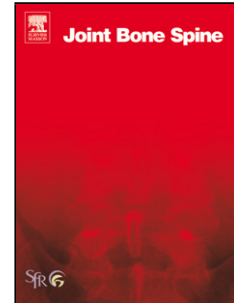


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Progress towards improved non-pharmacological management of fibromyalgia

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**Progress towards improved non-pharmacological management of fibromyalgia**

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## **1. Introduction**

Fibromyalgia (FM) is a chronic and disabling condition that affects about 3% of the adult population [1] and imposes a heavy burden on individuals and society. The implementation of successful strategies to assist patients in managing their condition and live a life worth living is, therefore, pivotal. Unfortunately, despite the progress in the understanding of FM over the last decades, its management remains challenging and, mostly, unsatisfactory for both patients and physicians. Additionally, patients frequently experience invalidation from their close relationships and even from health professionals [2], which adds considerably to their suffering [3].

## **2. Pharmacological management**

Overall, pharmacological approaches have held disappointing results [4], [5]. Besides the limited clinical efficacy, most medications only target one or two symptoms at best, while patients experience a constellation of disabling and distressing symptoms, including fatigue, unrefreshed sleep and cognitive dysfunction [6]. The poor symptom control and frequent side-effects lead to adherence problems [5]. Nonetheless, pharmacological approaches continue to be the mainstay treatment in many countries, despite being recommended only for severe FM with high levels of pain or sleep disturbance [7] or when first-line treatments fail. Emerging novel targets potentially relevant for FM [8] and new multi-target therapies need scientific verification.

Thus, debate continues about the best strategies for the management of FM, as reflected by discrepancies between existing evidence-based recommendations [9]. Nevertheless, there is general agreement on what the primary goals of FM management should be: improvement of quality of life, including symptoms, functioning and well-being [10].

### 3. Principles of care

Several governing principles guiding the care of people with FM are transversal to most recommendations: a) FM treatment should follow a personalized and stepped approach; b) shared-decision making and education should be an integral part of care; c) treatment goals should be feasible and aligned with the patient's personal goals [10]. Optimal treatments should therefore be individualized and tailored to psychiatric and medical comorbidities (that may demand specific treatment strategies), risk factors (e.g., trauma), maladaptive cognitive-affective processes (catastrophizing, perseverative thinking), and symptom's characteristics (e.g. predominance, severity, impact) [11] as well as patient's needs, preferences, and values [10]. Cost-benefit and accessibility of treatments and potential socioeconomic barriers should also be considered.

Non-pharmacological approaches, such as education, physical exercise, and psychological interventions, may be particularly appropriate for FM considering the multi-determined and dynamic nature of FM, the additional burden ensuing from psychiatric and medical comorbidities, and the influence that psychosocial processes may play in the development, maintenance and progression of the condition [12]. The targeting of multiple symptom domains and lower side effects of non-pharmacologic interventions may also be an advantage over medications [6]. For these reasons, non-pharmacological approaches are currently recommended as first-line treatment for FM by most recommendations [9]. Nonetheless, issues related to the availability, accessibility and implementation of some of these approaches and lack of familiarization of rheumatologists and general physicians with these techniques, undermine their broader adoption. New methods, such as eHealth and mHealth may prove useful to overcome some of these barriers.

#### **4. Patient education**

This is a key component in FM care. It: a) provides insight into FM's nature; b) promotes self-management by increasing knowledge about symptoms and underlying processes, their mutual influence, and the contributing role of behavioral patterns; c) validates personal experience, dismantles existing misconceptions about FM, and reduces (self-)stigma [12]; and d) favors informed and shared decision-making. Patient education's effects seem to be favored by its combination with other non-pharmacological modalities, such as exercise or psychological intervention [12,13].

#### **5. Physical exercise**

This is, to date, the only non-pharmacological intervention for FM with a “strong for” recommendation across guidelines [9]. It has been shown that physical exercise reduces key FM symptoms and improves function and quality of life [7,14]. Current modalities include aerobic exercise, resistance training, and stretching/flexibility exercises in land and water-based settings. Some studies have pointed to differential effects of distinct modalities and single or combined interventions, upon physical function, symptoms severity, quality of life and mood [15].

Exercise programs should follow a graded approach and be selected and adjusted according to the patient's specific needs (e.g., physical fitness, muscle strength), characteristics (e.g., age, BMI, comorbidities) [11] and personal preferences (e.g., activity type/frequency, individual/group format). Exercise-induced benefits are dependent on a regular and continued practice [16].

Promoting long-term adherence is a main challenge in this field [14]. Non-adherence should be timely addressed and tackled (e.g., using motivational interviewing). Also focusing on pleasurable physical activities that are integrated in daily life and other

behavioral change techniques such as nudging may be helpful in increasing long-term physical activity in FM.

## **6. Cognitive-Behavioral Therapy (CBT)**

CBT has received extensive empirical support over the years, being considered the gold-standard psychological intervention for FM. It is effective in reducing, in a dose-dependent manner [17], FM symptoms, negative affect and disability [18]. CBT is strongly recommended by most guidelines [9], especially for individuals who are emotionally distressed or have socioemotional/problem-solving deficits [7].

Despite this, CBT has been subject of criticism as well mostly due to: a) mixed findings regarding the size (often modest) and persistence of its effects [18]; b) methodological and sampling issues; c) uncertainty regarding treatment mediators/moderators [19]. This emphasizes the urge for high-quality research [20]. A debated question is the lack of or small effect on pain, which is the primary endpoint of FM trials, sometimes at the expense of other, equally burdensome, symptoms. Interestingly, a recent study showed that changes in pain-related outcomes, although desirable, are not *a sine qua non* condition for improvement to occur or for a treatment to be effective [21]. This calls attention to the need to systematically integrate, beyond symptom-focused measures, outcomes reflecting improvement of functioning, empowerment, well-being, and life satisfaction; as well as, next to generic outcomes, outcomes that fit individual needs and goals.

A new development in the field is the emergence of 3rd generation CBT. They involve mindfulness-, acceptance-, and value-based approaches. Most reviews and meta-analysis on mindfulness and acceptance-based interventions for fibromyalgia have concluded that these interventions are superior to control interventions and produce short-term improvements in key FM symptoms, depression, anxiety, mindfulness, and quality of life,

with small-to-moderate effects sizes [18,22]. Despite promising, these results should be interpreted with caution since they are largely based on low quality evidence. These new approaches are not only symptom-centered but also person-centered. This surely holds for another development in this field, compassion-based approaches. While mindfulness and acceptance are directed at better management of *symptoms and experiences*, compassion-based approaches are also directed at acceptance of *self* by learning to be non-judgmental, soothing, accepting and kind towards oneself [23]. Research shows the potential relevance of this construct in chronic pain [24].

Future studies should also provide insight into which mechanisms are being targeted, how changes in such mechanisms influence effects over time, which factors attenuate or amplify such effects and which ones favor treatment responsiveness [12,18]. Collectively, this knowledge will elucidate what works in which way for whom, and inform the development of optimized and customized disease models and psychological interventions.

## **7. Complementary and alternative therapies**

These therapies vary greatly in both contents and associated levels of evidence [25]. Balneotherapy, meditative movement therapies, or acupuncture have been associated with improvements in FM symptoms and quality of life [7], earning them a favorable recommendation from some guidelines [9]. Because most complementary and alternative therapies lack empirical support, with studies suffering from serious methodological flaws, further research aimed at clarifying their short and long-term effectiveness, underlying mechanisms, and benefit-risk ratio is pivotal, especially when considering the currency of these therapies among patients with FM [25].

## **8. Neuromodulation techniques**

Non-invasive brain stimulation such as transcranial direct-current stimulation, targeting areas implicated in pain processing and modulation, seem to have favorable effects on pain, sleep and fatigue, cognitive-affective symptoms, and quality of life [26]. Still, more studies are needed to provide conclusive evidence for the effectiveness of these techniques for FM, both as a stand-alone and add-on modality, to define optimal protocols and dosages, and to identify to whom these approaches may be best suited.

## **9. Summary and conclusion**

Despite theoretical considerations and empirical evidence supporting the benefits of non-pharmacological interventions, there is still a lot of room for improvement of treatment for FM. It has been advocated that the most effective strategy, especially in cases of severe symptoms or disability [7], may be to combine different interventions or components. While results are promising [4,13,27], future studies should examine which and how components should be combined and whether their interaction has additive or synergistic effects or even unexpected side-effects [6]. The development of a framework capable of integrating the current understanding on FM could prove valuable. It would provide insight into which mechanisms should be targeted by interventions, help to draw hypothesis regarding the expected impact of these interventions and above all inform the design of optimized interventions. Such work is currently underway by our team [28]. While we wait for further developments in these interventions and their accessibility, our clinical experience strongly indicates that patient education and engagement can go a long way in providing relief of pain and other symptoms, with emphasis on stress-related manifestations. It is especially important and rewarding that patients are helped to recognize the crucial detrimental role that chronic stress and fruitless ways of



management play in the fluctuation of their symptoms. The caring health professional may provide simple explanations on how psychological stress can sensitize the brain to respond with pain and fatigue. The interested health professional may stimulate patients to look for deeper self-understanding and to engage in mental and physical practices that foster relaxation, well-being and happiness. That seems to be, after all, a (if not “the”) common goal of all that seems to work in fibromyalgia, from anti-depressants to exercise and mindfulness!

#### **Disclosure of interest**

The authors declare that they have no conflicts of interest.

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#### **Authors Contributions**

**Ana M. Pinto:** Writing - Original Draft

**Rinie Geenen:** Writing - Review & Editing

**Paula Castilho:** Writing - Review & Editing

**José A. P. da Silva:** Writing - Review & Editing

## References

- [1] Branco JC, Bannwarth B, Failde I, et al. Prevalence of fibromyalgia: a survey in five European countries. *Semin Arthritis Rheum* 2010;39:448-53,
- [2] Santiago MG, Marques A, Kool M, Geenen R, da Silva JAP. Invalidation in patients with rheumatic diseases: clinical and psychological framework. *J Rheumatol* 2017;44:512-18.
- [3] Laroche F, Guérin J, Coste J, Trouvin AP, Perrot S. Importance of feelings of injustice in fibromyalgia, large internet survey on experiences of 4516 French patients. *Joint Bone Spine* 2019;86:808-10.
- [4] Nuesch E, Hauser W, Bernardy K, Barth J, Juni P. Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. *Ann Rheum Dis* 2013;72:955-62.
- [5] Häuser W, Walitt B, Fitzcharles MA, Sommer C. Review of pharmacological therapies in fibromyalgia syndrome. *Arthritis Res Ther* 2014;16:201.
- [6] Perrot S, Russell IJ. More ubiquitous effects from non-pharmacologic than from pharmacologic treatments for fibromyalgia syndrome: a meta-analysis examining six core symptoms. *Eur J Pain* 2014;18:1067-80.
- [7] Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017;76:318-28.
- [8] Ablin JN, Häuser W. Fibromyalgia syndrome: novel therapeutic targets. *Pain Manag* 2016;6:371-81.
- [9] Thieme K, Mathys M, Turk DC. Evidenced-based guidelines on the treatment of fibromyalgia patients: are they consistent and if not, why not? Have effective psychological treatments been overlooked? *J Pain* 2017;18:747-56.

- [10] Häuser W, Ablin J, Perrot S, Fitzcharles MA. Management of fibromyalgia: practical guides from recent evidence-based guidelines. *Pol Arch Intern Med* 2017;127:47-56, <https://doi.org/10.20452/pamw.3877>.
- [11] Häuser W, Perrot S, Clauw DJ, Fitzcharles MA. Unravelling fibromyalgia – steps toward individualized management. *J Pain* 2018;19:125-34.
- [12] Hassett AL, Gevirtz RN. Nonpharmacologic treatment for fibromyalgia: patient education, cognitive-behavioral therapy, relaxation techniques, and complementary and alternative medicine. *Rheum Dis Clin North Am* 2009;35:393-407.
- [13] Papadopoulou D, Fassoulaki A, Tsoulas C, Siafaka I, Vadalouca A. A meta-analysis to determine the effect of pharmacological and non-pharmacological treatments on fibromyalgia symptoms comprising OMERACT-10 response criteria. *Clin Rheumatol* 2016;35:573-86.
- [14] Bidonde J, Busch AJ, Schachter CL, et al. Mixed exercise training for adults with fibromyalgia. *Cochrane Database Syst Rev* 2019;5:CD013340.
- [15] Sosa-Reina MD, Nunez-Nagy S, Gallego-Izquierdo T, Pecos-Martín D, Monserrat J, Álvarez-Mon M. Effectiveness of therapeutic exercise in fibromyalgia syndrome: a systematic review and meta-analysis of randomized clinical trials. *Biomed Res Int* 2017;2017:2356346.
- [16] Häuser W, Klose P, Langhorst J, et al. Efficacy of different types of aerobic exercise in fibromyalgia syndrome: a systematic review and meta-analysis of randomised controlled trials. *Arthritis Res Ther* 2010;12:R79.
- [17] Glombiewski JA, Sawyer AT, Gutermann J, Koenig K, Rief W, Hofmann SG. Psychological treatments for fibromyalgia: a meta-analysis. *Pain* 2010;151:280-95.

- [18] Bernardy K, Klose P, Welsch P, Hauser W. Efficacy, acceptability and safety of cognitive behavioural therapies in fibromyalgia syndrome – a systematic review and meta-analysis of randomized controlled trials. *Eur J Pain* 2018;22:242-60.
- [19] Ehde DM, Dillworth TM, Turner JA. Cognitive-behavioral therapy for individuals with chronic pain: efficacy, innovations, and directions for research. *Am Psychol* 2014;69:153-66.
- [20] Morley S, Williams A, Eccleston C. Examining the evidence about psychological treatments for chronic pain: time for a paradigm shift? *Pain* 2013;154:1929-31.
- [21] Vowles KE, Witkiewitz K, Levell J, Sowden G, Ashworth J. Are reductions in pain intensity and pain-related distress necessary? An analysis of within-treatment change trajectories in relation to improved functioning following interdisciplinary acceptance and commitment therapy for adults with chronic pain. *J Consult Clin Psychol* 2017;85:87-98.
- [22] Haugmark T, Hagen KB, Smedslund G, Zangi HA. Mindfulness- and acceptance-based interventions for patients with fibromyalgia – a systematic review and meta-analyses. *PLoS One* 2019;14:e0221897.
- [23] Neff KD. Self-compassion: an alternative conceptualization of a healthy attitude toward oneself. *Self Identity* 2003; 2: 85-101.
- [24] Purdie F, Morley S. Compassion and chronic pain. *Pain* 2016;157:2625-7.
- [25] Cassisi G, Ceccherelli F, Atzeni F, Sarzi-Puttini P. Complementary and alternative medicine in fibromyalgia: a practical clinical debate of agreements and contrasts. *Clin Exp Rheumatol* 2013;31:S134-52.
- [26] Brighina F, Curatolo M, Cosentino G, et al. Brain modulation by electric currents in fibromyalgia: A structured review on non-invasive approach with transcranial electrical stimulation. *Front Hum Neurosci* 2019;13:40.

[27] Hauser W, Bernardy K, Arnold B, Offenbacher M, Schiltenwolf M. Efficacy of multicomponent treatment in fibromyalgia syndrome: a meta-analysis of randomized controlled clinical trials. *Arthritis Rheum* 2009;61:216-24.

[28] Pinto AM, Luís M, Palavra F, Hassett A, Geenen R, Da Silva JAP. Reconciling research fields in fibromyalgia: a proposed integrative model. *Clin Exp Rheumatol* 2019; S-130.

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