# Fibromyalgia

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|---|---|
| **Diagnosis/Condition:** | Fibromyalgia |
| **Discipline:** | Integrated |
| **ICD-10 Codes:** | M79.7 |
| **Origination Date:** | 08/2000 |
| **Review/Revised Date:** | 07/2024 |
| **Next Review Date:** | 07/2026 |

Fibromyalgia (FM) is a complex, chronic condition that causes widespread pain in the muscles and other connective tissues and is generally bilateral. Deep muscular pain is the most common symptom. Muscular rheumatism and fibrositis are historic terms for fibromyalgia. It is often associated with characteristic soft tissue "tender points", non-restorative sleep disorder, general fatigue, irritable bowel syndrome (IBS), muscle stiffness (especially in the morning), headaches, migraines, depression, and other systemic manifestations.[1] Current diagnostic parameters rely on the main sign of widespread pain throughout the body for at least three months, and no longer evaluate tender points as diagnostic. (See Appendix for evaluation forms). There are no specific organ pathologies associated, but many other conditions co-exist, including IBS, fatigue syndromes, interstitial cystitis, TMD disorders, POTS, and depression.[2] Fibromyalgia often results in disability and reduced quality of life.[3]

Fibromyalgia is more common in women compared to men, with the prevalence of fibromyalgia in the United States at 6.4% (7.7% in women and 4.9% in men).[4]

While no specific neurophysiologic abnormalities have been discovered, FM appears to be both a peripheral and a central nervous system disorder.[5] Its pathogenesis involves a disorder of the central modulation of pain, impairment of the descending inhibitory system, and hyperactivity of substance P.[6] Patients with FM exhibit prolonged pain after sensory stimulation. Banic et al found evidence of heightened withdrawal reflex indicating spinal cord hypersensitivity in FM and chronic whiplash patients.[7] The biopsychosocial model of illness clarifies the often multifactorial nature of FM. Experimental evidence in humans indicates that the response to stress lowers the pain threshold and contributes to central sensitization.[8,9] Prior history of physical and psychological trauma, such as PTSD and sexual abuse, along with anxiety and depression are predictive of chronic pain in general and may facilitate the onset of FM.[10,11]

The economic and social burden of FM is significant. A 2022 review (N=36) estimated a wide range of total annual direct costs per patient ($1,750 - $35,920).[12] Roughly one-quarter of people with fibromyalgia are work-disabled.[13] There is a higher risk for FM if other rheumatic disease is present. (e.g. OA, lupus, RA, or ankylosing spondylitis).

The most current European League Against Rheumatism (2017) clinical practice guideline incorporates both nondrug and drug treatments based on available scientific evidence or expert opinion. Non-pharmacological treatments involving active participation of patients seem to be more effective than passive physical measures. [14]

Recent research indicates that an interdisciplinary approach to FM treatment creates better outcomes.[15,16] Patients with FM tend to use more integrative healthcare (IH) and some modalities have been shown to be effective at relieving symptoms [17,18,19] Those who use IH have been shown to have lower insurance expenditures than those who do not.[20]

## Subjective Findings and History

Frequently observed symptoms and signs in FM include:

- Generalized pain and stiffness.
- Generalized weakness, myalgias, and arthralgias.
- Diffuse muscular and bilateral axial pain.
- Exercise intolerance-increased aching with excessive physical exercise.
- Migraine and tension headaches.
- Temporomandibular joint disorders (TMD).
- Problems with memory or clear thinking.
- Digestive issues (irritable bowel syndrome) or gastroesophageal reflux disease (GERD).
- As with other chronic pain conditions, co-morbid mood and anxiety disorders commonly occur in FM (29% and 27%, respectively)[21] and a lifetime diagnosis of a major mood disorder has been observed in as many as 74% of FM patients.[22]
- Nonrestorative sleep.
- Fatigue.
- Dysmenorrhea.
- Endometriosis.
- Lupus.
- Osteoarthritis.
- Restless leg syndrome.
- A 2021 meta-analysis of studies of respiratory disturbances suggests that respiratory disorders can also manifest with fibromyalgia.[23]
- Subjective numbness, swelling, tingling.
- Fever and sweating.
- Swollen glands.
- Dry eyes.
- Nocturnal myoclonus, restless legs syndrome.
- Female urethral syndrome.
- Vulvodynia or vaginismus.
- Concomitant reflex sympathetic dystrophy.
- COVID-19 infection may trigger FM or exacerbate preexisting FM.[24,25]

The American College of Rheumatology (ACR) eliminated the need of tender points for diagnosis (formerly ≥11 of 18 tender points was required). Diagnosis is now based on assessing: 1) Widespread Pain Index; and 2) Symptom Severity of: cognitive symptoms, unrefreshed sleep, fatigue, and number of somatic symptoms.

## Objective Findings[26,27]

- Subjective complaints may be out of proportion to the paucity of objective findings.
- As noted above, examination for tender points is not required to confirm the diagnosis.
- Minimal to no muscle hypertonicity.
- ROM is often within normal limits.
- There is no specific test to confirm diagnosis. Physical exam, lab, x-rays, and EMG studies may be normal. Sleep and muscle oxygenation studies may be abnormal.
- Laboratory Testing for Differential Diagnosis: CBC, ESR, Cyclic citrullinated peptide test, RF, thyroid function tests, ANA, celiac serology, Vitamin D status.
- Traditional Chinese Medicine (TCM) tongue, pulse, abdominal and meridian assessment findings will vary. A common pattern is *qi* and Blood stagnation combined with Cold and Damp (*Bi* Syndrome).[28]

## Assessment

Often patients will present already having had sufficient testing to allow for this differentiation. A therapeutic trial of treatment appropriate for FM with reasonable outcomes might suffice in lieu of a battery of further diagnostic testing. There appears to be a close relationship between the diagnosis of FM and chronic fatigue syndrome (CFS); also known as 'myalgic encephalomyelitis'. The majority of patients with CFS meet the tender point criteria for FM and approximately 70 percent of patients with FM meet the criteria for CFS.[29,30]

It Is important to consider other clinical entities that present with similar symptomatology. The list for differential diagnosis includes infections, muscle disorders, malignancies, autoimmune disease, hypermobility disorders, rheumatoid variants, substance abuse, and endocrinopathies such as diabetes and adrenal disorders.[31] Other entities to be considered in the differential diagnosis include subclinical hypothyroidism, inappropriate thyroid replacement medication dosage, vitamin and mineral deficiencies, inappropriate nutraceutical usage, and adverse effects of medication such as hormone replacement therapy (HRT).

## Treatment Plans

FM is managed as a chronic condition. Patient education and a prioritization of the obstacles to response for each individual, as well as evaluating for patient acceptance of various options are seen as essential steps in creating an effective treatment plan.[32] Healthcare professionals should be empathetic and not demonstrate negative attitudes. Certain guidelines recommend that "a therapeutic alliance would facilitate shared decision-making between the health care professional and the FMS-patient."[33,34] Patients should be active participants in their treatment plans.[35]

The most comprehensive guideline from the European League Against Rheumatism (EULAR) states that optimal management requires not only a more prompt diagnosis (current average is 2 years), but suggests that initial treatment should be patient education regarding FM. In addition, EULAR recommends a full assessment of pain, function, and the psychosocial parameters. Initial therapies are non-pharmacological approaches (e.g., exercise and if needed/requested IH treatments), with the aim of improving health related QOL. Additional individualized care can be recommended to address mental health (e.g., cognitive behavioral therapy) and pain/sleep disturbances (e.g., pregabalin), but these are

initiated *after* non-pharmacological approaches have been tried. Although some guidelines differ in their recommendations, a common theme among them is a patient-centered, multi-disciplinary approach. [36,37,Error! Bookmark not defined.] There is strong evidence for the effectiveness multidisciplinary interventions that combine cardiovascular exercise, cognitive behavioral therapy (CBT), and patient education.[38,39]

*Mind-Body Therapies:*

- Guided imagery and meditation can be effective adjunctive treatments.[40,41]
- Cognitive behavioral therapy (CBT) and associated approaches (e.g., acceptance and commitment therapy) have evidence to support its use.[42,43]
- Relaxation techniques, such as music therapy, biofeedback and progressive muscle relaxation (PMR) may be beneficial.[44,45,46,47]
- Sleep Hygiene.
    - Lengthy wind down period before bedtime.
    - Reduce television viewing before bedtime.
    - Regularity of sleep cycle.
    - Ergonomically optimal sleep positions.
    - Avoidance of stimulants.
    - Relaxation techniques and breathing exercises.
    - Nutritional considerations for sleep hygiene:
        - Magnesium.[48]
        - B complex, particularly thiamin, B-6, B-12, folate.
        - SAME (S-adenosylmethionine).[62]
        - Foods high in tryptophan.
        - Consider 5-Hydroxytryptophan (5-HTP) as a concentrated tryptophan source, one biochemical step removed from serotonin.
        - Malic acid.
        - Selenium.
        - CoQ10.[49,50]

*Diet:*

- Optimize nutrition with nutritional counseling, dietary assessment, or supplementation (see below). Be aware of anti-nutritional agents such as preservatives, nicotine and alcohol use, or toxic exposure. Plant based diets may be helpful.[51] Weight loss if needed appears to be beneficial.[52] Avoidance of certain foods is beneficial for some.[53]

*Herbal Medicine (Western):*

- Cannabinoids (mixed results).[54,55,56]
- Herbal therapy consideration:
    - Kava sp.
    - Hypericum sp.
    - Ginseng.
    - Valerian sp.

- Passiflora sp.
- Chlorella pyrenoidosa.
- Chinese herbal formulas have been used clinically for FMS and the associated symptoms.
- Ganoderma lucidum.[57]

*Homeopathy:*

- Efficacy was found for the functional somatic syndromes group (fibromyalgia and chronic fatigue syndrome).[58]

*Supplements and Nutrients:*

- Hormonal considerations:
  - Melatonin.
  - Calcitonin.
  - DHEAS.
  - Growth hormone (GH).

*Pharmaceuticals (Prescription):*

Patients with FM are frequently treated with analgesics, including opioids, despite an absence of evidence of their efficacy.

- FDA approved specifically for fibromyalgia:
  - Duloxetine (Cymbalta).
  - Milnacipran (Savella).
  - Pregabalin (Lyrica).
  - Gabapentin (Neurontin).
  - There is no evidence to show that opioids are effective in the treatment of FM.[59,60]
- For symptoms:[61]
  - Tricyclic antidepressants such as amitriptyline (Elavil)[62,63] and desipramine.
  - Other SSRIs, SNRIs,[64] and dual reuptake inhibitors, such as venlafaxine (Effexor), fluoxetine (*Prozac*), paroxetine (*Paxil*) or sertraline *(Zoloft*).
  - Cyclobenzaprine (Flexeril) (a central acting muscle relaxant).[65]
  - Anticonvulsants (Pregbalin, Gabapentin).[66]
  - NSAIDs and analgesics, such as ibuprofen (*Advil, Motrin*) or naproxen (*Aleve, Anaprox*), acetaminophen (Tylenol) and tramadol (Ultram).
- Pharmacological treatment, however, provides incomplete relief with coincident adverse effects of the drug. For example, pregabalin (Lyrica) shows some benefit in about 1 in 10 patients with 20-30% of patients experiencing adverse effects of somnolence and dizziness. Trials of mono- and combined drug therapy are generally of poor quality and the evidence for pharmacotherapy is weak.[67]

*Physical Modalities (Western):*

- Serial whole body cryotherapy.[68]
- Hyperbaric oxygen therapy.[69]

- Hydrotherapy[70,71] and/or hyperthermia[72] may be an effective intervention.
- Studies shows that balneotherapy (spa therapy) is effective.[73,74]

*Ancillary TEAM Modalities:*

- Traditional Chinese Exercise (e.g. Tai chi, Qi gong): A 2023 meta-analysis (12 RCTs; N=781) found these mind-body movement therapies effective "…to reduce pain, improve the quality of life and sleep, and relieve depression for FMS."[75]

*Movement and Exercise:*

- A 2022 study (18 RCTs; n=1184) concluded "that exercise may be a way to reduce depression, and pain and improve the quality of life in adult subjects with fibromyalgia and should be part of the treatment for this pathology."[76]
- Exercise is strongly recommended.[77] Aerobic exercise to tolerance (consider yoga, water aerobics, or walking). Consistency and moderation are critical.
- The addition of an aquatic exercise program to the usual care regime for fibromyalgia in women is cost effective in terms of both health care costs and societal costs.[78]
- There is some evidence for strength training. One report found comparable benefits comparing muscle strength training to an aerobic exercise program.[79]
- Yoga yielded significant effects on pain, fatigue, depression and health-related quality of life (HRQOL).[80]

*Manual Adjustments/Manipulation:*

- Chiropractic manipulation (mixed results).[81,82]
- Manual therapies, including massage and manipulation, based on patient tolerance and focusing on increasing functional capacity and patient independence.[83]
- Deep oscillation massage was shown to be safe and well tolerated in patients with moderate to severe grades of FMS.[84]
- Manual therapy protocol was effective for improving pain intensity, widespread pressure pain sensitivity, impact of FMS symptoms, sleep quality, and depressive symptoms.[85]

*Acupuncture (excluding pharmocoacupture):*

- There is a mounting body of research suggesting beneficial effects of acupuncture for the treatment of FM, including the current 2017 guideline from the European League Against Rheumatism.[86] The current evidence suggests that acupuncture is beneficial as an adjunct to current guideline recommended treatment options.
    - Systematic reviews suggest that acupuncture combined with usual care was more effective than usual care alone. (NB: Caution interpretation of findings due to the methodological quality of the clinical trials)
        - A 2022 meta-analysis (20 RCTs; n=1,497) concluded, "..low-to-moderate-quality level of evidence that suggests…acupuncture as an effective complementary treatment to medication and exercise for improving FM severity and symptoms…"[87]
        - A 2013 Cochrane Review (9 RCTs; n=395) concluded, "…low to moderate-level

evidence that compared with no treatment and standard therapy, acupuncture improves pain and stiffness…People with fibromyalgia may consider using EA alone or with exercise and medication."[88]

- A 2014 meta-analysis (9 RCTs; n=496) concluded that "Acupuncture combined with drugs and exercise could increase pain thresholds in the short-term..."[89]

*IV Therapies:*

- Intravenous micronutrient therapy (IVMT).[90,91]

## Outcomes Assessment Tools

- VAS/NRS/triple/quadruple VAS/NRS.
- McGill Pain Questionnaire.[92]
- Brief Pain Inventory.[93]
- Fibromyalgia Impact Questionnaire (FIQ).[94] (see below)
- Patient Reported Outcomes Measures (PROMs) focused on domain(s) of interest to the patient, e.g., pain, fatigue, functional status, sleep, mood, tenderness/stiffness, and problems with concentration/memory.[95]

## Resources for Clinicians

Fibromyalgia Impact Questionnaire is a useful tool in assessing functional abilities in daily life and measures patient status, progress, and outcomes. It is a self-administered instrument that is composed of 10 items and can be completed in about 10 minutes. (https://www.rheumatology.org/I-Am-A/Rheumatologist/Research/Clinician-Researchers/Fibromyalgia-Impact-Questionnaire-FIQ)[96]

## Resources for Patients

The National Fibromyalgia Association (NFA) is the largest nonprofit organization working to support people with fibromyalgia and other chronic pain illnesses.
http://www.fmaware.org/

Fibromyalgia Information Foundation (FIF) https://www.myalgia.com/

The Fibromyalgia section of the American College of Rheumatology web site.
http://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Fibromyalgia

NRS. Everything You Need to Know About Living Well with Fibromyalgia.
https://www.nrshealthcare.co.uk/articles/condition/fibromyalgia

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## Appendix

ACR Diagnostic Criteria

American College of Rheumatology (ACR) preliminary diagnostic criteria for FM were updated in 2011 (see questionnaire on pages 3 and 4). The older requirement of a tender point exam has been omitted and replaced with a symptom checklist.[97] The diagnosis is separated into two parts. The first part is called the Widespread Pain Index (WPI) in which the patient (and/or the clinician) endorses any of the 19 body regions of pain. The second part of the score is a Symptom Severity score (SS score) in which the patient's other symptoms are evaluated. Using both scores takes into consideration the pain as well as other bothersome symptoms. The researchers and authors of the study state: "*This criteria set has been approved by the American College of Rheumatology (ACR) Board of Directors as Provisional. This signifies that the criteria set has been quantitatively validated using patient data, but it has not undergone validation based on an external data set. All ACR-approved criteria sets are expected to undergo intermittent updates.*"

| Criteria Needed for a Fibromyalgia Diagnosis |
|---|
| 1. Pain and symptoms over the past week, based on the total of:<br>Number of painful areas out of 19 parts of the body<br>Plus level of severity of these symptoms:<br>• Fatigue.<br>• Waking unrefreshed.<br>• Cognitive (memory or thought) problems.<br>Plus a number of other general physical symptoms. |
| 2. Symptoms lasting at least three months at a similar level. |
| 3. No other health problem that would explain the pain and other symptoms. |
| Source: American College of Rheumatology, 2010 |

Wolfe, et al made revisions to the 2010/2011 ACR criteria stating that: "Fibromyalgia may now be diagnosed in adults when all of the following criteria are met":[98,99,100,101,102,103]

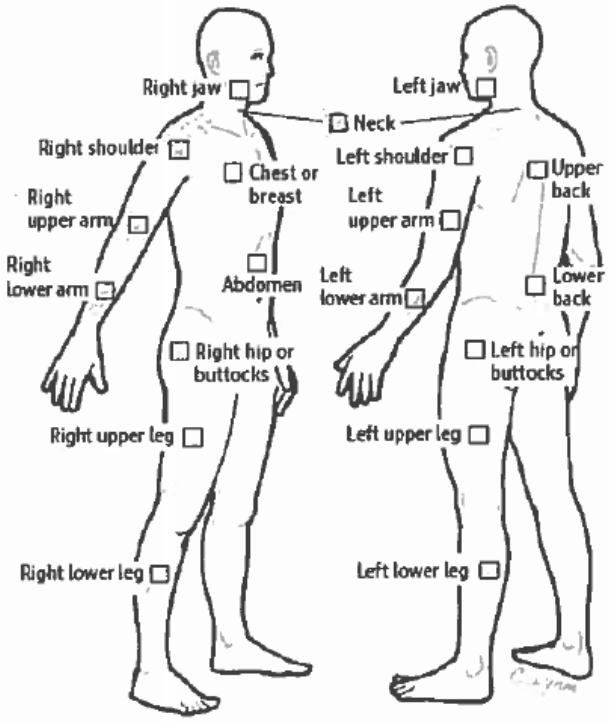
1. Generalized pain, defined as pain in at least 4 of 5 regions, is present.
2. Symptoms have been present at a similar level for at least 3 months.
3. Widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 OR WPI of 4–6 and SSS score ≥ 9.
4. A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.

# A New ACR Criteria

**Figure. Example of a Patient Self-report Survey for the Assessment of Fibromyalgia Based on Criteria in the 2011 Modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia[7]**

Widespread Pain Index
(1 point per check box; score range: 0-19 points)

(1) Please indicate if you have had pain or tenderness during the past 7 days in the areas shown below.
Check the boxes in the diagram for each area in which you have had pain or tenderness.




Symptom Severity
(score range: 0-12 points)

(2) For each symptom listed below, use the following scale to indicate the severity of the symptom during the past 7 days.
- No problem
- Slight or mild problem: generally mild or intermittent
- Moderate problem: considerable problems; often present and/or at a moderate level
- Severe problem: continuous, life-disturbing problems

| | No problem | Slight or mild problem | Moderate problem | Severe problem |
|---|---|---|---|---|
| Points | 0 | 1 | 2 | 3 |
| A. Fatigue | ☐ | ☐ | ☐ | ☐ |
| B. Trouble thinking or remembering | ☐ | ☐ | ☐ | ☐ |
| C. Waking up tired (unrefreshed) | ☐ | ☐ | ☐ | ☐ |

(3) During the past 6 months have you had any of the following symptoms?

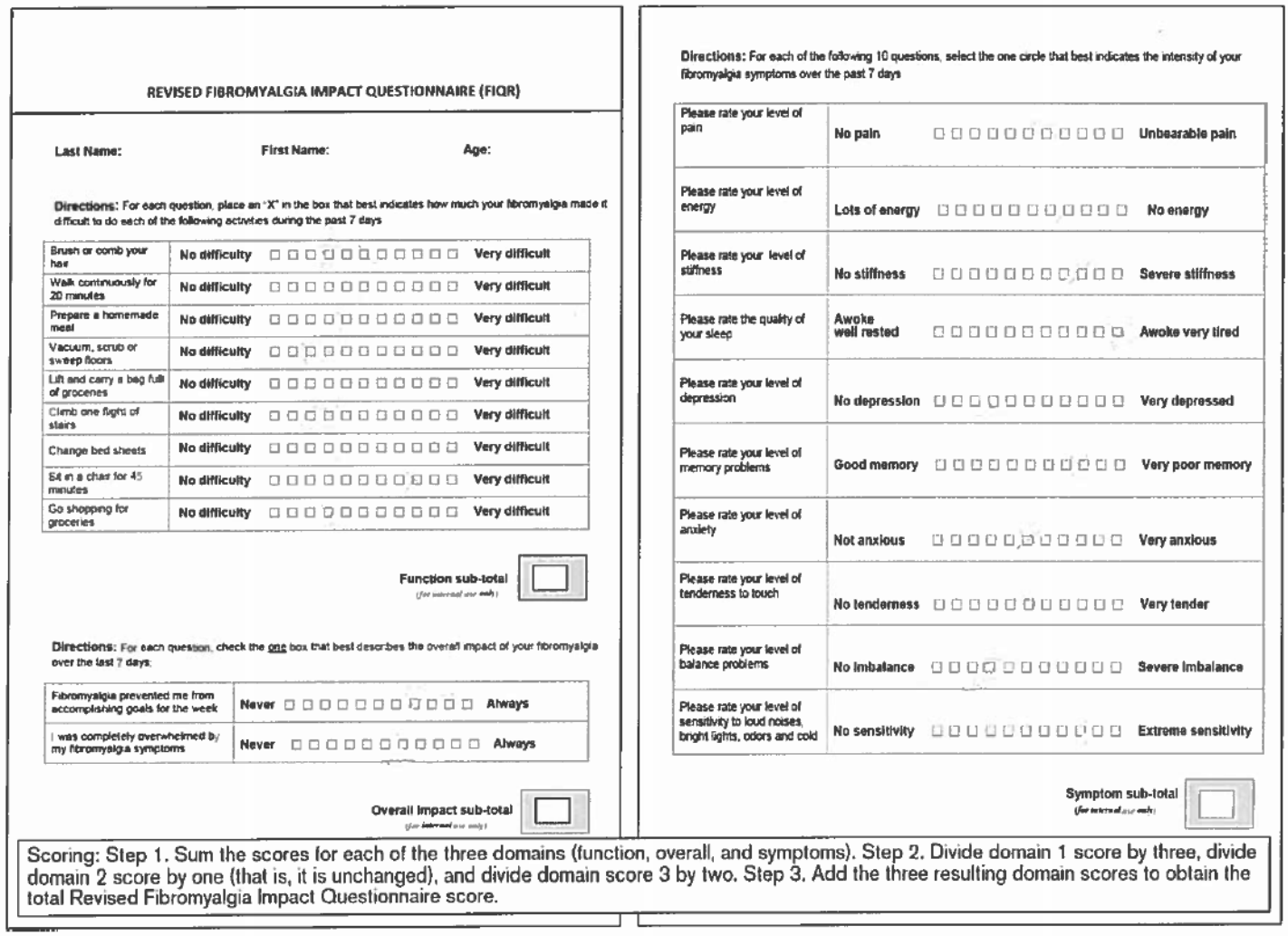
| Points | 0 | 1 |
|---|---|---|
| A. Pain or cramps in lower abdomen | ☐ No | ☐ Yes |
| B. Depression | ☐ No | ☐ Yes |
| C. Headache | ☐ No | ☐ Yes |

Additional criteria (no score)

(4) Have the symptoms in questions 2 and 3 and widespread pain been present at a similar level for at least 3 months?
☐ No ☐ Yes

(5) Do you have a disorder that would otherwise explain the pain?
☐ No ☐ Yes

ACR indicates American College of Rheumatology. Scoring information is shown in blue. The possible score ranges from 0 to 31 points; a score ≥13 points is consistent with a diagnosis of fibromyalgia. Additional scoring information and a printer-ready version of this survey that patients can complete are available online (eFigure 1 and eFigure 2 in the Supplement).



REVISED FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQR)

Last Name: First Name: Age:

**Directions:** For each question, place an "X" in the box that best indicates how much your fibromyalgia made it difficult to do each of the following activities during the past 7 days

| | | |
|---|---|---|
| Brush or comb your hair | No difficulty | Very difficult |
| Walk continuously for 20 minutes | No difficulty | Very difficult |
| Prepare a homemade meal | No difficulty | Very difficult |
| Vacuum, scrub or sweep floors | No difficulty | Very difficult |
| Lift and carry a bag full of groceries | No difficulty | Very difficult |
| Climb one flight of stairs | No difficulty | Very difficult |
| Change bed sheets | No difficulty | Very difficult |
| Sit in a chair for 45 minutes | No difficulty | Very difficult |
| Go shopping for groceries | No difficulty | Very difficult |

Function sub-total

**Directions:** For each question, check the one box that best describes the overall impact of your fibromyalgia over the last 7 days:

| | | |
|---|---|---|
| Fibromyalgia prevented me from accomplishing goals for the week | Never | Always |
| I was completely overwhelmed by my fibromyalgia symptoms | Never | Always |

Overall impact sub-total

**Directions:** For each of the following 10 questions, select the one circle that best indicates the intensity of your fibromyalgia symptoms over the past 7 days

| | | |
|---|---|---|
| Please rate your level of pain | No pain | Unbearable pain |
| Please rate your level of energy | Lots of energy | No energy |
| Please rate your level of stiffness | No stiffness | Severe stiffness |
| Please rate the quality of your sleep | Awoke well rested | Awoke very tired |
| Please rate your level of depression | No depression | Very depressed |
| Please rate your level of memory problems | Good memory | Very poor memory |
| Please rate your level of anxiety | Not anxious | Very anxious |
| Please rate your level of tenderness to touch | No tenderness | Very tender |
| Please rate your level of balance problems | No imbalance | Severe imbalance |
| Please rate your level of sensitivity to loud noises, bright lights, odors and cold | No sensitivity | Extreme sensitivity |

Symptom sub-total

Scoring: Step 1. Sum the scores for each of the three domains (function, overall, and symptoms). Step 2. Divide domain 1 score by three, divide domain 2 score by one (that is, it is unchanged), and divide domain score 3 by two. Step 3. Add the three resulting domain scores to obtain the total Revised Fibromyalgia Impact Questionnaire score.

The Fibromyalgia Network has a Criteria Survey based on the 2010 guidelines. (neuro.memorialhermann.org/uploadedFiles/_Library_Files/MNII/NewFibroCriteriaSurvey.pdf)

In 2013, the ACTTION-APS Pain Taxonomy (AAPT) was initiated by the Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks (ACTTION) public-private partnership with the U.S. Food and Drug Administration (FDA) and the American Pain Society (APS).[104]

The AAPT Diagnostic Criteria for Fibromyalgia Dimension 1:
Table 1. Core Diagnostic Criteria

1. Multi-site pain (MSP) defined as 6 or more pain sites from a total of 9 possible sites.
2. Moderate to severe sleep problems OR fatigue.
3. MSP plus fatigue OR sleep problems must have been present for at least 3 months.

NOTE: The presence of another pain disorder or related symptoms does not rule out a diagnosis of FM. However, a clinical assessment is recommended to evaluate for any condition that could fully account for the patient's symptoms or contribute to the severity of the symptoms.

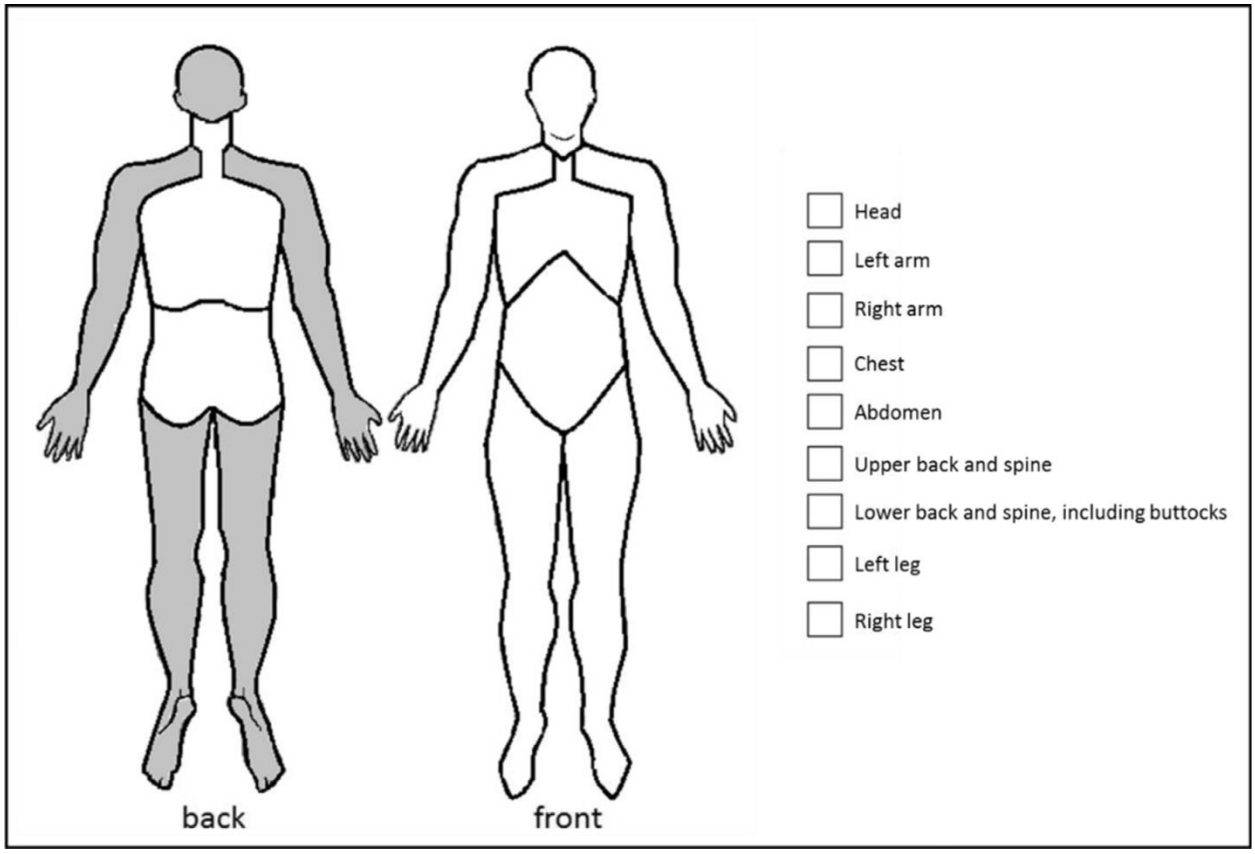



Figure 1. Number of painful body sites.
Patients are asked to check the areas in which they experience pain on the 2-view drawing (ignoring the pre- shaded areas). Alternatively, patients may use the checklist of body sites.
The number of separate sites are summed from a maximum of 9 body sites.

## References

[1] Ge HY, et al. The predetermined sites of examination for tender points in fibromyalgia syndrome are frequently associated with myofascial trigger points. *J Pain* 11:644-51, 2010.
[2] www.fmcpaware.org
[3] Vasileios P, Styliani P, Nifon G, Pavlos S, Aris F, Ioannis P, Managing fibromyalgia with complementary and alternative medical exercise: a systematic review and meta-analysis of clinical trials, Rheumatol Int. 2022 Nov;42(11):1909-1923. doi: 10.1007/s00296-022-05151-y. Epub 2022 Jul 7.
[4] Vincent A, Lahr BD, Wolfe F, Clauw DJ, Whipple MO, Oh TH, Barton DL, St Sauver J. Prevalence of fibromyalgia: a population-based study in Olmsted County, Minnesota, utilizing the Rochester Epidemiology Project. Arthritis Care Res (Hoboken). 2013 May;65(5):786-92.
[5] Rahman A, Underwood M, Carnes D. Fibromyalgia BMJ 2014; 348 :g1224
[6] Alessandra de Sousa Braz et al, Non-pharmacological therapy and complementary and alternative medicine in fibromyalgia, Rev Bras Reumatol. 2011 May-Jun;51(3):269-82.
[7] Banic B1, Petersen-Felix S, Andersen OK, Radanov BP, Villiger PM, Arendt-Nielsen L, Curatolo M. Evidence for spinal cord hypersensitivity in chronic pain after whiplash injury and in fibromyalgia. Pain. 2004 Jan;107(1-2):7-15.
[8] Kuehl, L. K., Michaux, G. P., Richter, S., Schachinger, H., & Anton F. (2010). Increased basal mechanical sensitivity but decreased perceptual wind-up in a human model of relative hypocortisolism. Pain, 194, 539-546.

[9] Rivat, C., Becker, C., Blugeot, A., Zeau, B., Mauborgne, A., Pohl, M., & Benoliel, J. (2010). Chronic stress induces transient spinal neuroinflammation, triggering sensory hypersensitivity and long-lasting anxiety-induced hyperalgesia. Pain, 150, 358-368.

[10] Institute for chronic pain. Understanding chronic pain. http://www.instituteforchronicpain.org/understanding-chronic-pain/what-is-chronic-pain/central-sensitization

[11] Hauser W, Kossevta M, et al. Emotional, Physical, and Sexual Abuse inFibromyalgia Syndrome: A Systematic ReviewWith Meta-Analysis. Arthritis Care & ResearchVol. 63, No. 6, June 2011, pp 808–820DOI 10.1002/acr.20328

[12] D'Onghia, M., et al., The economic burden of fibromyalgia: A systematic literature review. Semin Arthritis Rheum, 2022. 56: p. 152060.

[13] Burns JW, et al. Sleep stage dynamics in fibromyalgia patients and controls. *Sleep Med* 9:689-96, 2008.

[14] G J Macfarlane1, et al., EULAR revised recommendations for the management of fibromyalgia. BMJ,Annals of the Rheumatic Diseases Home Archive Volume 76, Issue 2.

[15] Sarzi-Puttini P, Sarzi-Puttini P, Buskila D, et al. Treatment strategy in fibromyalgia syndrome: where are we now? *Semin Arthritis Rheum*. 2008;37(6):353–65.

[16] Ablin J, Fitzcharles MA, Buskila D, et al. Treatment of Fibromyalgia Syndrome: Recommendations of Recent Evidence-Based Interdisciplinary Guidelines with Special Emphasis on Complementary and Alternative Therapies. *Evidence-Based Complementary and Alternative Medicine*. 2013. Review Article.

[17] Terry, R, Diehr PK, and E Ernst. An overview of systematic reviews of complementary and alternative medicine for fibromyalgia. *Clin Rheumatol*. 2011 May 26.

[18] Lind BK, WE Lafferty, PT Tyree, PK Diehr, and DE Grembowski. "Use of complementary and alternative medicine providers by fibromyalgia patients under insurance coverage". *Arthritis and Rheumatism*. 2007; 57 (1): 71-6.

[19] Wahner-Roedler DL, Peter L, Vincent A, et al. "Use of Complementary and Alternative Medical Therapies by Patients Referred to a Fibromyalgia Treatment Program at a Tertiary Care Center". Mayo Clinic Proceedings. 2005; 80 (1).

[20] Lind BK, Tyree PT, Diehr PK, and Lafferty WE. Comparison of health care expenditures among insured users and nonusers of complementary and alternative medicine in Washington state: A cost minimization analysis. *Journal of Alternative and Complementary Medicine.* 2010; 16 (4): 411-417.

[21] Epstein SA, Kay G, Clauw D, et al. Psychiatric disorders in patients with fibromyalgia. A multicenter investigation. *Psychosomatics*. 1999;40(1):57–63.

[22] Arnold LM, Hudson JI, Keck PE, et al. Comorbidity of fibromyalgia and psychiatric disorders. *J Clin Psychiatry*. 2006;67(8):1219–25.

23 Respiratory disturbances in fibromyalgia: A systematic review and meta-analysis of case control studies.Ortiz-Rubio A, Torres-Sánchez I, Cabrera-Martos I, López-López L, Rodríguez-Torres J, Granados-Santiago M, Valenza MC.Expert Rev Respir Med. 2021 Sep;15(9):1217-1227. doi: 10.1080/17476348.2021.1918547. Epub 2021 Apr 26.PMID: 33857393

[24] Goldenberg, D.L., How to understand the overlap of long COVID, chronic fatigue syndrome/myalgic encephalomyelitis, fibromyalgia and irritable bowel syndromes. Semin Arthritis Rheum, 2024. 67: p. 152455.

[25] Fialho, M.F.P., E.S. Brum, and S.M. Oliveira, Could the fibromyalgia syndrome be triggered or enhanced by COVID-19? Inflammopharmacology, 2023. 31(2): p. 633-651.

[26] Perrot S, Dickenson AH, Bennett RM. Fibromyalgia: harmonizing science with clinical practice considerations. *Pain Pract.* 2008; 8:177-89.

[27] Goldenberg DL. Diagnosis and differential diagnosis of fibro -myalgia. *Am J Med* 2009;122(Suppl 12):S14-21.

[28] Fu, X., Y. Li, and J. Yang, A survey of acupuncture for fibromyalgia syndrome. Shanghai Journal of Acupuncture and Moxibustion, 2004. 23(7): p. 46-48.

[29] Goldenberg DL, Simms RW, Geiger A, Komaroff AL. High frequency of fibromyalgia in patients with chronic fatigue seen in a primary care practice. *Arthritis Rheum*. 1990 Mar; 33(3):381-7.

[30] Aaron LA, Burke MM, and Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. *Arch Intern Med*. 2000 Jan 24;160(2):221-7.

[31] Wallace DJ. The fibromyalgia syndrome. *Annals of Medicine*. 1997 Feb; 29(1):9-21.

[32] Langhorst J, Häuser W, Lauche R, Perrot S, Alegre C, Sarzi Puttini. Complementary and alternative medicine for the treatment of fibromyalgia. *Evid Based Complement Alternat Med.* 2014;2014:408436.

[33] Fitzcharles MA, Ste-Marie PA, Goldenberg DL, et al. 2012 Canadian guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary, *Pain Research & Management.* 2013; 18(3): 119–126.

[34] Eich W, Häuser W, Arnold B, et al., Fibromyalgia syndrome. general principles and coordination of clinical care and patient education. *Schmerz*. 2012; 26(3): 268-275.

[35] Menzies V. Fibromyalgia Syndrome: Current Considerations in Symptom Management. *Am J Nurs*. 2016;116(1):24-32.
[36] Ablin J, Fitzcharles MA, Buskila D, Shir Y, Sommer C, Hauser W**.** Treatment of fibromyalgia syndrome: recommendations of recent evidence-based interdisciplinary guidelines with special emphasis on complementary and alternative therapies. *Evid Based Complement Alternat Med*. 2013;2013:485272.
[37] Fitzcharles MA, Shir Y, Ablin JN, Buskila D, Amital H, Henningsen P, et al. Classification and clinical diagnosis of fibromyalgia syndrome: recommendations of recent evidence-based interdisciplinary guidelines. *Evid Based Complement Alternat Med*. 2013;2013:528952.
[38] Carville, SF, Arendt-Nielsen A, Bliddal H, et al. EULAR evidence-based recommendations for the management of fibromyalgia syndrome. *Annals of the Rheumatic Diseases*. 2008; 67 (4): 536-541.
[39] Casale R, M Cazzola, G Arioli, RH Gracely, F Ceccherelli, F Atzeni, S Stisi, et al. "Non pharmacological treatments in fibromyalgia". *Reumatismo*. 2008; 60.
[40] Sephton SE, Salmon P, Weissbecker I, et al. Mindfulness meditation alleviates depressive symptoms in women with fibromyalgia: results of a randomized clinical trial. Arthritis Rheum. 2007 Feb 15;57(1):77–85.
[41] Zech N, Hansen E, Bernardy K, Häuser W. Efficacy, acceptability and safety of guided imagery/hypnosis in fibromyalgia - A systematic review and meta-analysis of randomized controlled trials. Eur J Pain. 2017;21(2):217-227.
[42] Cojocaru C M, Popa C O, Schenk A, Suciu B A, Szasz S, Cognitive-behavioral therapy and acceptance and commitment therapy for anxiety and depression in patients with fibromyalgia: a systematic review and meta-analysis, Med Pharm Rep. 2024 Jan;97(1):26-34. doi: 10.15386/mpr-2661. Epub 2024 Jan 29.
[43] Kundakci B, Kaur J, Li Goh S, Hall M, Doherty M, Zhang W, Abhishek A, Efficacy of nonpharmacological interventions for individual features of fibromyalgia: a systematic review and meta-analysis of randomised controlled trials, Pain. 2022 Aug 1;163(8):1432-1445. doi: 10.1097/j.pain. Epub 2021 Sep 24.
[44] Hassett AL, Radvanski DC, Sigal LH, et al. Preliminary results from a randomized controlled trial of heart rate variability biofeedback in fibromyalgia. Ann Rheum Dis. 2008 July;67(2 suppl):S638.
[45] Babu AS, Mathew E, Danda D, et al. Management of patients with fibromyalgia using biofeedback: a randomized control trial. Indian J Med Sci. 2007;61(8):455–61.
[46] Kayiran S, Dursun E, Ermutlu N, et al. Neurofeedback in fibromyalgia syndrome. Agri. 2007;19(3):47–53.
[47] Glombiewski JA, Bernardy K, Häuser W. Efficacy of EMG- and EEG-Biofeedback in Fibromyalgia Syndrome: A Meta-Analysis and a Systematic Review of Randomized Controlled Trials. Evid Based Complement Alternat Med. 2013;2013:962741.
[48] Sarac AJ, Gur A. Complementary and alternative medical therapies in fibromyalgia. Curr Pharm Des. 2006;12(1):47-57.
[49] Casale R, M Cazzola, G Arioli, RH Gracely, F Ceccherelli, F Atzeni, S Stisi, et al. "Non pharmacological treatments in fibromyalgia". Reumatismo. 2008; 60.
[50] Mehrabani S, Askari G, Miraghajani M, Tavakoly R, Arab A. Effect of coenzyme Q10 supplementation on fatigue: A systematic review of interventional studies. Complement Ther Med. 2019;43:181-187.
[51] Nadal-Nicolás Y, Miralles-Amorós L, Martínez-Olcina M, Sánchez-Ortega M, Mora J, Martínez-Rodríguez A, Vegetarian and Vegan Diet in Fibromyalgia: A Systematic Review. Int J Environ Res Public Health. 2021 May 6;18(9):4955. doi: 10.3390/ijerph18094955.PMID: 34066603 Review.
[52] D'Onghia M, Ciaffi J, Lisi L, Mancarella L, Ricci S, Stefanelli N, Meliconi R, Ursini F. Fibromyalgia and obesity: A comprehensive systematic review and meta-analysis. Semin Arthritis Rheum. 2021 Apr;51(2):409-424. doi: 10.1016/j.semarthrit.2021.02.007. Epub 2021 Mar 3.PMID: 33676126
[53] Pagliai G, Colombini B, Dinu M, Whittaker A, Masoni A, Danza G, Amedei A, Ballerini G, Benedettelli S, Sofi F. Effectiveness of a Khorasan Wheat-Based Replacement on Pain Symptoms and Quality of Life in Patients with Fibromyalgia. Pain Med. 2020 Oct 1;21(10):2366-2372. doi: 10.1093/pm/pnaa134.PMID: 32488245 Clinical Trial.
[54] Ste-marie PA, Fitzcharles MA, Gamsa A, Ware MA, Shir Y. Association of herbal cannabis use with negative psychosocial parameters in patients with fibromyalgia. Arthritis Care Res (Hoboken). 2012;64(8):1202-8.
[55] Fitzcharles MA, Ste-marie PA, Häuser W, et al. Efficacy, Tolerability, and Safety of Cannabinoid Treatments in the Rheumatic Diseases: A Systematic Review of Randomized Controlled Trials. Arthritis Care Res (Hoboken). 2016;68(5):681-8.
[56] Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W. Cannabis-based medicines for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2018;3:CD012182.
[57] Collado mateo D, Pazzi F, Domínguez muñoz FJ, et al. Ganoderma lucidum improves physical fitness in women with fibromyalgia. Nutr Hosp. 2015;32(5):2126-35.
[58] Davidson JRT, Crawford C, Ives JA, and Jonas WB. "Homeopathic treatments in psychiatry: A systematic review of randomized placebo-controlled studies". Journal of Clinical Psychiatry. 2011:72 (6): 795-805.

[59] Borchers AT, Gershwin ME. Fibromyalgia: A Critical and Comprehensive Review. Clin Rev Allergy Immunol. 2015;49(2):100-51.
[60] Davis F, Gostine M, Roberts BA, Risko R, Cappelleri JC, Sadosky A. Interpreting the Effectiveness of Opioids and Pregabalin for Pain Severity, Pain Interference, and Fatigue in Fibromyalgia Patients. Pain Pract. 2018;18(5):611-624
[61] Alciati A, Nucera V, Masala I F, Giallanza M, La Corte L, Giorgi V, Sarzi-Puttini P, Atzeni F, One year in review 2021: fibromyalgia, Clin Exp Rheumatol
. 2021 May-Jun;39 Suppl 130(3):3-12.
[62] 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(7):747-756.
[63] Häuser W, Petzke F, Üçeyler N, Sommer C. Comparative efficacy and acceptability of amitriptyline, duloxetine and milnacipran in fibromyalgia syndrome: a systematic review with meta-analysis. *Rheumatology* (Oxford). 2011;50(3):532-43.
[64] Derry S, Gill D, Phillips T, Moore RA. Milnacipran for neuropathic pain and fibromyalgia in adults. *Cochrane Database Syst Rev*. 2012;(3):CD008244.
[65] Tofferi JK, Jackson JL, O'malley PG. Treatment of fibromyalgia with cyclobenzaprine: A meta-analysis. *Arthritis Rheum*. 2004;51(1):9-13.
[66] Üçeyler N, Sommer C, Walitt B, Häuser W. WITHDRAWN: Anticonvulsants for fibromyalgia. *Cochrane Database Syst Rev*. 2017;10:CD010782.
[67] Thorpe J, Shum B, Moore RA, Wiffen PJ, Gilron I. Combination pharmacotherapy for the treatment of fibromyalgia in adults. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD010585. DOI: 10.1002/14651858.CD010585.pub2.
[68] Klemm P, Becker J, Aykara I, Asendorf T, Dischereit G, Neumann E, Müller-Ladner U, Lange U. Serial whole-body cryotherapy in fibromyalgia is effective and alters cytokine profiles. Adv Rheumatol. 2021 Jan 13;61(1):3. doi: 10.1186/s42358-020-00159-z.PMID: 33436106 Clinical Trial.
[69] Curtis K, Katz J, Djaiani C, O'Leary G, Uehling J, Carroll J, Santa Mina D, Clarke H, Gofeld M, Katznelson R, Evaluation of a Hyperbaric Oxygen Therapy Intervention in Individuals with Fibromyalgia. Pain Med. 2021 Jun 4;22(6):1324-1332. doi: 10.1093/pm/pnaa416.PMID: 33594439 Clinical Trial.
[70] McVeigh JG, McGaughey H, Hall M, et al. The effectiveness of hydrotherapy in the management of fibromyalgia syndrome: a systematic review. Rheumatol Int. 2008 Dec;29(2):119–30.
[71] Langhorst J, Musial F, Klose P, Hauser W. Efficacy of hydrotherapy in fibromyalgia syndrome—a meta-analysis of randomized controlled clinical trials. Rheumatology 2009;48:1155–9.
[72] Brockow T, Wagner A, Franke A, Offenbächer M, Resch KL. A randomized controlled trial on the effectiveness of mild water-filtered near infrared whole-body hyperthermia as an adjunct to a standard multimodal rehabilitation in the treatment of fibromyalgia. Clin J Pain. 2007;23(1):67-75.
[73] Evcik D, Kizilay B, Gökçen E. The effects of balneotherapy on fibromyalgia patients.Rheumatol Int. 2002 Jun;22(2):56-9.
[74] Ablin JN, Häuser W, Buskila D. Spa treatment (balneotherapy) for fibromyalgia-a qualitative-narrative review and a historical perspective. Evid Based Complement Alternat Med. 2013;2013:638050.
[75] Du, M., et al., Effectiveness of traditional Chinese exercise in patients with fibromyalgia syndrome: A systematic review and meta-analysis of randomized clinical trials. Int J Rheum Dis, 2023. 26(12): p. 2380-2389.
[76] Couto N, Monteiro D, Cid L, Bento T., Effect of different types of exercise in adult subjects with fibromyalgia: a systematic review and meta-analysis of randomised clinical trials. Sci Rep
. 2022 Jun 20;12(1):10391. doi: 10.1038/s41598-022-14213-x.
[77] Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017 Feb;76(2):318-328.
[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:R24.
[79] Winkelmann W. Häuser E. Friedel, et al., Physiotherapy and physical therapies for fibromyalgia syndrome. systematic review, meta-analysis and guideline, Schmerz.2012; 26(3):276-286.
[80] Langhorst J, Klose P, Dobos GJ, Bernardy K, Häuser W. Efficacy and safety of meditative movement therapies in fibromyalgia syndrome: a systematic review and meta-analysis of randomized controlled trials. Rheumatol Int. 2012;33(1):193–207.
[81] Salehi A, Hashemi N, Imanieh MH, Saber M. Chiropractic: Is it Efficient in Treatment of Diseases? Review of Systematic Reviews. Int J Community Based Nurs Midwifery. 2015 Oct;3(4):244-54.
[82] Ernst E. Chiropractic treatment for fibromyalgia: a systematic review. Clin Rheumatol. 2009;28(10):1175-8.

[83] Nadal-Nicolás Y, Rubio-Arias JÁ, Martínez-Olcina M, Reche-García C, Hernández-García M, Martínez-Rodríguez A, Effects of Manual Therapy on Fatigue, Pain, and Psychological Aspects in Women with Fibromyalgia..Int J Environ Res Public Health. 2020 Jun 26;17(12):4611. doi: 10.3390/ijerph17124611.PMID: 32604939 Clinical Trial

[84] Kraft K, Kanter S, Janik H. Safety and effectiveness of vibration massage by deep oscillations: a prospective observational study. Evid Based Complement Alternat Med. 2013;2013:679248.

[85] Castro-sánchez AM, Aguilar-ferrándiz ME, Matarán-peñarrocha GA, et al. Short-term effects of a manual therapy protocol on pain, physical function, quality of sleep, depressive symptoms, and pressure sensitivity in women and men with fibromyalgia syndrome: a randomized controlled trial. Clin J Pain. 2014;30(7):589-97.

[86] Macfarlane, G.J., et al., *EULAR revised recommendations for the management of fibromyalgia.* Ann Rheum Dis, 2017. **76**(2): p. 318 328.

[87] Valera-Calero, J.A., et al., Efficacy of Dry Needling and Acupuncture in Patients with Fibromyalgia: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health, 2022. 19(16).

[88] Deare, J.C., et al., *Acupuncture for treating fibromyalgia.* Cochrane Database Syst Rev, 2013. **5**: p. CD007070.

[89]Yang, B., et al., *Efficacy of acupuncture on fibromyalgia syndrome: a meta-analysis.* J Tradit Chin Med, 2014. **34**(4): p. 381-91.

[90] Ali A, Njike VY, Northrup V, et al.. Intravenous Micronutrient Therapy (Myers' Cocktail) for Fibromyalgia: A Placebo-Controlled Pilot Study. The Journal of Alternative & Complementary Medicine. 2009; 15 (3): 247-257.

[91] Massey PB. Reduction of fibromyalgia symptoms through intravenous nutrient therapy: results of a pilot clinical trial. Alternative Therapies in Health and Medicine. 2007; 13 (3).

[92] . The McGill Pain Questionnaire: major properties and scoring methods. Pain. 1975 Sep; 1(3):277-99.

[93] Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *Clin J Pain*. 2004;20:309–318.

[94] Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL. The Revised Fibromyalgia Impact Questionaire (FIQR): validation and psychometric properties *Arthritis Res Ther*. 2009; 11(4):R120. Epub 2009 Aug 10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2745803/table/T1/?report=objectonly

[95] Williams DA, Schilling S. Advances in the assessment of fibromyalgia. Rheum Dis Clin North Am. 2009;35(2):339-57.

[96] American College of Rheumatology Fibromyalgia Impact Questionaire. (FIQ) https://www.rheumatology.org/I-Am-A/Rheumatologist/Research/Clinician-Researchers/Fibromyalgia-Impact-Questionnaire-FIQ (accessed 06/23/20)

[97] American College of Rheumatology. Classification Criteria for Rheumatic Diseases, *Fibromyalgia,* 2010. https://www.rheumatology.org/Practice/Clinical/Patients/Diseases_And_Conditions/Fibromyalgia/

[98] Wolfe F, Clauw DJ, Fitzcharles MA, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum*. 2016;46(3):319-329.

[99] Ablin JN, Wolfe F. A Comparative Evaluation of the 2011 and 2016 Criteria for Fibromyalgia. *J Rheumatol*. 2017;44(8):1271-1276.

[100] Wolfe F, Egloff N, Häuser W. Widespread Pain and Low Widespread Pain Index Scores among Fibromyalgia-positive Cases Assessed with the 2010/2011 Fibromyalgia Criteria. *J Rheumatol.* 2016;43(9):1743-8.

[101] Wolfe F. Criteria for fibromyalgia? What is fibromyalgia? Limitations to current concepts of fibromyalgia and fibromyalgia criteria. *Clin Exp Rheumatol*. 2017;35 Suppl 105(3):3-5.

[102] Walitt B, Katz RS, Bergman MJ, Wolfe F. Three-Quarters of Persons in the US Population Reporting a Clinical Diagnosis of Fibromyalgia Do Not Satisfy Fibromyalgia Criteria: The 2012 National Health Interview Survey. *PLoS ONE*. 2016;11(6):e0157235.

[103] Wolfe F, Fitzcharles MA, Goldenberg DL, et al. Comparison of Physician-Based and Patient-Based Criteria for the Diagnosis of Fibromyalgia. *Arthritis Care Res* (Hoboken). 2016;68(5):652-9.

[104] Arnold LM, Bennett RM, Crofford LJ, et al. AAPT Diagnostic Criteria for Fibromyalgia. *J Pain*. 2019;20(6):611-628.