Fibromyalgia

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Faculty

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Contributing faculty, Lori L. Alexander, MTPW, ELS, MWC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, John M. Leonard, MD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for physicians, physician assistants, nurses, and other healthcare professionals involved in the diagnosis, treatment, and care of patients with fibromyalgia.

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Disclosure Statement

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Course Objective

The purpose of this course is to provide healthcare professionals with the information necessary to diagnose and treat fibromyalgia according to evidence-based or guideline-endorsed recommendations in order to improve patient quality of life.

Learning Objectives

Upon completion of this course, you should be able to:

- Outline the diagnostic criteria established for fibromyalgia, and discuss potential difficulties in establishing a diagnosis.
- 2. Identify appropriate treatment modalities for patients with fibromyalgia and patient education and follow-up needs.



Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also

included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Fibromyalgia is a complex rheumatic disorder characterized by chronic widespread musculoskeletal pain and focal tenderness (tender points), often accompanied by fatigue, other somatic complaints, and disturbances of affect and cognition [1]. The definition of the syndrome has been expanded to include the presence of fatigue, stiffness, and nonrestorative sleep; however, individuals with fibromyalgia usually have a broad range of additional symptoms and comorbidities [1; 2; 3]. The onset of fibromyalgia is insidious, symptoms wax and wane in intensity, and the course is variable [3; 4].

Acceptance of fibromyalgia as a discrete clinical entity (not associated with an apparent organic disease) has been slow [3; 5; 6; 7; 8]. In fact, at one time, there was a 40% bias of a person with fibromyalgia being labeled "neurotic" [3]. Despite increasing support for the validity of the syndrome, consensus is lacking about its cause, diagnosis, and optimal treatment [6; 8; 9].

Fibromyalgia has a substantial negative effect on physical, psychological, and social well-being, and the syndrome is associated with a significant burden in terms of both disability and healthcare costs. Fibromyalgia has been found to have a greater negative impact on quality of life than many other diseases, including osteoarthritis, chronic obstructive pulmonary disease, and permanent ostomies [9]. Activities of daily living and work within the home are often substantially limited. In a large survey of women 31 to 78 years of age, more than 25% had difficulty taking care of personal needs and bathing and more than 60% had difficulty doing light housework, going up/down one flight of stairs, walking one-half mile, or lifting/carrying 10 pounds [10]. The average survey respondent was assessed as having less functional ability than a typical woman in her 80s [10]. Approximately 20% to 50% of individuals with fibromyalgia are able to work few or no days; 36%

are absent from work two or more days each month; 31% have lost employment; and 26% to 55% receive disability or Social Security payments [5].

The economic burden is also high. According to studies of large U.S. claims databases, the healthcare costs of fibromyalgia are two to three times higher (compared with controls) as a result of more visits to the physician's office or emergency department and a higher number of prescription medications [11; 12]. Healthcare utilization and costs are high in the year preceding as well as following the initial diagnosis of fibromyalgia [12].

EPIDEMIOLOGY

According to prevalence and population estimates, fibromyalgia affects approximately 4 million people in the United States [13]. Determining the true prevalence is difficult because of the problems associated with defining its diagnosis according to the available criteria [5; 13]. The prevalence is estimated to be 2% to 8% of the population and increases with age [13; 14].

As with autoimmune diseases, the prevalence of fibromyalgia is higher among women than men, although data are conflicting. A female-to-male ratio of 6:1 to 9:1 has been reported in some studies [5; 12; 16]. However, estimates that use newer, symptom-based diagnostic criteria show a female-to-male ratio of 2:1 [13; 14].

The prevalence of fibromyalgia is 5% to 6% among patients seen in family or general medicine practice settings and among 15% to 20% of patients seen by rheumatologists [8]. As such, the syndrome is among the 100 most common diagnoses made in the family medicine setting, as well as one of the most common diagnoses in office-based rheumatology practice [8; 17]. Fibromyalgia is usually diagnosed between the ages of 20 and 55 years, but the prevalence increases with age, peaking at 70 to 79 years of age (at approximately 7% for women and 1% for men) [5].

The prevalence of fibromyalgia according to race/ethnicity in older studies has been inconclusive, as studies have either included a predominantly White population or have not specified the race/ethnicity of the subjects [13]. In general, the prevalence is similar among racial and ethnic groups [18]. There is no evidence of a higher prevalence of fibromyalgia in industrialized countries and cultures. Among a cohort of 266 individuals with systemic lupus, Black race had a negative association with fibromyalgia, and the prevalence has been low among Hispanic and Mexican individuals as well [19; 20].

PATHOGENESIS

Several etiologies for fibromyalgia have been postulated and explored; the syndrome has been thought to be an inflammatory condition, an autoimmune disease, an unexplained medical syndrome, or a psychiatric condition [3; 7; 8; 21; 22]. However, research has provided little or no evidence to support these bases, and the pathogenesis of the syndrome continues to be poorly understood [8; 9; 23].

Pioneering sleep studies in the 1970s demonstrated that people with fibromyalgia had abnormal sleep physiology, suggesting a central pathology [24]. Since then, substantial evidence has supported a mechanism of central sensitization, or the amplification of pain in the spinal cord through spontaneous nerve activity, expanded receptive fields, and augmented stimulus responses [4; 5; 6; 9]. Studies have also shown that, compared with healthy individuals, people with fibromyalgia experience pain differently and have physiologically lower pain thresholds [6]. Research has also indicated significant dysregulation of the hypothalamic-pituitary-adrenal axis is found in fibromyalgia [9]. In addition, there may be abnormalities of descending inhibitory pathways, neurotransmitters, or neurohumoral responses; low levels of serotonin and norepinephrine metabolites have been found in the cerebrospinal fluid of individuals with fibromyalgia [5; 6; 9].

Genetics is thought to be a factor in the susceptibility of fibromyalgia. Family clustering has been reported, and the risk for fibromyalgia is eight times higher for first-degree relatives of individuals with the syndrome [25]. Abnormalities in the serotonin transporter gene and the catecholamine-O-methyl transferase gene have been identified [5; 9; 26]. These abnormalities affect the metabolism or transport of serotonin and norepinephrine, which decrease the sensitivity of pain-processing systems through the descending central nervous system pain pathways [5].

POTENTIAL ENVIRONMENTAL RISK FACTORS

As with autoimmune diseases, several environmental risk factors have been thought to act as triggers for the development of fibromyalgia. Because research on the etiology of fibromyalgia is lacking, individuals' perceptions of triggers have been the source of some of the available information [27]. Perhaps as a result, data on the frequency of environmental triggers are conflicting, with some studies showing that half of all cases have a distinct physical or emotional trigger and other studies indicating that three-quarters of cases or more had no triggering event [9; 27; 28].

Psychiatric conditions have long been associated with fibromyalgia, and research suggests that such conditions may precede fibromyalgia and act as a trigger for the disease [6; 8]. In one study, when individuals were asked what they perceived to be a trigger for fibromyalgia, 73% attributed the development of the disease to emotional trauma or chronic stress; 24% noted emotional/physical abuse as an adult or child as a perceived trigger [27].

Injury/trauma and physical illness may also be triggers. Approximately one-third of individuals who attributed fibromyalgia to an environmental trigger noted physical injury (including those from a motor vehicle accident) as the perceived trigger [27]. Acute illness was perceived as a trigger in 27% of individuals in the same survey [27]. Viral infections have been

associated with the development of fibromyalgia, and hepatitis C, Epstein-Barr virus, human immuno-deficiency virus (HIV), parvovirus, and Lyme disease are thought to be viral triggers, but no causality has been established [6; 9; 28]. Other pain conditions, hyperprolactinemia, and autoimmune diseases have also been reported to be factors [9; 28].

ASSOCIATION WITH AUTOIMMUNE DISEASES

Several autoimmune diseases have been found in conjunction with fibromyalgia. In a retrospective study of 2,595 cases of fibromyalgia in a nationwide claims database, the likelihood of systemic lupus or rheumatoid arthritis was two to seven times greater than that for controls [29]. Other studies have confirmed an association between fibromyalgia and systemic lupus and rheumatoid arthritis, with reported rates of up to 65% and 57%, respectively [23]. High rates of Sjögren syndrome (up to 50%), and thyroiditis (up to 31%) have also been reported among individuals with fibromyalgia [3; 9; 30]. A small study has suggested that Hashimoto disease and/or subclinical hypothyroidism may be a predisposition to fibromyalgia; signs and symptoms of fibromyalgia were found in nearly one-third of individuals [30].

CLINICAL MANIFESTATIONS

Chronic, widespread musculoskeletal pain (on both sides of the body for at least three months) is the defining feature of fibromyalgia [1]. This pain is often associated with muscle tenderness (to palpation) adjacent to areas of tendon insertion [3; 31]. In addition, a constellation of other symptoms are common and vary across patients. Most patients complain of stiffness (especially in the morning), fatigue, sleep abnormalities, and difficulties of cognition, such as mental torpor, maintaining attention, and performing tasks that require rapid thought [1; 2; 3; 27; 31; 32; 33; 34].

The likelihood of depression is high among individuals with fibromyalgia [34]. Major depression has been identified in 20% to 62% of individuals with the syndrome [27; 28; 31; 34; 35]. Factors associated with major depression have included younger age, female gender, being unmarried, number of chronic conditions, and limitations in activities [34].

Cognitive dysfunction (often referred to as "fibrofog") affects approximately 40% of individuals [5]. The primary effect is on memory (working, episodic, and semantic), especially when tasks are complex and the individual's attention is divided [36]. Although memory impairment is not as common as many other symptoms, patients have considered them to be among the most troublesome, which is not surprising given that the impairment is equivalent to about 20 years of aging [27; 32; 36]. Attentional control/function is also commonly impaired in individuals with fibromyalgia [36; 37; 38]. Studies have indicated that cognitive dysfunction cannot be attributed solely to symptoms such as depression, anxiety, and sleep problems, but it does seem to be related to the level of pain [36; 37; 38].

DIAGNOSTIC EVALUATION

Fibromyalgia cannot be diagnosed on the basis of laboratory tests, imaging studies, or pathologic results. As a result, the diagnosis relies on a careful review of medical history and comprehensive physical examination. The American Pain Society guideline recommends that the physical examination include a complete joint examination, manual muscle strength testing, and a neurologic examination [4]. The ACR established diagnostic criteria for fibromyalgia in 1990, but the classification system, designed for use in clinical research rather than clinical practice, has many limitations [1; 2; 3; 39].

The lack of objective testing has led to substantial delays in the diagnosis of fibromyalgia, with a diagnosis confirmed only after many visits to healthcare professionals, referrals, diagnostic tests, and several possible diagnoses [5]. Nearly half of individuals with the disease consulted three to six healthcare providers before the diagnosis was made, and 25% saw more than six providers before diagnosis [27]. Physicians also acknowledge diagnostic delay, noting that an accurate diagnosis of a chronic pain disorder (including fibromyalgia) often is not made until after two to three years and consultations with 8 to 13 healthcare professionals [5].

A self-administered questionnaire developed in 2010 may aid in detecting fibromyalgia. The tool, Fibromyalgia Rapid Screening Tool (FiRST), was developed by a group of rheumatologists and pain experts and consists of six questions that can be answered with a yes/no response [40]. A score of five "yes" responses gave the highest rate of correct identification of fibromyalgia patients (87.9%), with a sensitivity of 90.5% and a specificity of 85.7% [40]. FiRST is meant to be used as an initial screening tool, with established diagnostic criteria used to subsequently confirm the diagnosis [40]. The current challenge in diagnosing fibromyalgia stems from many factors, including a wide range and variation in symptoms, a complex differential diagnosis, and difficulty with the established diagnostic criteria.

RANGE AND VARIATION IN SYMPTOMS

There is a wide range of symptoms and comorbidities associated with fibromyalgia, and they occur in a variety of combinations and differ in terms of severity. After the three primary manifestations (fatigue, stiffness, and sleep abnormalities), the most common symptoms are headaches (usually migraine), dry mouth, low back pain, and paresthesias (*Table 1*) [1; 3; 27; 31; 32; 33; 34]. In an online survey conducted by the National Fibromyalgia Association (NFA), 19 symptoms, affecting virtually all body systems, were noted by at least 25% of the respondents [27]. Nearly all individuals with fibromyalgia are polysymptomatic [27].

Most individuals with fibromyalgia describe pain as arising from muscles and joints and also have tender skin [3]. Pain is typically axial in distribution, and pain/stiffness usually occurs in the morning and evening [3]. Patients may note a feeling of swelling in the soft tissues, primarily around the joints, but there is no objective evidence of swelling [3; 28]. The American Pain Society recommends using self-reports as the primary source for pain assessment, focusing on such details as [4]:

- Type and quality of pain
- Source
- Location
- Duration
- Time course
- Pain affect
- Effects on quality of life

Several pain assessment tools may be useful in the setting of fibromyalgia (*Table 2*) [9; 22; 41].

Healthcare professionals should also ask about factors that may exacerbate musculoskeletal symptoms, as these symptoms are modulated in approximately 60% to 79% of individuals [1]. Emotional distress has been the most commonly reported exacerbating factor (83%), followed by changes in the weather (80%), sleeping problems (79%), and strenuous activity (70%) [27]. Many other factors are perceived to worsen symptoms, including fatigue, physical inactivity, mental stress, soft-tissue injuries, travel in a car or plane, and work-related conflict [3; 27].

Patient assessment must include evaluation of the severity of symptoms most often associated with fibromyalgia, as well as overall quality of life and functional assessment [4; 9; 22]. Most assessment tools used have been validated in other settings and are not fibromyalgia-specific. Healthcare professionals should ask patients about how their symptoms affect their ability to work, as physical limitations and cognitive dysfunction may result in an inability to maintain normal employment [3; 4]. A daily pain diary may also be useful in documenting how pain influences activities of daily living and quality of life [9].

COMMON SYMPTOMS OF FIBROMYALGIA			
Symptom	Reported Prevalence		
Stiffness	76% to 91%		
Fatigue	24% to 90%		
Sleep abnormalities	76%		
Headaches	47% to 75%		
Dry mouth	18% to 71%		
Low back pain	67%		
Paresthesias 44% to 67%			
Restless legs syndrome	32% to 64%		
Depression	20% to 62%		
Irritable bowel syndrome	36% to 60%		
Anxiety	30% to 56%		
Raynaud phenomenon	9% to 53%		
uscle spasms 46%			
Balance problems	45%		
Cognitive dysfunction (impaired memory and/or concentration)	40%		
Bloating	40%		
Sinus problems	37%		
Tooth disorders	32%		
Jaw pain	29%		
Bladder problems	26%		
Source: [1; 3; 5; 22; 27; 28; 31; 32; 33; 34; 35]	Table 1		

INSTRUMENTS FOR ASSESSMENT OF FIBROMYALGIA-RELATED SYMPTOMS		
Symptom	Assessment Tool	
Pain	Visual analog scale Brief Pain Inventory Short Form-McGill Pain Questionnaire Daily pain diary	
Fatigue	Visual analog scale Multidimensional Assessment of Fatigue Instrument Multidimensional Fatigue Inventory Fatigue Severity Scale	
Sleep	Visual analog scale Medical Outcomes Study Sleep Scale Pittsburgh Sleep Quality Index Sleep Assessment Questionnaire	
Depression/anxiety	Beck Depression Inventory Patient Health Questionnaire Beck Anxiety Inventory Hospital Anxiety and Depression Scale	
Quality of life/functional assessment	Fibromyalgia Impact Questionnaire Short Form-36 Health Survey	
Source: [9; 22; 41]		Table 2

COMORBIDITIES ASSOCIATED WITH FIBROMYALGIA				
Comorbidity	Prevalence			
	Lifetime	Current		
Any gastrointestinal problem	72%	34%		
Any psychiatric problem	68%	39%		
Depression	68%	39%		
Hypertension	49%	35%		
Any genitourinary problem	48%	5%		
Severe allergies	41%	21%		
Any endocrine problem	40%	28%		
Any lung problem	37%	19%		
Source: [43]		Table 3		

In relating their history, individuals will often focus on the symptoms that are of most concern or that are most troublesome. According to the NFA survey, the most troublesome symptoms were (in descending order): morning stiffness, fatigue, nonrestorative sleep, pain, forgetfulness, poor concentration, difficulty falling asleep, muscle spasms, anxiety, and depression [27]. In another study, 100 individuals with fibromyalgia ranked symptoms slightly differently, but the top five symptoms were similar: pain or physical discomfort, joint pain/aching, fatigue or lack of energy, poor sleep, and cognitive dysfunction [32].

Because of the predominance of fibromyalgia among women, there are few data on the clinical profile for men with the syndrome. The available research points to differences in the clinical presentation according to gender. Women tend to report more symptoms, to describe more symptoms as major problems, and to report greater life interference from pain [8; 18; 42]. Men have noted significantly lower health perceptions and more physical limitations [42]. With regard to specific symptoms, fatigue and sleep disorders are more common among women, with some studies showing a threefold higher rate [8]. "Pain all over" is also more frequently reported by women than men [8]. The most powerful discriminator between women and men with fibromyalgia is the number of tender points [8].

Comorbidities

Given the broad range of symptoms and conditions found in association with fibromyalgia, it is difficult to differentiate true comorbidities from manifestations of the syndrome itself [43]. For example, irritable bowel syndrome and restless legs syndrome are traditionally thought of as comorbidities but may be part of the overall clinical syndrome [1; 8; 43]. This is true for many autoimmune diseases but particularly for fibromyalgia, which has been described as overlapping with virtually every other unexplained syndrome [7]. In a study in which current and lifetime comorbidities associated with fibromyalgia, rheumatoid arthritis, and systemic lupus were evaluated, fibromyalgia was associated with significantly higher rates of depression and psychiatric conditions, gastrointestinal problems, and severe allergies (Table 3) [43].

COMPLEX DIFFERENTIAL DIAGNOSIS

The multitude of symptoms and comorbidities associated with fibromyalgia add to the complexity of making a differential diagnosis. Many other conditions can mimic widespread pain, and these conditions must be considered in the differential diagnosis (*Table 4*). Although objective testing cannot confirm a diagnosis of fibromyalgia, it can play an important role in ruling out other possible diagnoses. A CBC, ESR, muscle enzymes, liver function studies, and thyroid function tests can

DIFFERENTIAL DIAGNOSIS OF FIBROMYALGIA			
Diagnoses to Consider	Shared Manifestations	Distinguishing Features	
Myofascial pain syndrome	Painful, tender areas in the muscles, commonly affecting the axial muscles	Pain arising from trigger points in individual muscles during examination	
Chronic fatigue syndrome	Chronic pain and fatigue	Low-grade fever, enlargement of lymph glands, continuous subclinical inflammatory process, and acute onset of illness	
Rheumatoid arthritis	Joint pain/stiffness	Involvement of hands and feet, positive rheumatoid factor (in 80% to 90% of cases), radiographic evidence of joint erosion	
Systemic lupus erythematosus	Involvement of multiple systems, joint pain	Malar rash, positive antinuclear antibody test	
Hypothyroidism	Profound fatigue, muscle weakness, mental slowing	Weight gain, hair loss, increased TSH level	
Polymyalgia rheumatica	Pain/stiffness in sacrohumeral and pelvic girdle	Increased ESR (in 80% to 90% of cases), age older than 65 years, treatment with glucocorticoids resolves symptoms	
Spondyloarthropathy	Pain in neck, mid-thoracic, anterior chest wall, or lumbar regions	Pain localized to specific spinal areas, radiographic evidence of sacroiliitis, or radiographic changes in vertebral bodies	
Polyarticular osteoarthritis	Pain in multiple joints	Radiographic evidence of joint degeneration	
Polymyositis or other myopathies	Muscle weakness	Proximal, symmetrical muscles affected, increased serum levels of muscle enzymes, abnormal findings on EMG testing and on evaluation of biopsy samples	
Neuropathic pain syndromes	Tingling, numbness	Burning, shooting pain	
EMG = electromyography; ESR = es	rythrocyte sedimentation rate; TSH = thy	roid-stimulating hormone.	
Source: [3; 8; 28]		Table 4	

help identify other conditions [4]. However, given the high rate of conditions that occur concurrently with fibromyalgia, clinicians must remember that finding another diagnosis does not automatically rule out a diagnosis of fibromyalgia [3]. Differentiating fibromyalgia from other rheumatic diseases and conditions involving widespread pain is especially difficult. Individuals who have widespread pain and fibromyalgia are typically more symptomatic, dysfunctional, and depressed than people who have widespread pain without fibromyalgia [3].

DIFFICULTY WITH DIAGNOSTIC CRITERIA

The ACR designed the classification criteria for fibromyalgia for epidemiologic classification but noted that the criteria would also be useful for diagnosis [1]. However, the criteria are used by only about half of rheumatologists in routine practice and are seldom used in the primary care setting [3]. The classification system consists of two criteria: a history of widespread pain and pain in 11 of 18 tender point sites on digital palpation [1]. It has a sensitivity of 88%, a specificity of 81%, and an accuracy of 85%, but several important problems have been identified.

AMERICAN COLLEGE OF RHEUMATOLOGY DIAGNOSTIC CRITERIA FOR FIBROMYALGIA

Criteria

A patient satisfies diagnostic criteria for fibromyalgia if the following three conditions are met:

- WPI \geq 7 and SSS score \geq 5 or WPI 4-6 and SSS score \geq 9.
- Generalized pain is present, defined as pain in at least 4 of 5 regions (left upper, right upper, left lower, right lower, axial)
- Symptoms have been generally present at a similar level for at least three months.

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Ascertainment	
WPI	Note the number areas in which the patient has had pain over the last week. In how many of the following areas has the patient had pain? Score will be between 0 and 19.
	• Shoulder girdle, left
	Shoulder girdle, right
	Upper arm, left
	• Upper arm, right
	• Lower arm, left
	Lower arm, right
	Hip (buttock, trochanter), left
	Hip (buttock, trochanter), right
	• Upper leg, left
	• Upper leg, right
	• Lower leg, left
	• Lower leg, right
	• Jaw, left
	• Jaw, right
	• Chest
	• Abdomen
	Upper back
	Lower back
	Neck
SSS score	For the symptoms of fatigue, waking unrefreshed, and cognitive dysfunction, indicate the level of severity over the past week using the following scale: 0 = No problem 1 = Slight or mild problems, generally mild or intermittent
	2 = Moderate, considerable problems, often present and/or at a moderate level
	3 = Severe: pervasive, continuous, life-disturbing problems
	Considering somatic symptoms ^a in general, indicate whether the patient has:
	0 = No symptoms
	1 = Few symptoms
	2 = A moderate number of symptoms
	3 = A great deal of symptoms

^aSomatic symptoms that might be considered: muscle pain, irritable bowel syndrome, fatigue/tiredness, thinking or remembering problem, muscle weakness, headache, pain/cramps in the abdomen, numbness/tingling, dizziness, insomnia, depression, constipation, pain in the upper abdomen, nausea, nervousness, chest pain, blurred vision, fever, diarrhea, dry mouth, itching, wheezing, Raynaud phenomenon, hives/welts, ringing in ears, vomiting, heartburn, oral ulcers, loss of/change in taste, seizures, dry eyes, shortness of breath, loss of appetite, rash, sun sensitivity, hearing difficulties, easy bruising, hair loss, frequent urination, painful urination, and bladder spasms.

The final score will be between 0 and 12.

Source: [44] Table 5

A primary problem with the criteria is the focus on the tender point evaluation, which has been difficult for clinicians, especially primary care providers, to perform correctly [2; 3]. Perhaps equally as problematic is that widespread pain as the only criterion for diagnosis does not seem sufficient, given the broad range of symptoms associated with the syndrome [3]. A third major problem is the lack of a severity scale, which means that an individual with fibromyalgia may not satisfy the diagnostic criteria for the syndrome if symptoms or pain at tender points improve [3]. As a result of these drawbacks, the diagnosis of fibromyalgia often has been symptom-based, and researchers have sought ways to modify the criteria or use alternative approaches [2; 3; 39].

In one study to assess alternative approaches, survey criteria consisting of a Regional Pain Scale score of at least 8 and a fatigue score of at least 6 was found to be concordant with the ACR criteria in 72% of cases [39]. Clinical diagnosis (the clinician's impression irrespective of the ACR criteria) was concordant with the ACR criteria in 75% of cases. The authors concluded that all diagnostic methods have utility [39]. In another study, an effort to modify the criteria to include the three most common symptoms—morning stiffness, sleep disturbances, and fatigue—yielded a sensitivity of 81%, a specificity of 61%, and an accuracy of 72% [3].

To address the problems inherent in its classification system, the ACR published updated diagnostic criteria for fibromyalgia in 2016 [2]. The ACR used a symptom severity scale and the Regional Pain Scale (renamed the Widespread Pain Index) to construct a new case definition of fibromyalgia: a Widespread Pain Index (WPI) score of 7 or greater and a symptom severity score (SSS) of 5 or more OR a WPI score of 4–6 and a SSS of 9 or greater [2]. The WPI has been found to correlate well with findings of the tender point examination, eliminating the need for that examination [2]. The symptoms evaluated by the

SSS are fatigue, cognitive dysfunction, and waking unrefreshed (*Table 5*) [2; 44]. In addition, the new criteria minimizes misclassification of regional pain disorders and eliminates the confusing recommendation regarding diagnostic exclusion [44]. Another advantage is that the criteria can demonstrate change in the individual's health status and allows for fibromyalgia to be seen as part of a continuum [2].

TREATMENT

As with all chronic illnesses, the goal of treatment in fibromyalgia is to reduce symptoms, improve function, and engage the patient's involvement in self-care [22]. Studies have shown that treatment is most effective when it includes the combination of patient education, nonpharmacotherapy approaches (including exercise), and selective pharmacotherapy for persistent symptoms or comorbidities [4; 8; 45; 46; 47; 48].

Treatment guidelines for fibromyalgia have been established by the American Pain Society and EULAR, and subsequent systematic reviews and meta-analyses have provided further findings to support both pharmacologic and nonpharmacologic treatment [4; 46; 49]. Familiarity of guidelines and recommended treatments, especially among primary care providers, is low, and adherence is suboptimal [5; 50]. For example, a substantial number of people with fibromyalgia take pain medications that lack evidence for effectiveness or that are less effective than alternative options [27; 50].

In addition, the practice guidelines for fibromyalgia have many limitations, the most important of which is that their evidence base predates the FDA approval of three drugs for the treatment of the condition. The treatment guidelines may also lack clinical utility because of the crucial need to customize treatment of fibromyalgia according to the unique combination of symptoms in an individual patient.

A pooled analysis showed that pain reduction alone does not make people with fibromyalgia feel better; instead, improvements in fatigue, physical functioning, mood, and impact on daily living are important factors in feeling better [51]. These factors must therefore be considered when developing a treatment plan, and optimum treatment will depend on the level of various symptom involvement for the patient [5; 41]. Effective treatment of fibromyalgia may also necessitate guideline-based treatment for comorbidities (e.g., irritable bowel syndrome and restless legs syndrome) [41].

The approach most often used for initial management of fibromyalgia includes patient education and reassurance; an exercise program that combines stretching, aerobic conditioning, and strength training; and selective, low-dose monotherapy aimed at relieving symptoms that do not respond to nonpharmacologic measures.

NONPHARMACOLOGIC TREATMENT

Nonpharmacologic measures are important components of an effective fibromyalgia treatment plan. Strong evidence has been documented for exercise (aerobic and/or muscle-strength training), cognitive-behavioral therapy, and patient education, and the combination of the three components is recommended as the initial management approach [28; 45; 46; 48].

Patient Education

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The goal of patient education is to effect a change in the patient's perception of his or her role in managing and coping with symptoms [28]. Patients benefit from an explanation of the disease and reassurance regarding symptoms and prognosis; other topics for discussion are treatment options, sleep hygiene, the importance of conditioning and exercise, and the role of pharmacotherapy for comorbidities such as mood and sleep disorders. There is good evidence that patient education is an essential component of effective treatment [4; 45; 46; 48]. Even a single multidisciplinary educational program was associated with significant improvements in pain, fatigue, morning tiredness, stiffness, anxiety, and depression [45]. Education in a variety of formats has been found to be useful, including lectures, written materials, group discussions, demonstrations, and webbased programs [45; 52]. Healthcare professionals should encourage their patients to take advantage of many reliable online educational resources.

Language, cultural competency, and health literacy are significant issues, given the growing percentages of racial/ethnic populations. According to U.S. Census Bureau data from 2021, more than 44.8 million Americans are foreign-born, 67.2 million Americans (21.7% of the population) speak a language other than English at home, and more than 25.5 million (8.2% of the population) report that they speak English less than "very well" [84]. Clinicians should ask their patients what language they prefer for their medical care information, as some individuals prefer their native language even though they have said they can understand and discuss symptoms in English [85].

Most important, perhaps, is the fact that clinical consequences are more likely with ad hoc interpreters than with professional interpreters [86]. A systematic review of the literature showed that the use of professional interpreters facilitates a broader understanding and leads to better clinical care than the use of ad hoc interpreters, and many studies have demonstrated that the lack of an interpreter for patients with limited English proficiency compromises the quality of care. The use of professional interpreters improves communication (errors and comprehension), utilization, clinical outcomes, and patient satisfaction with care [15; 87].

Exercise

Exercise not only helps to alleviate many fibromyalgia symptoms but also helps to reverse the effects of deconditioning and improve physical fitness [8; 47; 53; 54; 55; 56]. In a study of 207 women who were actively treated with medication for confirmed fibromyalgia, progressive walking, simple strengthtraining exercises, and stretching activities led to several improvements, including higher scores for functional status, reduced fatigue, better mental health, reduced depression, and greater self-efficacy [53]. The benefits of exercise are enhanced when combined with targeted self-management education [28; 53].

A meta-analysis showed that supervised aerobic exercise training has beneficial effects on physical capacity and symptoms related to fibromyalgia and that strength training may also have benefits on some fibromyalgia symptoms [54]. Another meta-analysis published in 2010 showed that aerobic exercise has a significant positive effect on a variety of diseaserelated symptoms, with reductions in pain, fatigue, depressed mood, and limitations of health-related quality of life, as well as improved physical fitness [56]. A 2013 Cochrane review found low-quality evidence that resistance training (moderate-to-high intensity) improves functioning, muscle strength, pain, and tenderness in women with fibromyalgia [57]. Other low-quality evidence suggests that aerobic exercise is superior to resistance training for improving pain, but resistance training is superior to flexibility exercise training in women with fibromyalgia for improvements in pain and multidimensional function. Moderate-to-high resistance training is safe for women with fibromyalgia [57].

Both the American Pain Society and EULAR recommend exercise programs as part of treatment for fibromyalgia [46; 58]. The American Pain Society recommends beginning with low levels of exercise and working gradually to a goal of moderately intense aerobic exercise at least two to three times per week [58]. However, fewer than one-third of NFA survey

respondents said they engaged in aerobic exercise; more respondents said they participated in "gentle walking" (64%) and stretching (62%), and fewer noted use of physical therapy (24%) or strength training (18%) [27]. Aquatic physical therapy has also been recommended for relief of fibromyalgia-related stiffness [59].

A 2018 report provides evidence that a mind-body treatment approach, specifically a tai-chi program, is of equal or greater benefit than standard care aerobic exercise alone [60]. In this blinded, prospective study, 226 adults with fibromyalgia (widespread pain index ≥ 7 and severity score ≥ 5) were randomly assigned either to supervised aerobic exercise (24 weeks, twice weekly) or to one of four classic Yang-style tai chi interventions (12 or 24 weeks, once or twice a week). Participants were followed for 52 weeks; the primary outcome was change in the fibromyalgia impact questionnaire scores at 24 weeks compared with baseline. The results showed that improvement in symptom scores was greater for subjects in each of the tai chi groups than for those receiving aerobic exercise. A clinically significant difference was only observed when comparing the highest-intensity tai chi program (twice weekly for 24 weeks) with aerobic exercise. Benefit with respect to secondary outcomes (assessment scores for anxiety, depression, coping strategies, functional limitations, sleep, and quality of life) also favored the tai chi interventions. At 52 weeks the combined tai chi groups continued to show more improvement in primary and most secondary outcomes than the aerobic exercise group.

EULAR notes that exercises should be tailored to the individual patient, and modifications should be made according to the severity of symptoms [46]. For example, a sedentary individual with moderate-to-severe fibromyalgia should begin with breathing, posture, and relaxation training, move to flexibility exercises, then to strength and balance exercise, and finally, to aerobic exercise [55].

Cognitive-Behavioral Therapy

The goal of cognitive-behavioral therapy is to move patients toward more adaptive beliefs about their ability to cope with symptoms, which in turn increases self-management [47]. Cognitive-behavioral therapy is designed to help individuals improve the way they think about fibromyalgia and cope with the overall effects of its symptoms [8]. It is most effective when it focuses on a specific outcome, especially one that is the subject of the patient's maladaptive thoughts and expectations [8; 47].

A systematic review of 23 studies showed that of 30 psychological treatments for fibromyalgia, cognitive-behavioral therapy was associated with the greatest effect sizes, especially for short-term reduction in pain [61]. In addition to short-term and long-term reductions in pain, cognitive-behavioral therapy has been associated with reductions in sleep disturbances and depression and improvements in functional status [8; 46; 47; 58; 61]. Benefit is typically achieved in 10 to 20 sessions [28]. Despite recommendations for cognitive-behavioral therapy, it may be underutilized. According to the NFA survey, only 8% of respondents had used this strategy [27].

Cognitive-behavioral therapy has been significantly beneficial in many individuals with psychiatric illnesses, such as depression and anxiety disorders, and so may be most useful for individuals with fibromyalgia who have these symptoms [47]. The individuals most likely to respond are probably those who have greater emotional distress, fewer coping skills, or less social support [28; 47].

Other Approaches

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Relaxation techniques are often part of cognitive-behavioral therapy for fibromyalgia, and their effectiveness is generally accepted, even though direct evidence is lacking [47]. Relaxation/meditation was practiced by 47% of the NFA survey respondents [27]. Mindfulness-based stress reduction therapy has also been evaluated; however, only weak evidence exists for benefit in fibromyalgia [62].

The EULAR guidelines include a recommendation (level IIb) for heated pool treatment, with or without exercise, on the basis of studies showing improvement in pain and function [46]. A subsequent meta-analysis of 10 randomized controlled trials demonstrated moderate evidence that hydrotherapy has short-term beneficial effects on pain and health-related quality of life [63].

The lack of fully effective treatments has led patients—and sometimes their healthcare providers—to explore other options to help manage symptoms. Some of these options have no or weak evidence of effectiveness, and the approaches most commonly used by patients are often not recommended practices. For example, the three interventions used most often by the NFA survey respondents were resting (86%); distraction, such as reading or watching television (80%); and heat modalities, such as warm water or hot packs (74%) [27]. The issue is not that these methods are not helpful, rather that the use rates for these approaches are much higher than for many evidence-based recommended strategies [27].

Among the other approaches patients often try are complementary and alternative medicine; between 40% and 90% of individuals with fibromyalgia have tried at least one such method [27; 50; 64]. However, evidence indicates that most of these methods are ineffective. There is limited evidence to support spinal manipulation [65]. Evidence is also lacking on the effectiveness of herbal, nutritional, and dietary supplements (including St. John's wort, ginseng, valerian, melatonin, and botanical oil) for the symptomatic treatment of fibromyalgia [47; 65; 66]. Despite this, approximately 43% to 68% of people with fibromyalgia use such supplements, although they give low ratings for their effectiveness [27, 50]. Given the high rate of individuals with fibromyalgia who seek symptomatic relief from complementary and alternative methods, the American Pain Society guidelines recommend that clinicians ask their patients about their use of such practices and educate them about their effectiveness and possible negative interactions [4].

Methods with greater evidence of benefit include acupuncture and massage therapy. A 2013 Cochrane review found low-to-moderate level evidence that acupuncture (particularly electro-acupuncture) is effective for the treatment of fibromyalgia symptoms compared with no treatment or standard therapy [67]. Acupuncture in general may relieve pain and stiffness, and electro-acupuncture may improve overall well-being, fatigue, and sleep quality. A 2014 meta-analysis of nine randomized controlled trials found that massage therapy (for at least five weeks) has beneficial immediate effects on improving pain, anxiety, and depression in fibromyalgia patients [68]. However, no follow-up data are available to show long-term benefit. Long-term data are similarly unavailable for gigong, a somewhat popular Chinese medical exercise, but low-quality evidence exists for the short-term improvement of pain, quality of life, and sleep quality and very low-quality evidence exists for improvement of fatigue [69]. Increased psychological well-being is often reported by gigong practitioners.

PHARMACOLOGIC TREATMENT

No single drug has been found to manage all fibromyalgia symptoms, and a combination approach is often used [27; 41]. Antidepressants were the first medications used to treat fibromyalgia; drugs in this class include tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) [26; 41]. In general, antidepressants reduce pain through a direct effect rather than an indirect effect mediated by an effect on depression [41]. Other drugs that have been shown to be effective include anticonvulsant drugs, some analgesics/muscle relaxants, and nonbenzodiazepines (*Table 6*) [5; 26; 28; 41; 49; 58; 70].

Antidepressants

Both the American Pain Society and EULAR found strong evidence (level I) for the use of a tricyclic antidepressant (amitriptyline) for the treatment of fibromyalgia [4; 46]. The American Pain Society recommends using amitriptyline for the initial treatment of fibromyalgia, whereas EULAR notes that any of a number of antidepressants should be "considered" [4; 46]. According to a 2009 metaanalysis, there is strong evidence for an association between treatment with antidepressant medications and reductions in pain, depression, fatigue, sleep disturbances, depressed mood, and a better healthrelated quality of life for people with fibromyalgia [75]. Treatment with an antidepressant does not completely eliminate pain, but tricyclic antidepressants have been found to be more effective for pain relief than either SSRIs or SNRIs [4; 75]. Amitriptyline was the fifth leading "ever used" drug in the NFA survey (reported by 55% of respondents), with 42% of those using the drug saying it was helpful [27]. In addition, use of prescription antidepressants was the third-highest ranked intervention overall in the survey [27].



The European League Against Rheumatism recommends low-dose amitriptyline for the treatment of patients with fibromyalgia.

(https://ard.bmj.com/content/76/2/318. Last accessed July 6, 2023.)

Level of Evidence: A (Weak for)

Two of the three drugs approved by the FDA are SNRIs: duloxetine and milnacipran [5]. Duloxetine was approved on the basis of two trials. In the first study, duloxetine led to a clinically significant treatment response (at least a 30% reduction in pain severity on the Brief Pain Inventory) in more than half of the study participants [76]. Two doses were evaluated: 60 mg once daily and 60 mg twice daily; both doses were associated with significantly higher response rates than that for the placebo group [76].

PHARMACOLOGIC TREATMENTS USED IN FIBROMYALGIA				
Drug	Dose	Common Adverse Events	Comments	
Antidepressants				
Amitriptyline	25–50 mg PO at bedtime	Nausea, vomiting, dry mouth, dizziness, drowsiness, headache	Recommended by American Pain Society and EULAR	
Duloxetine	60 mg PO daily	Nausea, dry mouth, constipation, drowsiness, decreased appetite	Approved by FDA for fibromyalgia in 2008	
Milnacipran	50–100 mg PO twice daily	Nausea, headache, constipation, dizziness, hot flush, dry mouth	Approved by FDA for fibromyalgia in 2009	
Anticonvulsants				
Pregabalin	300-450 mg PO daily	Diarrhea, dizziness, blurred vision, dry mouth, vomiting	Approved by FDA for fibromyalgia in 2010	
Gabapentin	1,200-2,400 mg PO daily	Viral infections (in children), dizziness, somnolence, ataxia	Limited data on effectiveness	
Analgesics/Muscle Relaxants				
Cyclobenzaprine	10-30 mg PO at bedtime	Drowsiness, xerostomia, dizziness	Recommended by American Pain Society	
NSAIDs	_	_	No evidence to support use, but may be of benefit in treating comorbidities	
Glucocorticoids	_	_	No evidence to support use, but may be of benefit in treating comorbidities	
Opioids				
Low-dose (tramadol)	200-300 mg PO daily	Hot flush, dizziness, headache, constipation, nausea	Recommended by American Pain Society and EULAR	
Potent		_	Not recommended; should be used only if all other approaches have been exhausted	
Sedative Hypnotics	·	· 	<u> </u>	
Zolpidem	5-10 mg PO at bedtime	Headache, somnolence, dizziness	Improves sleep; no effect on pain	
Benzodiazepines and sedatives	_	-	Evidence of effectiveness is lacking	

Duloxetine also significantly improved function and quality of life. Similar results were achieved with the same doses of the drug in the other study [77]. Neither study showed improvement in sleep; however, duloxetine did not interfere with sleep [41; 49; 76; 77]. The drug was also well tolerated, and nausea was the most common side effect. Given the similarity in response with the two doses of duloxetine, the approval is based on the once-daily dose. A 2014 Cochrane review indicated that there is a lack of efficacy data, but that 60–120 mg daily doses were associated with a greater improvement in mental symptoms than in somatic physical pain [78].

Two studies of milnacipran demonstrated the effectiveness of the drug in achieving a composite endpoint of improvement in scores for pain (30% improvement on a visual analog scale), patient global assessment ("very much" or "much" improved), and physical component of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (six points) [79; 80]. The studies also evaluated the effect of the drug on pain only (improvement in pain and patient global assessment but not SF-36). Two doses were used: 50 mg twice daily and 100 mg twice daily. In both studies, milnacipran was associated with significant improvements in pain, fatigue, patient global assessment, and physical function [79; 80]. Further follow-up has shown the efficacy to be maintained for 12 months [41]. The drug was well tolerated; the most common side effects were mildto-moderate nausea and headache, both of which resolved with continued use of the medication [79; 80]. The FDA approved milnacipran at both doses.

A systematic review to compare the effectiveness of the three antidepressants demonstrated several differences [81]:

- Amitriptyline was superior to both duloxetine and milnacipran in reducing pain, sleep disturbances, fatigue, and limitations of health-related quality of life.
- Duloxetine was superior to milnacipran in reducing pain, sleep disturbances, and limitations of health-related quality of life.

- Milnacipran was superior to duloxetine in reducing fatigue.
- No differences in tolerability were found among the three drugs.

Anticonvulsants

The third FDA-approved drug for the treatment of fibromyalgia is pregabalin, an anticonvulsant agent. Several studies have shown pregabalin to significantly improve pain, patient global assessment, fatigue, and health-related quality of life, as well as sleep disturbances [41; 72; 82]. The effect of the drug has lasted for as long as six months [41]. The drug was well tolerated, with the common side effects being dizziness and sedation, which tended to resolve with time of treatment [41].

Anticonvulsants have been evaluated in several trials, and the American Pain Society found level II evidence for this class of drug, whereas the later EULAR guidelines note level I evidence for pregabalin specifically [4; 46; 49]. Another anticonvulsant drug, gabapentin, has also demonstrated efficacy with respect to pain, patient global assessment, function, and sleep [41; 70; 72]. Gabapentin has not been approved by the FDA to treat fibromyalgia, and the drug is not specifically noted in treatment guidelines [4; 46]. Approximately one-third of the respondents in the NFA survey said they had "ever used" gabapentin, and 46% who had used it considered the drug helpful [27]. The side effect profile of gabapentin is similar to that of pregabalin, but the pharmacokinetic and pharmacodynamic profile is not as favorable [41]. An overview of systematic reviews of anticonvulsants showed that both drugs had a modest effect on pain reduction, and it was not possible to conclude if one drug was better than the other [72]. The long-term safety and efficacy of both drugs is also unknown, and many patients are expected to discontinue therapy due to a high incidence of adverse effects. The overview found no evidence of clinical benefit with any other anticonvulsant, including carbamazepine [72].

Analgesics

With a primary symptom of pain, fibromyalgia has often been treated with analgesics. According to the NFA survey, acetaminophen, ibuprofen, and naproxen were the top three ever-used medications (94%, 87%, and 66%, respectively) [27]. Slightly more than one-third to about one-half of the survey respondents said that these medications were helpful [27]. In another study, nearly 30% of 434 women with fibromyalgia reported taking NSAIDs [50]. However, with no inflammatory mechanism, fibromyalgia is not expected to respond to NSAIDs, and there is no evidence to support the use of NSAIDs or glucocorticoids as a treatment modality [4; 46]. NSAIDs may be of benefit in relieving pain associated with comorbidities, such as osteoarthritis, rheumatoid arthritis, or systemic lupus, which may account for their high rate of use in the NFA survey [27; 41].

Strong evidence has also been documented for cyclobenzaprine, which has both muscle relaxant and tricyclic antidepressant properties [26; 58; 83]. A systematic review of five randomized controlled trials showed that individuals treated with cyclobenzaprine for fibromyalgia were three times as likely to report overall improvement and to note reductions in symptoms, especially sleep disturbances, than controls [83]. Among the NFA survey respondents, 64% had ever used cyclobenzaprine and 58% of these patients considered the drug to be helpful [27].

Neither the American Pain Society nor EULAR recommend the use of potent opioids for the treatment of fibromyalgia, noting that they should be used only if all other pharmacologic and nonpharmacologic options have been exhausted [4; 46]. The American Pain Society found moderate evidence (level II, III) and EULAR documented level I evidence for tramadol, a mild opioid [4; 46]. The drug is recommended in both guidelines and may be used alone or as an adjunctive measure [41; 46; 58]. The dose of tramadol should be increased slowly over time and should be tapered gradually when discontinued [4]. Caution should be used when prescribing tramadol because of the risk of dependence and abuse [46].

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Sedative Hypnotics

Benzodiazepines and sedatives are not recommended for the treatment of fibromyalgia symptoms [28]. Zolpidem, a short-acting nonbenzodiazepine sedative, has been used to improve sleep in people with fibromyalgia, but because zolpidem does not relieve pain, it is useful only as an adjunct medication, and it has not been included in treatment guidelines for fibromyalgia [4; 41; 46]. Approximately 41% of the NFA survey respondents said they had ever used the drug, and 64% of these individuals considered it helpful [27]. In general, prescription sleep medication was the intervention that respondents considered the most effective of all interventions [27].

FOLLOW-UP

Individuals with fibromyalgia should be followed up routinely to assess response to treatment. Follow-up visits also offer an opportunity for healthcare professionals to encourage their patients to comply with pharmacologic and nonpharmacologic treatment. Reinforcement for the need to exercise is especially important, as 68% to 83% of people with fibromyalgia have been found to not engage in aerobic exercise [27; 55]. Rates of exercise among the general population are below optimum, and people with fibromyalgia need added encouragement because of many symptoms that may be perceived as barriers (e.g., fatigue, pain).

One approach to enhance adherence to an exercise program is to begin pharmacologic treatment targeting the most distressing or severe symptoms and then provide education about exercise as symptoms begin to improve [28; 55]. It is especially important to address sleep disturbances and fatigue. In contrast to recommendations for the general population, increasing lifestyle activity is not effective as exercise for individuals with fibromyalgia; instead, clinicians should encourage their patients with fibromyalgia to conserve their energy in daily life in order to have the ability to comply with prescribed exercises [55].

The authors of one review of nonpharmacologic treatment suggest that clinicians use the acronym ExPRESS to follow principles of nonpharmacologic pain management [47]:

- Ex: Exercise
- P: Psychiatric (i.e., addressing psychiatric comorbidities to help improve pain and disability)
- R: Regain function (helping patients pace activities to avoid doing too much on days they feel well)
- E: Education (referral to reliable resources)
- S: Sleep hygiene
- S: Stress management (such as cognitivebehavioral therapy and relaxation techniques)

CONCLUSION

Fibromyalgia is a complex rheumatic disorder characterized by chronic widespread musculoskeletal pain and focal tenderness (tender points), often accompanied by fatigue, other somatic complaints, and disturbances of affect and cognition [1]. Fibromyalgia has a substantial negative effect on physical, psychological, and social well-being, and the syndrome is associated with a significant burden in terms of disability and healthcare costs.

After diagnosis, fibromyalgia symptoms will persist in most individuals, but the majority still report that they feel better overall than at the time of diagnosis [8; 28]. Better outcomes have been associated with greater self-efficacy, help-seeking behavior, increased level of exercise, and pacing of activities [28]. Therefore, it is important that healthcare professionals are equipped with the information necessary to diagnose and treat fibromyalgia according to evidence-based or guideline-endorsed recommendations in order to improve patient quality of life.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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Evidence-Based Practice Recommendations Citation

Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis.* 2017;76(2):318-328. Available at https://ard.bmj.com/content/76/2/318. Last accessed July 6, 2023.