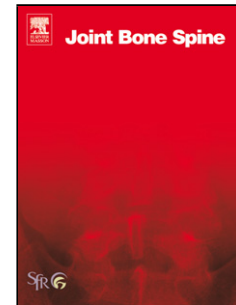


Journal Pre-proof

Physical activity in the treatment of fibromyalgia

Etienne Masquelier Dr Jacques D'haeyere



PII: S1297-319X(21)00074-9

DOI: <https://doi.org/doi:10.1016/j.jbspin.2021.105202>

Reference: BONSOI 105202

To appear in: *Joint Bone Spine*

Accepted Date: 4 January 2021

Please cite this article as: Masquelier E, D'haeyere J, Physical activity in the treatment of fibromyalgia, *Joint Bone Spine* (2021), doi: <https://doi.org/10.1016/j.jbspin.2021.105202>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier.

Physical activity in the treatment of fibromyalgia

Etienne Masquelier¹⁻², Jacques D'haeyere¹

¹ Centre Multidisciplinaire de Douleur Chronique – CHU UCL Namur – site Godinne, Belgique

² Institute of NeuroScience (IoNS) – Université catholique de Louvain, Belgique

Corresponding author's address:
Dr E. Masquelier
Centre de douleur chronique
CHU UCL Namur – site Godinne
Avenue Dr G. Thérasse, 1
B-5530 Yvoir, Belgique
etienne.masquelier@uclouvain.be
+32 81 42 36 80

Abstract

International treatment recommendations for fibromyalgia (FM) highlight the importance of adapted physical activity (APA) combined with patient education. Cognitive and behavioral therapies as well as an interdisciplinary approach can be proposed for more complex or severe clinical situations, with a biopsychosocial vision of rehabilitation.

To personalize the rehabilitation's therapeutic approach, a clinician can use simple and validated instruments for measuring physical performance that will highlight levels of physical conditioning, which range from low to very low in FM patients.

Several systematic reviews and meta-analyses have found strong evidence that supervised aerobic and resistance training programs reduce the pain intensity and significantly improve the quality of life and the physical and psychological functioning of female FM subjects. These therapeutic approaches appear safe and promising in terms of cost-effectiveness and should be the subject of more randomized controlled trials among male FM subjects and adolescents.

Keywords

Fibromyalgia – aerobic exercise – resistance training – interdisciplinary therapeutic programs – altered functional performance – adapted physical activity

Introduction

Fibromyalgia (FM) or FM syndrome is a form of diffuse chronic pain associated with other symptoms such as fatigue, sleeping and mood disorders, cognitive disorders, and physical deconditioning that has been present for at least 3 months. The etiology and pathophysiology of FM are complex since they involve various biological, psychological and social factors. This is a difficult diagnosis to make since the classification and diagnostic criteria are still in flux and there are no specific clinical or laboratory signs associated with this condition [1]. Its treatment requires a biopsychosocial vision of this high-cost disease for the society, in which the patient takes an active role in his/her health through a rehabilitation project [2,3].

A. International recommendations for fibromyalgia management

A recent publication [4] compared the four latest international evidence-based guidelines for the clinical management of FM patients (European, German, American and Canadian). The common element was that the highest ranking of recommendation was assigned to exercise, patient education, multidisciplinary care and cognitive-behavioral therapy. An algorithm was proposed by the EULAR in 2017 [5] that highlights the importance of exercise (adapted physical activity) and patient education as the basis for treatment.

B. Physical conditioning in fibromyalgia patients

Assessment of the patient's functional status and the impact of FM on their day-to-day life is crucial to set-up and guide the optimal personalized treatment approach that will be put into place. Given the complexity and heterogenous nature of FM, the symptoms, functional condition and quality of life can vary greatly from one patient to another, but also for the same patient over time [6].

When compared to control subjects, FM patients have low to very low physical conditioning associated with pain, fatigue, stiffness, fall risk, anxiety, depression. These are negatively correlated with quality of life [7]. Conversely, several studies have shown that better physical conditioning is consistently associated with lower levels of pain and better quality of life [8,9,10].

1. Reduced cardiorespiratory capacity

The 6-minute walking test is a valid, reproducible and sensitive measurement in FM, but it is not predictive of the patients' cardiovascular capacity (VO_2 max.) [11]. A systematic review [12] found moderate evidence that submaximal effort tests are reliable, valid and acceptable in the domain of chronic pain, and particularly FM, but that maximum effort tests are not valid because physical performance is limited, not by the patient's aerobic capacity but by their motivation and/or pain apprehension. In a Canadian review [13], 12 studies mention that cardiorespiratory capacity was reduced by 12% to 35% in FM patients compared to controls or to normal values during testing on a bicycle ergometer or treadmill.

2. Amplification of perceived exertion

Perceived exertion measures the intensity of an effort by integrating all the sensations and repercussion of exercise on the body. The Borg scale [14], which is used to measure perceived exertion, is significantly increased in FM patients during a submaximal cycle ergometer test [15] or during a 500 m walking test, the 60-step stairs climbing test, the measurement of maximum quadriceps strength or during activities of daily living [16,17,18]. The overscoring of perceived exertion appears to be a major sign of FM [15].

3. Reduced muscular strength and endurance

Several studies have found a significant reduction in muscle strength (upper and lower limbs) or dynapenia on various performance tests that are validated and reproducible in FM, such as the 30-second Arm Curl test, the 30-second chair stand test, or hand grip strength measurements [19,20,21]. The static endurance of shoulder abductor muscles was reduced by 80% in 16 FM patients compared to 85 controls in a study performed in Belgium [22].

4. Increased musculotendinous stiffness at the ankles and reduced walking speed and coordination

The feeling of abnormal stiffness can be quantified as a significant increase in the passive viscoelastic stiffness in the muscles around the ankle in younger and middle-aged FM patients, but paradoxically, not in older patients [23]. Reduction in walking speed, bradykinesia [24,25] and loss of motor agility can lead to a higher incidence of falls in FM [20,26].

5. Fear of movement, kinesiophobia

Kinesiophobia or an enhanced and irrational fear of movement is present in more than 38% of FM patients [27]. It is weakly but significantly correlated with the perceived disability level, pain intensity, depressive mood and inversely correlated with performance on a treadmill.

6. “Hyperactive” lifestyle

A premorbid “hyperactive” lifestyle [28], propensity to action with tendency to go beyond one’s limits, perception of elevated physical, cognitive or emotional allostatic overload, i.e., excessive and cumulative increase in the allostatic load (which corresponds to the physiological cost of maintaining stable equilibrium despite environmental changes) [29,30] are frequently seen in FM patients and they can contribute to or aggravate, over an extended period to time, physical deconditioning.

In a study of 45 FM patients, premorbid representational hyperactivity (i.e., their own representation of the activity level that they could previously accomplish) is associated with basic bodily needs neglect (such as feeding and rest), a level of self-oriented perfectionism and behavioral hyperactivity (i.e., effective engagement in several activities) is associated to a large number of children [31,32].

All these physical, cognitive and emotional deficiencies can progress into a cascade of deconditioning and severe physical and psychosocial disability (Figure 1).

7. Comparison of physical condition, quality of life, level of perceived disability in fibromyalgia versus the general population and in chronic rheumatological diseases

In a study with the self-reported International Fitness Scale (IFS) that evaluates the overall levels of physical conditioning, cardiorespiratory endurance, muscle strength, flexibility and balance, 65% to 80% of female patients with FM reported a low to very low level of physical conditioning, versus 8% to 50% in the control population [33].

Several studies have compared the quality of life of patients with FM to that of the general population based on the SF-36 or SF-12. Most published studies found significantly lower scores than in the general population with a larger gap on physical dimensions [34,35]. In comparison with patients who have rheumatoid arthritis, the SF-36 and SF-12 scores are often lower in patients with FM, although the differences are rarely significant [36]. The level of perceived disability measured by the Health Assessment Questionnaire (HAQ) in FM appears to be similar to the one measured in patients who have rheumatoid arthritis [37].

C. Exercise in fibromyalgia patients

An umbrella review published in 2020 analyzed 37 systematic reviews of which 16 had been published since 2014 [38]. The authors reported that aerobic exercise and strength training are the most used non-pharmacological treatment modalities for treating FM.

There is strong evidence that adapted physical activity reduces the intensity of the perceived pain, improves quality of life and the physical and psychological function of FM subjects. The incidence of side effects related to exercise programs is low, and to our knowledge, no serious adverse events have been reported in the literature. However, clinical observations show that FM patients have trouble performing high-intensity exercise because of pain and fatigue secondary to these efforts [39,40].

1. Aerobic exercise

The first study about a supervised cardiovascular fitness training program in FM patients was done in Canada in 1988 [41,42]. The FM patients in the aerobic exercise group increased their functional capacity and pain pressure threshold and reported improved overall well-being compared to a group who only did stretching exercises.

Over the past 30 years, a growing number of research articles, including systematic reviews and meta-analyses, have showed that regular aerobic exercise improves quality of life by reducing the pain level and improving function [43,44,45]. These treatment modalities have been the subject of the largest number of randomized controlled trials (RCT) and the best-quality methodology. However, the treatment effect remains weak (Table 1).

The intensity of the aerobic exercise should be between 40% and 80% of the maximum heart rate or at a perceived exertion level between 9 and 15 on the Borg scale [46].

2. Resistance exercise

Strength training is a specific type of physical activity in which progressively higher load is used to improve muscle strength, power or endurance. The progressive nature of the training is key: if the load or volume (repetitions) are not increased over time, the progress will be very limited. Modulation of the intensity of resistance training must be based on perceived exertion (e.g., Borg scale). The effectiveness of resistance training is currently low in the small number of RCTs done, although these are plagued by evaluation bias and low-quality methodology [33].

3. Stretching

The level of evidence for effectiveness of stretching exercises appears low to moderate; it is low if done alone and moderate when combined with aerobic exercise, leading to improved quality of life [47].

4. Aquatic exercise

The results of three systematic reviews [48,49,50] are positive in terms of the improvement in quality of life, sleep and physical performance (physical condition). The exercises proposed are mixed (aerobic, stretching, resistance, relaxation) and supervised. The withdrawal rate is comparable to a control group. Few adverse effects have been reported, although this aspect is not discussed in detail in these studies. The level of evidence for efficacy of water-based exercises appears to be low, thus it should be reserved for subgroups such as patients with physical deconditioning or older patients suffering from FM for a long time [48].

5. Mixed exercise training

A systematic review [51] including 29 RCTs with protocols involving at least two types of exercises (aerobic, resistance, stretching) found moderate evidence with likely improvement in quality of life, physical function and fatigue. Only physical function improved in every

participant in most studies although some had very weak methodology (selection bias, small sample size, etc.).

6. Meditative movement therapy

Meditative movement therapy such as yoga, tai-chi and Qi gong are alternative and complementary modalities that may be useful for patients who have low compliance with traditional exercise programs (i.e., cardiovascular and resistance training) and who continue to experience pain and fatigue [38]. These therapies appear effective for improving sleep quality but not for reducing the fatigue level due to a lower physical load than other exercise programs, which help to reduce the sympathetic tone and increase the parasympathetic activity [52].

D. Biological mechanisms explaining the treatment effect of exercise in fibromyalgia

The recent scientific literature points to several biological mechanisms that can explain the therapeutic effects of exercise in FM patients. The effects of exercise are not limited to a single physiological system and can affect the entire individual.

Regular exercise may have the ability to influence the nociceptive, neuroendocrine and autonomic system, along with cognitive ability and mood disorders in subjects with FM. As for the nociceptive system, the hypothesis of an effect of exercise on descending pain modulation has all its full meaning. Thus, cardiovascular fitness training three times per week for 20 weeks increases the level of serotonin and its metabolite 5-hydroxyindolacetic acid (5-HIAA), suggesting stimulation of the descending pain modulation [53]. Furthermore, the authors observed that the most physically active FM subjects were better able to modulate repeated painful thermal stimuli than minimally active FM subjects [54].

The hypothesis of an effect of exercise on the hypothalamic–pituitary–adrenal axis has been made based on the study by Genc et al. [39] who proposed 6 weeks of aerobic exercises in 50 FM subjects. This led to reduction in pain, morning stiffness and significant increase in growth hormone along with significant reduction in the serum cortisol levels.

A systematic review [55] showed that moderate to intense aerobic exercise done twice per week was effective by reducing the dysfunction of the autonomic nervous system and increasing heart rate variability. Furthermore, strength training reduced anxiety and depression symptoms while improving muscle strength in a systematic review of patients with fibromyalgia [56].

The effect of exercise on cognitive ability is still hypothetical but may turn out to be interesting. A Spanish study [57] showed that exercising in warm water improved cognitive functions such as working memory, episodic memory and semantic memory. Cherry et al [58] observed that the improvement in physical conditioning (mobility, strength, balance, flexibility) in subjects with FM was strongly correlated with the improvement in cognitive performance on working memory, cognitive flexibility, and attention tests.

A recent study [59] found a significant improvement in cognitive processing speed on the Stroop Color and Word Test (SCWT) after a 15-week exercise program. According to these authors, the underlying mechanisms may be related to amygdala activation observed in functional MRI, leading to better concentration and lower sensitivity to distractions.

E. Multimodal and interdisciplinary treatment approaches integrating exercise

Patient education is mentioned in the EULAR recommendations as one of the most useful and essential steps in the treatment approach for FM [60]. Two systematic reviews of patient education in FM [61,62] confirm that patient education itself has no proven effectiveness on

function and quality of life, even if it can alter the beliefs and/or perceptions about FM, contrary to the combination of patient education plus exercise (aerobic, resistance, stretching) on dry land or in water, which provides a significant reduction in pain levels along with improvement in quality of life (measured with the FIQ or SF36) and functionality (6-minute walking test) in the short, medium and long term.

Several older meta-analyses looked at the effects of non-pharmacological interventions on FM and showed that the combination of cognitive behavioral therapy (CBT) plus an exercise program is the most effective treatment for FM [63,64,65]

The “pacing activity” or change of rhythm appropriate for the management of physical and daily activities must be considered as an important element of multimodal treatment programs for FM with the need for personalization and customization [66,67,68].

The interdisciplinary biopsychosocial treatment strategy integrating exercise into a unit of place such as a chronic pain center shows the strongest evidence for forms of chronic disabling pain, especially FM, with the treatment results being maintained for more than 2 years [69].

F. Barriers and beliefs about physical activity

Several patients with FM do not believe that physical activity will reduce their level of perceived pain [70,71]. The first experience for a FM patient who is given a non-personalized exercise program is often negative, related to the feeling that FM and its consequences on day-to-day life is not well understood by the prescribing physician or the physical therapist. The main barriers to exercise in FM are the omnipresent fatigue, pain and fear of making the symptoms worse, especially after effort, but also the level of disability, mood disorders, weak self-efficiency for exercise and inadequate social support network [70].

G. Adherence to exercise programs

Several authors mention a large variability in the adherence rate to exercise programs [72,73]. More specifically, the mean compliance rate was 84% (range 54–100%) for a strength training program [56]. Several variables such as age, symptom severity and comorbidities may have an effect, as well as the lack of time stated by patients. Stoppage of exercise can also be explained by unsuitable personal beliefs about the effectiveness of these treatments or by high intensity or excessive intense exercise or by an overly high external health locus of control [74]. Moreover, a meta-analysis showed that supervised exercise programs at least 26 weeks in length could improve adhesion to exercise and symptoms (especially anxiety) versus short-term supervised exercise programs [75]. A Spanish meta-analysis on adherence to a walking-for-exercise program in female FM patients showed that encouragement by the doctors related to regular walking and supervision by a nurse yielded better adherence to this practice [76].

H. Health economic consequences of non-pharmacological treatments for fibromyalgia

While doctor hopping is thought to be costly for the individual and the community as a whole (multiple consultations, redundancy of supplementary examinations, inappropriate prescriptions, numerous hospitalizations) [77], three studies suggest promising cost-utility results of rehabilitation and physiotherapy in warm water along with group CBT and psychoeducation [78,79,80].

I. Exercise in children and adolescents with fibromyalgia

Very few RCTs have been done on exercise alone or in combination with other therapies (CBT, psychotherapy) in children or adolescents with FM. A Canadian study [81] found a significant decrease in pain and improvement in physical condition at 12 weeks after an

aerobic exercise program and meditative movements of Qi gong. A British study [82] showed the benefits of an intensive physical activity program (walking, going up stairs, squats, dance) combined with CBT for a minimum of 4 hours per week in 64 adolescents with FM. Quality of life and school function were improved while pain decreased.

CONCLUSIONS

An exercise program that is individualized and supervised over a set period allowing the patient to learn aerobic, strength and flexibility exercises must be considered as the treatment of choice for FM in close association with patient education. However, various research questions remain to be answered about the intensity, frequency, progression of the exercises, how to integrate these exercise programs into daily and professional activities, and also how to ensure adherence to these exercise programs.

Conflict of interest disclosure:

Conflicts of interest: none

Journal Pre-proof

References

- [1] Perrot S. Fibromyalgia: A misconnection in a multiconnected world? *Eur J Pain* 2019;23(5):866-873.
- [2] Arnold L, Choy E, Clauw D, et al. Fibromyalgia and chronic pain syndromes: a white paper detailing current challenges in the field. *Clin J Pain* 2016; 32(9):737-746.
- [3] Pinto A, Geenen R, Castilho P, et al. Progress towards improved non-pharmacological management of fibromyalgia. *Joint Bone Spine* 2020;87(5):377-379.
- [4] Thieme K, Mathys M, Turk D. 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(7):747-756.
- [5] Macfarlane G, Kronisch C, Dean L, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017; 76:318-328.
- [6] Harris R, Williams D, Mc Lean S, et al. Characterization and consequences of pain variability in individuals with fibromyalgia. *Arthritis Rheum* 2005; 52(11):3670-3674.
- [7] Castro-Pinero J, Aparicio V, Estévez-Lopez F, et al. The potential of established fitness cut-off points for monitoring women with fibromyalgia: the al-Andalus Project. *Int J Sports Med* 2017;38(5):359-369.
- [8] Carbonell-Baeza A, Aparicio VA, Sjostrom M. Pain and functional capacity in female fibromyalgia patients. *Pain Med* 2011;12:1667-1675.
- [9] De Bruijn ST, van Wijck AJ, Geenen R, et al. Relevance of physical fitness levels and exercise-related beliefs for self-reported and experimental pain in fibromyalgia: an explorative study. *J Clin Rheumatol* 2011;17:295-301.
- [10] Soriano-Maldonado A, Henriksen M, Segura-Jimenez V, et al. Association of physical fitness with fibromyalgia severity in women.: the al-Andalus project. *Arch Phys Med Rehabil* 2015b;96:1599-1605.
- [11] Pankoff B, Overend T, Lycy S, et al. Reliability of the six-minute walk test in people with fibromyalgia. *Arthritis Care Res* 2000; 13:291-295.
- [12] Ratter J, Radlinger L, Lucas C. Several submaximal exercise tests are reliable, valid and acceptable in people with chronic pain, fibromyalgia or chronic fatigue: a systematic review. *J Physiother* 2014; 60(3):144-150
- [13] Gaudreault N, Boulay P. Cardiorespiratory fitness among adults with fibromyalgia. *Breathe(Sheff)* 2018;14:e25-e33.
- [14] Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377-381.
- [15] Nielens H, Boisset V, Masquelier E. Fitness and perceived exertion in patients with fibromyalgia syndrome. *Clin J Pain* 2000;16:209-213.

- [16] Bachasson D, Guinot M, Wuyam B. Neuromuscular fatigue and exercise capacity in fibromyalgia syndrome. *Arthritis Care Res* 2013;65:432-440.
- [17] Palstam A, Larsson A, Bjersing J et al. Perceived exertion at work in women with fibromyalgia: explanatory factors and comparison with healthy women. *J Rehabil Med* 2014;46:773-780.
- [18] Huijnen IP, Verbunt JA, Meeus M, et al. Energy expenditure during functional daily life performances in patients with fibromyalgia. *Pain Pract* 2015; 15: 748-56.
- [19] Latorre-Roman P, Segura-Jimenez V, Aparicio V, et al. Ageing influence in the evolution of strength and muscle mass in women with fibromyalgia: the al-Andalus projet. *Rheumatol Int* 2015;35:1243-1250.
- [20] Goes S, Leite N, Shay B, et al. Functional capacity, muscle strength and falls in women with fibromyalgia. *Clin Biomech* 2012;27:578-583.
- [21] Larsson A, Palstam A, Bjersing J, et al. Controlled, cross-sectional, multi-center study of physical capacity and associated factors in women with fibromyalgia. *BMC Musculoskelet Disord* 2018;19:121.
- [22] Maquet D, Croisier J, Renard C, et al. Muscle performance in patients with fibromyalgia. *Joint Bone Spine* 2002;69:293-299.
- [23] Dierick F, Detrembleur C, Trintignac G, et al. Nature of passive musculoarticular stiffness increase of ankle in female subjects with fibromyalgia syndrome. *Eur J Appl Physiol* 2011;111:2163-2171.
- [24] Auvinet B, Bileckot R, alix A, et al. Gait disorders in patients with fibromyalgia. *Joint Bone Spine* 2006;73:543-546.
- [25] Heredia-Jimenez J, Latorre-Roman P, Santos-Campos M, et al. Spatio-temporal gait disorder and gait fatigue index in a six-minute walk test in women with fibromyalgia. *Clin Biomech* 2016;33:1-6.
- [26] Rutledge D, Martinez A, Traska T, et al. Fall experiences of persons with fibromyalgia over 6 months. *J Adv Nurs* 2013;69:435-448.
- [27] Turk DC, Robinson JP, Burwinkle T. Prevalence of fear of pain and activity in patients with fibromyalgia syndrome. *J Pain* 2004;5:483-490.
- [28] Van Houdenhove B, Neerinckx E, Onghena P, et al. Premorbid "overactive" lifestyle in chronic fatigue syndrome and fibromyalgia. An etiological factor or proof of good citizenship? *J Psychosom Res* 2001;51(4):571-576.
- [29] Sommela A, Chardhomme N, Masquelier E. La fibromyalgie: modèle de maladie de surcharge allostatique. Poster présenté à la Société française de la douleur, Nice 2017.
- [30] Martinez-Lavil M, Vargas A. Complex adaptive systems allostasis in fibromyalgia. *Rheum Dis Clin North Am* 2009;35(2):285-298.

- [31] Masquelier E, Scaillet N, Luminet O, et al. What's about overactive lifestyle in fibromyalgia and chronic fatigue syndrome? *Rev Med Suisse* 2011;7(301):1421-1422.
- [32] Grisart J, Scaillet N, Michaux M, et al. Determinants of representational and behavioral hyperactivity in patients with fibromyalgia syndrome. *Journal of Health Psychology*; 2020;25(8):1128-1137.
- [33] Alvarez-Gallardo I, Soriano-Maldonado A, Segura-Jimenez V, Carbonnel-Baeza A, Estévez-Lopez F, McVeigh J, Delgado-Fernandez M, Ortega F. International Fitness Scale 5IFIS): construct validity and reliability in women with fibromyalgia: the al-Andalus project. *Arch Phys Med Rehabil* 2016; 97(3):395-404
- [34] Jiao J, Vincent A, Cha S et al. Relation of age with symptom severity and quality of life in patients with fibromyalgia. *Mayo Clin Proc* 2014; 89(2):199-206.
- [35] Mas A, Carmona L, Valverde M, et al. Prevalence and impact of fibromyalgia on function and quality of life in individuals from the general population: results from a nationwide study in Spain. *Clin Exp Rheumatol* 2008;26(4):519-526.
- [36] Salaffi F, Sarzi-Puttini P, Girolilmetti R, et al. Health-related quality of life in fibromyalgia patients: a comparison with rheumatoid arthritis patients and the general population using the SF-36 health survey. *Clin Exp Rheumatol* 2009;27(5 suppl 5§):S67-74.
- [37] Raftery G, Bridges M, Heslop P, Walker D. Are fibromyalgia patients as inactive as they say they are ? *Clin Rheumatol* 2009; 28(6):711-714.
- [38] Andrade A, Dominski F, Sieczkowska S. What we already know about the effects of exercise in patients with fibromyalgia: an umbrella review. *Semin Arthritis Rheum* 2020; 14;S0049-0172(20)30022-6. Online ahead of print.
- [39] Genc A, Tu B, Aytur Y, et al. Does aerobic exercise affect the hypothalamic-pituitary-adrenal hormonal response in patients with fibromyalgia syndrome? *J Phys Ther Sci* 2015; 27(7):2225-2231.
- [40] van Santen M, Bolwijn P, Landewé R, et al. High or low intensity aerobic fitness training in fibromyalgia: does it matter? *J Rheumatol* 2020;29(3)582-587.
- [41] McCain G, Bell D, Mai F, et al. A controlled study of the effects of a supervised cardiovascular fitness training program on the manifestations of primary fibromyalgia. *Arthritis Rheum* 1988;31:1135-1141.
- [42] Masquelier E. Traitement non médicamenteux du syndrome fibromyalgique. Synthèse de littérature, ligne de conduite clinique. *Rev Rhumatisme* 2003;70(4):346-353.
- [43] Hauser 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* 2010a; 12: R79.
- [44] Kelley GA, Kelley KS. Exercise improves global well-being in adults with fibromyalgia: confirmation of previous meta-analytic results using a recently developed and novel varying coefficient model. *Clin Exp Rheumatol* 2011; 29(6 suppl 69):S60-S62.

- [45] Bidonde G, Busch A, Schachter C, et al. Aerobic exercise training for adults with fibromyalgia. *Cochrane Database Syst Rev* 2017;6:CD012700.
- [46] Moura Franco K, Lenoir D, dos Santos Franco Y, et al. Prescription of exercises for the treatment of chronic pain along the continuum of nociplastic pain: a systematic review with meta-analysis. *Eur J Pain* 2020;00:1-20.
- [47] Kim S, Busch A, Overend T, Schachter L, et al. Flexibility exercise training for adults with fibromyalgia. *Cochrane Database Syst Rev*. 2019; 9(9):CD013419.
- [48] Bidonde G, Busch A, Webber S, et al. Aquatic exercise training for fibromyalgia. *Cochrane Database Syst Rev* 2014b;10P:CD011336.
- [49] Lima T, Dias J, Mazuquin B, et al. The effectiveness of aquatic physical therapy in the treatment of fibromyalgia: a systematic review with meta-analysis. *Clin Rehabil* 2013;27:892-908.
- [50] Perraton L, Machotka Z, Kumar S, et al. Components of effective randomized controlled trials of hydrotherapy programs for fibromyalgia syndrome: a systematic review. *J Pain Res* 2009;2:165-173.
- [51] Bidonde G, Busch A, Schachter C, et al. Mixed exercise training for adults with fibromyalgia. *Cochrane Database Syst Rev* 2019;5:CD013340.
- [52] Estévez-Lopez F, Maestre-Cascales C, Russel D et al. Effectiveness of exercise on fatigue and sleep quality in fibromyalgia: a systematic review and meta-analysis of randomized trials.
- [53] Valim V, Natour J, Xiao Y, et al. Effects of physical exercise on serum levels of serotonin and its metabolite in fibromyalgia: a randomized pilot study. *Rev Bras Reumatol* 2013;53(6):538-541.
- [54] McLoughlin M, Stegner A, Cook D, et al. The relationship between physical activity and brain responses to pain in fibromyalgia. *J Pain* 2011;12(6):640-651.
- [55] Andrade A, Vilarino G, Serafim T, et al. Modulation of autonomic function by physical exercise in patients with fibromyalgia syndrome: a systematic review. *PM R* 2019; 11(10):1121-1131
- [56] Andrade A, Steffens R, Mendes S, et al. A systematic review of the effects of strength training in patients with fibromyalgia: a clinical outcomes and design considerations. *Adv Rheumatol* 2018;58(1):36.
- [57] Munguia-Izquierdo D. Assessment of the effects of aquatic therapy on global symptomatology in patients with fibromyalgia syndrome: a randomized controlled trial. *Randomized Controlled Trial* 2008;89(12):2250-2257.
- [58] Cherry B, Weiss J, Barakat B, et al. Physical performance as a predictor of attention and processing speed in fibromyalgia. *Arch Phys Med Rehabil* 2009;90(12):2066-2073.

- [59] Martinsen S, Flodin P, Löfgren M, et al. The role of long-term physical exercise on performance and brain activation during the Stroop colour word task in fibromyalgia patients. *Clin Physiol Funct Imaging* 2018; 38(3):508-516.
- [60] McFarlane GJ, Kronisch C, Dean L, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017;76(2):318-328.
- [61] Eligazagaray-Garcia I, Muriente-Gonzalez J, Gil-Martinez A. Education for patients with fibromyalgia. A systematic review of randomised clinical trials. *Rev Neurol* 2016;62:49-60.
- [62] Garcia-Rios MC, Navarro-Ledesma S, Tapia-Haro R, et al. Effectiveness of health education in patients with fibromyalgia: a systematic review. *Eur J Phys Rehabil Med* 2019; 55:301-313.
- [63] Rossy L, Buckelew SP, Dorr N, et al. A meta-analysis of fibromyalgia treatment interventions. *Ann Behav Med* 1999; 21:180-191.
- [64] Hadhazy Va, Ezzo J, Creamer P, et al. Mind-body therapies for the treatment of fibromyalgia. A Systematic review. *J Rheumatol* 2000;27:2911-2918.
- [65] Sim J, Adams N. Systematic review of randomized controlled trials of nonpharmacological interventions for fibromyalgia. *Clin J Pain* 2002; 18:324-336.
- [66] Thiem K, Gromnica-Ihle E, Flor H. Operant behavioral treatment of fibromyalgia: a controlled study. *Arthritis Rheum* 2003;49:314-320.
- [67] Thiem K, Turk DC. Heterogeneity of psychophysiological stress responses in fibromyalgia syndrome patients. *Arthritis Res Ther* 2006;8:R9.
- [68] Van Koulil S, Kraaijmaat F, van Lankveld W, et al. Cognitive-behavioral mechanisms in a pain-avoidance and a pain-persistence treatment for high-risk fibromyalgia patients. *Arthritis Care Res* 2011;63:800-807.
- [69] Guisti E, Castelnovo G, Molinari E. Differences in multidisciplinary and interdisciplinary treatment programs for fibromyalgia: a mapping review. *Pain Res Manag* 2017;2017:7261468.
- [70] Russel D, Alvarez Gallardo IC, Wilson I et al. 'Exercise to me Is a scary word': perceptions of fatigue, sleep dysfunction, and exercise in people with fibromyalgia syndrome – a focus group study. *Rheumatol Int* 2018; 38(3):507-515.
- [71] McVeigh JG, Lucas A, Hurley D, Basford J, Baxter G. Patient's perceptions of exercise therapy in the treatment of fibromyalgia syndrome: a survey. *Musculoskeletal Care* 2003; 1(2):98-107.
- [72] Bush A, Schachter C, Overend T, et al. Exercise for fibromyalgia: a systematic review. *J Rheumatol* 2008;35:1130-1144.

- [73] Pereira Campos R, Vazquez M. The impact of fibromyalgia on health-related quality of life in patients according to age. *Rheumatol Int* 2013;33(6):1419-1424.
- [74] Jones K, Liptan G. Exercise interventions in fibromyalgia: clinical applications from the evidence. *Rheum Dis Clin North Am* 2009;35:373-391.
- [75] McDowelll C, Cook D, Herring M. The effects of exercise training on anxiety in fibromyalgia patients: a meta-analysis. *Med Sci Sports Exerc* 2017;49:1868-1876.
- [76] Sanz-Banos Y, Pastor-Mira M, Lledo A, et al. Do women with fibromyalgia adhere to walking for exercise programs to improve their health? Systematic review and meta-analysis. *Disabil Rehabil* 2017:1-13.
- [77] Annemans L, Wessely S, Spaepen E, et al. Health economic consequences related to the diagnosis of fibromyalgia syndrome. *Arthritis Rheum* 2008; 58(3)895-902.
- [78] Gusi N, Tomas-Carus P. Cost-utility of an 8-month aquatic training for women with fibromyalgia: a randomized controlled trial. *Arthritis Res Ther* 2008;10(1):R24.
- [79] Luciano J, D'Amico F, Cerdà-Lafont M, et al. Cost-utility of cognitive behavioral therapy versus U.S. Food and Drug Administration recommended drugs and usual care in the treatment of patients with fibromyalgia: an economic evaluation alongside a 6-month randomized controlled trial. *Arthritis Res Ther* 2014;16(5):451.
- [80] Luciano J, Forero C, Cerdà-Lafont M, et al. Functional Status, Quality of Life, and Costs Associated with Fibromyalgia Subgroups: A Latent Profile Analysis. *Clin J pain* 2016;32(10):829-840.
- [81] Stephens S, Feldman B, Bradley N, et al. Feasibility and effectiveness of an aerobic exercise program in children with fibromyalgia: results of a randomized controlled pilot trial. *Arthritis Rheum* 2008;59(10):1399-1406.
- [82] Sherry D, Brack L, Tress J, et al. The Treatment of Juvenile Fibromyalgia with an Intensive Physical and Psychosocial Program. *J Pediatr* 2015;167(3):731-737.

Figure 1

Inspired from Préfaut C and Ninot G. *La réhabilitation du malade respiratoire chronique* [Rehabilitation of chronic respiratory disease patients] Paris: Masson, 2009:528p

Copyright © 2009 Elsevier Masson SAS. All rights reserved

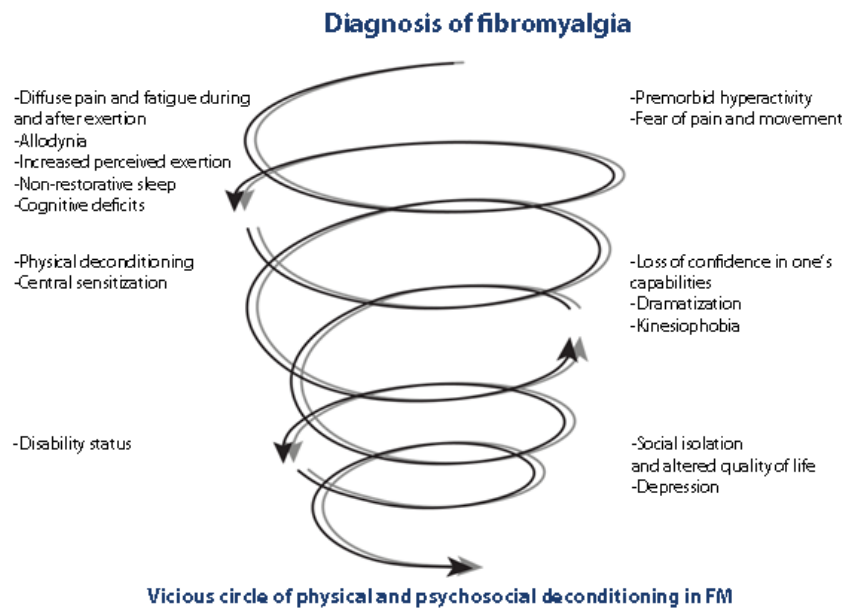


Table 1: Training on regular practice of supervised aerobic exercise in patients suffering from fibromyalgia (based on Bidonde, 2017)

Parameters (tools)	Number of RCT done	Exercise group vs control group (No. subjects)	Relative improvement* (95% CI)
Quality of life after 12 to 24 weeks (FIQ)	5	228 vs 144	15 % (5 %-24 %)
Pain after 6 to 24 weeks (VAS)	6	210 vs 141	18 % (7 %-30 %)
Fatigue after 14 to 24 weeks (VAS)	3	179 vs 107	8 % (-0.4 %-16 %)
Stiffness after 16 weeks (FIQ)	1	107 vs 36	11 % (1 %-21 %)
Physical function at 8 to 24 weeks (FIQ and SF-36)	3	159 vs 87	21.9% (-10.7-33.2 %)

**Relative improvement: mean difference/mean of pooled control groups; each variable is measured on a scale of 0 to 100, with lower scores being better. RCT: randomized controlled trials, VAS: visual analog scale, FIQ: Fibromyalgia Impact Questionnaire; SF-36: Short Form (36) Health Survey*