# Clinical Benefits of Current Therapies in Improving Quality of Life and Physical-Psychological Symptoms in Women with Fibromyalgia: An Integrative Review

**Benefícios Clínicos das Terapêuticas Atuais na Melhora da Qualidade de Vida e dos Sintomas Físico-psicológicos nas Mulheres com Fibromialgia: Uma Revisão Integrativa**

**Beneficios Clínicos de las Terapias Actuales en la Mejora de la Calidad de Vida y de los Síntomas Físico-Psicológicos en Mujeres con Fibromialgia: Una Revisión Integradora**

**RESUMO**

**Objetivo:** Esta revisão sistemática buscou avaliar os efeitos de terapias farmacológicas e não farmacológicas sobre dor, fadiga e depressão, com foco na melhoria da qualidade de vida de pessoas com fibromialgia. **Método:** Foi realizada uma revisão integrativa da literatura nas bases de dados Scielo, Lilacs e PubMed, contemplando estudos que investigaram diferentes intervenções terapêuticas aplicadas a indivíduos com diagnóstico de fibromialgia. **Resultados:** Os tratamentos farmacológicos tradicionais, como antidepressivos tricíclicos e anticonvulsivantes, demonstraram eficácia limitada, frequentemente associada a efeitos adversos e elevado índice de abandono. Por outro lado, terapias não farmacológicas, como cinesioterapia, pilates, exercícios aquáticos e programas multicomponentes (ex: FIBROWALK), mostraram-se eficazes na redução dos sintomas e na melhora da qualidade de vida. Estratégias como suplementação de vitamina D e uso de canabidiol apresentaram resultados ainda inconclusivos devido à escassez de evidências robustas. **Conclusão:** Intervenções não farmacológicas, especialmente as abordagens físicas e psicossociais, mostraram maior efetividade e abrangência terapêutica quando comparadas ao uso isolado de medicamentos, reforçando a importância de estratégias integradas no manejo da fibromialgia.

**DESCRITORES:** Fibromialgia; Terapêutica; Qualidade de Vida; Mulheres

**ABSTRACT**

**Objective:** This systematic review sought to evaluate the effects of pharmacological and non-pharmacological therapies on pain, fatigue, and depression, with a focus on improving the quality of life of people with fibromyalgia. **Method:** An integrative literature review was conducted in the Scielo, Lilacs, and PubMed databases, including studies that investigated different therapeutic interventions applied to individuals diagnosed with fibromyalgia. **Results:** Traditional pharmacological treatments, such as tricyclic antidepressants and anticonvulsants, have shown limited efficacy, often associated with adverse effects and a high dropout rate. On the other hand, non-pharmacological therapies, such as kinesiotherapy, Pilates, aquatic exercise, and multicomponent programs (e.g., FIBROWALK), have proven effective in reducing symptoms and improving quality of life. Strategies such as vitamin D supplementation and cannabidiol have yielded inconclusive results due to a lack of robust evidence. **Conclusion:** Non-pharmacological interventions, especially physical and psychosocial approaches, demonstrated greater effectiveness and therapeutic scope when compared to the isolated use of medications, reinforcing the importance of integrated strategies in the management of fibromyalgia.

**DESCRIPTORS:** Fibromyalgia; Therapeutics; Quality of Life; Women

**RESUMEN**

**Objetivo:** Esta revisión sistemática buscó evaluar los efectos de las terapias farmacológicas y no farmacológicas sobre el dolor, la fatiga y la depresión, con el objetivo de mejorar la calidad de vida de las personas con fibromialgia. **Método:** Se realizó una revisión bibliográfica integradora en las bases de datos Scielo, Lilacs y PubMed, incluyendo estudios que investigaron diferentes intervenciones terapéuticas aplicadas a personas con diagnóstico de fibromialgia. **Resultados:** Los tratamientos farmacológicos tradicionales, como los antidepresivos tricíclicos y los anticonvulsivos, han mostrado una eficacia limitada, a menudo asociada a efectos adversos y una alta tasa de abandono. Por otro lado, las terapias

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no farmacológicas, como la kinesioterapia, el pilates, el ejercicio acuático y los programas multicomponentes (p. ej., FIBROWALK), han demostrado ser eficaces para reducir los síntomas y mejorar la calidad de vida. Estrategias como la suplementación con vitamina D y el cannabidiol han arrojado resultados no concluyentes debido a la falta de evidencia sólida. **Conclusión:** Las intervenciones no farmacológicas, especialmente las físicas y psicosociales, demostraron mayor efectividad y alcance terapéutico en comparación con el uso aislado de medicamentos, reforzando la importancia de las estrategias integradas en el manejo de la fibromialgia.
**DESCRIPTORES:** Fibromialgia; Terapéutica; Calidad de Vida; Mujeres

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## INTRODUCTION

Fibromyalgia (FM) is a chronic syndrome characterized by widespread musculoskeletal pain, often accompanied by fatigue, sleep disturbances, memory problems, and mood changes. Although fibromyalgia can affect people of all ages and genders, it is more commonly diagnosed in women. The condition itself is a factor that causes significant functional and social impairment in this segment of society[1].

As already observed by Graminha et al. (2021)1, this debilitating condition significantly impacts women's quality of life, interfering with their daily activities, work, personal relationships, and mental health. Persistent pain and intense fatigue are symptoms that make it difficult to perform everyday tasks, often leading to time off work and social limitations[1].

In addition, a lack of understanding of the disease by society and even some healthcare professionals can result in late or incorrect diagnoses, exacerbating patients' suffering. The psychological impact is considerable, with many women developing depression and anxiety as a direct consequence of the condition[1].

Despite the overall picture of pain and loss of quality of life, treatment options for fibromyalgia are still very limited to pharmacological treatment, which, although effective, has many biases and adverse effects. Given this scenario, this integrative review sought to - to verify the scientific evidence regarding current therapies for the treatment of fibromyalgia and discuss the results of pioneering studies of alternative therapies for the relief of the symptoms of the disease, and other non-pharmacological therapies, comparing their clinical results with those of traditional drug therapies, such as antidepressants, anticonvulsants, and others. The aim in this context is to answer the following question: How could non-pharmacological treatment be used in conjunction with drug treatment to improve the quality of life of women with fibromyalgia?

The objective of this review is to analyze the clinical results of current pharmacological and non-pharmacological therapeutic options and demonstrate that, due to the multifactorial nature of the disease and the difficulty in finding treatments that address its complexity, there is a need to expand treatment protocols for fibromyalgia by including non-pharmacological therapies associated with


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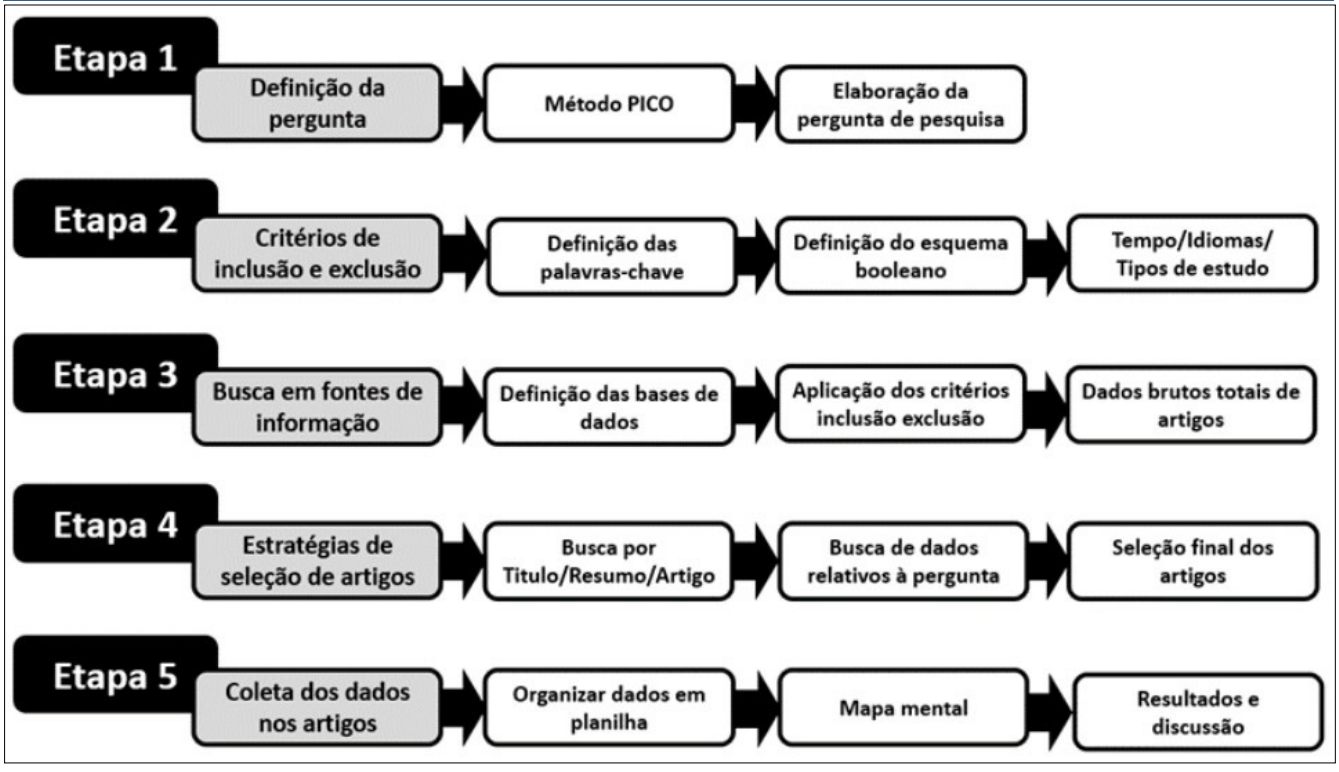
pharmacological treatment, because, in this way, in addition to obtaining better results in terms of increased quality of life and treatment adherence, we place the patient as an active agent in their treatment.

## METHODOLOGY

The review was conducted in five stages, following a rigorous methodology to ensure the reproducibility of the information found. The stages are listed in Figure 1.

**Figure 1: Research method used and its five stages of investigation**




The stages of this research are described below:

Stage 1 includes defining the research question and was obtained using the PICO method. Once the research question was defined, the keywords that would comprise the research were defined.

Step 2 consisted of defining the Boolean and non-Boolean scheme that would solve the research problem, as well as defining the eligibility criteria for articles, such as time [a], availability in Portuguese, English, and Spanish [b], direct relation to the object of study and its guiding question [c], no conflicts of interest [d], publication no more than five years ago [e], and presentation of a reliable and replicable research methodology with conclusive final results.

Stage 3 corresponded to the activity of defining the search sites, using the PubMed, ScienceDirect, and Lilacs portals. Also, via a non-Boolean scheme, articles from Google Scholar were included to complement the research.

Stage 4 was the selection phase of the articles found on the portals, which was followed by an initial verification by title and abstract, and those of interest were separated for analysis, aiming to answer the research question. The ROBANS (Risk of Bias Assessment Tool for Nonrandomized Studies) and Risk of Bias Tool 2 (RoB 2) methods were used for non-randomized and randomized studies, respectively.

Step 5 was the analysis of the results using spreadsheets and other instruments, with the aim of generating the results and discussion of the article.

## RESULTS

Considering the terms required in the research question according to GALVÃO et al. (2014), the items were established as shown in Table 1.

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**Table 1: Formulation of the research question**

| Definições do Acrônimo | P | I | C | O |
|---|---|---|---|---|
| | Population | Intervention | Comparison | Outcome |
| Componentes da pergunta | *People with fibromyalgia* | *Non-pharmacological treatments* | *Pharmacological treatments* | *Improved quality of life* |

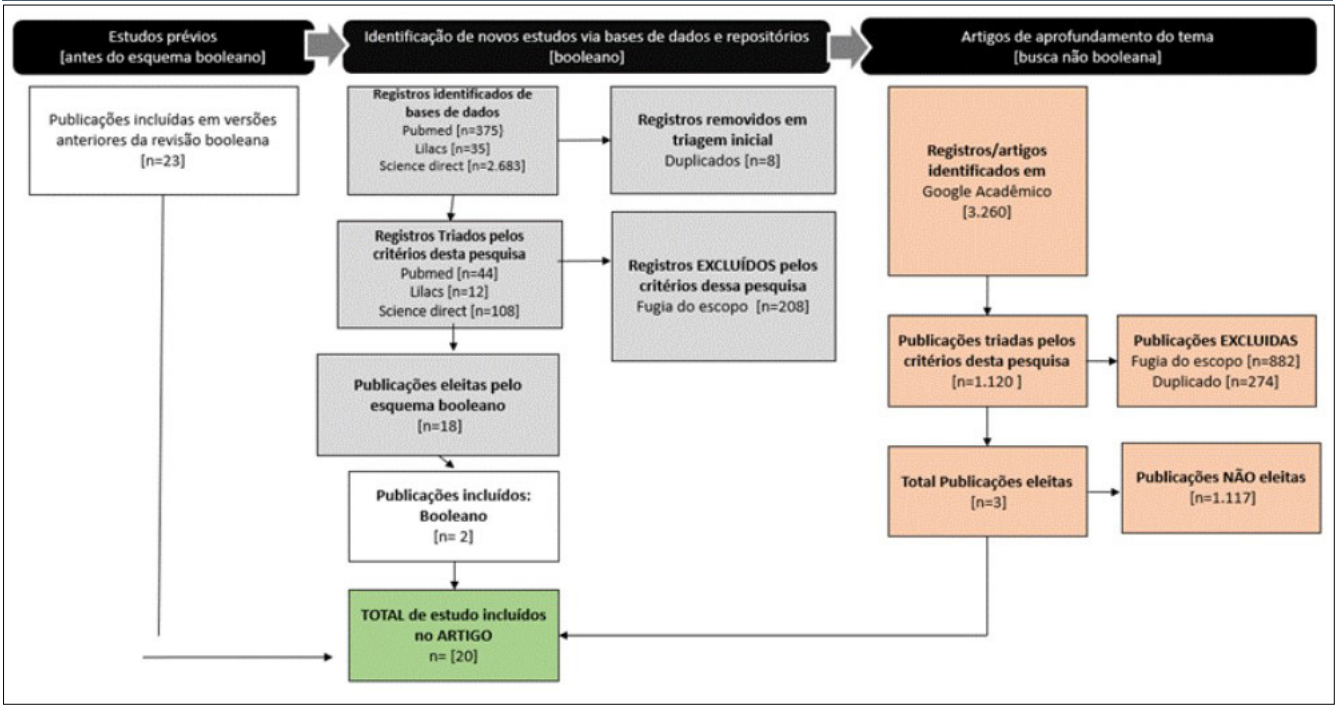
Source: the authors

The result of the question was expressed as follows: How could non-pharmacological treatment be used alongside drug treatment to improve quality of life in women with fibromyalgia?

Subsequently, the Boolean scheme for searching articles related to the question was defined, using the scheme used in the databases and presented below: ("fibromyalgia") AND ("treatment" OR "therapy" OR "intervention") AND ("non pharmacological" OR "multidisciplinary care") AND ("pharmacological treatment" OR "drug therapy" OR "medication") AND ("quality of life"); in the databases cited in the method.

A total of 167 articles were found, of which 20 met the selection criteria of the research to find propositions that answered the research question of the study, as shown in Figure 2.

**Figure 2: Overview of the results obtained via Boolean and non-Boolean schemes in the selected electronic media**




## DISCUSSION

### Impacts of FM on the lives of women with the disease

As briefly discussed in the introduction to this article, women are the segment of the population with the highest risk of developing FM, representing approximately 65 to 70% of FM cases1. The reasons for this prevalence are not yet known, but researchers have conducted case studies to analyze common characteristics among women with fibromyalgia, seeking to understand how this disease may be associated with impaired interpersonal relationships, causing mainly physical and psychological problems and a reduced quality of life.

In a study conducted by Graminha et al. (2021)[1], women with FM were selected and asked to complete a questionnaire on quality of life and outlook. Among the women analyzed in this article, 30% reported dissatisfaction with their social environment and 29% reported dissatisfaction with their interpersonal relationships. The same authors also discuss the biopsychosocial theory of the disease, which is based on the premise that women, whether for cultural or biological reasons, are more "demanded" than men socially.

This idea understands that, because they are often subjected to a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patriarchal culture, women are more exposed to stressful situations or social vulnerabilities, and are thus more predisposed to having suffered at some point in their lives psychological or sexual abuse, greater difficulty in professional advancement, or any other situation that has conditioned the development of the syndrome.

Given the scenario described above, there is an urgent need to seek therapies that alleviate symptoms and contribute to improving the quality of life and self-esteem of these women. To this end, treatment must be scientifically supported and place the patient as an active agent in their treatment. With comprehensive and multidisciplinary treatment, women with FM can experience a significant improvement in their quality of life, allowing them to lead more active and satisfying lives.

## Pharmacological and non-pharmacological treatments: current overview within the scientific context

Several therapeutic strategies, both pharmacological and non-pharmacological, have been studied with the aim of mitigating symptoms and improving patients' quality of life, as summarized in Table 2.

Among pharmacological treatments, the use of antidepressants and anticonvulsants stands out. In a meta-analysis4, only pregabalin and amitriptyline showed superior efficacy to placebo, while duloxetine did not show significant advantages. Similarly, Hussein M. Farag and Ismaeel Yunusa et al. (2022)[4] concluded that, despite symptom improvement with all drugs analyzed, only amitriptyline demonstrated better tolerability. The use of spironolactone, investigated by Ruwen Böhm et al. (2021)[5] ,did not significantly alter clinical outcomes, although a transient increase in serum potassium levels was observed.

In addition, studies on cannabidiol8 and vitamin D supplementation9 showed limited or inconclusive effects, highlighting the need for further investigation. Naltrexone, tested on two occasions[6,7], did not show superior efficacy to placebo, with adverse effects being reported in the intervention group in one of the studies.

**Table 2: summary of articles found in the Boolean scheme**

| AUTOR/ANO | PAÍS | OBJETIVO DO ESTUDO | MÉTODO | RESULTADOS | CONSIDERAÇÕES |
|---|---|---|---|---|---|
| Tânia Maria Hendges de Paula, Mariane Schäffer Castro et al, 2023 | Brasil | Efeitos da combinação de doses baixas de naltrexona e estimulação transcraniana por corrente elétrica direta na fibromialgia. | Ensaio clinico | A intensidade da dor, o desempenho funcional, os sintomas psicológicos e a qualidade de vida aumentaram significativamente em ambos os grupos (P<0,05) | Não houveram diferenças significativas entre os grupos |
| Ruth Izquierdo-Alventosa, Marta Inglés et al, 2020 | Espanha | Efeitos do exercicio de baixa intensidade na catastrofização da dor, ansiedade, depressão e outros sintomas em mulheres com fibromialgia | Ensaio clinico | Houve melhoraram significativamente no grupo que fez a atividade física após a interveção em todos os aspectos analisados. Houve piora do grupo controle no limiar da dor | Exercícios de baixa intensidade, com treinamento de resistência e coordenação, melhora as variáveis psicológicas, dor, a qualidade de vida e o condicionamento físico em mulheres com FM. |
| Daniela Matei 1, Rodica Trăistaru et al. 2024 | Romania | Efeitos de um programa de terapia cinética e um programa de modalidade física combinada sobre a fibromialgia | Ensaio clinico | A cinesioterapia foi superior na redução da dor tanto durante o tratamento e após três meses do término. A terapia combinada também obteve melhora da dor. Ambas melhoraram a qualidade de vida | Tanto a cinesioterapia quanto o programa de atividade combinada melhoraram os sintomas da FM |
| Pablo Tomas-Carus 1, Clarissa Biehl-Printes et al, 2022 | Espanha | Efeitos do treino respiratório na qualidade de vida e capacidade respiratória de mulheres com fibromialgia | Estudo de caso-controle | A pressão inspiratória máxima (PImáx) melhorou 17,5%. A pressão expiratória máxima melhorou 21,6%. O questionário sobre qualidade de vida melhorou em relação a função física, aspectos físicos, dor e vitalidade | O treinamento respiratório é uma terapia eficaz para terapia eficaz para melhorar a função respiratória e a qualidade de vida em mulheres com FM. |
| Mari Aguilera , Clara Paz Aguilera et al, 2022 | Espanha | Investigar a eficácia da Terapia Cognitivo-Comportamental (TCC) e da Terapia de Construção Pessoal (PCT) para sintomas depressivos em mulheres com fibromialgia | Estudo multicêntrico randomizado | As participantes reduziram de maneira significativa os sintomas depressivos, mas os autores não encontraram diferenças expressivas entre os resultados dos dois tipos de terapias | Ambas terapias aparentam igual eficácia nos sintomas depressivos das pacientes com FM |
| Mayte Serrat, Sònia Ferréset et al, 2022 | Espanha | Analisar a eficácia do FIBROWALK e do Programa de Fisioterapia Multicomponente (MPP) em comparação com o tratamento usual (TU) | Ensaio clínico | O FIBROWALK atingiu maiores melhorias em todos os resultados clínicos e os MPP no comprometimento funcional, percepção da dor, sintomas depressivos e cinesiofobia, em comparação ao TU. Em comparação ao MPP, o FIBROWALK mostrou efeitos superiores na melhora da dor, sintomas depressivos, ansiedade e função física | Há eficácia a curto prazo destes programas multicomponentes e há evidências de que técnicas cognitivo-comportamentais e baseadas em mindfulness podem ser clinicamente úteis |

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|---|---|---|---|---|---|
| Prados Oscar Cervilla 1, Elena Miró et al, 2020 | Espanha | Analisar se há maiores benefícios para a insônia de mulheres com fibromialgia ao realizar Terapia Cognitiva Comportamental Comibinada | Ensaio clínico | Houve melhoria no sono reparador, maior eficiência do sono, menos tempo acordado e mais tempo no estágio 4, resultando em melhora significativa na autopercepção da qualidade do sono | A terapia combinada pode conferir melhora nos aspectos relacionados à insônia em pacientes com FM |
| Carolina Chaves, Paulo Cesar T Bittencourt et al, 2020 | Brasil | Efeitos da ingestão do canabidiol por pessoas com fibromialgia | Ensaio clínico | Não houve diferença dos efeitos na analise global, Analisando itens isolados no FIQ, o grupo cannabis apresentou melhora significativa nos escores "sentir-se bem", "dor", "fazer trabalho" e "fadiga". O grupo placebo apresentou melhora significativa no escore de "depressão" | Estudos futuros ainda são necessários para avaliar os benefícios a longo prazo |
| Ruwen Böhm 1, Paul Westermann et al, 2021 | Alemanha | Eficácia da espirinololactona sobre os sintomas da fibromialgia | Ensaio clínico | A espironolactona não alterou significativamente nem os desfechos primários nem os secundários. Houve um aumento transitório nos níveis de potássio sérico | A espirinolactona não apresentou bons resultados no tratamento da FM |
| Carolina P Andrade , Antônio R Zamunér et al, 2019 | Brasil | Efeitos dos exercícios aquáticos na FM e resultados pós destreinamento | Ensaio clinico | No grupo intervenção houve aumento no consumo máximo de oxigênio (p=0, 01), aumento do limiar de dor a pressão (P=0,02) e bem estar | Mesmo que a terapia tenha contribuido tanto para aumentar o VO2 no TAV quanto no TCPE pico, após 16 semanas de destreinamento, os valores retornaram para perto do basal. |
| (Fernanda Fávero Alberti, Matheus William Becker, 2022) | Brasil | Efeitos da amitriptilina, pregabalina e duoloxetina na fibromialgia | Metanálise | Somente a pregabalina e a amitriptilina tiveram melhora clínica em relação ao placebo. Duoloxetina não apresentou relevancia em relação ao placebo | Todos os medicamentos analisados tiveram bons resultados, porém deve ser estimado a tolerabilidade e os possíveis efeitos adversos das terapias |
| (Daniel Rodríguez-Almagro 1, María Del Moral-García, 2023) | Espanha | Terapia baseada em exercícios físicos | Metanálise | Todos os exercícios físicos analisados resultaram em melhora clinica em algum aspecto | Importancia do tratamento não farmacológico na FM |
| Juan Rodríguez-Mansilla, Abel Mejías-Gil, 2023) | Espanha | Efeito dos exercícios de bem-estar e da fisioterapia com alongamentos na FM | Ensaio clinico | Houve melhora nos sintomas psicológicos, aumento de resistencia e amplitude de movimento e velocidade em ambas as terapias | A terapia de exercicios de bem-estar e fisioterapia tem grandes vantagens no tratamento de mulheres com FM |
| Ching-An Cheng , Ya-Wen Chiu et al 2019 | Taiwan | Efetividade do Tai Chi no tratamento da fibromialgia | Revisão sistemática e metanálise | Melhoria na qualidade do sono, alívio da depressão e fadiga, melhoria na qualidade de vida física e psicológica | Tai Chi oferece efeitos significativamente maiores no tratamento da fibromialgia em relação à terapia padrão |
| Nadal-Nicolás et al., 2021 | Espanha | Eficácia de dietas baseadas principalmente em vegetais em comparação com dietas onívoras, examinando os principais efeitos nos sintomas dos pacientes com FM e na melhoria da qualidade de vida | Revisão sistemática | Redução significativa da dor em repouso, melhora na qualidade do sono, redução da rigidez matinal, melhora no questionário geral do reumatologista, redução na intensidade da dor somática | Dietas vegetarianas e veganas podem proporcionar melhorias significativas em parâmetros bioquímicos, qualidade de vida, peso corporal e sintomas da fibromialgia |
| Hussein M Farag 1, Ismaeel Yunusa, 2022) | Estados Unidos | Comparação entre amitriptilina e duloxetina, pregabalina e milnaciprano | Metanálise | Apesar de melhora dos sintomas com todos os medicamentos, a amitriptilina foi a única que obteve tolerabilidade em relação ao placebo (OR, 0,78; 95% CrI, 0,31-1,66) | O tratamento deve levar em conta a individualidade e tolerabilidade do paciente |
| Suzy Araújo de Medeiros 1, Hugo Jário de Almeida Silva, 2020 | Brasil | Comparação entre os efeitos do pilates no solo e dos exercícios aeróbicos aquáticos na FM. | Ensaio clínico | Ambos grupos tiveram melhora na função física. O pilates obteve melhora na qualidade de vida, e o exercício aquático na melhora do sono. | Ambas as terapias tiveram resultados semelhantes |
| Karin Due Bruun, Prof Robin Christensen et al, 2024 | Dinamarca | Efeitos da baixa dose de Naltrexona em mulheres com FM | Ensaio clínico | O grupo intervenção teve uma mínima melhor na escala da dor em relação ao placebo. Efeitos colaterais do uso da Naltrexona foram relatados | O uso da Naltrexona não foi melhor que o placebo para o tratamento da FM |
| Kang Ku, Ming-Xi Lia et al, 2022 | China | Suplementação com vitamina D e os efeitos na FM | Metanálise | Houve melhora no questionário de impacto da FM com o uso da vitamina D (P < 0,001), mas não houve melhora na escala EVA ( P > 0,05). | A suplementação com vitamina D é eficaz na FM |

Source: The authors

On the other hand, non-pharmacological treatments are highly diverse and show promising results. Exercise-based strategies have shown consistent efficacy in several studies. Kinesiotherapy and low-intensity exercises, including aquatic and wellness exercises, have resulted in improved pain, functional performance, and quality of life[10,12,13,14]. Respiratory rehabilitation has also demonstrated positive effects on lung function and quality of life[15], the multicomponent FIBROWALK program[18] and com-


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bined Cognitive Behavioral Therapy[17] have shown significant clinical improvements in depressive symptoms, pain perception, and sleep.

In addition, alternative approaches such as Tai Chi[16], ,plant-based diets[20] and floor-based Pilates[11] have also been shown to be effective, especially in improving quality of life, pain, and psychosocial aspects. Finally, data consolidated in meta-analyses14 reinforce the importance of physical exercise as a first-line non-pharmacological treatment.

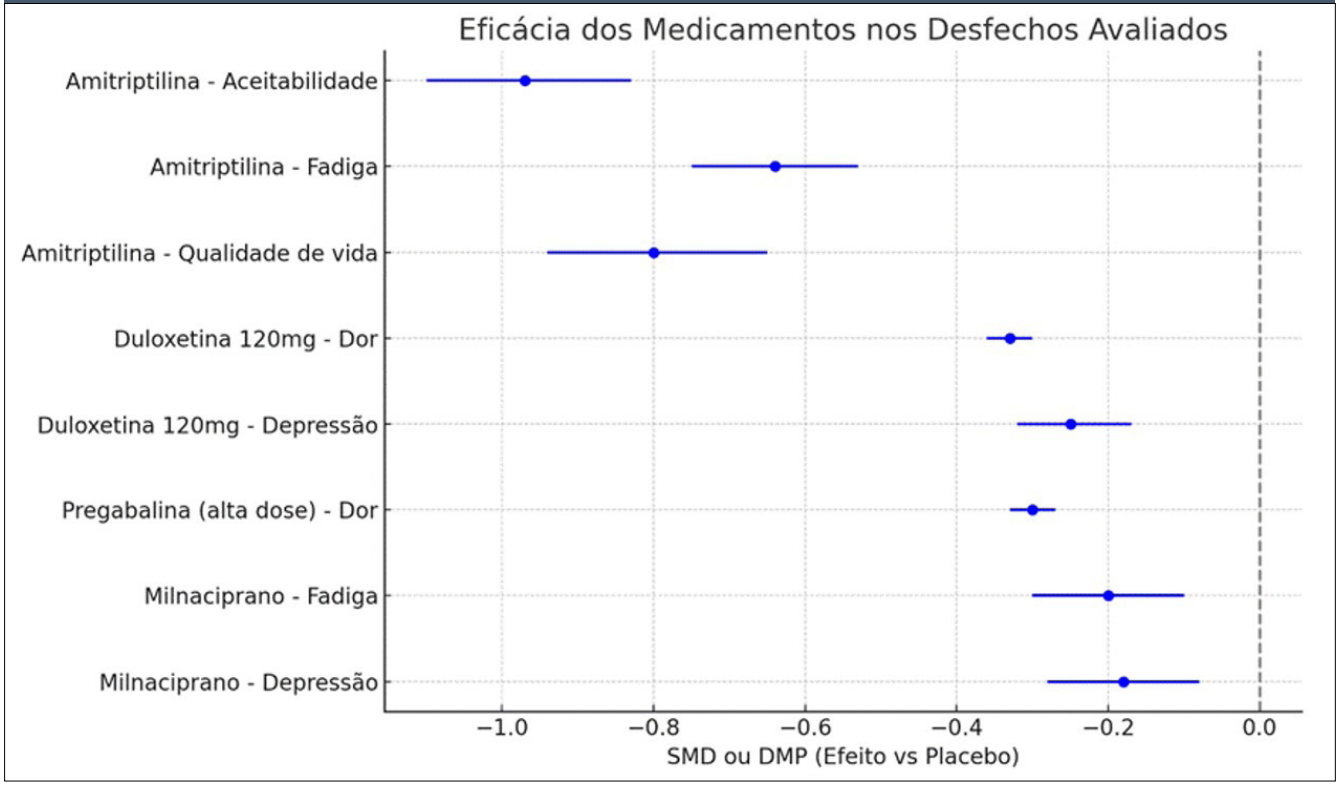
## Drug treatments for fibromyalgia and their relevant aspects today: advances and limitations

### Amitriptyline, pregabalin, and duloxetine: first-line drugs

Two recent meta-analysis studies evaluated the efficacy of pharmacological treatments for FM, focusing on amitriptyline, pregabalin, and duloxetine. The first meta-analysis included eight systematic reviews and 15 clinical trials, analyzing the effects of drugs in women with FM[3]. The results showed that pregabalin 450 mg was effective in improving pain in 30%, while amitriptyline 50 mg was superior in improving pain in 50%. Duloxetine 20 mg and 30 mg were no better than placebo. The risk of bias was analyzed using the Cochrane Collaboration's Rob 2.0 tool[3].

In a second meta-analysis, with 36 clinical trials, amitriptyline was compared with FDA-approved drugs (duloxetine, pregabalin, and milnacipran)[4]. The summary of the results can be seen in the following graph.

**Figure 1: Effects of drugs on different outcomes, including credibility intervals (CrI). Visual comparison of the magnitude and direction of the effect (negative values indicate improvement over placebo).**




### Use of potassium-sparing diuretics: spironolactone

A clinical trial investigated the efficacy of spironolactone, at a dose of 200 mg/day, in improving FM symptoms[5]. Forty-three women were randomized into two groups: placebo group (n=22) and intervention group (n=21). After an initial phase with doses of 50 mg, 100 mg, and 200 mg/day of spironolactone or placebo were administered between days 7 and 28. The primary outcome was the change in the FM Impact Questionnaire (FIQ-G, German version) score. Secondary endpoints included changes in pain (measured by the Numerical Rating Scale, NRS), mood (ADS), quality of life (SF-36), and changes in FIQ scores 14 days after the end of medication.

The results showed that spironolactone, at a dose of 200 mg/day, did not significantly alter the primary and secondary endpoints. In addition, there was a transient increase in serum potassium levels and a transient

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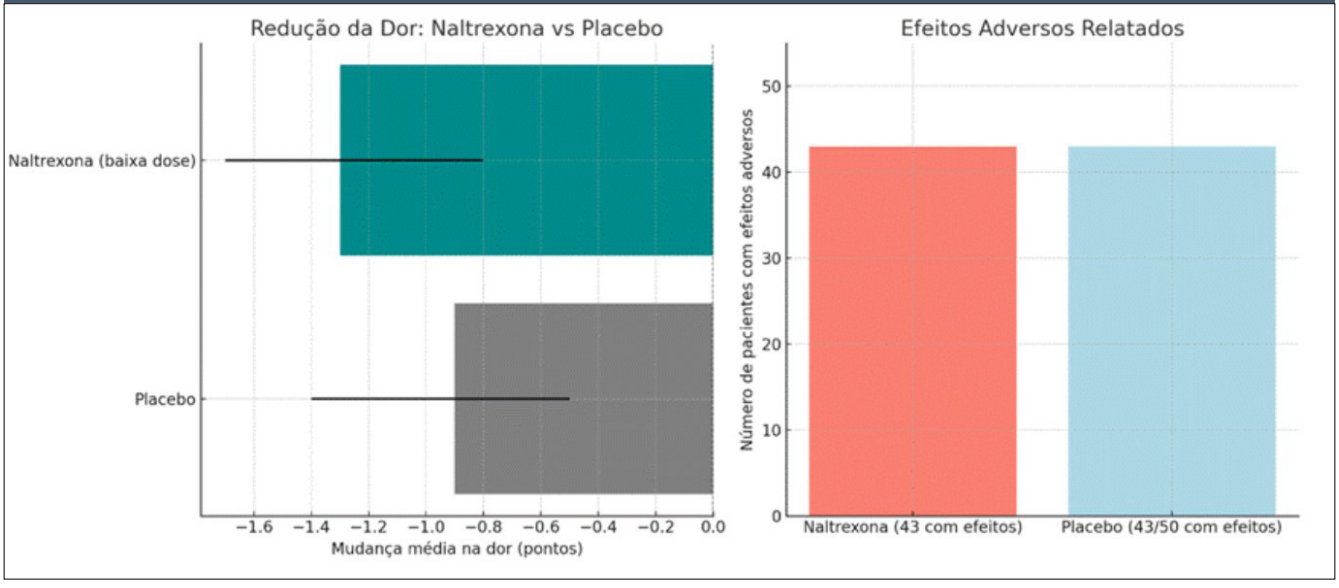
decrease in maximum glomerular filtration rate (GFR) after 2 weeks, but without clinical relevance [5].

### Naltrexone and transcranial stimulation

The single-center, randomized, double-blind clinical trial aimed to analyze the real effects of low-dose naltrexone (6 mg) in women with FM [6]. One hundred thirty-six participants were selected and allocated to an intervention group, which received the drug for 12 weeks, and a placebo group. The safety of the study was assessed in participants from the population with the intention to treat FM and who received at least one dose of their designated intervention, and the primary outcome was the change in the pain scale. The results are shown in Figure 2.

**Figure 2: The vertical dotted line represents no effect (zero). The further to the left of the line, the greater the reduction in pain. The naltrexone group showed a mean reduction in pain of -1.3 points (with a 95% confidence interval (CI): -1.7 to -0.8), indicating greater pain relief compared to placebo, while the placebo group had an average reduction of -0.9 points (95% CI: -1.4 to -0.5). The confidence intervals (horizontal black bars) show the uncertainty of the estimates. The adverse effect profile is high, being equal to or higher than that of placebo in absolute terms and proportionally higher.**




In another randomized, double-blind clinical trial, researchers combined low-dose naltrexone with transcranial direct current stimulation to assess the effects on FM symptoms in 86 women with FM, who were divided into four groups[7]. Several questionnaires were administered before and after the intervention. The results showed a significant reduction in pain in the groups that received active interventions, especially in the group that combined naltrexone and transcranial stimulation, which showed significant improvements in pain frequency and intensity, the impact of pain on daily activities, and emotions. In addition, depressive symptoms decreased after all active interventions. Despite the observed benefits, the presence of a placebo effect was noted, indicating the need for further studies to analyze this possible association[7].

### Cannabidiol and its current clinical use

A double-blind randomized clinical trial aimed to verify the efficacy of cannabidiol oil on FM symptoms[8]. To this end, the researchers selected 17 women from a socially vulnerable area in the Florianópolis region of Brazil, who received 18 weeks of treatment based on the ingestion of cannabis oil. The results were compared with a placebo. The initial dose of the medication was 1.22 mg of THC and 0.02 mg of CBD. The authors found that in the intervention group there was an increase in the FIQ score of $p = 0.005$ compared to the placebo group ($p < 0.001$), mainly for well-being, fatigue, and work performance. According to the researchers, there were no reports of adverse effects in either group. The authors concluded that cannabis oil was effective in improving FM symptoms, but reported that long-term monitoring of the effect of phytocannabinoids is necessary, as well as further exploration of other species.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### Non-pharmacological therapies for the treatment of fibromyalgia

In most of the studies analyzed in relation to non-pharmacological treatment for FM, specific questionnaires were used, such as the Numeric Rating Scale of Pain (NRS), Multidimensional Fatigue Inventory (MFI), Fibromyalgia Impact Questionnaire (FIQ), among others, were administered before and after intervention to analyze whether the results obtained were consistent with relief of disease symptoms and improvement in quality of life.

### Aquatic exercises and Pilates

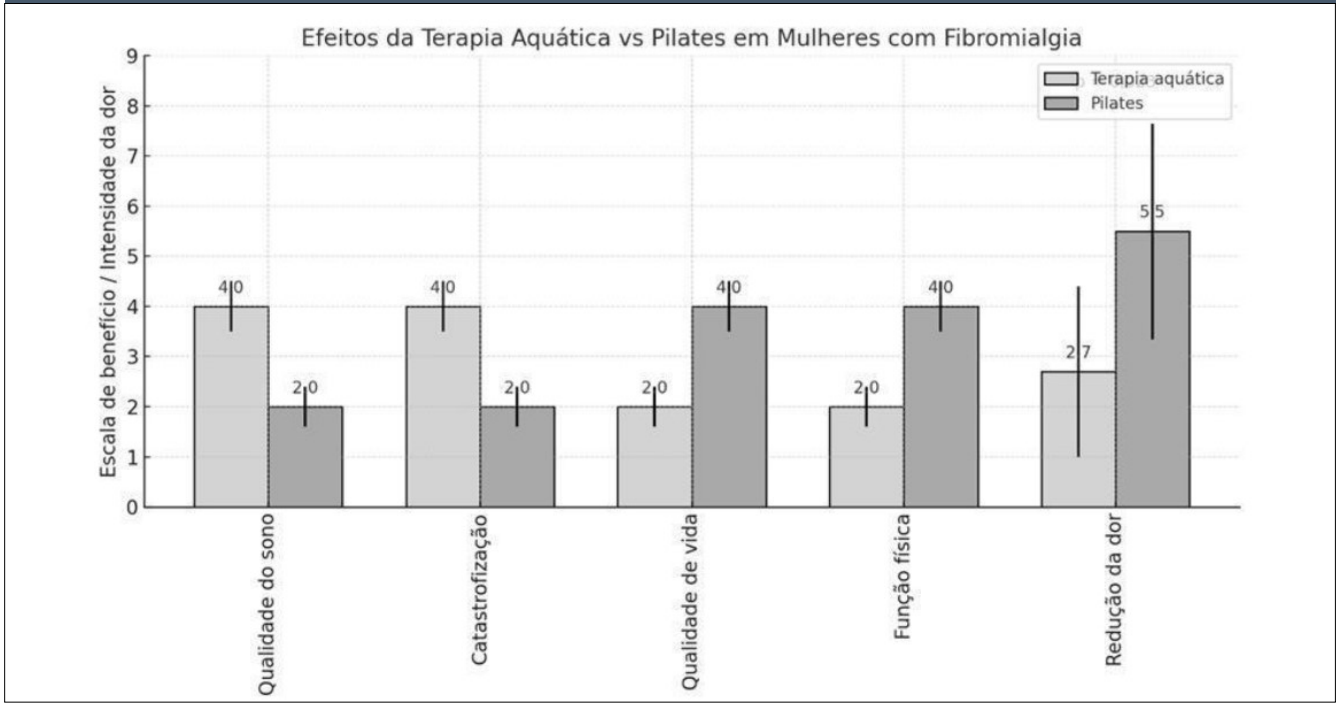
In a clinical trial, 54 women were randomly divided into an intervention group and a control group, each with 27 people. Both groups underwent cardiopulmonary capacity tests and assessment of BMI (body mass index) and $VO_2$ (oxygen consumption)for subsequent analysis of the improvement in $VO_2$in relation to BMI and clinical status[10].

The results were collected before the study and after 16 weeks of treatment followed by physical training to assess the magnitude of the effects of therapy on the patients' quality of life. The researchers found improvements in the intervention group in terms of increased $VO_2$relative to BMI (p=0.01), pain threshold (p=0.02), and perceived quality of life[10]. These results were not maintained after the detraining test (p>0.05). Finally, the researchers suggest that physical training should be done continuously throughout the lives of people with FM.

In the second study, a randomized blind clinical trial was conducted with 48 women, comparing the effects of Pilates on the floor and aquatic aerobic exercises. The interventions took place twice a week for 12 weeks, with pre- and post-intervention assessments. Both groups showed improvement in pain and physical function. However, quality of life and aspects assessed by the FABQ questionnaire improved only in the floor Pilates group, while sleep quality and reduction in catastrophic thoughts showed significant improvement only in the aquatic aerobic exercise group[11].

Although both studies had similar sample sizes and treatment durations, the article[10] found an advantage in aquatic therapy in terms of improving sleep quality and reducing catastrophic thoughts, while Pilates may be more effective in improving quality of life and physical function, according to the article researched[11]. The results are shown in the following graphs (Figure 4).

**Figure 4: The graph compares the effects of aquatic therapy and Pilates in women with FM, based on two separate studies. Aquatic therapy showed greater benefits in improving sleep quality and reducing catastrophic thoughts, while Pilates showed better results in quality of life and physical function. In both groups, a significant reduction in pain was observed, with a statistically significant advantage for aquatic therapy (p = 0.023). The bars represent the estimated mean or median values with their respective interquartile ranges (IQR).**

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### Kinesiotherapy

It is known that one of the consequences of pain in FM is kinesiophobia, i.e., fear of movement, which can cause patients to avoid physical activity, leading to decreased physical capacity and muscle deconditioning. This can result in a vicious cycle where lack of activity increases pain and disability. Against this backdrop, a clinical trial evaluated the effectiveness of a complex kinetic therapy program and a combined physical modality program on pain and other common symptoms of FM[12]. Seventy-eight women were included and divided into two groups: 39 participants underwent kinesiotherapy (aerobic exercise and Pilates) and 39 participated in a physical modality program (electrotherapy, including TENS and low-intensity laser, and thermotherapy). The researchers' results showed that kinesiotherapy was superior in reducing pain both during treatment and three months after its completion[12]. Both kinetic therapies relieved pain, as reported by patients and confirmed by tender point examinations and algometric assessments. Functional impairment was significantly influenced by the kinetic program, but there was no difference between therapies in the perception of functional impairment or the emotional consequences of FM. In conclusion, the authors determined that kinesiotherapy is more effective in reducing pain, but both nonpharmacological approaches demonstrated importance in the management of FM, promoting improvements in the functional and emotional well-being of participants.

Low-intensity physical exercises and strength training

A clinical trial sought to determine the effects of a low-intensity physical exercise program, combined with resistance training, strength training, coordination training, speed training, and increased pressure pain threshold, on pain improvement in women with FM, as well as the psychological effects on clinical acceptance and self-perception of functional capacity. To this end, 32 women with fibromyalgia, aged 30 to 70, who had already undergone pharmacological treatment for at least 3 months were screened. Women who were pregnant, using medications that could interfere with the results, and with clinical comorbidities were excluded from the study. As a result, the researchers observed that all psychological aspects evaluated (catastrophic pain, anxiety, stress, and depression) improved significantly in the intervention group, with increases of 7.31, 1.87, 2.43, and 7.32 points, respectively. The issue of pain acceptance increased by 4.94 points in the group that practiced physical activity. There was also a 9.8-point improvement in quality of life. Another interesting finding was related to gains in speed and physical endurance, with increases of 6.8 points. The control group did not improve in any of the variables analyzed, and even showed a worsening in the pressure pain threshold, with an average decrease of 0.25 kg/cm$^2$($p<0.05$). The authors therefore concluded that physical activity, even at low intensity, has great potential to improve physical endurance and reduce pain and improve quality of life in women with FM[13].

In another case-control study on the effects of physical training on FM, similar results were found[14]. To this end, the researchers selected 141 women diagnosed with FM, who were divided into a group that performed "wellness exercises" (a Chinese practice of movement, meditation, and breathing that improves circulatory capacity) and another group that underwent physical therapy. The sessions lasted 45 minutes and were held twice a week on alternate days. The study lasted 4 weeks, and the outcomes analyzed before and after the intervention were muscle range and endurance, as well as quality of life and respiratory capacity. As a result, a statistically significant improvement was observed in both groups after 5 weeks in terms of joint range of motion ($p = 0.004$), quality of life ($p = 0.002$), and strength ($p = 0.003$). There were no significant differences between the groups in any of the variables analyzed[14].

Tai Chi

Tai Chi may also be an effective treatment for FM, according to a systematic review and meta-analysis of randomized clinical trials [15]. Using studies published before May 2019 in PubMed, Medline, and the Physiotherapy Evidence Database, the effectiveness of the treatment was analyzed in relation to standard treatment, using the FM impact questionnaire (FIQ) and total score, pain score, sleep quality index, fatigue, depression, and quality of life. The results are shown in Figure 5.


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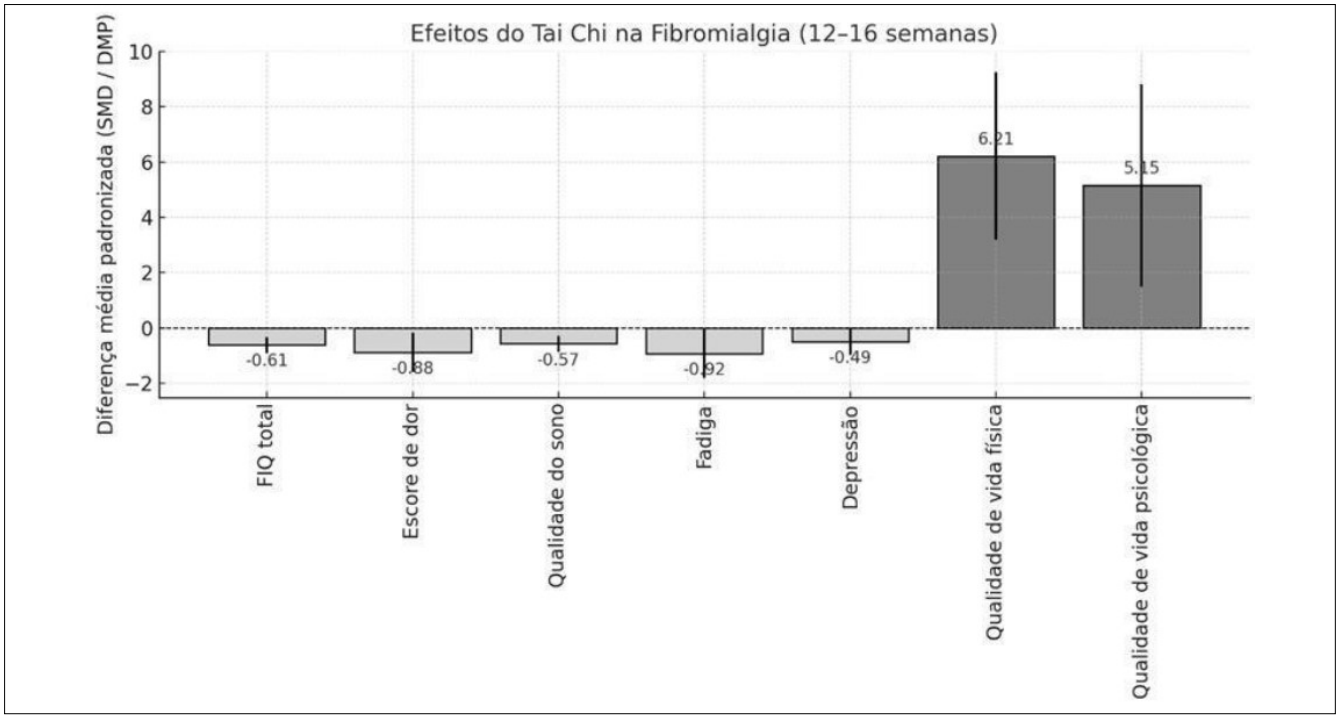
**Figure 5: The graph shows the positive effects of Tai Chi in women with FM after 12–16 weeks of practice. There was a significant reduction in the total FIQ questionnaire score, pain, fatigue, depression, and poor sleep quality (negative SMD/DMP values), indicating clinical improvement. In addition, a significant increase in physical and psychological quality of life (positive values) was observed. The bars represent the standardized mean difference (SMD or DMP), and the vertical lines indicate the 95% confidence intervals, reinforcing the statistical robustness of the findings.**




Finally, the authors understand that Tai Chi offers significantly greater effects in the treatment of FM compared to standard therapy and, therefore, according to them, it can be used as an alternative treatment. However, they point out that further studies are needed to prove this superiority with stronger evidence[15].

## Cognitive behavioral therapy

A randomized multicenter study investigated the effectiveness of two therapeutic approaches for FM in women diagnosed with depressive symptoms (n=106)[16]. Participants were allocated to two parallel groups: one with 55 women receiving Cognitive Behavioral Therapy (CBT) and the other with 51 women undergoing Personal Construction Therapy (PCT). All therapies were individual and modular to meet the needs of the patients, and the data were analyzed using linear mixed-effects models. It was observed that the participants significantly reduced their depressive symptoms, but the authors found no significant differences between the results of the two types of therapy during and after treatment, concluding that both appear to be equally effective in the depressive symptoms of patients with FM[16].

In line with the understanding of the psychological component as an important vehicle for additional clinical benefits for patients with FM, a study examined the effectiveness of two multicomponent video-based programs (FIBROWALK) and the Multicomponent Physical Therapy Program (MPP) compared to usual treatment (UT)[17]. FIBROWALK includes specific psychological aspects involving cognitive restructuring and mindfulness[17]. To this end, 330 patients with FM were randomly assigned to TU, TU + FIBROWALK, or TU + MPP groups in structurally equivalent programs with weekly videos on pain neuroscience education, therapeutic exercises, and self-management education[17]. When compared to TU alone, individuals in the FIBROWALK group achieved greater improvements in all clinical outcomes, and MPP showed greater improvements in functional impairment, pain perception, depressive symptoms, and kinesiophobia[17]. Compared to MPP, people in the FIBROWALK group showed superior effects in improving pain, depressive symptoms, anxiety, and physical function. Thus, the authors agree that there is short-term efficacy of these multicomponent programs (MPP and FIBROWALK), and consider that

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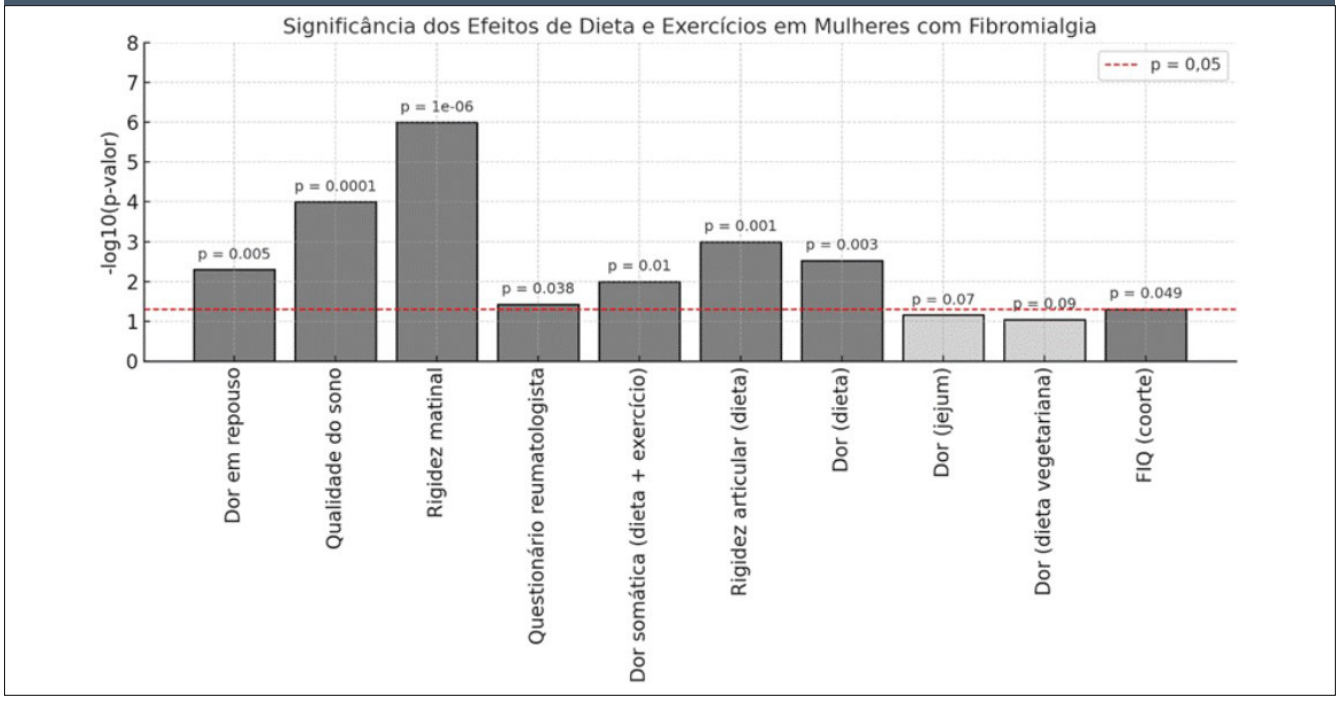
there is evidence that cognitive-behavioral and mindfulness-based techniques may be clinically useful in the context of multicomponent physical therapy treatment programs.

Another randomized clinical trial analyzed whether there are greater benefits for insomnia in women with FM when combining Combined Cognitive Behavioral Therapy for pain and insomnia[18]. Thirty-nine women with FM between the ages of 24 and 62 were recruited from the Rheumatology Service and Pain Unit of the Virgen de Las Nieves University Hospital and AGRAFIM (a local FM association), both in Granada, Spain[18]. Participants were assessed at baseline and post-treatment with the Pittsburgh Sleep Quality Index and an ambulatory polysomnography. The results showed that participants who received combined CBT showed more notable improvements in restorative sleep, greater sleep efficiency, less time awake, and more time in stage 4, resulting in significant improvement in self-perceived sleep quality, leading the authors to conclude that their study suggests that new approaches using this form of combined therapy may confer improvements in insomnia-related aspects in patients with FM[18].

### Nutritional guidelines

A systematic review sought to evaluate the effectiveness of diets based mainly on vegetables, such as vegan and vegetarian diets, in patients with FM compared to omnivorous diets, examining the main effects of these diets on patients' symptoms and improvement in their quality of life[19]. Six studies were used in this review, including four clinical trials and two observational cohorts. The results are shown in Figure 6.

**Figure 6: Statistical significance levels of the effects of different interventions in women with FM. Results with p < 0.05 (above the red line) indicate clinically relevant effects. It can be observed that integrated approaches (diet + exercise) appear to be more effective than isolated interventions.**




The authors suggest that vegetarian and vegan diets may provide significant improvements in biochemical parameters, quality of life, body weight, and FM symptoms. However, they understand that the variation in the methodological quality of the studies requires further well-controlled research to confirm these findings and provide solid dietary recommendations for patients with FM[19].

## CONCLUSION

Both therapeutic approaches (pharmacological and non-pharmacological) resulted in significant improvement in FM symptoms. Treatment with antidepressants and anticonvulsants, despite positive clinical effects, may be impaired depending on patient adherence, mainly due to adverse effects. There was no significant improvement with the use of spironolactone in relieving symptoms compared to placebo, in addition to presenting adverse effects.

Regarding the non-pharmacological therapies analyzed, there was a statistically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significant improvement in all modalities studied, mainly with the practice of physical activity, whether aquatic or terrestrial, enabling increased strength, endurance, and improvement in psychological symptoms.

We understand the importance of combining non-pharmacological options in the management of FM, since non-drug therapy can and should be implemented alongside standard pharmacological treatment, both because it leads to clinical improvement when these two therapeutic modalities are combined and because it enables real long-term rehabilitation of patients, so that they do not have to depend on medication for the rest of their lives. We can justify this conclusion by analyzing the results of articles [6-7], since the isolated use of naltrexone, in low doses, did not result in clinical improvement for FM symptoms, but when combined with other therapies, as in the case of study [6] with transcranial stimulation, better results were obtained.

We therefore conclude that, although there is clear evidence of the need for and effectiveness of drug therapies in the vast majority of FM cases, the results shown by this systematic review demonstrate that when combined with alternative therapies, they are not only more comprehensive but also provide more satisfactory results in improving the quality of life of women with FM.

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