these findings since there was a statistically significant results for the main effect of time for pain intensity and disability and the percentages of participants achieving the MCID duplicated on both outcomes from 4- to 8-weeks. Despite the statistically significant differences for the main effect of group on pain intensity, no statistical differences were found between groups neither for pain intensity nor for the PGIC in the clinical significance analysis.

Bourgault et al., (2015) defend that PGIC is an important outcome that could reflects clinical improvements in a programme combining exercise and education among FM individuals. Nevertheless, one cannot exclude that the improvement or worsening can be related to other factors, such as treatment convenience and costs, as well as other aspects of the side burden of the disease and medication, not considered by patients in their overall assessment of improvement (Dworkin et al., 2008).

Besides the MCID, another outcome measurement has been emerging to access treatment response based on patient's perception of their health: Patient acceptable symptomatic state (PASS). The PASS is defined as the score below which patients consider themselves well. At the end of a clinical trial, patients are classified as responders if their symptoms are less severe than their acceptable threshold (Tubach et al., 2006). The authors suggest that the most appropriate form to assess clinical improvement is to ask to the patient if they feel good rather than if they feel better. Moreover, patients report a major improvement only when they perceive their health state as satisfactory. Studies have been exploring the PASS among individuals with Rheumatoid Arthritis, Ankylosing Spondylitis, Chronic Low Back Pain, Hand Osteoarthritis and Knee Osteoarthritis (Tubach et al., 2012) but no study have searched for the effects of an intervention in the PASS in individuals with FM and the outcome measure was not yet been validated for Portuguese population.

Multiple studies have proved the effectiveness of a combined exercise and education for individuals with FM for coping with pain, disability and fatigue in the short, medium and long term. However, most of these studies did not have a non-pharmacological treatment on their control group, that is, they compared a combined exercise and education protocol to a waiting list (Bourgault et al., 2015; Lemstra & Olszynski, 2005; Cedraschi et al., 2004), no treatment (Giannotti et al., 2014), a conventional pharmacologic treatment (Martín et al., 2014; Castel et al., 2013; Luciano et al., 2011), or they used education only as a control group (Mannerkorpi et al., 2009). Moreover, the duration of the interventions, the type of exercise proposed, the content of the education sessions and the outcome measures differ from one study to another. This makes a comparison between these studies and our results difficult and inaccurate. Nevertheless, Rooks et al., (2007) and King et al., (2002) have investigated through a RCT the effectiveness of different non-pharmacological therapies, such as exercise, education or a combination of both.

In their study, Rooks et al., (2007) have searched for the effectiveness of a 16-weeks intervention program on function, symptoms, and self-efficacy in women with FM. They randomized the participants in four groups: aerobic exercise, strength exercise, education alone and combined education and strength. They have found statistically significant improvements in the FIQ score for aerobic, strength and

combined strength and education. Education alone seemed to not provide any benefits for any variable. Their between-group analysis revealed that only their combined education and strength group had a statistically significant results when compared to the education group on FIQ score (mean difference, −12.4; 95%CI, −23.1 to −1.7, p<.05). Concerning pain intensity, Rooks et al., (2007) have found statistically significant results for the between-subjects changes only in their aerobic and combined strength and education programs (-1.2 ± 2.4; -1.7 ± 2.1, p<.01).

King et al. (2002) have examined the effectiveness of a supervised aerobic exercise program, a self-management education program, the combination of exercise and education, and a control group without any intervention for women with fibromyalgia. The duration of their interventions was of 12 weeks with a follow-up at 3 months, and their outcome measures were disability, self-efficacy, 6 minutes' walk test (6MWT), tender point (TP) count and tenderness. Similarly to our results, the authors did not find significant group versus time interactions in their intention-to-treat or per-protocol analysis, but significant main effects for time were found from pre-test to follow-up for all measures, except 6MW. They have repeated their analysis using only subjects who complied with the study protocol, that is, if they did not miss 3 exercise sessions in a row, or a total of 12 of 36 exercise sessions and 6 of 14 education sessions. Interestingly, they have found a significant interaction for self-efficacy coping with other symptoms [F(6,65) = 3.48, p = 0.003] and the 6MW [F(6,63) = 2.87, p = 0.012]. Their results suggest that when a combined protocol of exercise and education is followed rigorously, individuals with FM could achieve a better sense of control over their symptoms and increase their fitness levels.

Among Portuguese population, some studies have searched for the effectiveness of interventions that combine exercise and education in individuals with FM. Prior to the implementation of our RCT, Fernandes and Caeiro (2019) have demonstrated the feasibility and acceptability of our protocol in a pilot study. The same intervention was implemented for the CONT (exercise) and EXP (exercise and education) groups, and non-parametric statistics were used for the analysis even though a comparison between groups was not explored in the study.

In terms of clinical significance, results were similar for the percentage of participants achieving the MCID in pain intensity, PGIC (pain) and PGIC (function). For the MCID in disability (FIQr), the results of Fernandes and Caeiro (2019) indicated that there was 0% of the participants in the EXP group attaining the MCID at the end of the intervention, while we found 63.3% in our study. This discrepancy is due to the use of different sources to calculate the MCID for FIQr. Fernandes (2019) used a 45.5% score reduction in the FIQr as a MCID, proposed by Surendran & Mithun (2018) whereas this study used the 14% reduction proposed originally by Bennett et al. (2009a) for the version of FIQ.

Parreira and Caeiro (2019) used a mixed methods approach to evaluate the effectiveness of the same 8-week physiotherapy program as we implemented – Fibromyalgia RehMove. On its quantitative analysis, pain intensity (NRPS), disability (FIQr) and PGIC were assessed, but the study did not include a control group. At the end of the intervention, they found a statistically significant pain intensity reduction, slightly inferior to our findings (-1.38, p =.001 vs -1.81, p<.001). Concerning the disability, the author's found a better improvement when compared to our study, although both were statistically significant (-21.6, p <.001 vs -13.99, p<.001).

In terms of clinical relevance, the percentage of participants achieving the MCID in pain intensity was similar in both studies (56.8% vs 63.3% in our study). For the MCID in disability (FIQ-R), Parreira and Caeiro (2019) used the same source as Fernandes and Caeiro (2019) and considered the 45.5% score reduction (Surendran & Mithun, 2018). They had 35.1% of participants attaining the MCID while this study present 63.3%. PGIC (pain and function) assessment at the end of the 8-weeks intervention showed that 70.3% and 78.4% of the participants achieve a MCID in these outcomes, respectively. These results were superior to our findings of 40% and 56.7%, respectively.

This study results are supported by current literature. According to the latest recommendations for the management of FM, the European League Against Rheumatism (EULAR) postulate that the only "strong" recommendation in terms of non-pharmacological treatment is in favour of exercise (Macfarlane et al., 2017). A

recent umbrella review confirmed that exercise improves pain intensity, quality of life and physical and psychosocial function (Andrade et al., 2020).

In this study, we have included both AE, STG and STR components to provide larger benefits to the participants. The intervention protocol is well described in every session and can be implemented at any environment with a small number of materials. We set the intensity of our aerobic sessions at 50% of Heart Rate Reserve (HRR), which corresponds to light to moderate intensity on Borg CR-10 scale (Andrade et al. 2017b). There was a concern that the 1-RM test could cause physical overload or increase symptoms. Instead, the modulation of resistance training was based on the self-perception of effort, which can also be measured with the Borg CR-10 scale after completing each working set (Morishita, Tsubaki, Takabayashi & Fu, 2018).

The EULAR suggests that initial management should also contain patient education about the condition (Macfarlane et al., 2017). Literature proposes that health education promotes self-management and improves health-related behaviours towards the disease. It can lead to greater patient autonomy, a lower intake of medication and less dependence on the health system (Perez-Aranda et al., 2017). On the other hand, patients seem to have a need for sharing and comparing their illness experiences to other people with a long history of FM (Salinen et al., 2011). They also do not feel heard or believed during their encounters with health professionals and report insufficient sharing of information or explanations relating to their conditions (Doebl, Macfarlane & Hollick, 2020).

To the authors` knowledge, this is the first clinical trial exploring a patient-centred education programme integrating FM patients` clinical narratives. It is well accepted that explaining complex biomedical theories work poorly for many FM patients (Hyland et al., 2016), especially considering their cognitive deficits, such as lack of concentration or memory problems (Pearson et al., 2020; Pires et al., 2018). The patient-centred education with a narrative-based approach implemented in the educative sessions allowed the participants to share their illness experiences, encouraging them to be more confident and autonomous when handling their condition. For that reason, it could have given to the participants a sense of being

listened, informed and encouraged to find realistic strategies to self-manage their conditions and have a more positive impact in their daily lives. However, this study design does not allow for the assessment of these considerations.

Drop-out and treatment compliance in FM are well discussed in the literature. Although several authors report the efficacy of rehabilitation programmes, poor compliance and high dropout rates reflect the difficulties that involve exercise and behaviour modification for patients with FM. Authors of RCTs have reported drop-out rates between 13% to 35% (Giannotti et al., 2014; Martín et al., 2014; Luciano et al., 2011; Mannerkorpi et al., 2009; Rooks et al., 2007; Lemstra & Olszynski, 2005; Cedraschi et al., 2004; King et al., 2002).

In this study, dropout causes, and frequencies were equal in both groups, which means that they were not influenced by the differences between the interventions. Most of these study interventions occurred during the pandemic year of 2020. The use of masks, cleaning hands and physical distancing was ensured, according to the recommendations of the World Health Organisation and Directorate-General of Health of Portugal (Direção-Geral da Saúde).

The drop-out rate was 43%, even though we initially expected it at 35%. This may have been related to the COVID19 pandemic because most of the interventions occurred during the pandemic year of 2020. Before the pandemic, the drop-out rate was 25% while during the pandemic it was above 50%. Participants who lived far away from the intervention site and did not have their own transport could have been more exposed in public transports. We speculate that this must have influenced our drop-out participants, which would explain the discrepancy between our expectations and our results. Nevertheless, one cannot exclude difficulties for FM patients to cope with pain after exercise, to handle stressful situations or other personal problems associated with deconditioning and psychosocial factors.

The participants who dropped out had a higher average disability score at the baseline compared to the participants who completed the study, although both presented severe disability. In terms of pain intensity, a high proportion of participants in both groups with severe pain was observed, although being slightly superior among those who dropped out.

Interestingly, among the drop out participants, the proportion of individuals that were not married (single, widowed or divorced) was higher compared to those who completed the interventions. On the contrary, there was a higher proportion of married persons (or living with significant others) accomplishing the intervention compared to those who dropped out. This is an interesting finding that led us to conclude that in this study, participants who were married had more probability to accomplish the intervention programme and those who were not married tended to drop out somewhere during the 8-weeks intervention period. These findings are supported by Martín et al. (2017) who found that being married was associated with a lower impact of FM. According to the authors, the marital relationship and the family life may lead to a greater social support and affect positively the adjustment of the disease in the patient´s life.

To maintain the baseline comparability of the compared groups, data was analysed according to the intention-to-treat analysis that includes all patients as originally allocated after randomization. Because of the high drop-out frequency, a robust and valid method to deal with the missing data - multiple imputation (MI) was selected. This advanced method has the potential to improve the validity of the results and preserve the study power. It aims to allow for the uncertainty about the missing data by creating several different plausible imputed data sets and appropriately combining results obtained from each of them (Sterne et al., 2009).

Other statistical methods are proposed in the literature for dealing with missing data. Complete-case analysis (CCA) arises as the most used method, but it involves excluding individuals with missing data from the analysis (Pedersen et al., 2017). This is an important issue since a large proportion of valuable data is ignored. Beyond that, authors suggest as a rule of thumb using CCA if the proportions of missing data are below approximately 5% (Jakobsen, Gluud, Wetterslev & Winkel, 2017), which is far from the 31.3% missingness of this study. Sensitivity analyses with worst-case and best-case scenarios is another method that could be used to deal with missing data. However, some authors state that this analysis can produce opposed results, can be difficult to interpret and yield biased estimates (Pedersen et al., 2017).

Using MI implies a potential bias because the missing data depends on the mechanism responsible for the lack of data itself and there is no standard procedure or valid test that can be used to assess the underlying correct mechanism (Pedersen et al., 2017; Jakobsen et al., 2017). Huges et al. (2019) suggest using the knowledge about the study and subject matter to decide which mechanism is responsible for the missing data.

In this study analysis, a missing at random (MAR) mechanism was assumed. First, the missing data was related to the withdrawals occurred due to personal or professional reasons, such as schedule incompatibility, lack of transportation or personal problems. As mentioned above, this was highly influenced by the COVID19 pandemic. Second, statistically significant associations between drop out participants and their marital status were observed. In conclusion, data were MAR because missing data was explained by associations with the observed data. Finally, Pedersen et al. (2017) argue that in most of clinical research, missing data are MAR.

Although there is no consensus about an established limit for the acceptable percentage of missing data when using MI, Pedersen et al. (2017) suggest as a rule of thumb a limit above 40%. In our study, a 33% of missingness was found and 20 imputed datasets were created, to achieve a desired efficiency of 99%, based on the recommendations of Newgard & Haukoos (2007).

To reduce the chance of bias, results between intention-to-treat and per-protocol analysis were compared. The use of MI method seemed to lead to small changes in the treatment effect compared to the complete case analysis. No differences were found for the group-by-time interaction and the main effect of time for pain intensity and disability. No differences were found for the main effect of group for disability. Still, some differences emerged for the main effect of group for pain intensity. The MI seemed to strengthen the effect of the CONT in the intention-to-treat analysis.

Strengths, limitations and future studies

Strengths

The randomized design, rigorous participant selection, equal sample size in each branch of the study, blind instrument assessor and participants, and the intention-to-treat analysis, were aspects that indicated a considerable internal validity in this study. Selection bias and confounding were reduced using random block size allocation, with treatment groups uniformly distributed and equal in size. Our double-blind methodology minimized the likelihood of differential treatment or assessments of outcomes and increased the robustness of the study. Although this study was constituted by a relatively small sample, it was determined a priori by a sample size calculation. Data were analysed according to the intention-to-treat analysis that included all patients as originally allocated after randomization. This is the recommended method in superiority trials to avoid bias.

It is generally accepted that patients who are attended at different health care levels or choose to participate by themselves in research studies present differences in terms of clinical and psychosocial features (Wolfe, 1990). They can have also different levels of symptoms severity, illness duration or self-efficacy (Boyer, Mira, Calatayud, Lopez-Roig & Cantero, 2009). Our sample size was obtained via three different forms: medical referral from two different hospitals (National Health Service); self-inscription through dissemination of the study in the local community; and dissemination in a patient association group. These aspects add strength to the external validity of this study results.

The exercise and education interventions were administered following a protocol that promoted improvement without exacerbating symptoms. The physiotherapist responsible for the interventions received training sessions for the implementation of the protocol. The exercise program was entirely described and included the type of exercise, frequency, intensity, volume and progression, for each session. Bodyweight mat exercises were implemented during most of this programme, adding external resistances such as elastic bands. A pre-planned format with learning outcomes and guiding questions to achieve the goals of each educative

session was also developed. Thus, this study protocol interventions can be implemented in any environment with a small number of materials.

Limitations

Data analysis did not provide follow-up after the end of the interventions. Considering that FM is a chronic condition associated with decreased quality of life and function, it is essential to understand and assess the outcomes at medium and long-term.

Since the intervention included pain neuroscience education and self-management strategies to improve health literacy, behaviours toward physical activity and coping strategies, it would be appropriate to assess and compare such outcomes in this study. These could have, hypothetically, showed better results in the group submitted to a combined exercise and education program.

Although the FIQr has been recommended by OMERACT for patients with FM, its MCID has not yet been established. Surendran & Mithun (2018) proposed a 45.5% improvement on the FIQr score as a MCID, but this score is much higher than the 14% obtained for the older Fibromyalgia Impact Questionnaire. To the authors` knowledge, this score has not been used in recent clinical trials. To reduce the risks of an underestimation of this study`s results, a conservative approach was chosen by using the 14% score reduction of the FIQ as a MCID.

The intervention's provider was aware of the study hypothesis. Although our special attention in reducing such bias through the implementation of a strict protocol for every session, it was not possible to avoid it. An audit during the interventions by recourse to an independent judge was planned but not implemented due to the pandemic restrictions in the intervention site.

There were drop-out participants over the course of the study, especially in the first 4-weeks after the beginning of the interventions. This is a common problem in clinical trials with FM participants, for reasons that may be attributed to the inherent nature of the condition. Missing data will always result in loss of statistical power and will be a limitation to consider when interpreting our trial results. The drop-out in this study was considerably superior to our expectations and this was attributed to the global pandemic occurred in 2020.

To deal with the missing data, a multiple imputation method was performed. This is more likely to generate valid estimates while appropriately accounting for the uncertainty in the imputation process and preserving study power. Moreover, the results of this imputation method were compared to a per-protocol analysis (complete case analysis) and showed small differences between the methods, particularly for the main effect of group on pain intensity.

Finally, drugs consumption were not monitored along the study. It is well established that FM individuals have higher use of pain-related medications such as antidepressants, long-acting opioids, analgesics, and muscle relaxants (Sicras-Mainar et al., 2009). Clinical trials exploring exercise interventions have already found benefits in reducing monthly medication consumption (Wang et al., 2018; Giannotti et al., 2014). Although the relationship between exercise and drug intake is not fully understood in patients with FM; showing a reduced medication intake may lead to a better medium-long terms results, and less costs for society.

Future studies

First, it seems critical to establish a MCID in the FIQr through a well-designed and high-quality study. This will allow for a more precise identification of the clinical relevance in trial results and find clearer treatment responders/non responders to the interventions.

It is necessary to develop the translation, cultural adaptation, and validation to European Portuguese of some outcomes measures to access the clinical benefits of the education and self-management programmes. Using the PASS in patients with FM could set other treatment-criteria besides the MCID to measure the treatment effects at the individual level and the Health Education Impact Questionnaire (heiQ) may constitute an appropriate form of measuring changes in self-management over time.

Secondary analysis of RCT's with larger sample sizes should be considered to explore and understand the variability within patients and their influence on treatment outcomes. This will allow for a better understanding about the subgroups of patients with FM who have better response to a specific treatment.

This study pointed out the marital status as a significant baseline characteristic in the patients who tend to drop-out. Futures studies should focus in identifying other characteristics of those who tend to drop-out and find strategies for a better treatment adherence and convenience.

Finally, the medium and long-term benefits of a combined education and exercise programme must be understood, extending the follow-up at 3, 6 and 12 months.

CONCLUSION

The present study found no significant interaction between our interventions and time, which suggests no superiority between a combined programme of exercise and education compared to exercise alone for pain intensity and disability.

This study interventions were both effective for decreasing pain intensity and disability from the baseline to the end of the interventions, with medium effects sizes.

In terms of clinical relevance, the proportion of participants achieving the MCID duplicated from 4-weeks to the end of the interventions for pain intensity, disability and patient's global impression of change. There was a higher proportion of participants in the EXP group achieving the MCID on pain intensity at 4- and 8-weeks. The group submitted to a combined program of education and exercise had more probability to attain the MCID on pain intensity and had better outcomes than the group submitted to exercise alone, although not statistically significant.

Drop-out participants in FM clinical trials are still an important concern, especially those containing exercise. Deconditioning, difficulties to cope with pain after exercise or psychosocial factors may have a strong correlation with withdrawals. In this study, drop-outs were severely affected by the COVID19 pandemic. Marital status had a significant influence on the accomplishment of this study interventions. This finding led to the conclusion that social support is a key factor for the engagement in exercise and education treatments among those suffering from FM.

Recent research have emphasised the need to assess education and self-management programs in clinical trials in patients with MSK chronic pain with outcomes measures that are specifically designed to measure the ability to manage the chronic condition, as well as health literacy and psychosocial, behavioural and lifestyle modifications. Future studies in individuals with FM exploring education programs and exercise should include outcomes measures to access self-efficacy towards the control over their symptoms, adaptative healthy behaviours and patients perceived health state.

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APPENDIX

APPENDIX I

Ethics committees' approval

IPS Instituto Politécnico de Setúbal
Escola Superior de Saúde

COMISSÃO ESPECIALIZADA DE ÉTICA EM INVESTIGAÇÃO

Parecer 42/AM/2019

SOLICITAÇÃO

Pedido de parecer à Comissão Especializada de Ética para Investigação da ESS-IPS pela docente Carmen Caeiro no âmbito do projeto SHARE (Saúde e Humanidades Actuando em Rede / Health and Humanities Acting Together). O SHARE enquadra-se nos projetos de desenvolvimento de atividades de investigação aplicada e de desenvolvimento tecnológico com potencial impacto no tecido empresarial e social, enquadrados nos domínios da Estratégia de Especialização Inteligente (RIS3), nacional e regional, tendo sido aprovado para financiamento pela Fundação para a Ciência e Tecnologia (FCT) (Ref.ª PTDC/LLTOUT/29231/2017). Insere-se no movimento emergente das humanidades médicas e prossegue trabalho pioneiro iniciado em 2009, no âmbito do projeto FCT Narrativa e Medicina: (Con)textos e Práticas Interdisciplinares (Ref.ª PTDC/CPC-ELT/3719/2012). Tem como investigadora principal a Professora Doutora Isabel Fernandes, docente na Faculdade de Letras da Universidade de Lisboa, instituição proponente do projecto. O projecto conta com a colaboração de uma equipa de investigadores, oriundos de diferentes áreas do conhecimento, como por exemplo as Humanidades, a Filosofia, a Psicologia, a Sociologia, a Medicina, a Fisioterapia, entre outras.

DOCUMENTAL

1. Dossier de submissão à CEEI;
2. Apêndice 1. Materiais de divulgação;
3. Apêndice 2. Ficha informativa para participantes;
4. Apêndice 3. Formulário de consentimento informado;
5. Apêndice 4. Caderno de instrumentos

ANÁLISE E PARECER

1. O presente estudo enquadra-se no âmbito do projeto SHARE -Saúde e Humanidades Actuando em Rede, financiado pela FCT e em colaboração da ESS com Faculdade de Letras da Universidade de Lisboa, pretende investigar os efeitos da combinação do exercício com uma abordagem educativa centrada nas narrativas dos utentes com fibromialgia comparativamente com a realização isolada de exercício.

2. Os participantes são indivíduos maiores de 18 anos com diagnóstico de fibromialgia que cumpram os critérios de seleção.

3. Método de colheita de dados através de: 1) Questionário de Caracterização Sócio-Demográfica e Clínica; 2) Escala Numérica de Dor (END); 3) Revised Fibromyalgia Impact Questionnaire – Versão Portuguesa (FIQr-PT); 4) EuroQol 5D-3L – Versão Portuguesa (EQ 5D-3L); e 5) Patient Global Impression of Change – Versão Portuguesa (PGIC-PT).

4. Formulário de consentimento evidencia os aspetos éticos - informação aos participantes, incluindo; assegurado o direito ao anonimato e à confidencialidade da informação prestada; a duração da participação e o direito de abandonar o projecto.

Considera-se que o estudo preenche os requisitos éticos, com preocupações relativas à proteção dos direitos dos participantes do estudo, pelo que se emite **parecer favorável**.

02 de maio de 2019

P´la CEEI

REPÚBLICA PORTUGUESA
SAÚDE

SNS SERVIÇO NACIONAL DE SAÚDE

CENTRO HOSPITALAR DE LISBOA OCIDENTAL, E.P.E.

CES **Comissão de Ética para a Saúde**

N.º Registo no RNEC: 20170700050

PARECER

Projeto de Investigação,

Título: "**Estudo sobre os efeitos da fisioterapia na população com fibromialgia**" (enquadrado no projeto SHARE – Saúde e Humanidades Atuando em Rede)

Investigadora Principal, externa ao CHLO: **Prof.ª Doutora Carmen Caeiro** (Instituto Politécnico de Setúbal)

Investigador Principal no CHLO: **Prof.º Doutor Fernando Pimentel-Santos** (Serviço de Reumatologia do CHLO–HEM e FCM–UNL)

Serviço no CHLO onde decorrerá o estudo: **Serviço de Reumatologia do CHLO**

Após reunião de 03 de junho de 2019 e estando o estudo de acordo com as normas de submissão impostas por esta CES, deliberou-se emitir **parecer favorável** à realização do mesmo.

A Comissão de Ética para a Saúde solicita aos Investigadores Principais que, quando da conclusão deste estudo, lhe seja enviada uma síntese dos resultados e conclusões do mesmo.

Ouvido o Relator, o processo foi votado pelos Membros da Comissão de Ética para a Saúde do Centro Hospitalar de Lisboa Ocidental presentes em reunião de 03 de junho de 2019:

Presidente: Dra. Paula M. R. Peixe

Dra. Lucília Carvalho, Dr. Carlos Neves, Enf.ª Clara Carvalho,

Dra. Helena Farinha, Padre João Valente, Dra. Maria João Pais e Dr. Rui Campante Teles

Pelo exposto, emitiu-se a 11 de junho de 2019, **parecer favorável**.

Presidente da Comissão de Ética para a Saúde

Dra. Paula M. R. Peixe

Paula M. R. Peixe
Presidente da Comissão
de Ética para a Saúde do CHLO

Comissão de Ética para a Saúde (CES) do CHLO
Hospital de Egas Moniz | Rua da Junqueira, 126 - 1349-019 Lisboa
Telefone: 210 432 665 | Correio eletrónico: anavalho@chlo.min-saude.pt

Para C.A.
26.11.2019
DIRETOR CLINICO DO CHS, EPE
NUNO [illegible]

DELIBERAÇÃO:
O CA autoriza
CENTRO HOSPITALAR DE SETÚBAL, EPE
O CONSELHO DE ADMINISTRAÇÃO
2019-11-27

NOTA DE SERVIÇO

PARA: Exma. Sra. Dra. Elisa Carvalhão, Gestora do Gabinete de Investigação e Desenvolvimento.
DE: Sr. Pedro Santos, Secretário do Gabinete de Investigação e Desenvolvimento

22-11-2019

ASSUNTO: Autorização à realização do Estudo: "Estudo sobre os efeitos da fisioterapia na população com fribromialgia", a realizar no Serviço da Unidade Multidisciplinar de Terapêutica da Dor do Centro Hospitalar de Setúbal, E.P.E.

Trata-se de um estudo, cuja Investigadora Principal é a Exma. Sra. Prof.ª Carmen Caeiro realizar no serviço da Unidade Multidisciplinar de Terapêutica da Dor do Centro Hospitalar de Setúbal, E.P.E. (ver anexo e processo devidadamente instruído).

O estudo teve o parecer favorável da CES. (em anexo)

A realização deste estudo tem como objectivo investigar os efeitos de um programa de fisioterapia constituído por exercício terapêutico e educação centrada nas narrativas dos utentes comparativamente a um programa de fisioterapia constituído apenas por exercício terapêutico.

À consideração superior,

Pedro Santos

DESPACHO

tomei conhecimento.
Ao Exmo Sr. Dr. Nuno Fachada, solicita-se autorização para a realização do estudo em anexo
EMP
26-11-2019

Tomei conhecimento
Ao Sec do GID, para informar o IP da deliberação do CA.
EMP
28-11-2019

ACTA Nº 48 / 19

APPENDIX II

Participant information sheet and Informed consent - an example ajusted to the requirements from the Ethics Committee of Centro Hospitalar de Lisboa Ocidental

CENTRO HOSPITALAR DE LISBOA OCIDENTAL, E.P.E.

HOSPITAL DE EGAS MONIZ

Ficha Informativa para Participantes

Estudo sobre os efeitos da fisioterapia na população com fibromialgia

Gostaríamos de convidá-la(o) a participar neste estudo. Antes de tomar qualquer decisão, é importante que compreenda as razões pelas quais esta investigação está a ser conduzida e o nível de envolvimento que lhe é pedido. Por favor, utilize o tempo de que necessitar para ler a informação que se segue. Poderá falar com outras pessoas sobre este estudo, se o desejar.

Este documento inclui duas partes: a parte 1 apresenta-lhe informação sobre o propósito deste estudo e o nível de envolvimento que lhe será pedido; a parte 2 oferece-lhe informação mais detalhada sobre a forma como o estudo será conduzido.

Se algum aspecto não for claro ou se desejar mais informação por favor não hesite em colocar as suas questões. Utilize o tempo de que necessitar para decidir se deseja ou não participar neste estudo.

Parte 1 | O propósito do estudo e o nível de envolvimento que lhe é pedido

Que instituições estão envolvidas neste estudo?

O presente estudo enquadra-se no âmbito do projeto SHARE (Saúde e Humanidades Atuando em Rede), aprovado pela Fundação para a Ciência e Tecnologia (FCT), com o número 029231. O projeto tem como entidade proponente a Faculdade de Letras da Universidade de Lisboa (representada pela Professora Doutora Isabel Fernandes), contando com a colaboração da Escola Superior de Saúde do Instituto Politécnico de Setúbal (representada pela Professora Doutora Carmen Caeiro). Neste estudo específico há a colaboração do Serviço de Reumatologia do CHLO, Hospital de Egas Moniz (representado pelo Prof. Doutor Fernando M. Pimentel dos Santos).

Qual é o propósito deste estudo?

O propósito deste estudo é avaliar os efeitos da fisioterapia em indivíduos com fibromialgia**.** Mais especificamente, pretende-se comparar os efeitos de duas intervenções de fisioterapia distintas, centradas na realização de exercício físico e educação, recomendadas pela investigação internacional e pelas diretrizes nacionais para pessoas com fibromialgia.

Porque fui convidada(o)?

Foi convidada(o) por ter diagnóstico de fibromialgia e idade entre os 18 e os 65 anos. Adicionalmente, na avaliação realizada foi excluído um conjunto de situações que poderiam exigir precauções especiais em qualquer uma das intervenções a realizar, nomeadamente a presença de outras patologias (cardiovascular, pulmonar, metabólica, neurológica, renal, oncológica, inflamatório-reumática e osteoarticular), intervenções cirúrgicas recentes (cardiotorácica, coluna vertebral ou membro inferior há menos de um ano), gestação, incapacidade física incompatível com a prática de exercício físico ou a realização de tratamento de fisioterapia semelhante ao proposto nos últimos três meses.

Tenho mesmo que participar?

A decisão é sua. Iremos descrever-lhe o estudo ao longo desta ficha informativa. Terá o tempo que necessitar para a ler e colocar questões. Caso aceite participar, solicitaremos o seu consentimento informado. É livre de desistir do estudo a qualquer momento, sem que tenha que o justificar.

O que acontece, se aceitar participar?

Será integrada(o), aleatoriamente, numa das intervenções de fisioterapia em estudo. Em qualquer uma delas, será integrada(o) num grupo de seis pessoas com diagnóstico de fibromialgia que irão realizar fisioterapia conduzida por uma fisioterapeuta.

O que terei que fazer?

Terá que frequentar as sessões de fisioterapia que irão decorrer durante um período de 8 semanas. Cada sessão terá uma duração aproximada de 60 a 90 minutos. Estão previstas duas sessões presenciais por semana e uma sessão que será realizada por si, de forma autónoma, sendo esta última realizada em casa, mas monitorizada pela fisioterapeuta responsável pela sua intervenção.

Para além das sessões de fisioterapia, ser-lhe-á solicitado que responda a questionários sobre o seu estado de saúde, que pretendem avaliar os efeitos da intervenção. Estes questionários serão aplicados em três momentos ao longo das sessões de fisioterapia (início - 1ª semana; meio – 4ª semana; e, fim – 8ª semana) e num quarto momento (três meses após o término da fisioterapia). O primeiro momento de aplicação dos questionários será realizado presencialmente, os seguintes, via telefone, num horário selecionado de acordo com a sua conveniência. O tempo estimado para resposta a estes questionários é de cerca de 10 a 15 minutos.

Quais são as possíveis vantagens em participar?

A participação neste estudo permitir-lhe-á usufruir, de forma gratuita, de sessões de fisioterapia, centradas na realização de exercício e educação, cujo formato e conteúdos são atualmente recomendados para pessoas com fibromialgia. Não lhe podemos prometer que este estudo a(o) ajude de alguma forma. Contudo, podemos garantir-lhe que a informação que retirarmos dele irá ajudar-nos a compreender melhor os efeitos da fisioterapia em indivíduos com fibromialgia, o que poderá contribuir para melhorar os cuidados de saúde prestados a pessoas com este problema no futuro.

Quais são as possíveis desvantagens ou riscos se aceitar participar?

Não são esperadas quaisquer implicações negativas para as pessoas que participarem neste estudo.

E se houver algum problema?

Qualquer queixa que tenha sobre este estudo, sobre a forma como foi abordada(o) ou qualquer dano associado serão considerados. Na parte 2 deste documento, poderá encontrar mais informação sobre este aspecto.

A minha participação neste estudo será confidencial?

Sim. Seguiremos um conjunto de princípios éticos de forma a assegurar que a sua participação será mantida em confidencialidade. Na parte 2 deste documento poderá encontrar mais informação sobre este aspecto.

Se a informação disponibilizada na parte 1 lhe despertou interesse em participar, por favor leia a informação adicional apresentada na parte 2 antes de tomar qualquer decisão.

Parte 2 | A forma como o estudo será conduzido

O que acontece se eu não aceitar participar no estudo?

A sua participação é totalmente voluntária e é livre de desistir do estudo a qualquer momento, sem que tenha que o justificar. Se desistir do estudo, não utilizaremos quaisquer dados que lhe digam respeito.

E se houver algum problema?

Se tiver alguma queixa sobre qualquer aspecto deste estudo, deverá falar com a investigadora responsável pelo estudo, Professora Doutora Carmen Caeiro através de email (carmen.caeiro@ess.ips.pt) ou via contacto telefónico (265 709 382). Nessa situação, faremos o nosso melhor para responder às suas questões.

Se pretender informação adicional, ou se desejar fazer uma reclamação poderá contactar a direção da Escola Superior de Saúde do Instituto Politécnico de Setúbal, através do telefone 265 709 300 (Diretor – Professor Doutor António Manuel Marques) ou o Diretor de Serviço de Reumatologia do CHLO, Hospital de Egas Moniz (Professor Doutor Jaime C. Branco) através do telefone 210 432 508.

A minha participação neste estudo será confidencial e anónima?

Toda a informação relacionada com a sua identidade será mantida em estrita confidencialidade e será mencionada de forma codificada e anónima. Será utilizado um código nos questionários a que irá responder para ocultar a sua verdadeira identidade. Os seus dados serão trabalhos conjuntamente com os de outros participantes, sem que seja possível identificá-la(o).

O que irá acontecer às informações que eu der sobre mim?

A informação recolhida através dos questionários será introduzida de forma codificada numa base de dados para análise posterior. Os questionários preenchidos serão armazenados pela investigadora responsável pelo estudo, em local seguro, na Escola Superior de Saúde do Instituto Politécnico de Setúbal, de forma a impedir o acesso a outras pessoas. Os questionários serão preservados por um período máximo de cinco anos após o término do estudo.

O que irá acontecer com os resultados deste estudo?

Os resultados serão utilizados exclusivamente para fins de investigação e poderão ser publicados em revistas científicas. Não será mencionada a sua verdadeira identidade em qualquer circunstância.

Quais as fases seguintes deste estudo?

Está prevista a realização de uma segunda fase, onde será estudada a percepção dos participantes sobre a intervenção. Caso tenha interesse, poderá ser contactada(o) no futuro, para obter mais informações sobre essa segunda fase e, eventualmente, continuar a participar.

Gratos pela atenção dispensada,

Carmen Caeiro

Investigadora do projeto SHARE, responsável pelo estudo
Professora Adjunta no Departamento de Fisioterapia da Escola Superior de Saúde do Instituto Politécnico de Setúbal

Fernando M. Pimentel Santos

Investigador do projeto SHARE,
Coordenador do estudo no CHLO, Hospital de Egas Moniz
Professor Auxiliar na NOVA Medical School | Faculdade de Ciências Médicas, Universidade NOVA de Lisboa

Isabel Fernandes

Investigadora responsável pelo projeto SHARE
Professora Catedrática na Faculdade de Letras da Universidade de Lisboa

Declaração de Consentimento Informado

Estudo sobre os efeitos da fisioterapia na população com fibromialgia

Declaro que aceito participar no estudo sobre os efeitos da fisioterapia, centrada na realização de exercício físico e educação, na população com fibromialgia. Este estudo enquadra-se no âmbito do projeto SHARE (Saúde e Humanidades Atuando em Rede), aprovado pela Fundação para a Ciência e Tecnologia (FCT). O projeto tem como entidade proponente a Faculdade de Letras da Universidade de Lisboa (representada pela Professora Doutora Isabel Fernandes – responsável pelo projeto), contando com a colaboração da Escola Superior de Saúde do Instituto Politécnico de Setúbal (representada pela Professora Doutora Carmen Caeiro – responsável pelo presente estudo) e com Serviço de Reumatologia do CHLO, Hospital de Egas Moniz (representado pelo Prof. Doutor Fernando M. Pimentel dos Santos – coordenador local).

Li e compreendi a ficha informativa. Foram-me explicados o objetivo e procedimentos envolvidos no estudo. As minhas questões foram esclarecidas de forma satisfatória.

Compreendi que a minha participação é voluntária e que não foram identificados riscos/consequências negativas associadas à participação neste estudo.

Tomei conhecimento de que o convite para integrar o estudo resultou da verificação de um conjunto de critérios nomeadamente ter diagnóstico médico de fibromialgia e idade entre os 18 e os 65 anos. Adicionalmente, foi excluída a presença de situações que pudessem exigir precauções especiais na intervenção realizada como a presença de outras patologias, intervenções cirúrgicas recentes, gestação, incapacidade física incompatível com a prática de exercício físico ou a realização de tratamento de fisioterapia semelhante ao proposto nos últimos três meses.

Tenho conhecimento de que irei integrar, aleatoriamente, um grupo de seis pessoas que irão realizar uma ou duas intervenções possíveis em fisioterapia, ambas centradas na realização de exercício físico e educação. Ambas são recomendadas para o tratamento de pessoas com fibromialgia.

Compreendi o tempo estimado para a minha participação. Tenho conhecimento que a intervenção tem uma duração prevista de 8 semanas, com a realização de 2 sessões presenciais por semana e uma sessão realizada de forma autónoma por mim, com monitorização do fisioterapeuta. A duração estimada para as sessões é de cerca de 60 a 90 minutos.

Compreendi, também, que irei responder a questionários em quatro momentos ao longo da realização do estudo, autorizando os contactos telefónicos para este efeito. A duração estimada para as avaliações é de cerca de 10 a 15 minutos.

Sei que a informação referente à minha identificação pessoal será mantida anónima e confidencial e apenas manuseada pelos investigadores deste estudo e utilizada para fins de investigação. Compreendi que os dados serão armazenados de forma segura.

Sei que a minha participação é voluntária, que tenho o direito de não participar no estudo e que sou livre de abandoná-lo em qualquer momento, sem qualquer consequência, prejuízo e sem necessidade de justificação.

Para esclarecimento de qualquer dúvida adicional, sei que poderei recorrer ao coordenador do estudo no CHLO, Hospital de Egas Moniz, Prof. Doutor Fernando Pimentel-Santos através do email: pimentel.santos@nms.unl.pt, ou através do telefone 210 432 508 do Serviço de Reumatologia.

Em caso de dúvida, sei que poderei recorrer ao encarregado de proteção de dados desta instituição, Dra. Maria João Lupi, através do email: dpo@chlo.min-saude.pt.

☐ Tenho interesse em ser contactada(o), via telefone, no futuro para eventual continuação de participação numa segunda fase deste estudo.

A preencher pelo participante

Nome do Participante _____

Assinatura do Participante _____

Data de Assinatura _____

A preencher por duas testemunhas (apenas no caso de o participante não ser capaz de assinar o consentimento).

"Confirmo que presenciei o consentimento informado ao participante acima mencionado. Confirmo que o participante foi devidamente informado e deu o seu livre consentimento para a sua participação no ensaio."

Nome da Testemunha nº 1 _____

Assinatura da Testemunha nº 1 _____

Data de Assinatura _____

Nome da Testemunha nº 2 _____

Assinatura da Testemunha nº 2 _____

Data de Assinatura _____

A preencher pelo Médico Investigador

Nome do Médico Investigador /
Nº Cédula Profissional _____

Assinatura do Médico Investigador _____

Data de Assinatura _____

APPENDIX III

Outcome measures

ESCALA NÚMERICA DA DOR (END)

Assinale com um “X” o número que melhor classifica a intensidade atual da sua dor, sendo que a 0 corresponde a classificação “Sem Dor” e a 10 a classificação “Dor Máxima” (Dor de intensidade máxima imaginável).

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

REVISED FIBROMYALGIA IMPACT QUESTIONNAIRE – VERSÃO PORTUGUESA

Instruções:

Para cada uma das seguintes nove questões, assinale com uma cruz (x) a caixa que melhor indica em que grau a fibromialgia dificultou cada uma das seguintes tarefas **na última semana**. Se não desempenhou alguma das atividades neste período, indique a dificuldade com que desempenhou pela última vez essa atividade. Se não pode desempenhar uma atividade, assinale a última caixa à direita.

Pentear ou escovar o seu cabelo	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Caminhar continuamente durante 20 minutos	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Preparar uma refeição	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Aspirar, esfregar ou varrer o chão	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Levantar e carregar um saco cheio de mercearias	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Subir um lanço de escadas	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Mudar os lençóis da cama	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Estar sentado numa cadeira durante 45 minutos	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**
Fazer compras de supermercado	**Sem dificuldade**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Muita dificuldade**

Instruções: Para cada uma das seguintes duas questões, assinale com uma cruz (x) a caixa que melhor indica impacto global da sua fibromialgia, **ao longo da última semana:**

A fibromialgia impediu-me de cumprir os meus objetivos da semana	**Nunca**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Sempre**
Estive completamente perturbada(o) pelos meus sintomas de fibromialgia	**Nunca**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	**Sempre**

Instruções: Para cada uma das dez questões que se seguem, assinale com uma cruz (x) a caixa que melhor descreve a intensidade destes sintomas comuns de fibromialgia, **ao longo da última semana**.

Por favor avalie o seu nível de dor

sem dor ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **dor insuportável**

Por favor avalie o seu nível de energia

muita energia ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **sem energia**

Por favor assinale o seu nível de rigidez

sem rigidez ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **rigidez grave**

Por favor assinale a qualidade do seu sono

acorda muito descansada ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **acorda muito cansada**

Por favor avalie o seu nível de depressão

sem depressão ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **muito deprimida**

Por favor avalie o seu nível de problemas de memória

boa memória ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐☐ **memória muito fraca**

Por favor avalie o seu nível de ansiedade

sem ansiedade ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐☐ **muita ansiedade**

Por favor avalie o seu nível de dor quando lhe tocam ou apertam

sem dor ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐☐ **muita dor**

Por favor avalie o seu nível de problemas de equilíbrio

Sem desequilíbrio ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Grave desequilíbrio**

Por favor avalie o seu nível de sensibilidade a ruídos fortes, luzes brilhantes, cheiros e frio

sem sensibilidade ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **extrema sensibilidade**

Patient Global Impression Change Scale – Versão Portuguesa

Desde o início do tratamento nesta instituição, como é que descreve a mudança (se houve) nas **suas limitações para realizar atividades do dia-a-dia**, em relação à sua fibromialgia (selecione UMA opção):

Sem alterações (ou a condição piorou)	☐ 1
Quase na mesma, sem qualquer alteração visível	☐ 2
Ligeiramente melhor, mas sem mudanças consideráveis	☐ 3
Com algumas melhorias, mas a mudança não representou qualquer diferença real	☐ 4
Moderadamente melhor, com mudança ligeira, mas significativa	☐ 5
Melhor, e com melhorias que fizeram uma diferença real e útil	☐ 6
Muito melhor, e com uma melhoria considerável que fez toda a diferença	☐ 7

Desde o início do tratamento nesta instituição, como é que descreve a mudança (se houve) na sua **dor,** em relação à sua fibromialgia (selecione UMA opção):

Sem alterações (ou a condição piorou)	☐ 1
Quase na mesma, sem qualquer alteração visível	☐ 2
Ligeiramente melhor, mas sem mudanças consideráveis	☐ 3
Com algumas melhorias, mas a mudança não representou qualquer diferença real	☐ 4
Moderadamente melhor, com mudança ligeira, mas significativa	☐ 5
Melhor, e com melhorias que fizeram uma diferença real e útil	☐ 6
Muito melhor, e com uma melhoria considerável que fez toda a diferença	☐ 7

PainDETECT Questionnaire – Versão Portuguesa

painDETECT

QUESTIONÁRIO SOBRE DOR

Data: ..... **Paciente:** **Apelido:** **Nome:**

Como avalia a sua dor **agora**, neste momento?

0 1 2 3 4 5 6 7 8 9 10

ausente máxima

Qual a intensidade da dor **mais forte** que sentiu nas últimas 4 semanas?

0 1 2 3 4 5 6 7 8 9 10

ausente máxima

Em média, qual a intensidade da dor que sentiu nas últimas 4 semanas?

0 1 2 3 4 5 6 7 8 9 10

ausente máxima

Assinale a imagem que melhor descreve a evolução da sua dor:

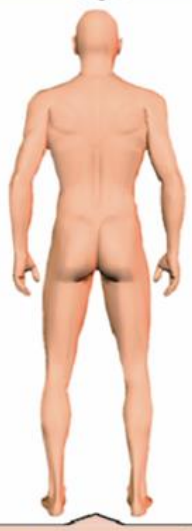
Dor constante com ligeiras variações ☐

Dor constante com crises de dor ☐

Crises de dor sem dor nos intervalos ☐

Crises frequentes de dor com dor nos intervalos ☐

Por favor indique **a principal zona de dor**



A sua dor espalha-se a outras regiões do corpo?
sim ☐ não ☐
Se sim, indique a direcção para onde a dor se espalha.

Sofre de sensação de queimadura ou ardor (p. ex., como se tocasse em urtigas) nas zonas indicadas?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

Sente uma sensação de picada ou formigueiro na zona da dor (como formigas a caminhar ou uma vibração eléctrica)?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

Um toque superficial (com roupa, cobertor) nesta zona provoca dor?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

Tem crises repentinas de dor na zona afectada, como choques eléctricos?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

O frio ou o calor (como a água do banho) provoca-lhe dor ocasional nesta zona?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

Sofre de sensação de dormência nas zonas que indicou?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

Uma leve pressão nessa zona, por ex., com um dedo, desperta dor?

nenhuma ☐ insignificante ☐ ligeira ☐ moderada ☐ forte ☐ muito forte ☐

(A preencher pelo médico)

nenhuma	insignificante	ligeira	moderada	forte	muito forte
x 0 = 0	x 1 =	x 2 =	x 3 =	x 4 =	x 5 =

Pontuação total ☐☐ **de 35 no máximo**

R. Freynhagen, R. Baron, U. Gockel,T.R. Tölle, CurrMed ResOpin Vol 22, 2006, 1911-1920

PD-Q - Portugal/Portuguese - Final version - 25 Jun 07 - Mapi Research Institute.
f:\institut\cultadap\project\4101\study4101\final_versions\pd-qporq.doc-25/06/2007

painDETECT

Pontuação do questionário sobre dor

Data: ..... **Paciente:** Apelido: ..... Nome: .....

Por favor introduza aqui a pontuação total obtida no questionário sobre dor:

Pontuação total | |

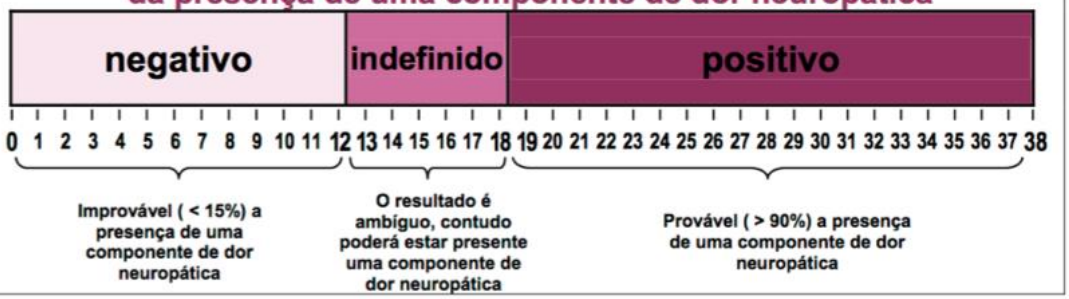
Por favor, adicione os valores seguintes de acordo com o padrão de evolução da dor assinalado e a irradiação da dor. Em seguida calcule a pontuação final:

	Dor constante com ligeiras variações	0	
	Dor constante com crises de dor	-1	se assinalou esta opção ou
	Crises de dor sem dor nos intervalos	+1	se assinalou esta opção ou
	Crises frequentes de dor com dor nos intervalos	+1	se assinalou esta opção
	Irradiação da dor?	+2	se respondeu que sim

Pontuação final | |

Resultado do despiste

da presença de uma componente de dor neuropática



Esta ficha não substitui o diagnóstico médico.
Destina-se ao despiste da presença de uma componente de dor neuropática.

DFNS

pain

R. Freynhagen, R. Baron, U. Gockel,T.R. Tölle, CurrMed ResOpin Vol 22, 2006, 1911-1920

APPENDIX IV

Exercise and Education protocol

Intervention program			
Week	**Session**	**Exercise**	**Education**
1	1	**Warm-up** **Motor control training:** cognitive stage of activation of deep neck flexors, scapular stabilizers muscles and core muscles of lumbar spine. **Stretching.**	**Topic 1: Pain and disability narratives.** The goal of this session is to understand the participants' cognitions, beliefs, and attitudes towards pain as well as the response behaviours adopted in their daily lives. Participants are invited to tell their story while the physiotherapist seeks to understand and interpret the events associated with fibromyalgia over time. **Topic 2: Expectations towards the programme.** Participants are invited to discuss their expectations. The goal is to understand what they expect from the programme as well as their objectives.
	2	**Warm-up** **Aerobic training:** 2'' warm-up + 6'' of fast walk (flat ground) at 50% HRR. **Motor control and strength:** 1x8 RM + glutes bridge, hold 5-10sec, 3reps + prone trunk extension + plank exercise (elbow and knee support), hold 5-10sec, 3reps. **Stretching.**	**Topic 3: Cognitions and response behaviours towards pain.** Participants are invited to talk about their experience of pain. The first goal is to understand how psychosocial factors are contributing to the maintenance of the problem (pain catastrophizing, fear-avoidance beliefs, low levels of self-efficacy). The second goal is to assess the response behaviour of each participant (active/passive coping strategies, kinesiophobia, dependence on the help of other people, such as family, health professionals, etc.). **Topic 4: Individual goals:** Participants are invited to set at least two priority goals centred on their individual needs, to be reassessed throughout the program.
	3	**Aerobic training (autonomous):** 6'' walk (flat ground) at 50% HRR.	
2	4	**Warm-up** **Motor control and strength**: 1x10 RM + glutes bridge, hold 5-10sec, 5reps + prone trunk extension + plank exercise (elbow and knee support), hold 5-10sec, 5reps. **Stretching.**	**Topic 5: The contribution of psychosocial factors.** Participants are invited to talk about the reasons, from their perspective, that justify their pain and fatigue. The main goal is to assess the meaning that each participant attributes to his/her pain and fatigue in his/her clinical condition. Then, the physiotherapist should use stories and metaphors to help participants understand pain, challenging their beliefs and cognitions.
	5	**Warm-up** **Aerobic training:** 3'' warm-up + 8'' of fast walk (flat ground) at 50% HRR. **Motor control and strength**: 1x10 RM + glutes bridge, hold 5-10sec, 5reps + prone trunk extension + plank exercise (elbow and knee support), hold 5-10sec, 5reps. **Stretching.**	
	6	**Aerobic training (autonomous):** 8'' walk (flat ground) at 50% HRR.	
3	7	**Warm-up** **Motor control and strength**: circuit training 2x6 RM + glutes bridge with alternated knee Flx/Ext, hold 10-15sec, 5reps + 4-point kneeling, hold 5-10sec, 3reps + plank exercise (elbow and knee support), hold 10-15sec, 5reps. **Stretching.**	**Topic 6: Understanding the neurophysiology of pain.** Participants are invited to talk about pain: what it is and how can it be explained. The main goal is to develop the discussion started in the previous session, initiating the reconceptualization of pain and changing illness perceptions. Participants are expected to understand the diversity of factors that can influence pain and fatigue. The second goal is to introduce pain neurophysiology education but only when participants start questioning their own explanations and ideas of pain.
	8	**Warm-up** **Aerobic training:** 3'' warm-up + 10'' of fast walk (flat ground) at 50% HRR. **Motor control and strength**: circuit training 2x6 RM + glutes bridge with alternated knee Flx/Ext, hold 10-15sec, 5reps + four-point kneeling hold 5-10sec, 3reps + plank exercise (elbow and knee support), hold 10-15sec, 5reps. **Stretching.**	
	9	**Aerobic training (autonomous):** 10'' walk (flat ground) at 50% HRR.	
4	10	**Warm-up** **Motor control and strength:** circuit training 2x8 RM + glutes bridge with alternated knee Flx/Ext, hold 10-15sec, 5reps + four-point kneeling with alternated arm lift, hold 5-10sec, 3reps + plank exercise (elbow and knee support), hold 10-15sec, 5reps. **Stretching.**	**Topic 7: Mid-term assessment of goals**. Participants are invited to review and summarise their improvements through the programme. The aim is to assess the impact the programme has had on achieving their goals. The physiotherapist assists the participants in evaluating their gains and understanding their needs not yet met. New goals should be considered.
	11	**Warm-up** **Aerobic training:** 3'' warm-up + 12'' of fast walk (flat ground) or 5'' fast, 2'' slow, 5'' fast, at 50% HRR. **Motor control and strength**: circuit training 2x8 RM + glutes bridge with alternated knee Flx/Ext, hold 10-15sec, 5reps + four-point kneeling with alternated arm lift, hold 5-10sec, 3reps + plank exercise (elbow and knee support), hold 10-15sec, 5reps. **Stretching.**	
	12	**Aerobic training (autonomous):** 12'' walk (flat ground) at 50% HRR.	
5	13	**Warm-up** **Motor control and strength:** circuit training 2x10 RM + clamshell exercise + four-point kneeling with alternated arm lift, hold 10-15sec, 5reps + plank exercise (elbow support), hold 10-15sec, 5reps. **Stretching.**	**Topic 8: Fibromyalgia Flare-up management.** Participants are invited to discuss possible strategies to increase their activity levels. The goal is to find strategies to manage pain and fatigue while increasing their levels of physical activity. Everyone is invited to formulate strategies that are useful for themselves or the group.

	14	**Warm-up** **Aerobic training:** 3'' warm-up + 15'' of fast walk (flat ground) or 7'' fast, 1'' slow, 7'' fast, at 50% HRR. **Motor control and strength:** circuit training 2x10 RM + clamshell exercise + four-point kneeling with alternated arm lift, hold 10-15sec, 5reps + plank exercise (elbow support), hold 10-15sec, 5reps. **Stretching.**	
	15	**Aerobic training (autonomous):** 15'' walk (flat ground) at 50% HRR.	
6	16	**Warm-up** **Motor control and strength:** circuit training 3x8 RM + clamshell exercise + four-point kneeling with alternated leg Ext., hold 10-15sec, 5reps + plank exercise (elbow support), hold 10-15sec, 5reps. **Stretching.**	**Topic 9: Factors influencing flare-up management.** Participants are invited to present self-management strategies used at home to gradually increase their activity levels as well as to deal with pain and fatigue. Through group interaction, everyone should be empowered to find realistic strategies to control pain and recognise the reasons for the success or failure of the strategies they have been using. After the discussion, the physiotherapist introduces the factors that may influence and impact flare-ups management, such as biological and psychosocial aspects.
	17	**Warm-up** **Aerobic training:** 3'' warm-up + 17'' of fast walk (flat ground) or 8'' fast, 1'' slow, 8'' fast, at 50% HRR. **Motor control and strength:** circuit training 3x8 RM + clamshell exercise + four-point kneeling with alternated leg Ext., hold 10-15sec, 5reps + plank exercise (elbow support), hold 10-15sec, 5reps. **Stretching**	
	18	**Aerobic training (autonomous):** 17'' walk (flat ground) at 50% HRR.	
7	19	**Warm-up** **Motor control and strength:** circuit training 3x10 RM + clamshell exercise + four-point kneeling superman, hold 10-15sec, 5reps + plank exercise (elbow support), hold 15-20sec, 5reps. **Stretching.**	**Topic 10: The role of the context in persistent pain.** The participants invite a guest (usually a family member or a work colleague) to this session. The goal is to allow participants to summarize the main learnings by themselves while simultaneously involving those who are closed to them in the process.
	20	**Warm-up** **Aerobic training:** 3'' warm-up + 20'' of fast walk (flat ground) or 9'' fast, 1'' slow, 9'' fast, at 50% HRR. **Motor control and strength:** circuit training 3x10 RM + clamshell exercise + four-point kneeling superman, hold 10-15sec, 5reps + plank exercise (elbow support), hold 15-20sec, 5reps. **Stretching.**	
	21	**Aerobic training (autonomous):** 20'' walk (flat ground) at 50% HRR.	
8	22	**Warm-up** **Aerobic training:** 3'' warm-up + 20'' of fast walk (flat ground) or 9'' fast, 1'' slow, 9'' fast, at 50% HRR. **Motor control and strength:** circuit training 3x10 RM + clamshell exercise + four-point kneeling superman, hold 15-20sec, 5reps + plank exercise (elbow support), hold 15-20sec, 5reps. **Stretching.**	
	23	**Warm-up** **Motor control and strength:** circuit training 3x10 RM + clamshell exercise + four-point kneeling superman, hold 15-20sec, 5reps + plank exercise (elbow support), hold 15-20sec, 5reps. **Stretching.**	**Topic 11: The experience of participating in the programme**. Participants are invited to review their participation along the programme. First, participants should summarize main learnings and outline strategies for the post-intervention. Afterwards, the goal is to promote the maintenance of efficient self-management strategies and healthy behaviours while identifying the most beneficial type of physical activity and exploring options for exercise available in the area of residence of each participant. **Topic 12: Final assessment of goals.** Participants are invited to assess the goals set in topic 7. The physiotherapist should promote a discussion to understand the reasons why participants may not have achieved their individual goals while exploring future ambitions.
	24	**Aerobic training (autonomous):** 20'' walk (flat ground) at 50% HRR.	

Warm-up: each session starts with 10 minutes warm-up "head to toes" exercises.
Motor control and strength: supine position: alt scapular protraction, alt knee flex/ext, alt arm flex/ext, alt hip flex/ext, alt horizontal shoulder ABD/ADU. Full range of motion at moderate to high speed (2 sec) with controlled eccentric action (1 sec). Rest 1 minute between series. Using theraband if necessary, from week 5.
Aerobic Training: 50% HRR (light to moderate intensity on Borg CR-10 scale).
Stretching: major muscles groups of the neck, shoulders, elbows, wrists, trunk, hip, and knee in pain-free range, holding the stretch for 15-20 seconds, repeated 3 times.
Abbreviations: HRR: heart rate reserve**; RM:** repetition maximum; **Reps:** repetitions; **Sec:** seconds; **Alt:** alternated; **Flx:** flexion; **Ext:** extension; **ABD:** abduction; **ADD**: adduction.

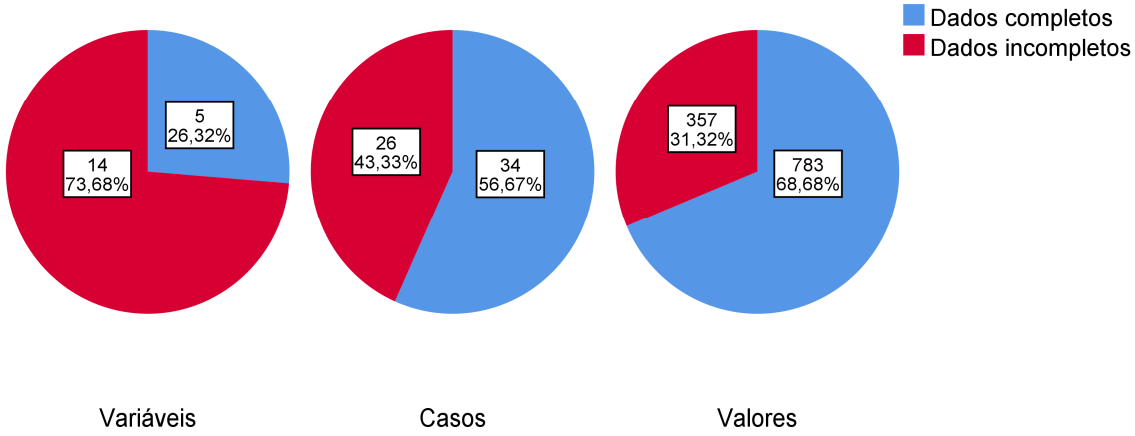
APPENDIX V

SPSS Output: Multiple imputation

Imputações múltiplas

Valores omissos

Resumo geral de valores omissos

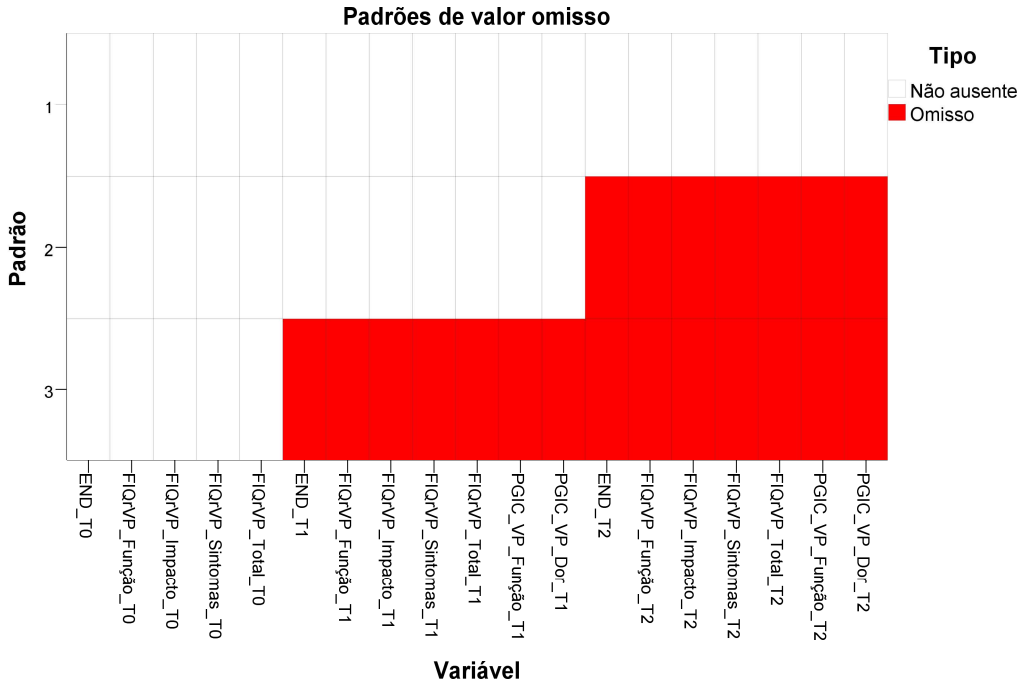


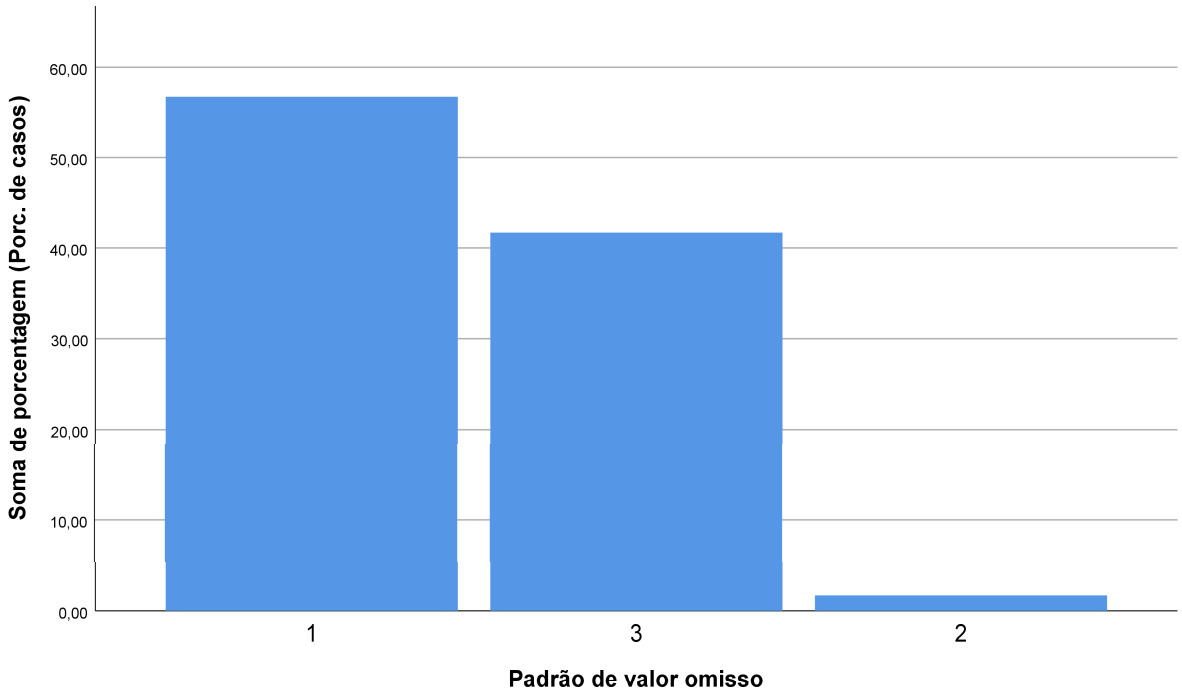
Resumo da variável[a,b]

	Omisso				
	N	Porcentagem	N válido	Média	Erro Desvio
PGIC_VP_Dor_T2	26	43,3%	34	4,65	1,390
PGIC_VP_Função_T2	26	43,3%	34	5,09	1,083
FIQrVP_Total_T2	26	43,3%	34	50,09	18,357
FIQrVP_Sintomas_T2	26	43,3%	34	26,03	8,590
FIQrVP_Impacto_T2	26	43,3%	34	8,47	5,456
FIQrVP_Função_T2	26	43,3%	34	15,47	5,910
END_T2	26	43,3%	34	4,68	1,838
PGIC_VP_Dor_T1	25	41,7%	35	3,71	1,405
PGIC_VP_Função_T1	25	41,7%	35	4,14	1,375
FIQrVP_Total_T1	25	41,7%	35	56,51	16,757
FIQrVP_Sintomas_T1	25	41,7%	35	28,86	8,139
FIQrVP_Impacto_T1	25	41,7%	35	10,63	5,225
FIQrVP_Função_T1	25	41,7%	35	17,03	5,079
END_T1	25	41,7%	35	5,89	2,069

a. Número máximo de variáveis mostradas: 25

b. Porcentagem mínima de valores omissos para variável a ser incluída: 10,0%


Padrões de valor omisso
Tipo
Não ausente
Omisso
Padrão
1
2
3
END_T0
FIQrVP_Função_T0
FIQrVP_Impacto_T0
FIQrVP_Sintomas_T0
FIQrVP_Total_T0
END_T1
FIQrVP_Função_T1
FIQrVP_Impacto_T1
FIQrVP_Sintomas_T1
FIQrVP_Total_T1
PGIC_VP_Função_T1
PGIC_VP_Dor_T1
END_T2
FIQrVP_Função_T2
FIQrVP_Impacto_T2
FIQrVP_Sintomas_T2
FIQrVP_Total_T2
PGIC_VP_Função_T2
PGIC_VP_Dor_T2
Variável


Soma de porcentagem (Porc. de casos)
60,00
50,00
40,00
30,00
20,00
10,00
0,00
1
3
2
Padrão de valor omisso

Imputações múltiplas

Especificações de imputação

Método de imputação	Automático
Número de imputações	20
Modelo para variáveis de escala	Regressão Linear
Interações incluídas nos modelos	(nenhum)
Porcentagem máxima de valores omissos	100,0%
Número máximo de parâmetros no modelo de imputação	100

Valores imputados

Resultados de imputação

Método de imputação		Uniforme
Iterações de método de especificação totalmente condicional		n/a
Variáveis dependentes	Imputado	END_T1,FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2,FIQrVP_Impacto_T2, FIQrVP_Sintomas_T2,FIQrVP_Total_T2, PGIC_VP_Função_T2,PGIC_VP_Dor_T2
	Não imputado (muitos valores omissos)	
	Não imputado (nenhum valor omisso)	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0
Sequência de imputação		END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2,FIQrVP_Impacto_T2, FIQrVP_Sintomas_T2,FIQrVP_Total_T2, PGIC_VP_Função_T2,PGIC_VP_Dor_T2

Modelos de imputação

	Modelo		Valores omissos	Valores imputados
	Tipo	Efeitos		
END_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0	25	500
FIQrVP_Função_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1	25	500
FIQrVP_Impacto_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1	25	500
FIQrVP_Sintomas_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1	25	500
FIQrVP_Total_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1	25	500
PGIC_VP_Função_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1	25	500
PGIC_VP_Dor_T1	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1	25	500
END_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1	26	520
FIQrVP_Função_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2	26	520
FIQrVP_Impacto_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2	26	520

Modelos de imputação

	Modelo		Valores omissos	Valores imputados
	Tipo	Efeitos		
FIQrVP_Sintomas_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2,FIQrVP_Impacto_T2	26	520
FIQrVP_Total_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2,FIQrVP_Impacto_T2, FIQrVP_Sintomas_T2	26	520
PGIC_VP_Função_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2,FIQrVP_Impacto_T2, FIQrVP_Sintomas_T2,FIQrVP_Total_T2	26	520
PGIC_VP_Dor_T2	Regressão Linear	END_T0,FIQrVP_Função_T0,FIQrVP_Impacto_T0, FIQrVP_Sintomas_T0,FIQrVP_Total_T0,END_T1, FIQrVP_Função_T1,FIQrVP_Impacto_T1, FIQrVP_Sintomas_T1,FIQrVP_Total_T1, PGIC_VP_Função_T1,PGIC_VP_Dor_T1,END_T2, FIQrVP_Função_T2,FIQrVP_Impacto_T2, FIQrVP_Sintomas_T2,FIQrVP_Total_T2, PGIC_VP_Função_T2	26	520

APPENDIX VI

SPSS Output: ANOVA assumptions assessment

Resumo de processamento do caso

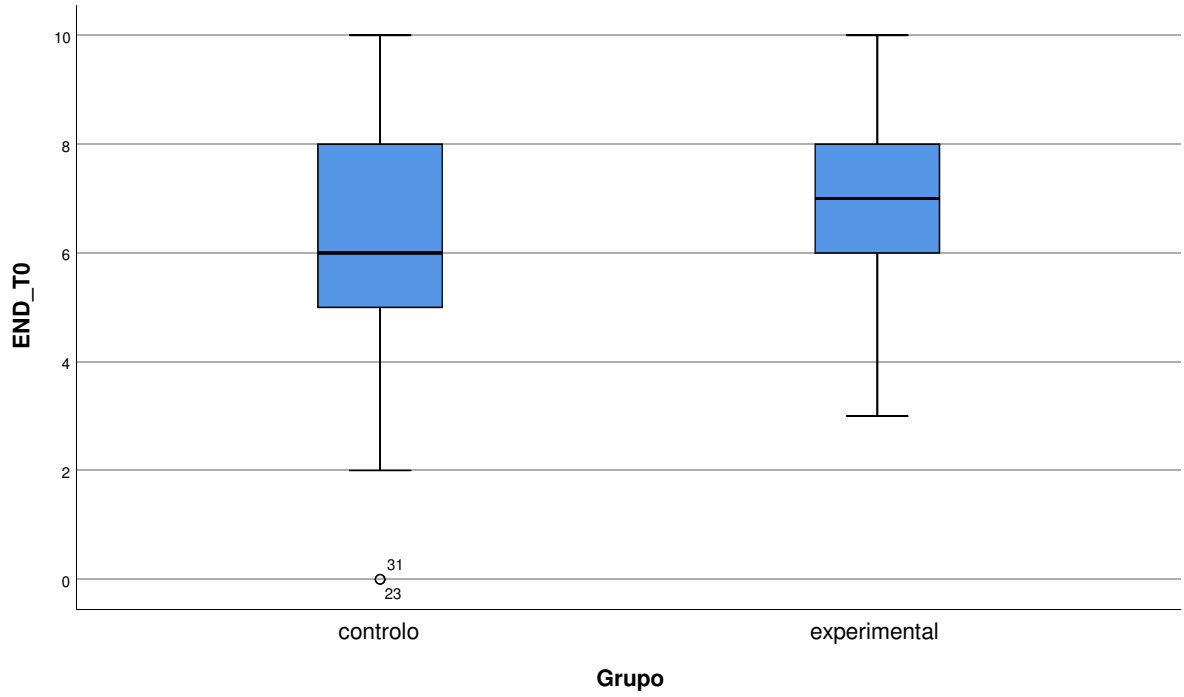
		Casos					
		Válido		Omisso		Total	
	Grupo	N	Porcentagem	N	Porcentagem	N	Porcentagem
END_T0	controlo	30	100,0%	0	0,0%	30	100,0%
	experimental	30	100,0%	0	0,0%	30	100,0%
FIQrVP_Total_T0	controlo	30	100,0%	0	0,0%	30	100,0%
	experimental	30	100,0%	0	0,0%	30	100,0%
END_T1	controlo	30	100,0%	0	0,0%	30	100,0%
	experimental	30	100,0%	0	0,0%	30	100,0%
FIQrVP_Total_T1	controlo	30	100,0%	0	0,0%	30	100,0%
	experimental	30	100,0%	0	0,0%	30	100,0%
END_T2	controlo	30	100,0%	0	0,0%	30	100,0%
	experimental	30	100,0%	0	0,0%	30	100,0%
FIQrVP_Total_T2	controlo	30	100,0%	0	0,0%	30	100,0%
	experimental	30	100,0%	0	0,0%	30	100,0%

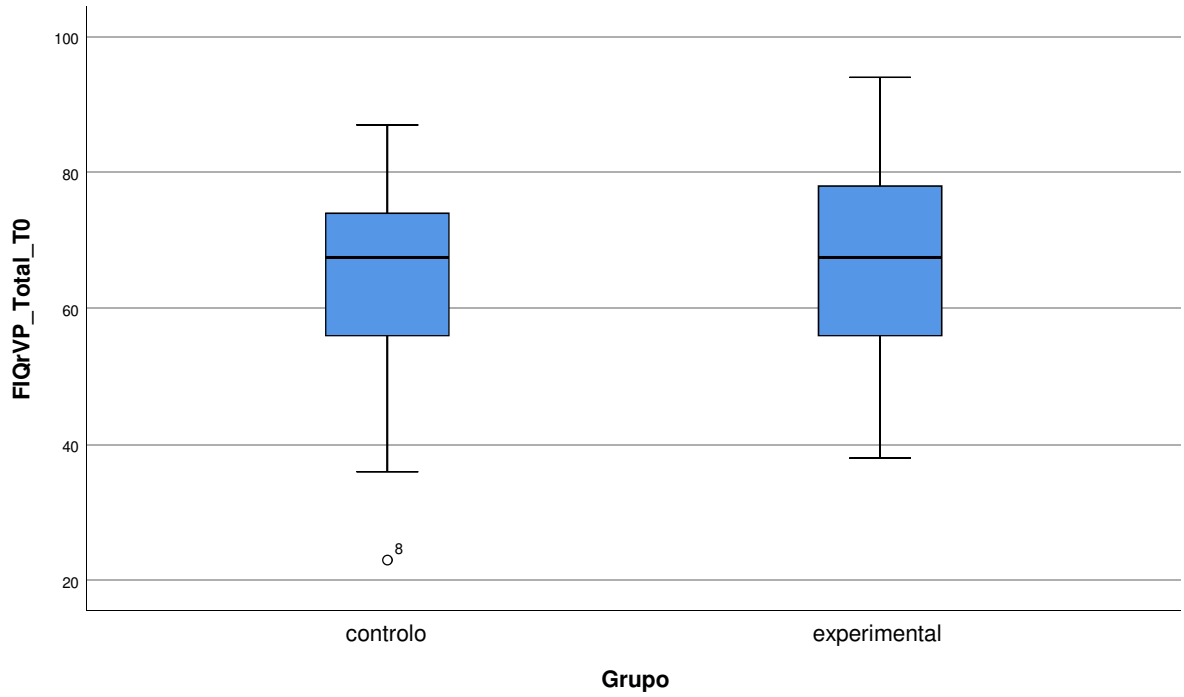
Testes de Normalidade

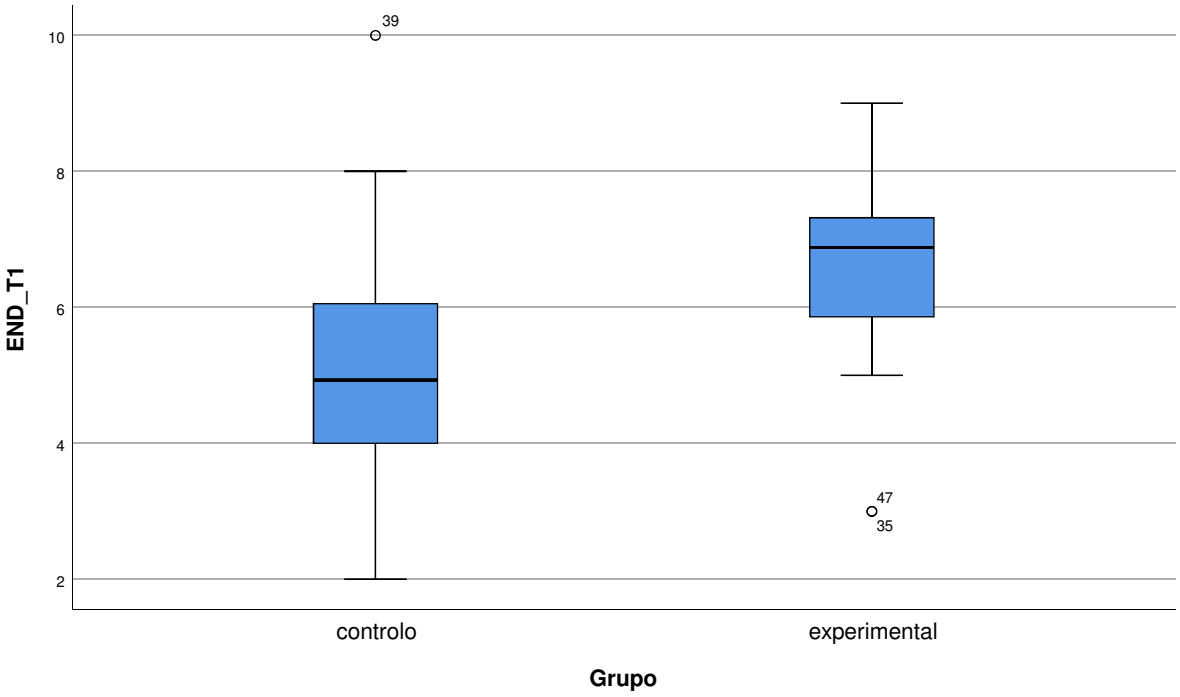
		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Grupo	Estatística	df	Sig.	Estatística	df	Sig.
END_T0	controlo	,178	30	,016	,939	30	,086
	experimental	,144	30	,114	,957	30	,255
FIQrVP_Total_T0	controlo	,128	30	,200*	,948	30	,153
	experimental	,128	30	,200*	,963	30	,365
END_T1	controlo	,113	30	,200*	,954	30	,214
	experimental	,145	30	,110	,922	30	,030
FIQrVP_Total_T1	controlo	,076	30	,200*	,991	30	,994
	experimental	,088	30	,200*	,987	30	,971
END_T2	controlo	,125	30	,200*	,968	30	,492
	experimental	,157	30	,056	,966	30	,437
FIQrVP_Total_T2	controlo	,120	30	,200*	,955	30	,226
	experimental	,148	30	,093	,969	30	,508

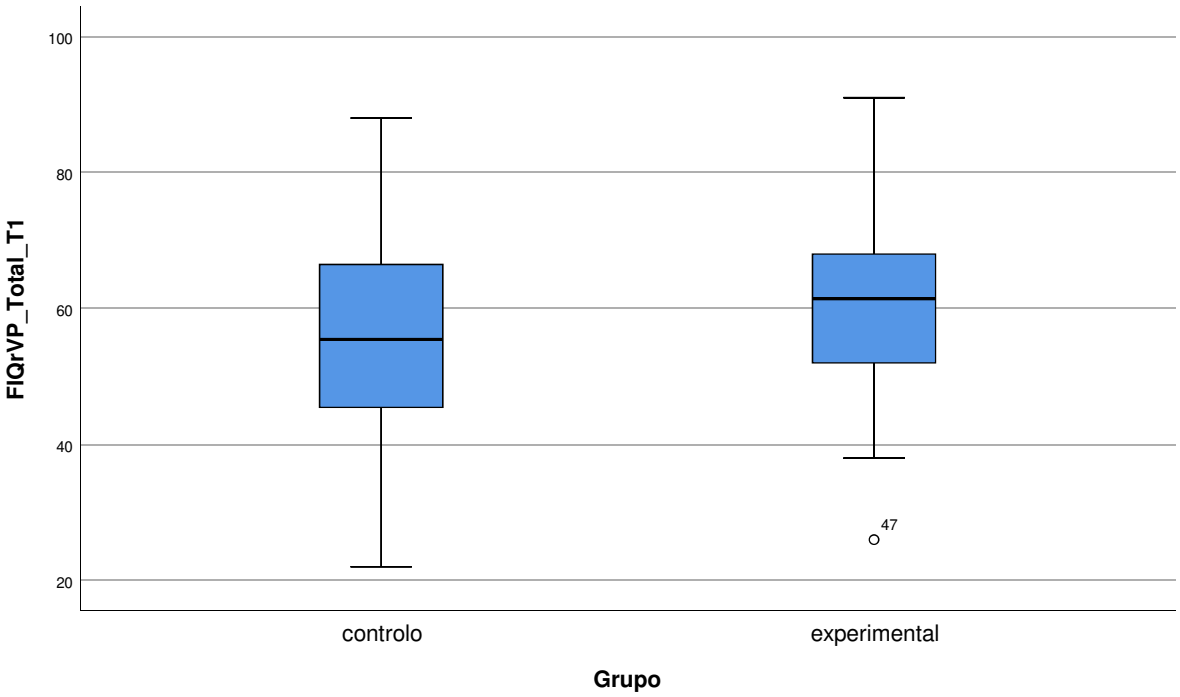
*. Este é um limite inferior da significância verdadeira.

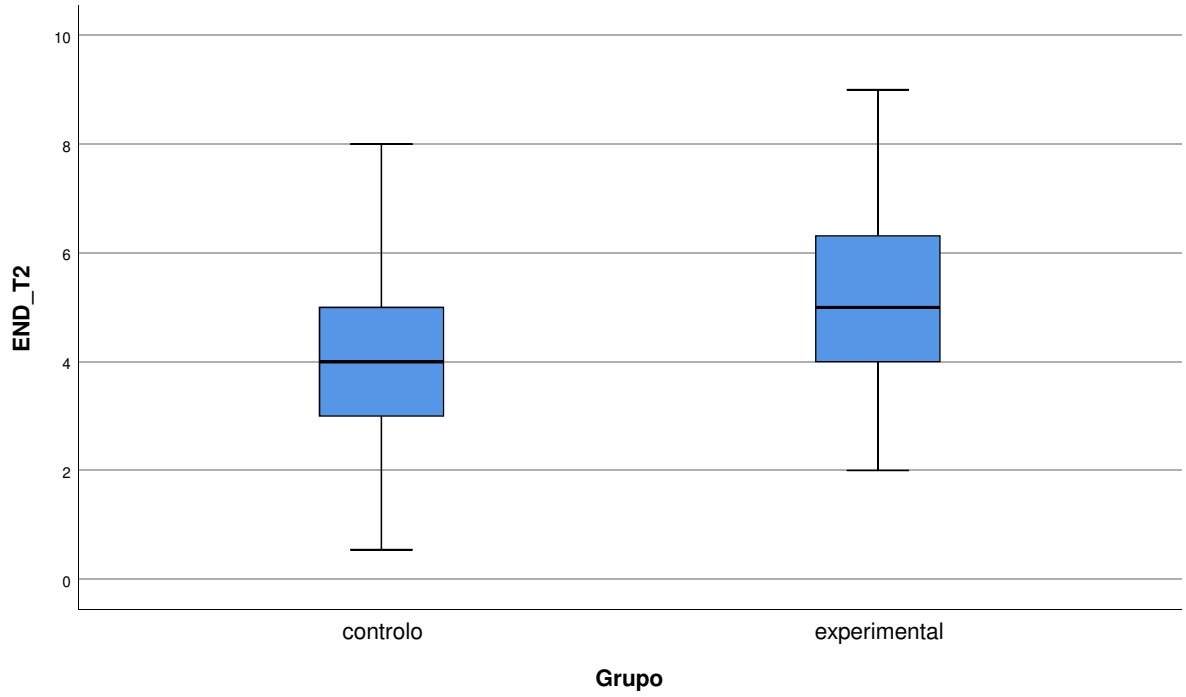
a. Correlação de Significância de Lilliefors

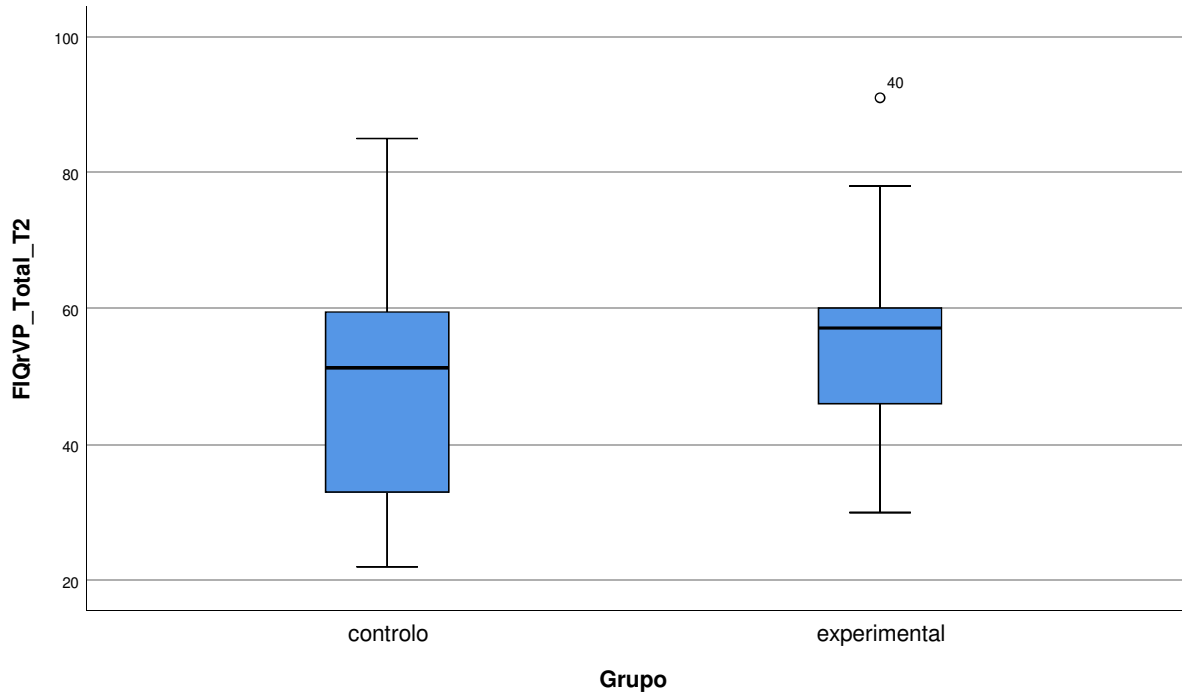

END_T0
10
8
6
4
2
0
31
23
controlo
experimental
Grupo


FIQrVP_Total_T0
100
80
60
40
20
8
controlo
experimental
Grupo


END_T1
10
8
6
4
2
39
47
35
controlo
experimental
Grupo


FIQrVP_Total_T1
100
80
60
40
20
47
controlo
experimental
Grupo





Resumo de processamento do caso

		Casos				
		Válido		Omisso		Total
	Grupo	N	Porcentagem	N	Porcentagem	N
END_T1	controlo	30	100,0%	0	0,0%	30
	experimental	30	100,0%	0	0,0%	30

Resumo de processamento do caso

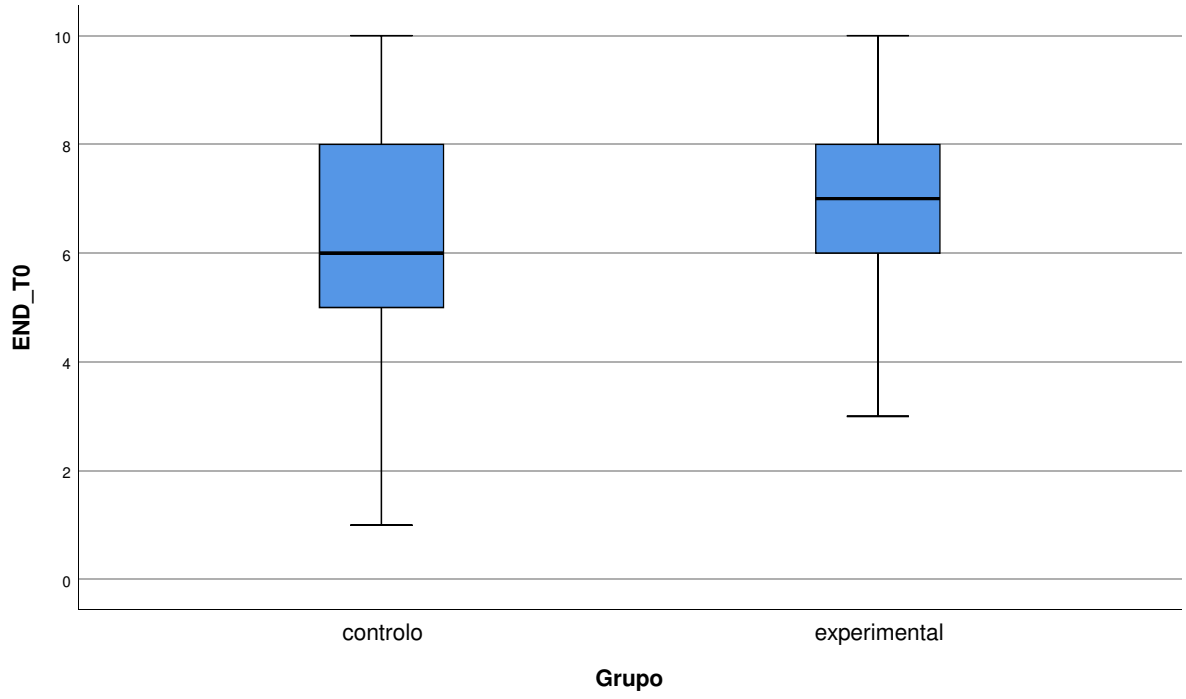
		Casos	
		Total	
	Grupo	Porcentagem	
END_T1	controlo	100,0%	
	experimental	100,0%	

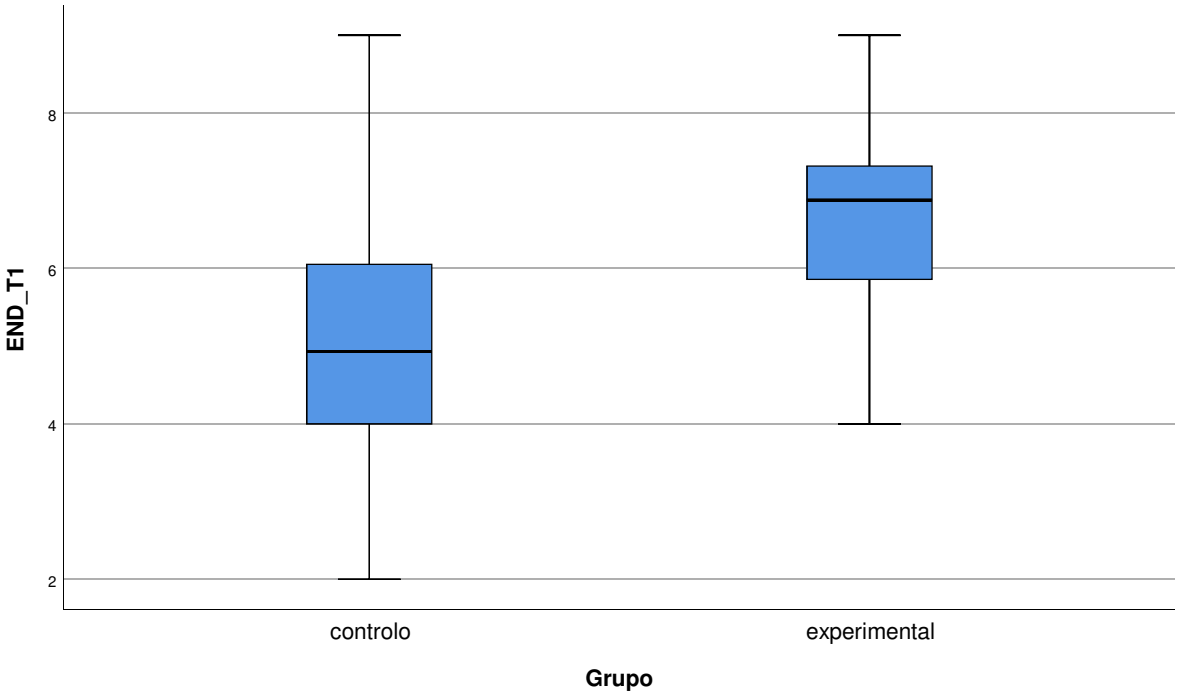
Testes de Normalidade

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Grupo	Estatística	df	Sig.	Estatística	df	Sig.
END_T1	controlo	,113	30	,200*	,954	30	,214
	experimental	,146	30	,101	,959	30	,291

*. Este é um limite inferior da significância verdadeira.

a. Correlação de Significância de Lilliefors




END_T1
8
6
4
2
controlo
experimental
Grupo

Teste de igualdade de variâncias do erro de Levene[a]

		Estatística de Levene	gl1	gl2	Sig.
END_T0	Com base em média	2,136	1	58	,149
	Com base em mediana	1,845	1	58	,180
	Com base em mediana e com df ajustado	1,845	1	52,79	,180
	Com base em média aparada	2,012	1	58	,161
END_T1	Com base em média	3,447	1	58	,068
	Com base em mediana	3,322	1	58	,074
	Com base em mediana e com df ajustado	3,322	1	52,22	,074
	Com base em média aparada	3,420	1	58	,070
END_T2	Com base em média	,109	1	58	,742
	Com base em mediana	,190	1	58	,664
	Com base em mediana e com df ajustado	,190	1	57,34	,664
	Com base em média aparada	,108	1	58	,744

Testa a hipótese nula de que a variância do erro da variável dependente é igual entre grupos.

a. Design: Intercepto + Grupo
Design Dentre-Sujeitos: Time

Teste de igualdade de variâncias do erro de Levene[a]

		Estatística de Levene	gl1	gl2	Sig.
FIQrVP_Total_T0	Com base em média	,318	1	58	,575
	Com base em mediana	,485	1	58	,489
	Com base em mediana e com df ajustado	,485	1	54,04	,489
	Com base em média aparada	,389	1	58	,535
FIQrVP_Total_T1	Com base em média	,116	1	58	,735
	Com base em mediana	,115	1	58	,735
	Com base em mediana e com df ajustado	,115	1	57,75	,735
	Com base em média aparada	,115	1	58	,735
FIQrVP_Total_T2	Com base em média	1,068	1	58	,306
	Com base em mediana	,726	1	58	,398
	Com base em mediana e com df ajustado	,726	1	57,56	,398
	Com base em média aparada	1,114	1	58	,296

Testa a hipótese nula de que a variância do erro da variável dependente é igual entre grupos.

a. Design: Intercepto + Grupo
Design Dentre-Sujeitos: Time

Teste de caixa de igualdade de matrizes de covariância[a]

M de Box	14,736
F	2,318
gl1	6
gl2	24373,132
Sig.	,031

Testa a hipótese nula de que as matrizes de covariância observadas das variáveis dependentes são iguais entre grupos.

a. Design: Intercepto + Grupo
Design Dentre-Sujeitos: Time

Teste de caixa de igualdade de matrizes de covariância[a]

M de Box	4,473
F	,704
gl1	6
gl2	24373,132
Sig.	,647

Testa a hipótese nula de que as matrizes de covariância observadas das variáveis dependentes são iguais entre grupos.

a. Design: Intercepto + Grupo
Design Dentre-Sujeitos: Time

Teste de esfericidade de Mauchly[a]

Medida: Dor

Efeito dentre-sujeitos	W de Mauchly	Aprox. Qui-quadrado	gl	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Limite inferior
Time	,860	8,612	2	,013	,877	,918	,500

Testa a hipótese nula para a qual a matriz de covariâncias de erro das variáveis transformadas ortonormalizadas é proporcional em relação a uma matriz identidade.

a. Design: Intercepto + Grupo
Design Dentre-Sujeitos: Time

b. Pode ser usado para ajustar os graus de liberdade dos testes de significância dentro da média. Os testes corrigidos são exibidos na tabela Testes de efeitos dentre-sujeitos.

Teste de esfericidade de Mauchly[a]

Medida: Incapacidade

Efeito dentre-sujeitos	W de Mauchly	Aprox. Qui-quadrado	gl	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Limite inferior
Time	,863	8,374	2	,015	,880	,921	,500

Testa a hipótese nula para a qual a matriz de covariâncias de erro das variáveis transformadas ortonormalizadas é proporcional em relação a uma matriz identidade.

a. Design: Intercepto + Grupo
Design Dentre-Sujeitos: Time

b. Pode ser usado para ajustar os graus de liberdade dos testes de significância dentro da média. Os testes corrigidos são exibidos na tabela Testes de efeitos dentre-sujeitos.

APPENDIX VII

SPSS Output: Two-way mixed model ANOVA

Fatores dentre-sujeitos

Medida: Dor

Time	Variável dependente
1	END_T0
2	END_T1
3	END_T2

Fatores entre sujeitos

		Rótulo de valor	N
Grupo	1	controlo	30
	2	experimental	30

Estatística Descritiva

	Grupo	Média	Erro Desvio	N
END_T0	controlo	5,87	2,432	30
	experimental	7,00	1,800	30
	Total	6,43	2,197	60
END_T1	controlo	5,01	1,776	30
	experimental	6,56	1,201	30
	Total	5,79	1,694	60
END_T2	controlo	4,05	1,779	30
	experimental	5,19	1,587	30
	Total	4,62	1,768	60

Testes de efeitos dentre-sujeitos

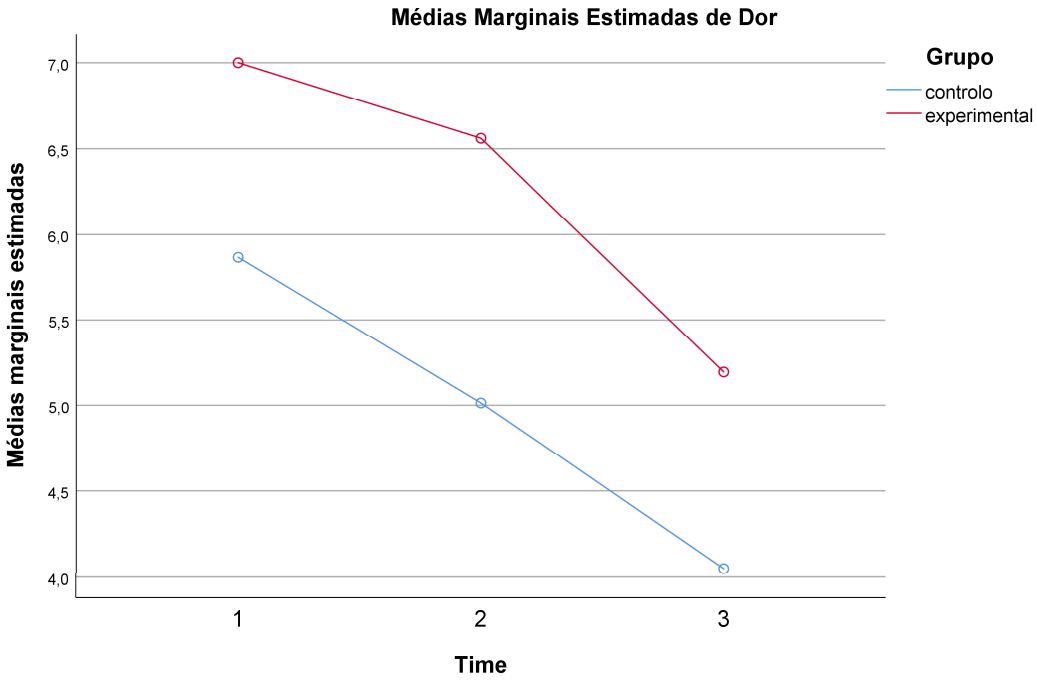
Medida: Dor

Origem		Tipo III Soma dos Quadrados	gl	Quadrado Médio	F	Sig.	Eta parcial quadrado
Time	Esfericidade considerada	101,167	2	50,583	42,486	,000	,423
	Greenhouse-Geisser	101,167	1,754	57,676	42,486	,000	,423
	Huynh-Feldt	101,167	1,836	55,115	42,486	,000	,423
	Limite inferior	101,167	1,000	101,167	42,486	,000	,423
Time * Grupo	Esfericidade considerada	1,661	2	,831	,698	,500	,012
	Greenhouse-Geisser	1,661	1,754	,947	,698	,482	,012
	Huynh-Feldt	1,661	1,836	,905	,698	,488	,012
	Limite inferior	1,661	1,000	1,661	,698	,407	,012
Erro (Time)	Esfericidade considerada	138,109	116	1,191			
	Greenhouse-Geisser	138,109	101,735	1,358			
	Huynh-Feldt	138,109	106,462	1,297			
	Limite inferior	138,109	58,000	2,381			

1. Grupo * Time

Medida: Dor

Grupo	Time	Média	Erro Erro	Intervalo de Confiança 95%	
				Limite inferior	Limite superior
controlo	1	5,867	,391	5,085	6,649
	2	5,013	,277	4,459	5,568
	3	4,049	,308	3,433	4,665
experimental	1	7,000	,391	6,218	7,782
	2	6,561	,277	6,006	7,115
	3	5,195	,308	4,579	5,811



Fatores dentre-sujeitos

Medida: Incapacidade

Time	Variável dependente
1	FIQrVP_Total_T0
2	FIQrVP_Total_T1
3	FIQrVP_Total_T2

Fatores entre sujeitos

		Rótulo de valor	N
Grupo	1	controlo	30
	2	experimental	30

Estatística Descritiva

	Grupo	Média	Erro Desvio	N
FIQrVP_Total_T0	controlo	63,93	15,387	30
	experimental	67,47	15,701	30
	Total	65,70	15,515	60
FIQrVP_Total_T1	controlo	55,05	14,414	30
	experimental	61,43	14,154	30
	Total	58,24	14,524	60
FIQrVP_Total_T2	controlo	47,62	15,900	30
	experimental	55,81	14,096	30
	Total	51,72	15,460	60

Testes de efeitos dentre-sujeitos

Medida: Incapacidade

Origem		Tipo III Soma dos Quadrados	gl	Quadrado Médio	F	Sig.
Time	Esfericidade considerada	5876,175	2	2938,088	35,062	,000
	Greenhouse-Geisser	5876,175	1,760	3339,502	35,062	,000
	Huynh-Feldt	5876,175	1,842	3190,693	35,062	,000
	Limite inferior	5876,175	1,000	5876,175	35,062	,000
Time * Grupo	Esfericidade considerada	165,731	2	82,865	,989	,375
	Greenhouse-Geisser	165,731	1,760	94,187	,989	,367
	Huynh-Feldt	165,731	1,842	89,990	,989	,370
	Limite inferior	165,731	1,000	165,731	,989	,324
Erro (Time)	Esfericidade considerada	9720,511	116	83,798		
	Greenhouse-Geisser	9720,511	102,057	95,246		
	Huynh-Feldt	9720,511	106,816	91,002		
	Limite inferior	9720,511	58,000	167,595		

Testes de efeitos dentre-sujeitos

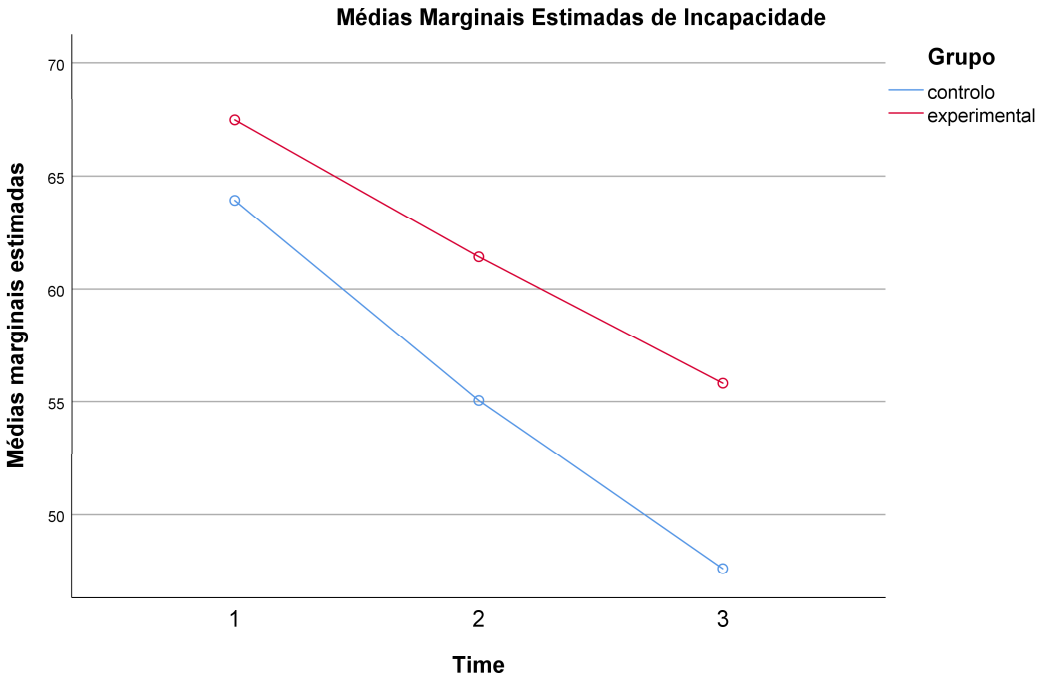
Medida: Incapacidade

Origem		Eta parcial quadrado
Time	Esfericidade considerada	,377
	Greenhouse-Geisser	,377
	Huynh-Feldt	,377
	Limite inferior	,377
Time * Grupo	Esfericidade considerada	,017
	Greenhouse-Geisser	,017
	Huynh-Feldt	,017
	Limite inferior	,017
Erro (Time)	Esfericidade considerada	
	Greenhouse-Geisser	
	Huynh-Feldt	
	Limite inferior	

1. Grupo * Time

Medida: Incapacidade

Grupo	Time	Média	Erro Erro	Intervalo de Confiança 95%	
				Limite inferior	Limite superior
controlo	1	63,933	2,838	58,252	69,614
	2	55,047	2,608	49,826	60,267
	3	47,617	2,743	42,126	53,108
experimental	1	67,467	2,838	61,786	73,148
	2	61,430	2,608	56,210	66,651
	3	55,813	2,743	50,322	61,304


Médias Marginais Estimadas de Incapacidade
Médias marginais estimadas
70
65
60
55
50
1
2
3
Time
Grupo
controlo
experimental

2. Time

Estimativas

Medida: Dor

Time	Média	Erro Erro	Intervalo de Confiança 95%	
			Limite inferior	Limite superior
1	6,433	,276	5,880	6,986
2	5,787	,196	5,395	6,179
3	4,622	,218	4,186	5,057

Comparações por Método Pairwise

Medida: Dor

(I) Time	(J) Time	Diferença média (I-J)	Erro Erro	Sig.[b]	95% Intervalo de Confiança para Diferença[b]	
					Limite inferior	Limite superior
1	2	,646*	,233	,023	,071	1,222
	3	1,812*	,176	,000	1,378	2,246
2	1	-,646*	,233	,023	-1,222	-,071
	3	1,165*	,183	,000	,713	1,617
3	1	-1,812*	,176	,000	-2,246	-1,378
	2	-1,165*	,183	,000	-1,617	-,713

Baseado em médias marginais estimadas

*. A diferença média é significativa no nível ,05.

b. Ajustamento para diversas comparações: Bonferroni.

2. Time

Estimativas

Medida: Incapacidade

Time	Média	Erro Erro	Intervalo de Confiança 95%	
			Limite inferior	Limite superior
1	65,700	2,007	61,683	69,717
2	58,239	1,844	54,547	61,930
3	51,715	1,940	47,832	55,598

Comparações por Método Pairwise

Medida: Incapacidade

(I) Time	(J) Time	Diferença média (I-J)	Erro Erro	Sig.[b]	95% Intervalo de Confiança para Diferença[b]	
					Limite inferior	Limite superior
1	2	7,461*	1,765	,000	3,110	11,813
	3	13,985*	1,866	,000	9,385	18,585
2	1	-7,461*	1,765	,000	-11,813	-3,110
	3	6,523*	1,335	,000	3,232	9,815
3	1	-13,985*	1,866	,000	-18,585	-9,385
	2	-6,523*	1,335	,000	-9,815	-3,232

Baseado em médias marginais estimadas

*. A diferença média é significativa no nível ,05.

b. Ajustamento para diversas comparações: Bonferroni.

Testes de efeitos entre sujeitos

Medida: Dor

Variável transformada: Média

Origem	Tipo III Soma dos Quadrados	gl	Quadrado Médio	F	Sig.	Eta parcial quadrado
Intercepto	5673,029	1	5673,029	773,376	,000	,930
Grupo	73,214	1	73,214	9,981	,003	,147
Erro	425,454	58	7,335			

3. Grupo

Estimativas

Medida: Dor

Grupo	Média	Erro Erro	Intervalo de Confiança 95%	
			Limite inferior	Limite superior
controlo	4,976	,285	4,405	5,548
experimental	6,252	,285	5,680	6,823

Comparações por Método Pairwise

Medida: Dor

(I) Grupo	(J) Grupo	Diferença média (I-J)	Erro Erro	Sig.[b]	95% Intervalo de Confiança para Diferença[b]	
					Limite inferior	Limite superior
controlo	experimental	-1,276*	,404	,003	-2,084	-,467
experimental	controlo	1,276*	,404	,003	,467	2,084

Baseado em médias marginais estimadas

*. A diferença média é significativa no nível ,05.

b. Ajustamento para diversas comparações: Bonferroni.

Testes de efeitos entre sujeitos

Medida: Incapacidade

Variável transformada: Média

Origem	Tipo III Soma dos Quadrados	gl	Quadrado Médio	F	Sig.	Eta parcial quadrado
Intercepto	617083,344	1	617083,344	1224,752	,000	,955
Grupo	1640,365	1	1640,365	3,256	,076	,053
Erro	29222,914	58	503,843			

3. Grupo

Estimativas

Medida: Incapacidade

Grupo	Média	Erro Erro	Intervalo de Confiança 95%	
			Limite inferior	Limite superior
controlo	55,532	2,366	50,796	60,269
experimental	61,570	2,366	56,834	66,306

Comparações por Método Pairwise

Medida: Incapacidade

(I) Grupo	(J) Grupo	Diferença média (I-J)	Erro Erro	Sig.[a]	95% Intervalo de Confiança [a]...
					Limite inferior
controlo	experimental	-6,038	3,346	,076	-12,736
experimental	controlo	6,038	3,346	,076	-,660

Comparações por Método Pairwise

Medida: Incapacidade

(I) Grupo	(J) Grupo	95% Intervalo de Confiança para [a]...
		Limite superior
controlo	experimental	,660
experimental	controlo	12,736

Baseado em médias marginais estimadas

a. Ajustamento para diversas comparações: Bonferroni.

APPENDIX VIII

Comparison between intention-to-treat and per-protocol analysis

Two-way mixed-model ANOVA - Intention-to-treat and Peer-protocol analysis

Intention-to-treat					Peer-protocol				
Primary Outcome	***df***	***F***	***p***	***η2***	*Primary Outcome*	***df***	***F***	***p***	***η2***
Pain Intensity (NRPS 0-10)					**Pain Intensity (NRPS 0-10)**				
Group-by-time interaction	1.836, 106.462	0.698	0.488	0.012	**Group-by-time interaction**	2, 64	1.327	0.273	0.040
Time effect	1.836, 106.462	42.486	**<0.001***	0.423	**Time effect**	2, 64	16.630	**<0.001***	0.342
Group effect	1, 58	9.981	**0.003***	0.147	**Group effect**	1, 32	2.185	0.149	0.064
Secondary Outcome					*Secondary Outcome*				
Disability (FIQr 0-100)					**Disability (FIQr 0-100)**				
Group-by-time interaction	1.842, 102.057	0.989	0.370	0.017	**Group-by-time interaction**	2, 64	1.093	0.341	0.033
Time effect	1.842, 106.816	35.062	**<0.001***	0.377	**Time effect**	2, 64	11.68	**<0.001***	0.267
Group effect	1,58	3.256	0.076	0.053	**Group effect**	1,32	1.243	0.273	0.037

Abbreviations: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; df: degrees of freedom; η2: effect size. *statistically significant.

Pairwise comparaisons - Within-Subjects effects: Intention-to-treat and Peer-protocol analysis

Intention-to-treat				Peer-protocol			
Pain Intensity (NRPS 0-10)	**Mean Dif.**	**95% CI**	**p-value[a]**	***Pain Intensity (NRPS 0-10)***	**Mean Dif.**	**95% CI**	**p-value[a]**
Baseline (T0) - 4 weeks (T1)	0.65	(0.71 - 1.22)	**0.023***	Baseline (T0) - 4 weeks (T1)	0.56	(-0.34 - 1.46)	0.380
4 weeks (T1) - 8 weeks (T2)	1.17	(0.71 - 1.61)	**<0.001***	4 weeks (T1) - 8 weeks (T2)	1.24	(0.45 - 2.03)	**0.001***
Baseline (T0) - 8 weeks (T2)	1.81	(1.38 - 2.25)	**<0.001***	Baseline (T0) - 8 weeks (T2)	1.80	(1.08 - 2.53)	**<0.001***
Disability (FIQr 0-100)				***Disability (FIQr 0-100)***			
Baseline (T0) - 4 weeks (T1)	7.46	(3.11 - 11.81)	**<0.001***	Baseline (T0) - 4 weeks (T1)	6.47	(-0.61 - 13.56)	**<0.001***
4 weeks (T1) - 8 weeks (T2)	6.52	(3.23 - 9.82)	**<0.001***	4 weeks (T1) - 8 weeks (T2)	6.66	(1.00 - 12.33)	**0.017***
Baseline (T0) - 8 weeks (T2)	13.99	(9.39 - 18.59)	**<0.001***	Baseline (T0) - 8 weeks (T2)	13.14	(5.44 - 20.83)	**<0.000***

Abbreviations: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; Dif: difference; CI: Confidence Interveal. [a]Bonferroni adjustment; * Statistically significant, p< 0.005

Pairwise comparaisons - Between-Subjects effects: Intention-to-treat and Peer-protocol analysis

Intention-to-treat				Peer-protocol			
Pain Intensity (NRPS 0-10)	**Mean Dif.**	**95% CI**	**p-value[a]**	***Pain Intensity (NRPS 0-10)***	**Mean Dif.**	**95% CI**	**p-value[a]**
Experimental - Control	1.28	(0.47 - 2.08)	**0.003***	Experimental - Control	0.84	(-0.32 - 2.00)	0.149
Disability (FIQr 0-100)				***Disability (FIQr 0-100)***			
Experimental - Control	6.04	(-0.66 - 12.74)	0.076	Experimental - Control	5.62	(-4.65 - 15.877)	0.273

Abbreviations: NRPS: Numeric Rating Pain Scale; FIQr: Fibromyalgia Impact Questionnaire Revisited; Dif: difference; CI: Confidence Interveal. [a]Bonferroni adjustment; * Statistically significant, p< 0.005

APPENDIX IX

SPSS Output: Clinical significance of the outcomes

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * END_T1_DICHO	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * END_T1_DICHO

			END_T1_DICHO		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	22	8	30
		% em Grupo	73,3%	26,7%	100,0%
	experimental	Contagem	20	10	30
		% em Grupo	66,7%	33,3%	100,0%
Total		Contagem	42	18	60
		% em Grupo	70,0%	30,0%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	,317[a]	1	,573		
Correção de continuidade[b]	,079	1	,778		
Razão de verossimilhança	,318	1	,573		
Teste Exato de Fisher				,779	,389
Associação Linear por Linear	,312	1	,576		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 9,00.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * END_T2_DICHO	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * END_T2_DICHO

			END_T2_DICHO		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	14	16	30
		% em Grupo	46,7%	53,3%	100,0%
	experimental	Contagem	11	19	30
		% em Grupo	36,7%	63,3%	100,0%
Total		Contagem	25	35	60
		% em Grupo	41,7%	58,3%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	,617[a]	1	,432		
Correção de continuidade[b]	,274	1	,600		
Razão de verossimilhança	,618	1	,432		
Teste Exato de Fisher				,601	,300
Associação Linear por Linear	,607	1	,436		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 12,50.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * FIQR_T1_DICHO	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * FIQR_T1_DICHO

			FIQR_T1_DICHO		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	16	14	30
		% em Grupo	53,3%	46,7%	100,0%
	experimental	Contagem	16	14	30
		% em Grupo	53,3%	46,7%	100,0%
Total		Contagem	32	28	60
		% em Grupo	53,3%	46,7%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	,000[a]	1	1,000		
Correção de continuidade[b]	,000	1	1,000		
Razão de verossimilhança	,000	1	1,000		
Teste Exato de Fisher				1,000	,602
Associação Linear por Linear	,000	1	1,000		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 14,00.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * FIQR_T2_DICHO	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * FIQR_T2_DICHO

			FIQR_T2_DICHO		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	8	22	30
		% em Grupo	26,7%	73,3%	100,0%
	experimental	Contagem	11	19	30
		% em Grupo	36,7%	63,3%	100,0%
Total		Contagem	19	41	60
		% em Grupo	31,7%	68,3%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	,693[a]	1	,405		
Correção de continuidade[b]	,308	1	,579		
Razão de verossimilhança	,695	1	,404		
Teste Exato de Fisher				,580	,290
Associação Linear por Linear	,682	1	,409		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 9,50.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * PGIC_VP_Dor_T1 (Categorizado)	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * PGIC_VP_Dor_T1 (Categorizado)

			PGIC_VP_Dor_T1 (Categorizado)		
			Clinically Stable	Clinical improvement	Total
Grupo	controlo	Contagem	21	9	30
		% em Grupo	70,0%	30,0%	100,0%
	experimental	Contagem	25	5	30
		% em Grupo	83,3%	16,7%	100,0%
Total		Contagem	46	14	60
		% em Grupo	76,7%	23,3%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	1,49[a]	1	,222		
Correção de continuidade[b]	,839	1	,360		
Razão de verossimilhança	1,507	1	,220		
Teste Exato de Fisher				,360	,180
Associação Linear por Linear	1,466	1	,226		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 7,00.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * PGIC_VP_Dor_T2 (Categorizado)	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * PGIC_VP_Dor_T2 (Categorizado)

			PGIC_VP_Dor_T2 (Categorizado)		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	11	19	30
		% em Grupo	36,7%	63,3%	100,0%
	experimental	Contagem	18	12	30
		% em Grupo	60,0%	40,0%	100,0%
Total		Contagem	29	31	60
		% em Grupo	48,3%	51,7%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	3,270[a]	1	,071		
Correção de continuidade[b]	2,403	1	,121		
Razão de verossimilhança	3,301	1	,069		
Teste Exato de Fisher				,120	,060
Associação Linear por Linear	3,216	1	,073		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 14,50.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * PGIC_VP_Função_T1 (Categorizado)	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * PGIC_VP_Função_T1 (Categorizado)

			PGIC_VP_Função_T1 (Categorizado)		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	17	13	30
		% em Grupo	56,7%	43,3%	100,0%
	experimental	Contagem	19	11	30
		% em Grupo	63,3%	36,7%	100,0%
Total		Contagem	36	24	60
		% em Grupo	60,0%	40,0%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	,278[a]	1	,598		
Correção de continuidade[b]	,069	1	,792		
Razão de verossimilhança	,278	1	,598		
Teste Exato de Fisher				,792	,396
Associação Linear por Linear	,273	1	,601		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 12,00.

b. Computado apenas para uma tabela 2x2

Resumo de processamento de casos

	Casos					
	Válidos		Omissos		Total	
	N	Porcentagem	N	Porcentagem	N	Porcentagem
Grupo * PGIC_VP_Função_T2 (Categorizado)	60	100,0%	0	0,0%	60	100,0%

Tabulação cruzada Grupo * PGIC_VP_Função_T2 (Categorizado)

			PGIC_VP_Função_T2 (Categorizado)		
			Clinically Stable	Clinical Improvement	Total
Grupo	controlo	Contagem	7	23	30
		% em Grupo	23,3%	76,7%	100,0%
	experimental	Contagem	13	17	30
		% em Grupo	43,3%	56,7%	100,0%
Total		Contagem	20	40	60
		% em Grupo	33,3%	66,7%	100,0%

Testes qui-quadrado

	Valor	gl	Significância Assintótica (Bilateral)	Sig exata (2 lados)	Sig exata (1 lado)
Qui-quadrado de Pearson	2,700[a]	1	,100		
Correção de continuidade[b]	1,875	1	,171		
Razão de verossimilhança	2,731	1	,098		
Teste Exato de Fisher				,170	,085
Associação Linear por Linear	2,655	1	,103		
N de Casos Válidos	60				

a. 0 células (0,0%) esperavam uma contagem menor que 5. A contagem mínima esperada é 10,00.

b. Computado apenas para uma tabela 2x2