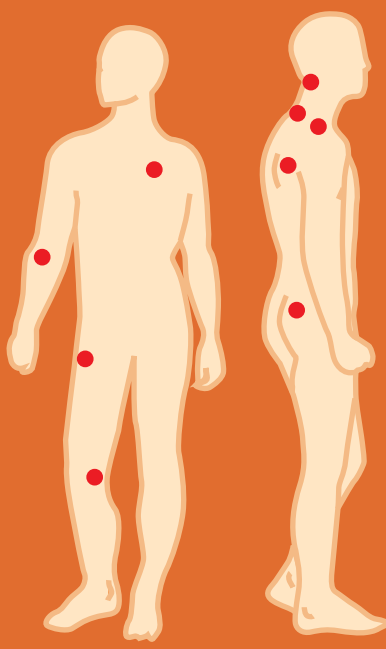
FIBROMYALGIA SYNDROME

WHAT DO WE KNOW ABOUT CAUSES AND TREATMENT OPTIONS?



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Introduction

Fibromyalgia syndrome (FMS) is a debilitating disorder characterized by symptoms of musculoskeletal pain, fatigue, sleep disturbance and changes in cognitive function. It is often associated with a number of other medical disorders. In the early 1970's, FMS began to emerge on the scene as a syndrome that was distinct from other rheumatologic diseases, though the World Health Organization did not recognize it as a disease until 1992. In some countries, FMS is estimated to affect about 1-2% of the general population[1-3] though some have suggested a prevalence as high as 5%[4,5]. FMS has been ranked as the highest chronic illness associated with long-term disability, pain and poor self-rated health[6]. The estimated health utilization and costs for FMS have been estimated to be $2,274 per patient per year in the U.S.[7], 3245 euro ($4,348 U.S.) in Spain and 4,331 euro ($5,803 U.S.) in Germany[8], numbers that are significantly higher when loss of work and productivity are considered.

Despite the fact that FMS is a fairly common disorder, it still remains undiagnosed in 3 of 4 people who present with symptoms. This may in part be due to the overlap that common FMS symptoms share with a number of other disorders. In addition, the criteria needed to make the diagnosis of FMS has evolved and changed over the years. To date, there is no cure for FMS and the conflicting information on effective treatments has been a source of frustration for both providers and their patients. This has led several professional organizations to develop guidelines based on evidence from well-designed studies to help clinicians and FMS patients better choose among available therapies with scientifically proven effectiveness. Towards that end, The American Pain Society[9], the European League Against Rheumatism (EULAR)[10] and the Association of Scientific Medical Societies of Germany[11] have put forth guidelines of available treatments for FMS based on extensive literature reviews, expert opinion and committee consensus. Both pharmacological and non-pharmacological therapies received high ratings by different organizations[12]. Further, the overwhelming consensus is that no single therapeutic approach can be expected to be effective in all individuals with FMS. Therefore, a treatment plan is more likely to be successful if it is multifactorial and includes elements from different treatment modalities.

This short book is intended to give you the most updated information about what causes FMS and will review a number of effective treatment modalities along with a comprehensive list of references supporting the information presented. In addition, information about adaptations that can be made at work to decrease stress, minimize symptoms and improve productivity will be provided.

What is fibromyalgia syndrome and who is at risk?

FMS is a chronic disorder characterized by widespread muscle pain, joint stiffness, fatigue and sleep disturbance.

- FMS occurs in almost all ethnic groups and is not limited to industrialized countries, with the exception of China where epidemiologic studies have revealed a very low prevalence[13]. It is not known why the prevalence of FMS in China is so low, but it is thought that this may be due to differences in environmental exposure, genetics or a combination of both.
- Though FMS affects all age groups, the incidence increases with age and it is more common in individuals over 50 years old[14].
- Women are diagnosed with FMS far more often than men, except during childhood where girls and boys are equally affected. Fortunately, children are more than likely to outgrow their symptoms.
  Even though one study reported that the majority of the participants with FMS who were interviewed could not identify a specific factor that precipitated the onset of symptoms[15], certain physical and psychological factors or stressors may trigger symptoms or increase one's susceptibility.
- For instance, psychiatric problems such as anxiety, somatization (experiencing physical symptoms for which no organic cause can be found), panic disorder, posttraumatic stress are more common among individuals with FMS compared to those with other rheumatic diseases[16] and depression has been shown to worsen symptoms[17-20].
- Infections have also been linked to triggering FMS. In particular viruses such as Coxsackie[21] Parvovirus[22] or bacteria such as Borrelia[23] may be involved.
- Vaccinations have also been considered as possible triggers[24], though more recently the evidence supporting this has been questioned[25].
- Physical trauma[26], emotional distress, chronic stress[27] and exposure to certain environmental chemicals[28] may also trigger FMS symptoms.

In addition to environmental factors, studies of families have pointed to a role for genetics. For instance, the incidence of FMS is greater in first-degree relatives of those diagnosed with the disorder[29-30]. First degree relatives are not only 8 times more likely to develop FMS compared with the general population, but they also can suffer from greater tenderness even in the absence of pain and are much more likely to have other pain syndromes such as headaches and irritable bowel syndrome.

Did you know?

Despite the fact that FMS is a fairly common disorder, it still remains undiagnosed in 3 of 4 people who present with symptoms.

Common symptoms of fibromyalgia syndrome (FMS)

FMS is a disorder that has widespread effects throughout the body. Almost everyone with a diagnosis of FMS has complaints of **pain, chronic fatigue** and **sleep disturbance**. Painful morning stiffness that can last up to several hours during the day is a common feature. The pain is not confined to the musculoskeletal system however, since tension and migraine headaches, jaw and facial tenderness are not uncommon complaints. Individuals often complain of **sleeping poorly** and waking up "unrefreshed" in the morning. Yet, despite feeling sleep-deprived, people often have difficulty taking a nap during the day. **Gastrointestinal complaints** can range from abdominal pain, bloating and constipation to nausea and diarrhea. Bladder problems such as increased urinary frequency and urgency are also found.

Some people will experience parasthesias such as numbness or tingling in the face, arms, hands or feet. There may also be a feeling of swelling in the hands and feet, though no swelling is apparent on examination. There may be increased **sensitivity to odors, noises, bright light** and **cold**. There can be reduced tolerance for exercise that is sometimes accompanied by heart palpitations and dizziness and increased muscle pain after exercising is often reported. In addition to these physical symptoms, individuals with FMS often complain of "**brain fog**" or problems with memory, concentration and difficulties performing simple mental tasks. **Depression** and **anxiety** are also very common.

FMS symptoms overlap with other medical disorders

Because the symptoms of FMS overlap with a number of other disorders, it's important to investigate if other medical conditions are present before arriving at a definitive diagnosis (Table 1). In many cases, the history and physical examination combined with carefully chosen laboratory studies can help the clinician distinguish among the various contenders. For example, rheumatoid arthritis and other inflammatory rheumatic diseases may present with widespread musculoskeletal pain and morning stiffness similar to FMS, but can often be distinguished by the presence of joint inflammation, swelling and deformity or the presence of rashes that are not seen in FMS.

Laboratory studies and x-rays are also useful in helping to nail the diagnosis. Individuals with hypothyroidism can be chronically fatigued with poor quality sleep and generalized muscular pain. Here, obtaining thyroid function studies will help differentiate the disorders. Adrenal insufficiency can lead to chronic fatigue. Here again, laboratory studies are useful in helping to sort things out. Certain psychiatric disorders such as post-traumatic stress disorder (PTSD), anxiety and depression may also underlie a number of the symptoms seen in FMS and in some cases, treating the mental health disorder can alleviate the symptoms altogether[31]. In older individuals, diffuse muscular pain can also be a presenting complaint of multiple myeloma, a relatively rare cancer of the blood. A careful family and/or personal history of cancer can be helpful.

In summary, it is important for both patients and their providers to be aware of the overlap in symptoms between FMS and a number of other physical and mental disorders, so that the correct diagnosis can be made and the appropriate treatment instituted.

Table 1: Differential diagnoses of fibromyalgia and corresponding diagnostic testing options.

Differential diagnosis	Differential diagnosis
Adrenal dysfunction	Morning serum cortisol, urinary catecholamine metabolites
Anemia	CBC with differential, RBC indices (MCV, MHC, MCHC)
Bone marrow disease	WBC differential, ESR, CRP, CMP
Chronic fatigue syndrome	Clinical history
Functional disorders (e.g., intestinal dysbiosis, subtle endocrine imbalances, postviral immune suppression)	Standard laboratory testing yields unclear results
Hypothyroidism	Thyroid function tests (T3, T4, TSH)
Lyme disease	Lyme titer, CMP
Psychiatric conditions (e.g., anxiety, depression, PTSD)	Refer to DSM-IV
Multiple sclerosis	MRI scan, lumbar puncture, evoked potential testing Muscular tender points on physical examination
Phenomenological Referred Myofascial Pain Rheumatoid autoimmune disorders (e.g., rheumatoid arthritis, ankylosing spondylitis, scleroderma)	Rheumatic profile (rheumatoid factor, ESR/CRP), ANA
Sleep disorders	EEG sleep studies
Spinal facet pain or sacroiliac joint pain	Radiologic studies (MRI scan, CT scan), bone scans (minimal diagnostic assistance)
Spinal disc herniation	MRI scan
Systemic inflammation or infection	WBC differential, ESR, CRP, CMP
Vitamin and/or mineral deficiency	B vitamins, magnesium, malic acid, complete nutrition assessment

ANA, antinuclear antibody; CBC, complete blood count; CMP, complete metabolic profile; CRP, C-reactive protein; CT, computerised tomography; DSMIV, diagnostic and statistical manual of mental disorders; EEG, electroencephalogram; ESR, erythrocyte sedimentation rate; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MRI, magnetic resonance imaging; PTSD, posttraumatic stress disorder; RBC, red blood cell; T3, triiodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone; WBC, white blood cell.

When considering the different diagnoses in someone presenting with symptoms consistent with FMS, it is not always the case that it will be an either/or situation. Several of the very same disorders previously discussed have been shown to co-exist with FMS (Table 2). Rheumatic conditions, chronic fatigue syndrome, irritable bowel syndrome, headache and psychiatric conditions such as anxiety and depression are anywhere from two to seven times more likely to be present in individuals with a diagnosis of FMS[1].

Table 2: Conditions often associated with fibromyalgia.

Muscoloskeletal	Genitourinary	Gastrointestinal	Miscellaneous
Nondermatomal paresthesia	Dysmenorrhea	Irritable bowel syndrome	Tension/migraine headaches
Temporomandibular joint syndrome	Interstitial cystitis	Esophageal dysmotility	Cognitive dysfunction
Hypermobility syndrome	Vulvodynia		Anxiety disorders
Rheumatoid Arthritis	Female urethral syndrome		Hyperventilation
Systemic lupus erythematosus	Vulvar vestibulitis		Allergy
Sjögren syndrome	Premenstrual syndrome		Vestibular disorders
Osteoarthritis			Ocular disorders
Chronic fatigue syndrome			Reynaud phenomenon
Carpal tunnel syndrome			Lyme disease
Myofascial pain syndrome			Mitral valve prolapse

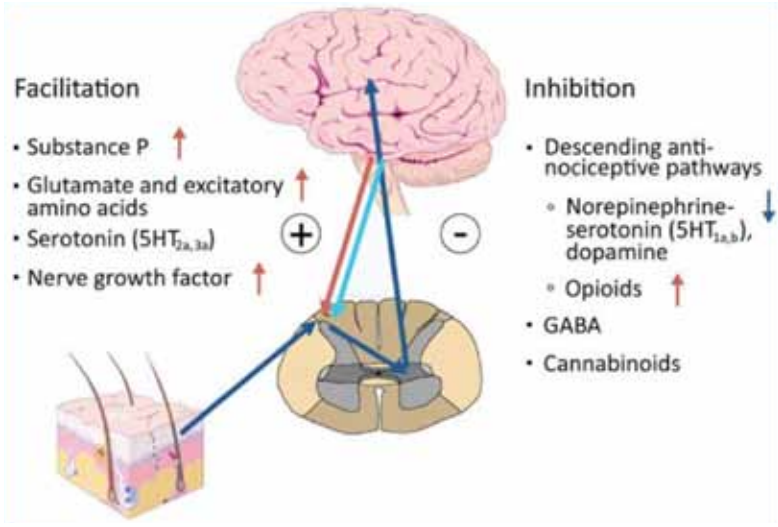
Abnormal pain pathway

Pain is one of the central features of FMS. The association between FMS and other painful conditions such as irritable bowel syndrome, tension-type headaches, migraines, temporomandibular disorder, chronic pelvic pain, interstitial cystitis, painful bladder syndrome and chronic prostatitis[32] has led researchers to investigate whether abnormalities in the pain processing pathways may be contributing factors. Over the years, research has indeed uncovered certain alterations in the way pain signals are transmitted and perceived by individuals with FMS. Under normal circumstances, the perception of pain involves two main groups of neural pathways called " *ascending and descending pathways*" (Figure 1). Peripheral nerves, those outside of the spinal cord, transmit signals to the spinal cord that are in turn sent through the ascending pathway to the brain for processing.

The descending pain pathways can modulate the intensity with which the brain perceives those signals. In FMS, the two main pathways function abnormally in such a way that the pain signal coming in from the periphery is amplified, something that has been termed "*central amplification*". Individuals with FMS perceive pain at a lower threshold than healthy controls[33]. They also have an increased response to painful stimuli, something called "*hyperalgesia*" and a heightened sensitivity to stimuli that are not normally painful, termed "*allodynia*". There can also be increased sensitivity to pressure, heat, cold, even auditory and electrical stimuli[33,34]. Imaging studies have supported these observations by showing that the pain processing brain centers in people with FMS are more active when they are presented with the same stimulus as a healthy control[35].

What exactly is underlying these changes? Normally, our perception of pain is a result of a balance between painful signals travelling up the spinal cord to our brain and a sort of dampening or inhibitory pathway that modulates its impact. In FMS, there appears to be both increased excitability of central nerve cells and a decrease in inhibitory mechanisms. Higher levels of substances called neurotransmitters that work to increase the effect of sensory input have been found in the cerebral spinal fluid and brains of individuals with FMS compared to healthy controls. Conversely, levels of neurotransmitters that process signals in the inhibitory descending pathway, such as norepinephrine and serotonin, are lower in the cerebral spinal fluid of those with FMS (Figure 1)[32,36,37]. Since many of these neurotransmitters have an effect on mood, energy and sleep, these imbalances may also explain fatigue, mood disorders and sleep problems that are often seen with FMS.

Figure 1- Neural pathways and neurotransmitters that influence pain sensitivity



In addition to the interactions between the central and peripheral nervous systems, enhanced pain perception may chronically activate the sympathetic nervous system, the part of our nervous system particularly involved in stress. This chronic activation of the sympathetic nervous system can lead to muscle contractions that may contribute to fatigue. In addition, when muscles do not receive enough oxygen, glial cells, those cells that surround and protect nerve cells in the brain, release inflammatory chemicals that probably contribute to the symptoms of fibromyalgia in unknown ways.

Autonomic nervous system dysfunction

A number of FMS symptoms appear to be due abnormal regulation of the autonomic nervous system (ANS)[38], the part of our nervous system that regulates heart rate, blood pressure, breathing and bowel function. This may explain the increase in heart rate that can sometimes occur when someone with FMS goes from a sitting to a standing position. The heart rate can increase rapidly more than 30 beats per minute, even though the blood pressure stays normal or may even be slightly elevated. This phenomenon is called postural orthostatic tachycardia syndrome (POTS) and can often lead to dizziness and palpitations. POTS may also contribute to exercise intolerance, headache, sleep abnormalities and cognitive difficulties. Many people can develop symptoms while standing, eating, showering or performing light exercise. In some individuals, the symptoms can be very debilitating. Fortunately, most people can expect improvement in their symptoms with the treatment options that are available (see pharmacological management of POTS).

Chronic stress

The biochemical consequences of stress may also be important in the development of FMS symptoms and dysregulation of the hypothalamic-pituitary axis (HPA) is the central player in this scenario. Normally, during times of stress, cortisol levels increase. Different studies have shown that higher levels of cortisol are found in people with FMS, especially in the evening, and that these may be associated with disrupted sleep patterns[39-41]. Low levels of growth hormone may also contribute to sleep disruption in FMS. Growth hormone tends to be secreted during stage 4 of sleep or deep sleep[42], and this is the stage of sleep that is most disturbed in people with FMS. This stress response may have even broader implications. For instance, studies that have examined skin biopsies from tender points in individuals with FMS have found changes consistent with the effects of chronic stress, namely evidence of demyelinated nerve cells and inflammation of peripheral nerve fibers[43].

Oxidative stress and free radicals

Oxidative stress and abnormal regulation of our immune system are also thought to contribute to FMS. Some studies have suggested that individuals suffering from FMS have a high level of oxidative stress and free radicals in their bodies [44,45] that may be contributing to musculoskeletal symptoms. These free radicals accumulate in little organelles in our cells called mitochondria that produce 90% of our energy. Mitochondria depend on a number of important compounds like coenzyme Q, niacin and magnesium to name a few, in order to neutralize these free radicals that can cause damage to many important structures within the cell. The observation that some individuals with FMS have low levels of some antioxidant nutrients like magnesium[46] and selenium[47,48] implies that oxidative stress may be contributing to the disease process.

Immune system dysfunction

Some studies have suggested that certain cytokines may be deregulated in FMS[49]. Cytokines are protein molecules that modulate our immune system and are known to play a role in a number of symptoms such as fatigue, fever, sleep, pain, stress and aching.

All of these observations provide different windows through which we are beginning to understand what may be behind some of the most troubling FMS symptoms. But the story is likely to be more complicated because genetic and environmental factors also determine to a large degree how processes like central amplification actually function in individuals[50]. Many of the genes that have been investigated such as the serotonin transporter gene[51,52], dopamine D4 receptor gene[53] and the catecol-O-methyltransferase[54,55] are all associated with neurotransmitters that, as already mentioned, are the key players in our pain processing pathways.

In summary, our understanding of what factors may underlie FMS has improved considerably over the years. Abnormalities in pain processing pathways, oxidative stress and our immune system may all be playing a role, albeit against a background of environmental and genetic influences.

Making a diagnosis of fibromyalgia syndrome

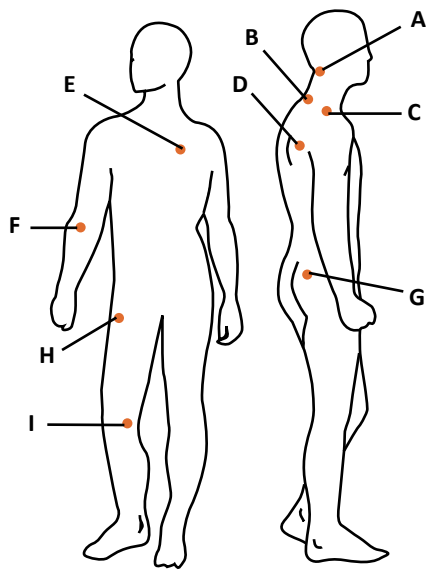
Criteria for diagnosis

Because FMS often presents as a constellation of symptoms, it has been challenging to come up with specific diagnostic criteria. In many cases, it was a diagnosis of exclusion after other conditions were ruled out. Therefore, in 1990, the American College of Rheumatology (ACR) established the following guidelines for establishing a diagnosis of FMS:

1) musculoskeletal pain that has been present for at least 3 months and is located in all four body regions (divided horizontally at the waistline and vertically at the midline) and in the axial skeleton.

2) pain elicited on palpation in 11 out of 18 tender points designated by the ACR (Figure 2).

Figure 2- Fibromyalgia tender points.



A) Occiput: bilateral, at the suboccipital muscle insertions.

B) Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5-C7.

C) Trapezius: bilateral, at the midpoint of the upper border.

D) Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.

E) Second rib: bilateral at the costochondral junction, just lateral to the junctions on upper surfaces.

F) Lateral epicpndyle: bilateral, 2cm distal to the epicondyles.

G) Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.

H) Greater trochanter: bilateral, posterior to the trochanteric prominence.

I) Knee: bilateral, at the medial fat pad proximal to the joint line.

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Some criticized this scheme as being too restrictive because it focused primarily on pain while ignoring other important symptoms. Further, an estimated 80% of people with fibromyalgia actually had fewer tender points than required by this criteria[56]. As a result, in 2010, the ACR put forth a new set of criteria that included symptoms of sleep disturbance, fatigue and cognitive problems (Table 3). In place of the tender point count, patients now described 19 body regions in which pain had been experienced during the past week. Each area was given one point for a total of 19 points. The final number was referred to as the Widespread Pain Index (WPI).

The second part of the evaluation was the symptom severity score (SS). Here individuals ranked symptoms on a scale of 1-3: for example, fatigue, waking unrefreshed, memory or cognitive loss, headache, weakness, bowel problems, nausea, dizziness etc. A diagnosis of FMS was made if the following conditions were met: *a WPI of at least 7 and SS scale score of at least 5* ***OR*** *WPI of 3-6 and an SS scale score of at least 9*.

Table 3 - New American College of Rheumatology (ACR) diagnostic criteria for symptom severity (SS)

Fatigue	Waking unrefreshed	Cognitive symptoms
0= No problem	0= No problem	0= No problem
1= Slight or mild problems; generally mild or intermittent	1= Slight or mild problems; generally mild or intermittent	1= Slight or mild problems; generally mild or intermittent
2= Moderate; considerable problems;often present and/or at a moderate level	2= Moderate; considerable problems;often present and/or at a moderate level	2= Moderate; considerable problems;often present and/or at a moderate level
3= Severe: pervasive, continuous; life disturbing problems	3= Severe: pervasive, continuous; life disturbing problems	3= Severe: pervasive, continuous; life disturbing problems

In 2011, a further modification of these criteria was proposed 30 (Tables 4-5). The criteria became completely patient driven and no longer required a physician to assess the extent of the symptoms, which had been a previous component of the SS scale. Three more questions were added about abdominal pain, depression and headaches. In addition, a new FMS symptom scale was developed that added the WPI and SS scores together for a total score of 31. An FS score of 13 or higher was found to be the best predictor of FMS. Since these new criteria were primarily developed for the purpose of improving research tools for epidemiologic studies, they have not been widely adopted. In the end, the most widely used criteria for the diagnosis of FMS is that provided by the WPI and SS scales.

Table 4 - Key features of the ACR 1990 classification criteria for fibromyalgia

Widespread pain	*Tender points*
Pain in the left/right side of the body, pain above/below the waist. In addition, axial skeleton pain (cervical spine or anterior chest or thoracic spine or low back) must be present.	Pain, on digital palpation (4kg/cm2 applied over 4 seconds), must be present in at least 11 of the following 18 specified tender-point bilateral sites: occiput, low cervical, trapezius, supraspinatus, second rib, lateral epicondyle, gluteal, greater trochanter, and knee.

Table 5

ACR 2010 and modified classification criteria for fibromyalgia

Widespread pain index (WPI)
Note the number of areas in which the patient has had pain over the past week (0-19 points). The following are the areas to be considered: shoulder girdle, hip (buttock,trochanter), jaw, upper back, lower back, upper arm, upper leg, chest, neck, abdomen, lower arm, and lower leg (all these areas should be considered bilaterally).

SS scale score
Fatigue, waking unrefreshed, cognitive symptoms (e.g., working memory capacity, recognition memory, verbal knowledge, anxiety, and depression). For each of these 3 symptoms, 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 in general, indicate whether the patient has the following:

- 0= no symptoms
- 1= few symptoms
- 2= a moderate number of symptoms
- 3= a great deal of symptoms

Final score between 0 and 12

Criteria
A patient satisfies diagnostic criteria for fibromyalgia if the following 3 conditions are met:
i WPI≥ 7/19 and SS scale score≥ 5 OR WPI 3-6 and SS scale score≥ 9
ii symptoms have been present at a similar level for at least 3months
iii the patient does not have a disorder that would otherwise explain the pain

Other helpful diagnostic tests

Once the diagnosis of FMS is made, other diagnostic tests may be useful in further investigating certain specific symptoms. For instance, complaints of dizziness and heart palpitations, especially when going from sitting or lying down to a standing position, can be evaluated with a tilt table test[57] or standing test[38]. If a sustained increase in heart rate of at least 30 beats per minute is seen, this suggests a diagnosis of POTS.

Further, for individuals with cognitive dysfunction, the standard tests used to evaluate memory such as the Wechsler Memory Scale may not be sensitive enough to detect cognitive deficits in someone with FMS. In fact, individuals with FMS usually perform well on many of these standard tests. As it turns out, this is because distractions play a large role in the memory problems associated with FMS and so, when faced with a test that is administered under distraction-free conditions, FMS individuals will often perform well. To test the importance of distractions, researchers tested 35 patients with FMS and 35 patients with complaints of memory loss for other reasons as a control group[58]. When there were no distractions during the test, only 31.4% of FMS patients had difficulty with at least one of the tasks. When a source of distraction was added, that number rose to 85.7%. The test that picked up this discrepancy was the Auditory Consonant Trigram (ACT). Another test named the Stroop Test was used to reveal difficulties with reading words and naming colors that were unique to FMS patients compared to other patients with memory loss[59]. These two tests represent recent diagnostic tools that can better identify and evaluate cognitive deficits in people with FMS that previously went undetected.

What types of treatment are available for FMS?

The main goals of FMS treatment should be to relieve pain, improve sleep disturbances and physical function as well as identify and treat any co-existing disorders. In order to be maximally effective and beneficial, all approaches to management need to multifaceted and geared to each individual's physical, emotional and social circumstances. What follows is a wide range of treatment components that have been shown to be effective in managing FMS, several of which have been recommended to varying degrees in guidelines put forth by professional organisations such as the American Pain Society, the European League Against Rheumatism and the Association of Scientific Medical Societies of Germany.

Non-Pharmacological Management of FMS

o Education

It's important to seek out educational programs that offer a wide range of information about topics such as FMS symptoms, the course of the illness, associated disorders, potential causes, psychosocial factors that influence pain, the various pharmacologic and non-pharmacologic treatment options, along with self-management instructions. For instance, if you have symptoms of POTS, you can learn about the importance of avoiding aggravating factors such as extreme heat or dehydration, stopping or changing medications that could be contributing to the symptoms such as diuretics and vasodilators, and you can be encouraged to wear elastic support hose and engage in an exercise program that is properly supervised and gradual[38].

Learning about self-management strategies is an important part of any educational program. One example of a self-management strategy might centre on the area of sleep. Certain behavioural changes can be recommended that will optimize conditions for more restful sleep. For instance, you can plan on going to bed at a regular time and always sleep in your bed (avoiding using a chair for example); you can take a warm bath before going to bed, keep the room dark and private and try to maintain the room temperature constant. This is obviously just one small example of the wide range of self-management tools that can be shared

Educational programs are most effective when they are combined with other interventions. It's been shown, for example, that education in self-management leads to a better response to group exercise such as walking, strength training and stretching activities[60]. In addition, those who participate in clinical education in addition to their usual care have reported improvement in physical functioning, fatigue, stiffness, anxiety and depression. Another important facet of education is open and direct communication between you and your providers. Your expectations need to be clearly identified, so that realistic goals can be set and the response to therapy properly assessed. Openly discussing the possibility that complete pain relief may not always be achieved opens the door for considering a variety of useful strategies that can improve your quality of life and sense of emotional and physical well-being.

For instance, one study found that women who began to see pain as a warning signal that there was too much stress in their lives, found that they were better able to change goals and daily obligations in order to maintain their improved status[61]. In addition, acceptance-based approaches for pain management can be successfully used with other intervention strategies. Studies have shown that greater acceptance of chronic pain is associated with improved emotional, physical and social functioning[62]. This approach involves admitting that a cure for the pain may not occur, shifting your focus away from pain to non-pain aspects of your life and rejecting the idea that pain is a personal weakness. FMS education should therefore be an integral part of any treatment plan and has been shown to have a positive effect on symptoms and overall sense of well-being.

o Dietary changes

Many people diagnosed with FMS consider making changes in their diet and adding nutritional supplements to help manage their symptoms. In a recent survey of one hundred and one women with FMS, 30% had changed their dietary habits and most of them used nutritional supplements with the most common being magnesium[63]. An immediate benefit of changing your diet is weight loss. Being overweight can worsen FMS symptoms and obese individuals with FMS (body mass index or BMI>30) have been shown to have a higher pain sensitivity and decreased quality of life[64]. But the effects of dietary changes may have even broader implications. Because chronic inflammation and oxidative stress may be important contributors to the development of FMS, diets rich in antioxidants may provide a number of benefits. Individuals eating vegan diets based on uncooked living food have reported improvement in joint stiffness and pain and also showed higher levels of beta- and alfa-carotenes, lycopen and lutein, vitamin C and E in their serum compared to those eating a regular diet[65].

Vegetarian diet

Studies have also shown that this kind of dietary intervention is beneficial in FMS. For instance, eating a raw, pure vegetarian diet consisting of fruits, salads, carrot juice, tubers, grain products, seeds and dehydrated barley grass juice for seven months led to significant improvements in almost all symptoms except body pain[66]. Another study however, found that when compared to antidepressant medication, a six-week intervention of a vegetarian diet did not improve fatigue, insomnia or sleep[67]. These latter results may suggest that a six-week dietary intervention may not be long enough to see noticeable differences in symptoms.

Avoiding certain substances may also be of benefit. Monosodium glutamate (MSG) and aspartame are thought to potentially act as excitatory neurotransmitters that may be toxic to nerve cells when used in excess. While MSG is usually associated with Chinese restaurant food, it can also be found in many common food products such as canned soup, beef and chicken stock, frozen dinners, fast foods and instant meals such as seasoned mixtures of instant noodles. In a small study of just four patients with FMS, eliminating these products from their diet led to a complete resolution of symptoms within months[68]. More studies are obviously needed with larger groups of individuals to confirm these results.

Nutritional and vitamin supplements

What about the impact of certain nutritional deficiencies? Vitamin D levels have been reported to be lower in individuals with FMS[69]. However, whether low vitamin D levels are directly linked to musculoskeletal pain is unknown [70] and more studies are needed to determine how vitamin D deficiency may be impacting FMS symptoms. Some, [48,71] but not all studies [47,72] have shown decreased levels of trace elements like magnesium, zinc and selenium in individuals with FMS.

What about the impact of certain nutritional deficiencies? Vitamin D levels have been reported to be lower in individuals with FMS[69]. However, whether low vitamin D levels are directly linked to musculoskeletal pain is unknown [70] and more studies are needed to determine how vitamin D deficiency may be impacting FMS symptoms. Some, [48,71] but not all studies [47,72] have shown decreased levels of trace elements like magnesium, zinc and selenium in individuals with FMS. These elements are very important in maintaining the oxidant/antioxidant balance in the body and taking vitamin C, E and magnesium supplementation may be of possible benefit[73]. Lower levels of melatonin have been found in individuals with FMS and melatonin replacement has been reported to reduce complaints. Since melatonin has a good safety profile, the authors of this study recommended using it as a treatment that may help with sleep disturbances, especially when a deficiency is found[74]. Though the number of reliable studies is limited, there is evidence that nutritional supplements may be beneficial in improving FMS symptoms. Further, they have been generally found to be safe with mild side effects.

5-HTP or 5-hydroxytryptophan is a chemical that the body makes from an essential amino acid called tryptophan. Once tryptophan is converted to 5-HT, it is changed to serotonin, a neurotransmitter that enhances communication between brain cells. While tryptophan is found in the foods we eat, it is difficult to increase 5-HT levels by diet alone, which is why a supplement, made from the seeds of an African plant called Griffonia simplicifolia has been made available. 5-HT is often used to treat depression and has also been investigated to a limited extent in FMS. Two studies and one review have suggested the 5-HT improves a number of FMS symptoms when given alone or in combination with certain antidepressants [75-77]. In one double-blind study of 50 people with FMS, taking 300 mg per day of 5-HT for 30 days led to decreased pain and tender points along with improved sleep, morning stiffness, anxiety and fatigue when compared to those individuals who were taking placebo[78]. Side effects associated with 5-HT are mild, short term and usually are limited to digestive problems and possible allergic reactions.

Chlorella pyreinoidosa is a single-cell green algae that grows in fresh water. It has the highest concentration of chlorophyll of any known plant and is also rich in protein, vitamins, minerals and other essential nutrients. As a dietary supplement, it has been linked to anti-cancer activity, promotion of growth and healing, and stimulation of the immune system. In a small but well-designed double-blind trial, 37 participants with FMS were randomised to receive 10 gram chlorella tablets and a 100 ml extract or placebo plus extract, daily for three months[79]. More participants taking chlorella versus placebo reported a decrease in pain associated with tender points and improved functionality. In addition, for some subjects, deep sleep and anxiety also improved. Chlorella also appears to be safe with no toxic effects reported in animals or humans. Mild gastrointestinal symptoms such as loose bowels, cramping or nausea have been reported with preparations that include broken cell walls.

Acetyl-L-carnitine (ALCAR or LAC) is a nutritional supplement that is synthesized in order to help the body make more of a chemical called L-carnitine. Carnitine plays an important role in energy production within cells and LAC has been used to help manage a wide range of conditions such as depression, memory loss and stroke. It also acts as an antioxidant and may provide potential benefits for the central nervous system and heart. The main dietary source of carnitine is from red meat, especially mutton. Symptoms of carnitine deficiency include weakness, fatigue and exercise intolerance. While these are also common symptoms among people with FMS, it is not known whether carnitine deficiency is actually a feature of FMS. Still, in a double-blind trial, 102 patients with FMS were randomised to receive 1500 mg daily of LAC for eight weeks or placebo (following a two week protocol of oral and intramuscular LAC or placebo). Both groups reported an improvement in symptoms. However, those receiving LAC found that the decrease in tender points, depression and pain persisted for a longer period of time[80]. LAC was well tolerated in this study. In general, side effects are mild and include nausea, vomiting, abdominal cramps and headache.

Super Malic is a nutritional supplement that is a combination of magnesium, an essential mineral, and malic acid, a substance that is made by the body and also found in apples and other fruits. Evidence that Super Malic alleviates FMS symptoms is limited. One small study reported beneficial effects of Super Malic in relieving muscle pain. This trial was carried out in two phases. Twenty-four patients with FMS were randomised to receive 200 mg of malic acid and 50 mg of magnesium or a placebo[81]. The first phase of the study lasted four weeks and was carried out in a blinded fashion so that the participants did not know whether they were taking placebo or Super Malic. At the end of this phase, there were no significant improvements in either group. In the second phase of the study, participants knew what they were taking and were allowed to increase the dose as needed. After six months, the group taking Super Malic reported significant improvement in the severity of pain and tenderness. Only mild gastrointestinal side effects were reported.

SAMe or S-adenosylmethionine is derived from an amino acid called methionine and adenosine triphosphate (ATP) and is commonly used to treat depression and osteoarthritis. Though the body makes all of the SAMe that it requires, deficiencies in methionine, B-12 and folate may decrease SAMe levels. Three out of four double-blind trials found SAMe to be helpful in improving symptoms of FMS. In most of the trials, the supplement was given intravenously or by muscle injection, sometimes in combination with pills[82-85]. In one trial, 44 people with FMS took 800 mg tablets of SAMe or placebo for six weeks[84]. Those taking SAMe reported improvements in disease activity, mood, pain at rest and morning stiffness. SAMe appears to be quite safe as determined in human and animal studies with the most common side effect being stomach or digestive distress.

Collagen, **ascorbigen** and **co-enzyme Q10** with **Gingko biloba** have also been shown to be beneficial in reducing symptoms such as pain and improving quality of life [80,84,86-89]. In a very small randomised study, those who used topical capsaicin (found in cayenne peppers) in addition to their regular medical treatment reported significant improvements in pain compared to those taking a placebo[90]. And though two thirds of participants who took **D-ribose** daily for three to four weeks reported significant improvement in FMS symptoms [91], this study was not randomised and no placebo was used.

In summary, the evidence to date suggests that adopting a vegetarian diet, losing weight, and using nutritional supplements may improve symptoms of FMS. While some deficiencies in trace minerals such as magnesium, selenium, zinc and lower levels of vitamin D and melatonin have been reported in individuals with FMS, it is unclear how much these contribute to the disorder. Lastly, it is important to work together with your healthcare provider before using nutritional supplements and you should both carefully review the evidence regarding the potential benefits, risks and importantly, possibility of dangerous interactions with other medications that you may be taking.

o Exercise

Which forms of exercise are beneficial for fibromyalgia syndrome?

Aerobic exercise and strength training have been most consistently linked to improvements in FMS symptoms. In 2010, a review of 28 randomised controlled trials found that exercise, practiced two to three times per week for at least four to six weeks reduced pain, fatigue, depressed mood and improved quality of life, though there did not appear to be a significant effect on sleep disturbances[92]. The exercise level needed to be at least of moderate intensity and consistently maintained in order for the positive effects on pain to persist. It is not necessary to stick to only one form of exercise, as a combination of aerobic exercise, strengthening and flexibility has also been shown to improve physical and mental health[93]. The exercise program must be tailored to your baseline level of fitness and must take into account the severity of your symptoms, so that you will not be discouraged or harmed. Group exercise may be better than home-based programs because of the increased supervision that is often available. If you have a good baseline physical level of functioning, you may be able to participate in group exercise programs offered to healthy individuals. If your functional level is more limited, however, you should start very gradually with walking, stretching and other low effort activity.

There are types of mind body exercise that have also been found to be beneficial in reducing FMS symptoms. **Tai Chi,** for one, is a form of ancient Chinese martial arts that combines slow, graceful, purposeful movements with controlled breathing and relaxation. It works by redistributing the body's vital energy termed "qi". Individuals with FMS who participated in twice weekly 90 minute sessions for 12 weeks that was based on an eight-form Yang style program[94] had significant improvements in pain, sleep, functional mobility and balance compared to those who were enrolled in an educational program alone[95]. The improvement in functional mobility also suggests that Tai Chi may be helpful in decreasing falls and improving performance of daily tasks[96].

A particular form of **Qigong**, Chaoyi Fanhuan Qiqong[97] has also been associated with improved pain, sleep, physical and mental function in individuals with fibromyalgia[98]. In this randomised trial, participants practiced at home for 45-60 minutes for eight weeks. The important observation here was that the benefits extended even beyond the end of the program.

Water exercises and **balneotherapy** – spa bathing - also have a place in FMS therapy. There is no clear consensus that water exercises are more beneficial than land exercises, though many of the studies have not provided sufficient information about the details of the water therapy to really compare the outcomes[99]. In balneotherapy, natural mineral and thermal waters or mud application is often used. Four randomised trials have concluded that there is a benefit to balneotherapy[100].

It's not clear exactly how this therapy relieves chronic pain, but hot stimuli is known to increase the pain threshold in nerve endings. The pain relief may therefore be due to the effects of the water temperature combined with the hydrostatic pressure on the skin. Spa therapy also leads to the release of beneficial hormones such as adrenocorticoptropic hormone (ACTH), prolactin and growth hormone (GH). Since FMS seems to involve dysregulation of the hypothalamic-pituitary-adrenal axis (HPA) that oversees the production many of these hormones, it may explain why spa therapy is beneficial.

Principles for prescribing and starting an exercise program

Even in the face of evidence that supports the benefits of exercise, poor compliance with exercise recommendations is the biggest obstacle to having those benefits realised in the lives of individuals with FMS. In fact, it has been reported that 83% of individuals with FMS do not engage in aerobic exercise and the majority of those tested have below-average fitness levels. Shockingly, the average 40-year old with FMS has been found to be as physically unfit as an 80-year-old without the disorder[101,102]! There are several physiologic reasons for the difficulties that someone with FMS must overcome in order to engage in and sustain an exercise program. Pain and fatigue are some of the biggest challenges and there are a several observations that might explain why these symptoms may be aggravated when someone with FMS begins an exercise program. Normally, exercise is thought to decrease pain because the body increases its production of endorphins (a natural analgesic) and activates the descending inhibitory pain pathways that blunt the impact of painful signals[103,104]. There is evidence that special type of receptors in the brain called μ-opioid receptors that bind endorphins may be saturated in individuals with FMS making them less responsive to these natural analgesics[105].

As a result, pain may be felt more acutely. In addition, while muscle contraction in healthy individuals leads to inhibition of pain perception through the descending inhibitory pain pathways, this does not occur in individuals with FMS [106]. Quite the opposite, a sustained muscle contraction in FMS results in an increased response to painful stimuli or hyperalgesia.

Abnormalities in the stress response system may also explain why exercise can be poorly tolerated in FMS. Low blood pressure, fatigue and orthostatic tachycardia, a rapid heart rate when suddenly assuming an upright position, are manifestations of this dysfunction. In addition, growth hormone, which is important for repair of muscle damage, does not increase as much in response to exercise in individuals with FMS[107]. So muscles may feel sore for longer. And finally, when an individual's exercise program is in excess of what they can reasonably tolerate, the immune system produces chemicals called inflammatory cytokines that result in a 'sickness syndrome' leading to extreme fatigue [108,109].

Given these limitations, any exercise program that you may wish to undertake needs to be individualised to order to take into account the physiologic obstacles that you may be facing. One recommendation is that an exercise program should be undertaken only after several components of the medical management have been optimised such as education, nutrition, medications or supplements and after any co-existing medical conditions have been evaluated and treated. A general recommendation is that if you are a sedentary person with moderate to severe FMS, aerobics should be the last step in a progression of exercises. You may benefit more from starting with breathing exercises, posture and relaxation, followed by flexibility and then strength and endurance training[110].

Finally, adopting a set of helpful principles before prescribing or starting an exercise program is likely to increase the chances of success of both sustaining the regimen and achieving your goals (see Table 6).

Table 6 - Ten principles for prescribing exercise in fibromyalgia [110].

Principles for prescribing exercise in fibromyalgia
1. Treat peripheral pain generators to minimise central sensitisation
2. Minimise eccentric muscle work i.e. muscle lengthening against resistance
3. Program low-intensity non-repetitive exercise
4. Recognise the importance of restorative sleep
5. Screen for and treat autonomic dysfunction
6. Evaluate for risk of poor balance and risks for falling
7. Modify exercise for common comorbidities (central sensitivity syndromes)
8. Address obesity and deconditioning
9. Conserve energy daily to exercise

o Acupuncture

Acupuncture is one of the oldest forms of therapy in traditional Chinese medicine. Sharp, thin needles are inserted into the body at specific points such that the body's energy flow is adjusted and altered to flow in healthier patterns. Acupuncture has been used for a variety of illnesses and is widely used in the United States especially for pain relief [111]. The U.S. National Institute of Health (NIH) concluded that acupuncture could be a useful adjunct as part of a comprehensive management program for people with FMS[112].

Three randomised trials have investigated the effectiveness of acupuncture in FMS. In one study, acupuncture was added to the standard treatment of antidepressants and exercise in 58 women with FMS[113]. Acupuncture sessions were given twice weekly for a total of 20 sessions lasting 20 minutes. Three months following the end of treatment, those who received acupuncture had significant improvements in pain with a decreased number of tender points. However, these improvements were no longer evident at the 2-year mark suggesting that treatment may need to be repeated. Acupuncture treatments not only decreased pain, but also lead to greater improvement in fatigue and anxiety[114], even when compared to treatment with an antidepressant[115]. Acupuncture appears to be a safe treatment for a number of symptoms associated with FMS. If acupuncture is something that you would like to consider, it is important to find a trained professional with experience in treating chronically painful disorders like FMS.

o Psychological therapy

Emotional distress is often cited as one of the top six most common exacerbating factors of FMS symptoms[116]. Mental stress, worrying, chronic stress and emotional trauma are common triggers[27], along with psychological vulnerability to stress and a frightening stressful cultural environment[117]. A number of psychological treatment modalities have been shown to be beneficial in improving FMS symptoms, enhancing coping strategies and quality of life and should be an integral part of FMS management.

Cognitive-behavioural therapy

Cognitive-behavioural therapy (CBT) and operant-behavioural therapy (OBT) are two forms of psychotherapy that have been used to help manage FMS. CBT is a form of psychotherapy that focuses on changing negative emotions that lead to dysfunctional thinking and changing behaviour patterns that contribute to poor coping strategies. In general, the goal of CBT is to reduce negative emotions and pain perception while increasing self-efficacy, physical functioning and coping strategies. The aim of OBT is to reduce painful behaviour (that is often reinforced by other's reaction to the demonstration of pain) and to reinforce alternative, healthier behaviours. Physical exercise also tends to be a part of an operant learning program[118]. Randomised clinical trials have shown that CBT leads to improvements in coping with pain, reduces depressed moods and decreases health-care seeking behavior in individuals with FMS[119]. In this review, however, there appeared to be no significant effect of CBT on the pain itself, fatigue, sleep or health-related quality of life. In contrast, ten out of 14 randomized controlled trials evaluating CBT and OBT in the management of FMS did demonstrate significant improvement in measures of pain intensity, disability and mood with half of the studies reporting positive effects that were maintained at six months[120]. Approximately half of the individuals reported at least a 50% reduction in pain, six to twenty-four months after therapy had been discontinued. How well people responded to therapy depended to some extent on the degree of physical and functional impairment before treatment. Those with lower levels of physical impairment before treatment responded the best, while those with high levels of physical impairment were actually at some risk of deteriorating after therapy[121]. This underscores the importance of ensuring that therapy is tailored to meet individual needs and that appropriate follow-up is carried out.

Cognitive Hypnotherapy

Cognitive hypnotherapy has been used for pain management in a number of disorders[122]. This approach typically involves hypnotic induction using suggestions for changes in perception, behaviour and coping. In addition, the individual is often taught how to use hypnosis to reduce pain throughout their daily life. In a Dutch randomised controlled trial, 40 individuals with FMS who received 8 one hour sessions of hypnotherapy for three months reported reduced pain intensity and fatigue and improvement in their sleep pattern, compared to those who received massage only[123]. In a study comparing hypnotherapy to physical therapy, those individuals enrolled in hypnotherapy showed superior results in the areas of improved muscle pain, fatigue, sleep disturbance and their own overall assessment of the outcome[124]. Hypnosis has also been shown to be superior to relaxation for the treatment of FMS pain[124]. Guided imagery may also be useful in managing pain and anxiety[125], improving quality of life and reducing psychological symptoms[126]. In spite of the limitations that have been identified in several studies[127], both hypnosis and guided imagery have been recommended as adjuncts to both pharmacological and non-pharmacological treatments in the guidelines put forth by the Association of Scientific Medical Societies of Germany[128].

Relaxation training

Relaxation training alone has not been shown to be as effective for pain reduction in FMS when compared to CBT, hypnotherapy, bath or massage therapy[129-131], though it is recommended as part of a multicomponent therapy. In terms of biofeedback, the results of studies are varied. Some studies describe benefits in terms of pain, depression and general quality of life[132], while others report long-term improvement in sleep and depression (after two years), but no effect on pain[133]. Both the American Pain Society and the Association of the Scientific Medical Societies of Germany do not recommend single therapy biofeedback.

Written emotional disclosure

Written emotional disclosure (ED) is a psychological intervention that has been shown to yield health benefits in several different populations including those with FMS. Initial studies in healthy college students found that those who were randomly assigned to disclose their deep thoughts and feelings about some personal trauma showed a drop in visits to the health center, decreased symptoms and improved psychological well-being[134,135]. ED has also been shown to have detectable benefits on the immune system[136,137]. Because surveys have shown that the rates of abuse, trauma and injury are higher in individuals with FMS[138], researchers have investigated whether written ED might be effective in reducing symptoms in this population. In a study in which 92 patients with FMS were randomised to a trauma-writing group, a control writing group or usual care, the trauma-writing group reported significant reductions in pain, fatigue and improved psychological well-being four months after the writing intervention[139]. The writing groups wrote for 20 minutes, once a week for three weeks. At a 10-month follow-up, however, the benefits were not maintained suggesting that the writing intervention needs to be repeated and incorporated into a total model of care. It is also interesting that the improvements were not immediately visible. The emotional benefits did not surface until three to four months after the intervention. In fact, a negative mood tended to ensue immediately after the writing intervention. Guidelines from both the American Pain Society and the Association of the Scientific Medical Societies of Germany recommend writing interventions as an adjunct to CBT/OBT, exercise and pharmacotherapy.

You should be carefully evaluated before undergoing any form of psychological therapy, since the efficacy of a chosen treatment depends on a number of variables. For instance, individuals that are less physically impaired tend to respond well with decreasing pain to behavioural methods; while those with more severe physical impairment are more likely to have improvements in their overall level of physical impairment rather than in the area of pain. One study reported that those who report low pain intensity, high emotional distress and more physician visits, may even develop worse physical impairment after psychotherapy[140].

Pharmacological Management of FMS

As we have seen, the pathways involved in pain and other symptoms associated with FMS are complex. In considering the role of drug therapy, it is important to note that no single class of medication will work for everyone. The classes of drugs most commonly used include antidepressants, analgesics, anti-epileptic, muscle relaxants and sedatives/hypnotics.

Analgesics

Though non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently used medications to treat FMS, there is little evidence that they are effective. Ibuprofen and naproxen, for instance, were found to be no more effective than placebo[141]. Nonetheless, in a survey of 1042 patients, 66.1% thought that NSAIDs were more effective than acetaminophen[142] There is also some evidence that NSAIDs may be more effective when taken in combination with medications such as tricyclic antidepressants and anticonvulsants[143]. One reason why NSAIDs and acetaminophen may be less effective is because they act primary through mechanisms that don't really target central pain, but rather work peripherally.

Nevertheless, given the complex nature of FMS, there are still likely to be individuals with 'peripheral' components to their symptoms or who have other co-existing inflammatory conditions that would respond to NSAIDs or acetaminophen. The use of opiate analgesics is generally not recommended for the treatment of FMS[10,12,144]. In addition to the limited number of randomised trials,[145] opiates have well known side-effects that include cognitive dysfunction, constipation, the development of tolerance requiring larger and larger doses and addiction. Opiates have been shown to increase pain sensitivity[146]. Yet despite these observations, a recent survey with 2 596 respondents showed that hydrocodone and oxycodone preparations were among the most consistently used medications and were felt to be the most effective[27].

Tramadol is an analgesic with both opioid and antidepressant properties that is indicated for short-term management of pain (i.e. 5 days). It is also not a controlled substance. The most common side effects that limit how well it is tolerated, are nausea and skin rashes, though the nausea can be lessened when it is combined with acetaminophen [147].

It should also be used with caution with any other medications that lower the seizure threshold. Tramadol 's primary benefits have been in alleviating pain, improving sleep and physical function in individuals with FMS [148,149]. Though it has been recommended by EULAR, it is not approved by the U.S. Federal Drug Administration (FDA) for treatment of FMS.

Antidepressants

There are currently two antidepressants approved by the U.S. FDA for the treatment of FMS: duloxetine and milnacipran. These antidepressants belong to the class of drugs called serotonin-norepinephrine reuptake inhibitors (SNRIs). Both medications have been shown in randomised, blinded, controlled trials to improve the pain associated with FMS[150]. Duloxetine is often considered in patients with significant depression[151] and milnacipran may be helpful when significant fatigue or cognitive dysfunction are present[152]. Nausea, insomnia, headaches are common side effects which may limit their use.

Amitriptyline has been shown to be most effective in terms of improving sleep quality, with modest improvement reported in stiffness and tenderness[153]. Side effects such as sedation, dry mouth and constipation make it poorly tolerated at high doses so that smaller doses are often taken at bedtime. Further, when there is a history of heart, kidney or liver disease, it should be used with caution[147].

Anticonvulsants

Pregabalin is an anticonvulsant approved by the U.S. FDA for the treatment of FMS. In a double-blind placebo controlled trial, pregabalin effectively decreased pain[154], though it had significant side effects such as weight gain, dizziness, sleepiness or insomnia, swelling, nausea and anxiety.

Sedatives

Sodium oxybate is derived from a compound called gamma-hydroxybutyrate (GBH) that acts as a neurotransmitter that influences the activity of neurons in the central nervous system. It also stimulates the release of growth hormone. In randomised trials, sodium oxybate significantly improved sleep, pain and fatigue in FMS patients[155]. In spite of these results, in 2010 it was not approved by U.S. FDA for treatment of FMS, primarily because of concerns about abuse. Common side effects include headache, nausea, dizziness and sleepiness.

Pharmacologic management of POTS

The U.S. FDA has not approved any specific drug for the management of POTS and there have not been any studies that have properly evaluated pharmacologic management. Medications such as, udrocortisone that help to correct low blood volume, propranolol that blunts the rapid increase in heart rate and midodrine that constricts blood vessels, have all been used. Octreotide is another class of medication that has been used in treating POTS[156], but side effects of abdominal pain and diarrhoea have limited its use. In general, about 40-60% of those treated with medications for PTOS experience improvement in their symptoms[38] .

General principles of therapy

The main goal of therapy for individuals with FMS should be aimed at improving function, decreasing symptoms and fostering the development of healthy coping strategies for dealing constructively with a chronic illness. The choice of treatment options needs to be carefully reviewed by you and your provider and should be based on a clear understanding of the risks, benefits and costs. The results of a chosen comprehensive treatment approach need to be carefully monitored on a regular basis to ensure that the benefits outweigh the risks and that progress is being made. Many of the active treatments such as various forms of exercise, psychological support and dietary changes can be continued long term and in several cases have been proven to be superior to standard medical treatment[11]. In some cases, the positive effects of these active treatments persist even after the end of therapy. In contrast, according to Association of the Scientific Medical Societies, evidence supporting the benefits of pharmacological agents has been mostly studied for up to six months. Therefore, the decision to continue medications should only be considered if you and your doctor see persistent benefits at regular check-ups[11] and consideration should be given to a drug holiday after six months[157].

Working with fibromyalgia

One of the common challenges and sources of stress for individuals with FMS surrounds the issue of work. If you are still in the work force, trying to balance the demands of the job with new physical limitations can be daunting. Feelings of isolation, frustration and hopelessness are not uncommon. This is where education both for the employee and employer can offer helpful guidelines[158]. A first step is to get a clear assessment of the limitations that you are experiencing and how they affect your job performance. Consider discussing FMS with your employer and providing him/her with pamphlets to better acquaint them with the disorder.

A well-informed employer will usually be more willing to implement certain accommodations to fit your needs, many of which are simple and inexpensive. For example, a simple workstation analysis by an occupational therapist can establish good ergonomic habits that may ease symptoms.

- For office workers, adjustments can be made to the position of the keyboard, monitor and mouse on the computer. Chairs can be adjusted or new chairs purchased to ensure that your legs are at a 90-degree angle to the floor, and your arms at a 90-degree angle to the keyboard. Telephone headsets, anti-glare computer screens, portable angle writing surfaces, document holders and forearm supports for typing are just a few of the useful tools available.
- For individuals working in factories, a padded floor mat and a nearby stool, where periodic rests can be easily taken, can reduce fatigue. Also, using padded gloves can decrease excessive vibrations.
- For individuals with fine motor impairment, using built-up pens, light pressure pens, large calculators and light touch keyboards, may be of benefit. You should inquire about closer parking spaces, automatic door openers and the possibility of placing your workstation close to frequently used areas such as copiers, lunchrooms and restrooms.

You might also inquire about altering break schedules, flexible working hours and even working from home for part of the week. There are also a number of simple behavioural changes that you can adopt to help alleviate symptoms in the workplace. Giving your body a break by taking time for walking and stretching to alleviate muscle strain and pacing yourself by switching between large and small tasks are two simple adjustments that can have enormous benefits.

Being diagnosed with FMS can also present an opportunity to re-evaluate your situation and consider a complete career change. As one author stated after realising that chronic pain had derailed her career aspirations in academia, "The first step is to accept your current circumstances rather than torturing yourself with comparisons of where you once were and would have liked to be… Acceptance can be liberating " [159]. Focusing on what you *are* able to do and exploring things that you enjoy will often lead to new opportunities. Some general guidelines are to look for work that is meaningful to you, low stress, flexible and comfortable. Sources such as online searches, friends, previous colleagues, libraries and self-help books can provide a wealth of information. Professionals such as occupational therapists can suggest adaptive changes that may be needed in your work environment and career counsellors and life coaches can help you to evaluate different options and offer support. With the technology available today, many fields such as consulting work, online businesses and freelance work can be managed from home.

Online interventions in fibromyalgia

The use of modern information technology in the area of healthcare has made it possible to deliver a number of innovative strategies for designing interventions that provide education, support and interactive services to individual patients. These services cannot only delivered through home computers, but also through tablets and smart phones. Though a review of online FMS resources concluded that most were of low quality and failed to provide accurate, comprehensive information[160], there have been a few projects that have yielded useful information.

In 2008, an internet-based adaptation of the Arthritis Self-Management Program (ASMP), designed for patients who could not attend small groups, was evaluated and found to be effective in changing health-related behaviours[161]. Though primarily geared towards patients with arthritis, patients with FMS also participated. The program included education on symptoms, fatigue management, doctor-patient communication and problem solving and required participants to log in at least three times for a total of one to two hours. Several other reviews of online programs that have targeted patients with rheumatoid arthritis, osteoarthritis and FMS have reported that participants had improvements in pain, global health, physical functioning and self-efficacy[162-164]. In 2012, an internet-based intervention for people with FMS was developed, called "SMARTLog" or SMART self-monitoring and review tool. Participants logged in to record daily activities, health-related behaviors, stressors and symptom levels. This information was then used to build a personal database. Data was then analysed in order to identify which personal behaviours predicted changes in symptom levels and this information was shared with the participant. Individuals who participated at least three to 4.5 times per week, over three to five months had significant improvements in pain, memory, gastrointestinal problems, depression, fatigue and concentration[164].

The SMARTLog program should be available in the near future at www.collinge.org. These programs are likely to become increasingly popular if they continue to demonstrate effectiveness and patient satisfaction. Fibromyalgia syndrome is a complex, debilitating disorder that affects millions of people worldwide. In addition to its impact on individual quality of life, nations are becoming increasingly aware of the staggering healthcare costs and loss of productivity associated with this disorder. Over the years, research has begun to shed light on some of the factors that may be underlying FMS symptoms and we are gaining a greater appreciation of the benefits that various non-pharmacologic and pharmacologic treatments and therapies have to offer.

The approach to treatment should entail careful individual evaluation and should encourage your active participation in designing a comprehensive plan. The guidelines put forth by the Association of the Scientific Medical Societies of Germany can provide a good source of information regarding the wide range of treatment options that are likely to be effective (Tables 7-9). Finally, there is increasing recognition that simple changes can be made in the workplace to address any number of potential limitations that you may be facing. And while a career change is always an option, you and your employer both should freely consult professional sources for information on a wide array of inexpensive adaptations that can be easily incorporated into the work environment. Information technology may be providing innovative, effective and easily accessible programs with the potential to yield measurable benefits for those coping with FMS.

Table 7 - Treatments with strong recommendations for the management of adult fibromyalgia syndrome

Therapy	Strength of consensus
Patient education	
Information on diagnosis and therapeutic options	Strong
Patient education within multicomponent therapy	Strong
Patient-centered communication	Strong
Exercise	
Aerobic exercise	Strong
Psychotherapy	
Cognitive-behavioral therapy (CBT)	Strong
Multicomponent therapy	
Multicomponent therapy	Strong
Pharmacological therapy	
Amitriptyline	Strong

Table 8 - Recommended treatments for the management of adult fibromyalgia syndrome

Therapy	Strength of consensus
Physiotherapy and physical therapy	
Balneo- and spa therapy	Strong
Whole body heat	Strong
Psychotherapy	
Hypnotherapy/guided imagery	Consensus
Written emotional disclosure (ED)	Strong
Pharmacological therapy	
Fluoxetine	Strong
Paroxetine	Strong
Duloxetine	Strong

Table 9 - Treatments with open recommendations for the management of adult fibromyalgia syndrome

Therapy	Strength of consensus
Physiotherapy and physical therapy	
Whole body cold therapy	Consensus
Low energy laser	Consensus
Magnet field therapy	Consensus
Ultrasounds and electrotherapy	Consensus
Lymph drainage	Consensus
Osteopathy	Consensus
Transcranial magnet stimulation	Consensus
Physiotherapy	Consensus
Functional training	Strong
Occupational therapy as part of multicomponent therapy	Majority
Psychotherapy	
Relaxation training as part of multicomponent therapy	Strong
Psychodynamic therapy	Majority
Pharmacological therapy	
Cyclobenzaprine	Strong
Sertraline	Strong
Tramadol or Tramadol/Aminoacetophen	Strong
Pregabalin	Strong
Tropisetron	Consensus
Pramiprexol	Consensus
Complementary and alternative therapies	
Homeopathy	Consensus
Vegetarian diet	Consensus
Elimination diet	Consensus
Acupuncture as part of multicomponent therapy	Consensus
Tai-Chi, Qi-Gong as part of multicomponent therapy	Strong
Music therapy as part of multicomponent therapy	Strong
Body therapies (Body-awareness, Feldenkrais, music therapy) as part of multicomponent therapy	Strong

Resources

National Fibromyalgia Association (NFA)-non-profit
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Glossary of terms

Adrenal insufficiency: a condition where the adrenal glands that are located above the kidneys do not produce enough steroid hormones.

Central nervous system: part of the nervous system that consists of the brain ad spinal cord.

Cerebral spinal fluid: a clear fluid that surrounds the brain and spinal cord.

Cortisol: a hormone that is made in the adrenal glands

Double-blind trial: an experimental study in which neither the individuals participating in the experiment nor the person administering the intervention know which intervention is being evaluated i.e. a placebo versus a medication.

Glial cells: cells in the nervous system that surround nerve cells or neurons and have a supportive and protective function. Unlike neurons, they do not conduct electrical impulses.

Growth Hormone: a hormone secreted by the pituitary gland that promotes growth, cell reproduction and regeneration.

HPA-hypothalamic-pituitary-axis: a network that includes the hypothalamus and pituitary located in the brain and the adrenals, located above the kidneys, that regulates a complex network of hormonal activity.

Hypothyroidism: a condition in which the thyroid gland does not make enough thyroid hormone.
Interstitial cystitis: long term inflammation of the bladder wall.

Mitochondria: structures located within cells that provide the energy the cell requires in order to carry out its many functions.

Norepinephrine: also known as noradrenaline, is a hormone and neurotransmitter that is important in the 'fight or flight response' and affects many aspects of the cardiovascular system.

Neurotransmitters: chemicals that transmit signals from neurons to other cells in the body.

Peripheral nervous system: part of the nervous system that lies outside of the brain and spinal cord.

Prostatitis: inflammation of the prostate gland.

Serotonin: also known as 5-hydroxytryptamine is a neurotransmitter that is found in the gastrointestinal tract, blood cells called platelets and in the central nervous system.

Sympathetic nervous system: one part of the autonomic nervous system (the involuntary nervous system) that regulates the 'fight or flight response' and is important for maintaining homeostasis.

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