

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF MEDICALLY UNEXPLAINED SYMPTOMS (MUS): CHRONIC PAIN AND FATIGUE

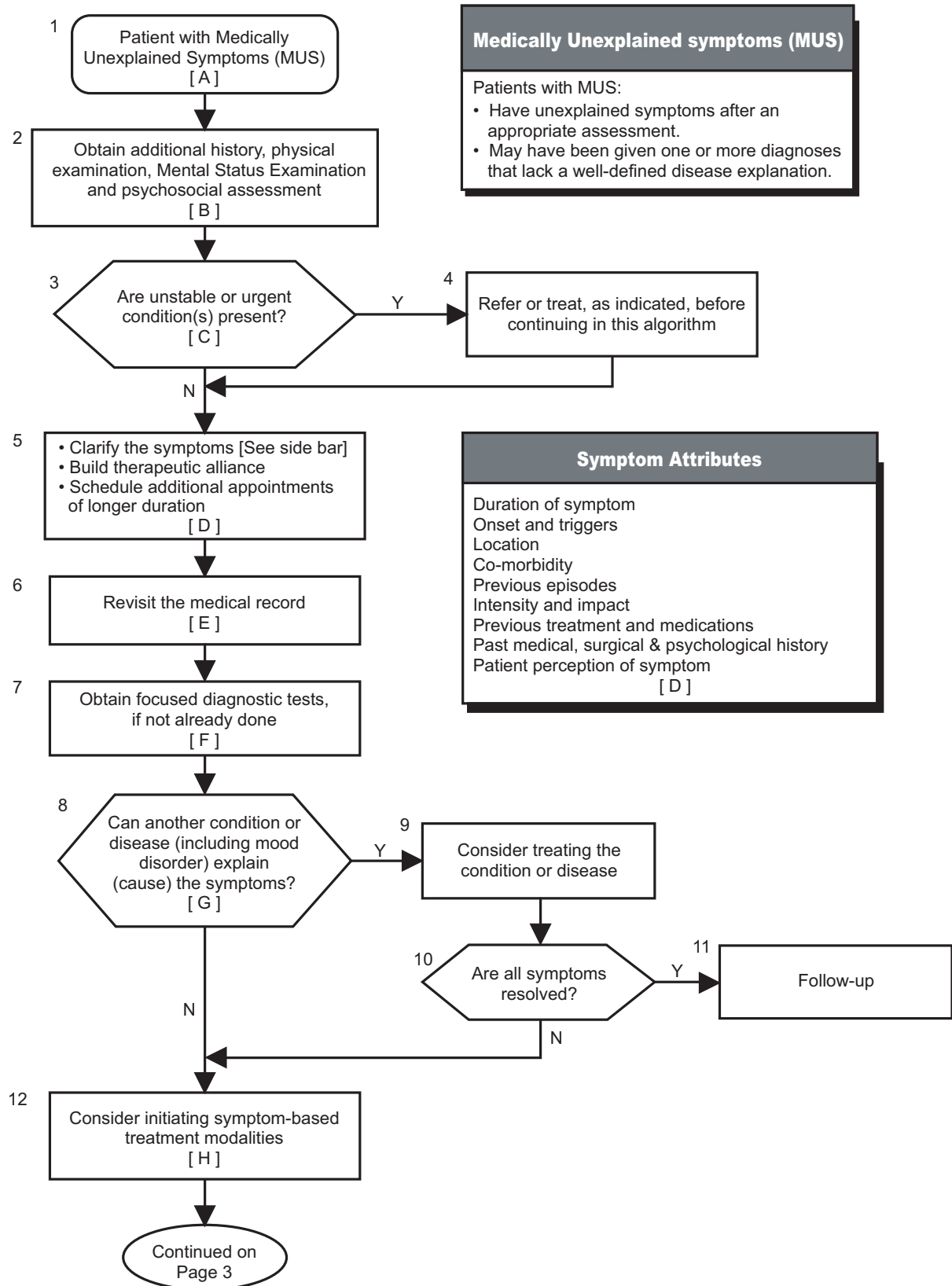
Guideline Summary

PRIMARY CARE

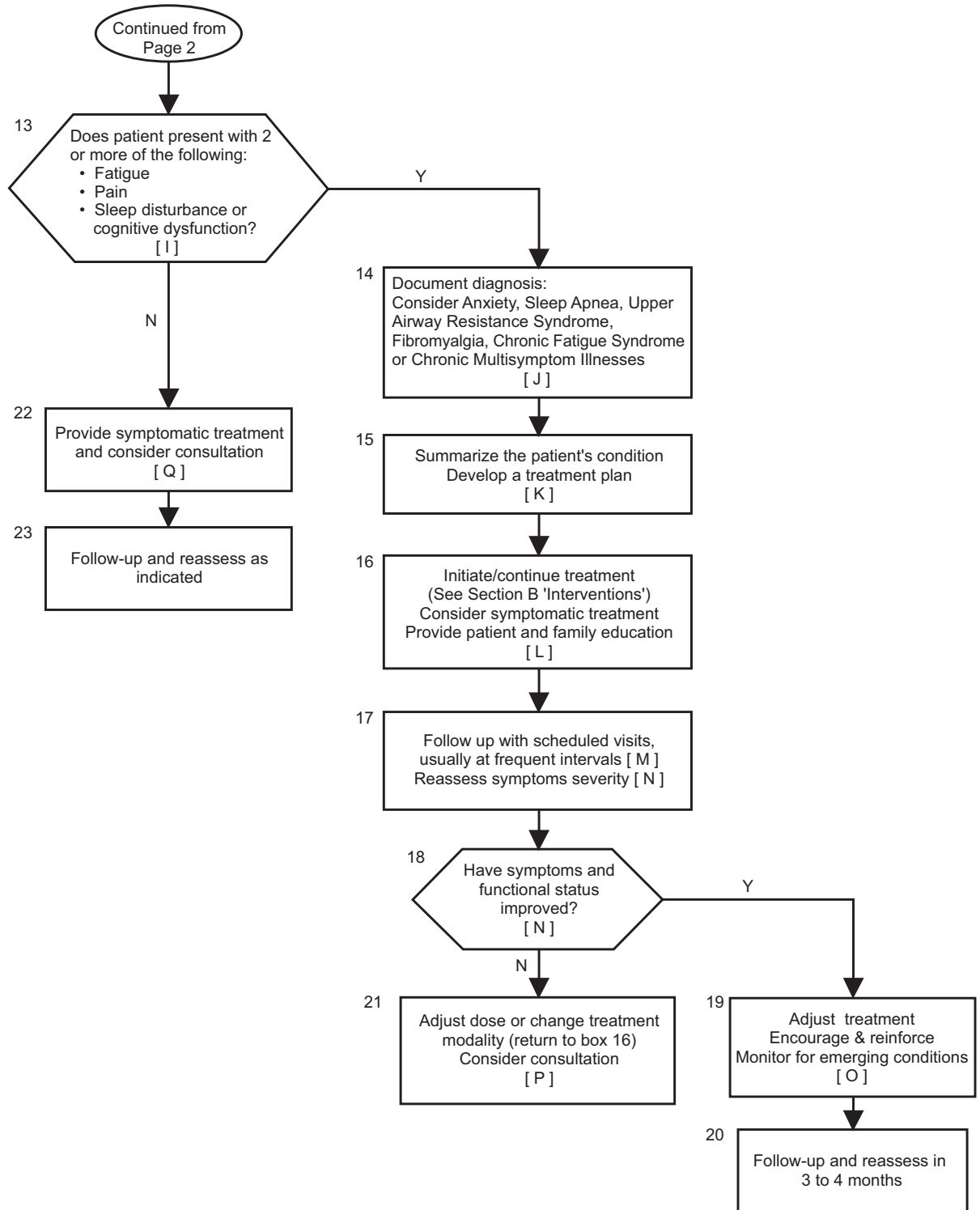
GUIDELINE SUMMARY

- Establish that the patient has MUS.
- Obtain a thorough medical history, physical examination, and medical record review.
- Minimize low yield diagnostic testing.
- Identify treatable cause (conditions) for the patient's symptoms.
- Determine if the patient can be classified as Chronic Multi-Symptom Illness (CMI) (i.e., has two or more symptoms clusters: pain, fatigue, cognitive dysfunction, or sleep disturbance).
- Negotiate treatment options and establish collaboration with the patient.
- Provide appropriate patient and family education.
- Maximize the use of non-pharmacologic therapies:
 - Graded aerobic exercise with close monitoring.
 - Cognitive behavioral therapy (CBT)
- Empower patients to take an active role in their recovery.

Clinical Practice Guideline for Management of Medically Unexplained Symptoms: Chronic Pain and Fatigue



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PRIMARY CARE

MEDICALLY UNEXPLAINED SYMPTOMS

Patients managed by this guideline have symptoms that remain relatively unexplained after an appropriate medical assessment that includes focused diagnostic testing. Patients are often given multiple labels that lack a well-defined disease explanation. Usual clinical features include a relative lack of objective signs and a chronic symptom course often marked by exacerbations, remissions, and recurrences. Therefore, clinical management must be based largely upon patient report, rather than specific findings on clinical examination or diagnostic testing. A compassionate approach to patients with medically unexplained symptoms (MUS) is essential.

ASSESSMENT AND DIAGNOSIS

A thorough and early review of all sources of information can help in validating the patient's health concerns, while communicating care and understanding—the necessary building blocks to an effective patient-clinician partnership. Sources of information include: all medical records, medical history and psychosocial assessment, review of systems, physical examination and mental status examination (MSE), routine test results, and standard health assessments.

Additional medical history: In obtaining a medical history, the clinician should focus on key symptoms that may suggest a well-defined disease explanation.

Physical examination: Patients with unexplained symptoms have often been examined several times in the past. However, important details may have been overlooked due to time constraints or the frequency that clinicians encounter such complaints in the absence of objective findings. Setting aside time for a detailed and thorough examination is critical for the assessment and may also help in building an alliance with the patient, who in many cases was seen by several clinicians.

Mental Status Examination (MSE): A careful MSE should be performed, including assessment of appearance, behavior, mood and affect, cognition, thought content and processes, and insight and judgment. A useful screen for cognitive impairment in elderly patients consists of four questions from the Mini-Mental State Examination (MMSE) (i.e., orientation to time,

orientation to place, memorizing and repeating three non-related items, and spelling “world” backwards).

Psychosocial Assessment: A psychosocial assessment is critical in evaluating the patient with unexplained symptoms and should include a screening for suicidal ideation and substance use disorders. The Patient Health Questionnaire (PHQ) is an excellent screening tool for assessing the presence of the most common psychiatric conditions associated with complaints of fatigue: depression, symptoms, and anxiety.

Unstable/Urgent Conditions

Unstable or urgent conditions represent situations that mandate immediate attention. A complete discussion of diagnosis and management of the entire range of possible urgent conditions is beyond the scope of this guideline. These conditions are generally recognized and managed by the astute primary care clinician and include (but are not limited to) the following:

- Suicidal ideation or psychosis
- Objective evidence of joint swelling
- Fever (over 101.1 degrees F/38.4 degrees C)
- Significant weight loss
- Focal findings on neurological examination
- Severe anemia or elevated white blood cells

Symptoms

Patients who present with unexplained pain or fatigue often carry a cluster of symptoms that must be understood as accurately as possible. Taking an accurate history is an essential part of the diagnostic work-up. The following brief standardized assessment measures are recommended for routine recording in the medical record:

For pain: "On a 0 to 10 scale, 0 being no pain and 10 being pain as bad as you can imagine, what number would you say your pain has been over the past week?"

For symptoms other than pain: "On a 0 to 10 scale, 0 being no (insert SYMPTOM) and 10 being (insert SYMPTOM) as bad as you can imagine, what number would you say your (insert SYMPTOM) has been over the past week?"

For symptom impact: "During the past week, how much have your symptoms interfered with your usual

work or activities, 0 being does not interfere at all and 10 being completely interferes?"

The clinician should initiate a complete initial symptom assessment (e.g., symptom duration, onset, triggers, and severity for new symptoms not previously assessed).

Duration: The duration of the symptoms until time of presentation is variable and patients may have spent years seeing numerous clinicians and undergoing extensive evaluations without ever obtaining a diagnosis. Many patients may relate the onset of their symptoms to a significant event (e.g., severe illness, trauma, military mobilization, and viral illness). Some patients may present with symptoms after sustaining central/axial skeletal trauma, such as a motor vehicle accident with resultant whiplash.

Exploring the history and clarifying the details may require several visits. However, the more the clinician can create an atmosphere of calmness and interest in the details, the more likely it is that important aspects of the history will be elicited. Details that may not seem important to the patient to mention in a hurried history may emerge in a subsequent or follow-up visit and provide important clues in determining a diagnosis.

Location: Pain location is important as it may provide useful information to help guide further assessment and treatment. Asking patients to indicate on their bodies where they feel pain can help to assess the distribution (location) of pain. It is also useful to employ a standard pain drawing, consisting of a line drawing outline of the front and back of a human body.

Co-morbidity: Other chronic illnesses may occur as co-morbid conditions, including:

- Thyroid disease
- Rheumatic disease
- Sleep apnea
- Neurological disease
- Depression

Irritable bowel syndrome, migraine headaches, and multiple-chemical sensitivity occur more frequently in patients with Chronic Fatigue Syndrome/Fibromyalgia (CFS/FM). The elderly individual also has a higher risk

for the presence of malignancy, which should be kept in mind during the evaluation. It is important not to ignore co-morbidities that may represent a true underlying condition that will require treatment.

Previous episodes: The patient may have had prior episodes of similar symptoms in the past, as well as prior treatments.

Patient perception of symptoms: Patients should be given the opportunity to relate their experiences and complaints, at each visit, in their own way. Although time-consuming and likely to include much seemingly irrelevant information, this has the advantage of providing considerable information concerning the patient's intelligence, emotional make-up and attitudes about their complaints. This also provides patients with the satisfaction that they have been "heard-out" by the clinician, rather than merely being asked a few questions and exposed to a series of laboratory tests based on "high technology."

As the patient relates the history, important nonverbal clues are often provided. The clinician should observe the patient's attitude, reactions, and gestures while being questioned, as well as his or her choice of words or emphasis. The impact from the symptoms may range from annoying to totally disabling and patient perceptions regarding the cause and impact are important to understand in managing the disorder. Stressors such as occupational and family issues should also be explored.

The BATHE technique provides a time-efficient way to address the impact of patients' symptoms on their level of function. The BATHE technique addresses the following topics:

- **Background:** "What is going on in your life?"
- **Affect:** "How do you feel about it?"
- **Trouble:** "What troubles you the most about the situation?"
- **Handle:** "What helps you handle that?"
- **Empathy:** "This is a tough situation to be in. Anybody would feel (down, stressed, etc.). Your reaction makes sense to me."

Questions that may prompt patients to provide important attributes of their symptoms are summarized in the following table.

Symptom Attributes	Questions
Duration	<ul style="list-style-type: none"> • Has the symptom existed for days, weeks, or months? • Has the symptom occurred only intermittently? • Particularly with regard to pain and fatigue, can the patient define if these symptoms occurred only two or three days per month or constantly? • Is the symptom seasonal? • Are there times of the day when the symptom is worse?
Onset	<ul style="list-style-type: none"> • Can the patient recall exactly how the symptom began? • Were there triggering events, either physical or emotional? • Was the onset subtle and gradual, or dramatic and sudden? • Have the triggering events tended to be the same over time or are there changing patterns?
Location	<ul style="list-style-type: none"> • Is the symptom localized or diffuse? • Can the patient localize the symptom by pointing to it? • If the pain is diffuse, does it involve more than one body quadrant?
Co-morbidity	<ul style="list-style-type: none"> • Does the patient have any diagnosed co-existing illnesses? • What is the time relationship between the onset and severity of the co-existing illnesses and the symptoms of fatigue and/or pain? • What are the symptoms other than pain and/or fatigue? • Are there co-morbid diagnoses? • Are there changes in the patient's weight, mood, or diet?
Previous episodes	<ul style="list-style-type: none"> • If the symptoms are episodic, what is the pattern in regard to timing, intensity, triggering events, and response to any prior treatment?
Intensity and impact	<ul style="list-style-type: none"> • How severe are the symptoms (use the 1 to 10 Numerical Rating Scale [NRS])? • Ask the patient to describe any new limitations they have experienced compared to their usual life-style, including limitations in physical endurance or strength (e.g., climbing stairs, shopping, and amount or quality of their sleep).
Previous treatment and medications	<ul style="list-style-type: none"> • Exploring this aspect of the history may be complicated and require obtaining prior medical records, or having an authorized telephone conversation with the prior treating clinician. Ask the patient to bring in their medication bottles on a subsequent visit and document the exact names of the medications. Find out which medications have/have not been helpful.
Past medical, surgical and psychological history	<ul style="list-style-type: none"> • This area includes chronic and major acute illnesses and injuries, allergies, surgical procedures, and hospitalizations. The psychological history may take several visits to clarify, depending upon the ease with which the patient can articulate their emotional status and past and present issues. Explore stressors such as occupational and family issues.
Patient perception of symptoms	<ul style="list-style-type: none"> • Often omitted from the history-taking are questions designed to gain some understanding of what the patient believes is happening. Ask the patient about their hunches and fears.

Build Therapeutic Alliance

The lack of diagnosis or effective treatment can make the management of patients with unexplained symptoms challenging. It may also cause frustration for both the patient and the provider. A high level of patient trust and faith in the clinician is required in order to maintain continuity of care and continue patient management through regular follow-up appointments. The initial evaluation helps establish a special partnership between the patient and clinician. To strengthen the partnership with the patient, the clinician should:

- Acknowledge and indicate commitment to understand the patient's concerns and symptoms.
- Encourage an open and honest transfer of information that will provide a more comprehensive picture of the patient's concerns and medical history.
- Indicate commitment to allocate sufficient time and resources to resolving the patient's concerns.
- Avoid open skepticism or disapproving comments in discussing the patient's concerns.

At each patient visit, the clinician should consider the following:

- Ask if there are unaddressed or unresolved concerns.
- Summarize and explain all test results.
- Schedule follow-up visits in a timely manner.
- Explain that outstanding or interim test results and consultations will be reviewed during the follow-up visits.
- Offer to include the concerned family member or significant other in the follow-up visit.

Revisit The Medical Record

Review the patient's medical record for co-morbidities, prior episodes, occurrences of other unexplained symptoms, prior evaluations, and the nature and extent of prior therapy. The review should include the following:

- Complete medical history
- Family and social history
- Occupational and deployment history
- Exposure to possible risks, hazards, and toxic agents
- Prescription history, including over-the-counter medications and herbs
- Clinical notes
- Other documented history and physical examinations

- Radiological, laboratory and other ancillary test results
- Effectiveness of previous therapies and reasons for past treatment failures or successes

Diagnostic Tests

After a complete history and physical examination, there are several routine laboratory tests that will assist in completing the patient assessment:

- Complete blood count
- Electrolytes
- Blood urea nitrogen
- Creatinine
- Glucose
- Calcium
- Phosphate
- Liver function tests
- Total protein
- Thyroid-stimulating hormone
- Erythrocyte sedimentation rate
- Urinalysis

The clinician also should ensure that health care maintenance is up to date. The following tests should only be ordered if the history or physical examination results strongly suggest the need:

- Serological tests for:
 - Epstein-Barr virus
 - Lyme disease (in the absence of polyarthritis, history of tick bite, or erythema chronicum migrans)
 - Immunologic function testing
- Neuroimaging

Other Conditions/Diseases That Can Explain (Or Cause) The Symptoms

After obtaining a detailed history, completing a thorough physical examination, obtaining laboratory test results, and using a screening tool (e.g., the PHQ) the clinician should determine whether an explanatory or causal condition can be diagnosed or whether the symptoms remain medically unexplained.

The following examples of the patient's description may indicate a related diagnosis. In most instances, the symptoms of CFS can be distinguished from the closely related phenomena of somnolence, muscle weakness, neuromuscular fatigability, depressed mood, or anhedonia.

Patient's Description	Clinician's Interpretation
<ul style="list-style-type: none"> • Reduced muscle power at rest • Difficulty walking or lifting weights 	<ul style="list-style-type: none"> • Muscle weakness (e.g., myopathy or polymyositis)
<ul style="list-style-type: none"> • Loss of muscle power over time with activity 	<ul style="list-style-type: none"> • Neuromuscular fatigability (e.g., myasthenia gravis)
<ul style="list-style-type: none"> • Physical and mental fatigue at rest 	<ul style="list-style-type: none"> • Central fatigue (e.g., multiple sclerosis)
<ul style="list-style-type: none"> • Lack of motivation to commence tasks • Lack of pleasure from tasks undertaken 	<ul style="list-style-type: none"> • Anhedonia (e.g., major depression)
<ul style="list-style-type: none"> • Daytime sleepiness • Short sleep latency 	<ul style="list-style-type: none"> • Somnolence (e.g., sleep apnea or narcolepsy)
<ul style="list-style-type: none"> • Breathlessness at rest or on exercise 	<ul style="list-style-type: none"> • Dyspnea • Weakness (e.g., airflow limitation, cardiac failure, or anemia)
<ul style="list-style-type: none"> • Muscle or joint pain • Fever or malaise 	<ul style="list-style-type: none"> • Inflammation (e.g., systemic lupus erythematosus) • Infection (e.g., influenza)

When considering depression, the clinician should assess whether the symptoms are causing the depression or the depression is resulting in physical complaints. Physical illness may cause psychosocial distress through a direct biological link, such as through neurotransmitters involved in both pain and mental disorders. Physical symptoms may cause emotional distress by overwhelming an individual's ability to cope. Distress may increase unhealthy behaviors that increase the risk of such symptoms. The disordered sleep and changes in autonomic nervous system functioning associated with stress may cause these symptoms. Finally, both mental disorders and MUS may be found together in some people, simply by chance.

Symptom-Based Treatment Modalities

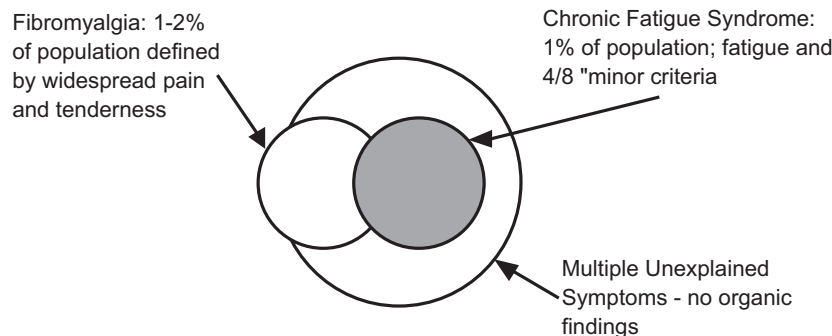
Although the criteria for CFS require six months duration of symptoms prior to making the diagnosis, the initiation of appropriate treatments for unexplained symptoms and for myalgias may be considered earlier. There is a point in the course of the diagnostic work-up and clinical monitoring at which the symptoms may appear to be "unexplained." The time that elapses in reaching this point varies.

- Early interventions should include restoration of sleep and management of pain.
- The clinician must maintain an ongoing vigilance to the possibility of emerging diagnosable conditions.

Patients Who Present With 2 or More of the Following: Fatigue, Pain, Sleep Disturbance, or Cognitive Dysfunction

Chronic unexplained symptoms are very common in the general population. In many instances, these symptoms occur in isolation (e.g., fatigue and headaches). However, it is also common for these symptoms to aggregate in individuals, leading to hypothesized "syndromes" that have been given a variety of terms, such as CFS, FM, and somatoform disorders. There are substantial data suggesting that overlapping illnesses have common mechanisms and respond to similar types of interventions. Careful assessment of fatigue, pain, cognitive difficulties, sleep disturbance, and associated physical symptoms, considering their impact on the patient in isolation and aggregate, will allow the clinician to reach an appropriate diagnosis.

OVERLAPPING CHRONIC MULTI-SYMPTOM ILLNESS



Fatigue

Persistent fatigue is the primary manifestation of CFS and is present in over 90 percent of FM patients, as well. Patients may describe their fatigue in various ways. It is also present in otherwise healthy patients and in a wide array of other illnesses. Fatigue should be differentiated from transient tiredness. Patients report a diminished ability to perform mental and physical tasks because of fatigue, and that those tasks increase their fatigue.

Fatigue is not substantially improved by rest, including sleep, naps, or cessation of activities. The patient may also describe sleep disturbance—unrefreshing sleep that may be characterized by difficulty falling asleep, frequent awakening, abnormal limb movements (such as myoclonus), or sleep apnea.

Pain

Pain is the primary manifestation in FM and is very common in CFS. Patients complain of muscle and joint pain, but are usually unable to differentiate between muscle and joint area pain. Pain usually becomes widespread (typically bilateral and above and below the waist) and is poorly localizable (meaning it occurs "all over"). Occasionally patients will complain only of unilateral body pain. The characteristic of widespread pain indicates a central nervous system etiology.

"Widespread pain" is defined as occurring in at least three quadrants: above and below waist, right and left side of the body, and axial. The pain-drawing methodology may be helpful because it allows the patient to indicate the location of their pain on a line drawing of the human body. This method permits a systematic and standard method to assess pain location and determine whether the patient meets the "widespread pain" criteria.

On examination there is increased tenderness, often very marked, to palpation in characteristic locations, defined as "tender points" (TPs)—pain on digital palpation. Although there is controversy regarding the assessment and usefulness of evaluating TPs, three options have been offered:

1. Simple count of the number of TPs may be misleading unless a carefully standardized assessment is followed (see bullet 3 below).
2. Myalgic scores, which use a dolorimeter for patients to rate the amount of pressure required for each point to become painful. The "myalgic score" is the sum of the amount of pressure for all aggregated TPs. The average myalgic score can be determined by dividing the summed score by 18. The advantage of using this approach is that there is a greater range of scores and although the number of positive TPs may not change over time or as a result of treatment, the myalgic score may be responsive to time and treatment.
3. Manual Tender Point Survey (MTPS) have the following advantages: a) it follows a standard protocol and has an instructional booklet and tape, b) it does not require a dolorimeter, and c) it provides a range of scores similar to the myalgic score, while at the same time it permits determination of the absolute number of TPs so that the ACR criteria can be used.*

*Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990; 33(2):160-72.

Headache and sore throat are common complaints in patients with CFS. The headache should be of a new type, different from that previously experienced, with a new pattern or severity. Patients often complain of a myriad of other vague pain, unexplained by clinical evaluation, either at the same time or over time (e.g., urethral symptoms, pelvic pain, tension, or migraine). However, these complaints are not included in the definition of CFS/FM.

Cognitive Difficulties

Neurocognitive difficulties are common in CFS/FM and may include the following:

- Forgetfulness
- Memory disturbance
- Problems with concentration

Sleep Disturbance

Poor sleep is a frequent complaint in FM and some patients have objective abnormalities noted in sleep studies. But even though disturbed sleep likely plays a significant role in symptom expression in some patients, and may contribute to some of the physiologic abnormalities (e.g., low IGF-1), the aggregate data do not

support the notion that disturbed sleep alone is causing this illness.

Sleep disturbances, common in CFS, may include unrefreshing sleep (i.e., waking up feeling unrefreshed) that may be characterized by difficulty falling asleep, frequent awakening, abnormal limb movements (e.g., myoclonus), or sleep apnea. A shift from regular night-time sleep to day-time naps and a late-night to late-morning sleep cycle is sometimes noted. It is known that chronic disruption of the normal sleep pattern can induce symptoms in healthy volunteers, including fatigue, musculoskeletal pains, irritability and concentration impairment.

Associated Physical Symptoms

While the recognized criteria for CFS/FM emphasize the presence of chronic pain and fatigue, it is nonetheless important to note that patients suffering from CFS/FM generally present a number of physical symptoms that complicate the approach to diagnosis. The clinician who is alert to the possibility of MUS will find it easier to make the diagnosis and not become unduly alarmed. The subjective symptoms associated most frequently with CFS/FM are included in the following table.

Cardiovascular System <ul style="list-style-type: none"> • Palpitations • Raynaud's phenomenon 	Endocrine System <ul style="list-style-type: none"> • Generalized fatigue • Excessive sweating, localized or generalized • Hypoglycemia (e.g., sudden severe hunger, headache, sudden anxiety, tremulousness/shakiness, sweating, confusion, and unconsciousness/coma) • Dry skin • Hair loss
Eyes, Ears, Nose & Throat <ul style="list-style-type: none"> • Dry eyes • Dry mouth • Sore throat • Sinusitis • Rhinorrhea 	Musculoskeletal System <ul style="list-style-type: none"> • Costochondritis • Temporo-mandibular dysfunction • Muscle spasms (including nocturnal myoclonia) • Coccydynia
Respiratory System <ul style="list-style-type: none"> • Asthma • Dyspnea • Cough 	Central Nervous System <ul style="list-style-type: none"> • Disturbance of mood • Chronic headaches, migraines • Generalized dysesthesia (e.g., burning sensation, heat, numbness, chills, pins and needles, subjective sensation of swelling) • Hypersensitivity to noise, odors and air conditioning • Insomnia • Tendency to drop things • Tinnitus • Double vision • Balance problems and dizziness • Dry eyes or excessive tearing
Digestive System <ul style="list-style-type: none"> • Dry mouth • Dysphagia (e.g., "lump" in the throat, difficulty swallowing, and sore throat) • Dyspepsia • Irritable bowel (diarrhea or constipation) 	
Genitourinary System <ul style="list-style-type: none"> • Irregular menstrual cycles • Dysmenorrhea • Irritable bladder (urgency of urination) 	

CFS AND FM DEFINITIONS

Chronic Fatigue Syndrome

CFS is the current term used to describe a syndrome involving a set of defined (yet in many ways, non-specific) symptoms and behaviors that include, as a defining element, severe disabling fatigue and a combination of associated symptoms including cognitive impairments (memory and concentration), sleep disturbances and musculoskeletal pain. The condition has been described for centuries using a variety of nomenclatures (e.g., febricula, nervous exhaustion, neurasthenia, epidemic neuromyasthenia, benign myalgic encephalomyelitis, royal free disease, and chronic mononucleosis). To date, no clear pathophysiology or etiologies have been established, and current evidence points to a heterogeneous and multi-causal pathogenesis. In 1994, an international study group coordinated by the Centers for Disease Control (CDC) established the most widely accepted criteria for case definition of CFS.

A case of chronic fatigue syndrome is defined by the presence of:

Clinically evaluated, unexplained, persistent or relapsing fatigue that is of new or definite onset; is not the result of ongoing exertion; is not alleviated by rest; and results in substantial reduction in previous levels of occupational, educational, social, or personal activities.

And

Four or more of the following symptoms that persist or reoccur during six or more consecutive months of illness and do not predate the fatigue:

- Self-reported impairment in short term memory or concentration
- Sore throat
- Tender cervical or axillary nodes
- Muscle pain
- Multi-joint pain without redness or swelling
- Headaches of a new pattern or severity
- Unrefreshed sleep
- Post-exertional malaise lasting >24 hours

Fibromyalgia

FM is the current term used to describe a syndrome involving a set of defined (yet in many ways, non-specific) symptoms and behaviors that include, as a defining element, widespread musculoskeletal pain and tenderness. The condition has been described for centuries using a variety of nomenclatures (e.g.,

muscular rheumatism, fibrositis, fibromyositis, and psychogenic rheumatism). To date, no clear pathophysiology or etiologies have been established. In 1990, a committee of the ACR established the most widely accepted criteria for case definition of FM. The ACR criteria include both of the following:

1. History of widespread pain of at least 3 months duration.
Definition. Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.
2. Pain in 11 of 18 tender point sites on digital palpation (performed with an approximate force of 9 lb/4 kg).
Definition. Pain, on digital palpation, must be present in at least 11 of the following 18 sites:

Occiput: Bilateral, at the suboccipital muscle insertions.

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

Trapezius: bilateral, at the midpoint of the upper border.
Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.

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

Lateral epicondyle: bilateral, 2 cm distal to the epicondyles.

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

Greater trochanter: bilateral, posterior to the trochanteric prominence.

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

For a tender point to be considered "positive" the subject must state that the palpation was painful. "Tender is not to be considered 'painful'."

*The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia.

Concurrent symptomatology is nearly universal and includes fatigue, headaches (both migraine and musculoskeletal), paresthesias, hearing/ocular/vestibular complaints, cognitive difficulties (memory and concentration), "allergic" and chemical/photo sensitivity symptoms, non-cardiac chest pain, palpitations, dyspepsia, irritable bowel syndrome, chronic sinusitis, heartburn, irritable bladder, and affective/somatoform disorders.

Labeling

There is insufficient evidence to allow clinicians to predict the impact that diagnostic labels such as FM syndrome, CFS, multi-chemical sensitivity (MCS), CMI, or Gulf War Illness (GWI) will have on the clinical course of patients with these symptoms. There is evidence, however, to suggest that the clinician should consider the following potential impacts:

- Assigning specific diagnostic labels may have implications in the clinical course for a particular individual with MUS.
- There may also be negative effects of labeling. A diagnostic label may sometimes unnecessarily cause a patient to define him or herself as ill, an effect that could be especially problematic in occupational health care settings.
- The potential risks and benefits of applying a particular diagnostic label to unexplained symptom clusters should be weighed by the clinician and discussed with the patient prior to applying such a diagnostic label.
- The clinician should consider generic approaches to managing MUS; such approaches may be useful, without having to rely on specific diagnostic labels.

TREATMENT

Treatment Plan

Assure that the patient understands the meaning and impact of CFS/FM syndrome on their life and the potential improvement a recommended treatment may offer. A final acceptable treatment plan should be negotiated with the patient and documented in the medical record.

- Prepare a summary of the problems and potential treatment plans prior to meeting the patient.
 - Develop a problem list with an assessment of problem severity and urgency for treatment.
 - Develop treatment options for discussion with the patient.
- Educate the patient.
 - Discuss the general concept of MUS and how problems associated with this diagnosis apply to the patient.
 - Evaluate the patient's understanding.
 - Describe treatment options and the associated risks and benefits.
 - Describe the prognosis of the illness.

- Collaborate with the patient and determine the patient's preferences.
 - Determine the patient's goals for recovery.
 - Explore and discuss the patient's beliefs regarding his or her illness.
 - Determine if the patient agrees with the priority and severity of the problems and urgency for treatment.
 - Determine the level of the patient's agreement with the recommended treatment or one of the alternative options.
 - Determine the patient's motivation to begin treatment and identify barriers to treatment.
 - Obtain the patient's consent to the treatment plan.
- Empower the patient for self-management.
 - Move the responsibility of patient improvement from the treatment team to the patient.
 - Encourage a change in life-style, including exercise, diet, sleep hygiene, stress reduction, relaxation training, leisure activity schedule, and pacing.
- Implement the treatment plan.
 - Coordinate treatment plan activities.
 - Establish a referral and interdisciplinary team approach, if indicated.
- Follow-up.
 - Monitor treatment progress and patient improvement.
 - Establish a regular follow-up schedule throughout and after treatment.

Role of the Primary Care Manager (PCM)

In the course of the assessment, the primary care provider should also serve as the primary care manager (PCM) and develop a problem list that summarizes the findings of specialty consultations and diagnostic procedures related to the diagnosis of CFS/FM or CMI. The PCM should determine the severity of each identified problem and the impact it will have on the patient's functional ability and quality of life, so that a baseline can be established against which improvements can be assessed. The PCM should also identify problems for which treatment is most urgently recommended. The most urgent treatments may be defined as those treatments expected to result in the greatest improvement when addressing the most severe problems.

Role of Consultants

The PCM is not expected to directly provide treatment, but is expected to serve as the focal point for a multi-disciplinary approach to treatment that may span the continuum of care, beginning with self-management. The treatment team may include those from whom prior consults have been obtained, such as physical therapy, nutrition, social work, psychology, rheumatology, and significant others within the patient's social network. The PCM, with patient consent, may find it useful to involve the patient's employer/supervisor, spouse, and friends in the defined treatment team.

Mental health professionals should provide input into implementing psychotherapies and psychopharmacology in outpatient or partial hospitalization settings. Social workers should help build family and social support networks, or recommend changes in the patient's living situation, in order to create a positive support network. Within the most intensive treatment setting within the continuum of care, residential treatment may be required to assure the presence of a support network.

Continuum of Care

A continuum of care should cover a range of levels of intensity, including self-care in the home through outpatient treatment, partial hospitalization, residential treatment, and hospitalization. Patients may be encouraged to use wellness centers and gyms as part of the plan to improve physical conditioning, diet, and stress management. In outpatient settings, the patient may be willing to keep a diary of symptoms, events, and diet that can be reviewed by the outpatient provider.

Substance use disorders commonly occur in all patient populations, but are commonly missed in comprehensive medical assessments. The PCM should be sensitive to the harmful and potentially addictive use of alcohol, medication, and illicit drugs that transcend all three areas. Treatment programs that comprehensively address addiction recovery have high success rates and should be expected to significantly improve the patient's quality of life and functional level.

Initiate/Continue Treatment

CFS/FM has significant negative impact on the patient's physical, mental and social well-being. Multi-disciplinary treatment should cover these three main areas. Interventions expected to improve physical well-being include a graduated exercise regimen (monitored through physical therapy, exercise trainers, and social supports), improved sleep habits, and medication (monitored by the physician). Mental well-being may be improved through individual or group therapy, medication, and creating a supportive social network. Social well-being may be improved through resolving legal, financial, occupational, or recreational problems.

The expected outcome of intervention should be to significantly alter the patient's lifestyle and improve the identified problem areas, rather than discover a disease etiology or "cure."

- With early recognition, patient education, and effective multi-modal management, most patients with CFS/FM condition can lead a fairly normal life.
- The optimal intervention for FM would include non-pharmacologic treatments, specifically graded aerobic exercise, and cognitive-behavioral therapy, in addition to appropriate medication management, as needed for sleep and pain symptoms.
- The optimal interventions for CFS would include non-pharmacologic treatments, cognitive-behavioral therapy and moderate aerobic exercise, in addition to appropriate medication management as needed for associated depression, insomnia or myalgia, and sleep hygiene.

The following tables summarize the therapies for CFS and FM and the potential benefit or harm of these interventions based on evidence from randomized controlled trials. The significance of the results of the research is indicated using the "Recommendation" (R) grading system described in Appendix 1 (e.g., R = A indicates significant benefits that are based on good clinical trails).

THERAPY INTERVENTIONS FOR FIBROMYALGIA

R=Recommendation A=Randomized Control Trial B=Clinical Studies C=No Benefit or Harm D=Harmful

R	Maximum Benefit	Some Benefit	Possible Benefit	Possibly Harmful
A		<ul style="list-style-type: none"> • Cognitive Behavioral Therapy (CBT) • Graded Aerobic Exercise • Antidepressant (TCA) 		
B		<ul style="list-style-type: none"> • Tramadol* • SAME** • SSRI (R = B/C) • NSAIDs (R = B/C) 	<ul style="list-style-type: none"> • Acupuncture • Biofeedback • Trigger point injection • Stretching 	<ul style="list-style-type: none"> • Alprazolam
C		<ul style="list-style-type: none"> • Sleep education • Other antidepressants (non-SSRI, non-TCA) 	<ul style="list-style-type: none"> • Massage therapy • Relaxation therapy • Myofascial release • Spinal manipulation • Hypnotherapy • Magnesium 	<ul style="list-style-type: none"> • Antiviral • Antifungal • Antibiotics
D				<ul style="list-style-type: none"> • Bed rest

*Tramadol - Non-formulary medication. Available by physician request using the non-formulary process.

**SAME is a nutritional supplement that VA does not provide. Is available as over the counter product.

THERAPY INTERVENTIONS FOR CFS

R=Recommendation A=Randomized Control Trial B=Clinical Studies C=No Benefit or Harm D=Harmful

R	Maximum Benefit	Some Benefit	Possible Benefit	Possibly Harmful
A	<ul style="list-style-type: none"> • Cognitive Behavioral Therapy (CBT) • Graded Aerobic Exercise 			
B		<ul style="list-style-type: none"> • MAOI • NADH 		
C		<ul style="list-style-type: none"> • Sleep education • SSRI • Other anti- depressants (non-SSRI, non-TCA) 	<ul style="list-style-type: none"> • Relaxation • Flexibility exercise • Essential fatty acids • Magnesium • Low-dose, short term corticosteroid (R = B/C) 	<ul style="list-style-type: none"> • Florinef, alone
D				<ul style="list-style-type: none"> • Bed rest • Corticosteroid High-dose or Replacement • Anti-viral • Anti-fungal • Immune therapy

PHARMACOLOGIC AGENTS FOR CFS/FM⁽¹⁾

Agent	Dose Studied	Effective	Adverse Effects	Comments
Anti-depressants: Amitriptyline	Initial: 10 to 25 mg/day Maximum: 75 mg/day	Yes	<ul style="list-style-type: none"> ■ Sedative and anticholinergic effects ■ Cardiac toxicity 	<ul style="list-style-type: none"> ■ The agent is only effective in approximately 30% of patients. ■ Tachyphylaxis can occur with continued treatment. ■ Anticholinergic side effects may limit use. ■ Not recommended for use in the elderly.
Cyclobenzaprine	5 to 40 mg/day	Yes	<ul style="list-style-type: none"> ■ Anticholinergic and central nervous system effect 	<ul style="list-style-type: none"> ■ Side effects may limit use. ■ Tachyphylaxis can occur with continued treatment.
Fluoxetine	Initial: 10 mg/day Range: 20 to 40 mg/day Maximum: 60 mg/day	Equivocal	<ul style="list-style-type: none"> ■ Most commonly sexual dysfunction 	
Venlafaxine	37.5 to 300 mg/day	Possibly	<ul style="list-style-type: none"> ■ Headache ■ Sexual dysfunction 	<ul style="list-style-type: none"> ■ The extended release form given during the day as a single morning dose or BID dosing may be most effective.
Citalopram	Initial: 20 mg/day Range: 20 to 40 mg/day Maximum: 40 mg/day, if indicated	No	<ul style="list-style-type: none"> ■ Sexual dysfunction ■ Nausea 	
Alprazolam	0.5 to 3.0 mg/day	Unknown	<ul style="list-style-type: none"> ■ Sedative and hypnotic effects 	
Analgesics: Tramadol*	50 to 400 mg/day	Yes	<ul style="list-style-type: none"> ■ Nausea ■ Dizziness 	<ul style="list-style-type: none"> ■ Dual mechanism of action may address altered neurotransmitters and pain signals of FM.
NSAIDs	Dose range recommended by drug manufacturer	Equivocal	<ul style="list-style-type: none"> ■ If risk of bleeding avoid NSAIDs 	<ul style="list-style-type: none"> ■ Intolerance is common ■ Efficacy is less than in other rheumatic conditions where inflammation is present.
Opioids	Dose range recommended by drug manufacturer	Unknown	<ul style="list-style-type: none"> ■ Sedative effects ■ Nausea 	<ul style="list-style-type: none"> ■ There is no clinical evidence to show efficacy. ■ Tolerance or dependence may develop with long-term use. ■ If used regularly, long-acting formulations are preferred.
S-adenosyl-L-methionine (SAME)**	<ul style="list-style-type: none"> ■ 200 mg/day subq ■ 400 mg/day IV ■ 800 mg/day orally 	Possibly	<ul style="list-style-type: none"> ■ None documented 	<ul style="list-style-type: none"> ■ Drug is available in the United States orally, as an over-the-counter dietary supplement.
Sleep: Melatonin**	3 to 6 mg/day	Equivocal	—	<ul style="list-style-type: none"> ■ May help a limited number of patients who have difficulty initiating sleep.
Other: Magnesium and malic acid	600 to 2000 mg/day	Unknown	<ul style="list-style-type: none"> ■ Diarrhea ■ Nausea 	

⁽¹⁾Adapted from Leventhal LJ. Management of fibromyalgia. Ann Int Med 1999; 131:850-8. Other guidance regarding pharmacotherapy for CFS can be found in Reid S, et al. Chronic Fatigue Syndrome. BMJ 2000; 320(7230):292-96.

*Tramadol - Non-formulary medication. Available by physician request using the non-formulary process.

**SAME and Melatonin are nutritional supplements that VA does not provide. Are available as over the counter products.

Sleep Hygiene

In patients with CFS, behavioral approaches to sleep-wake cycle disturbances are likely to be more successful than pharmacologic approaches, as the latter do not induce normal sleep. Cognitive and educational management approaches should be aimed at promoting an understanding of the role of disordered sleep, and dispelling any irrational fears or inappropriate beliefs about sleep. Relaxation training and stress management may be useful for some patients.

The aim of sleep management is to establish a regular, normalized sleep-wake pattern. Patients should be encouraged to:

- Restrict the night-time sleep period to about eight hours.
- Avoid going to bed too early in the evening.
- Avoid stimulants during the evening period.
- Wake at a regular time in the morning (e.g., 7 am).
- Arise from bed at a regular time in the morning (e.g., by 8 am).
- Reduce (to less than 30 minutes) or abolish daytime naps.
- Engage in daytime physical and mental activities (within the limits of the individual's functional capacity).

If a patient with CFS has a concurrent *primary* sleep disorder (e.g., sleep apnea, restless leg syndrome or narcolepsy), specific intervention is required. The goals of sleep management should be to establish a regular, unbroken, night-time sleep pattern and to improve perceptions of the quality of sleep.

Brief Introduction to Cognitive Behavioral Therapy

CBT has been found to be particularly beneficial for patients with CFS/FM. If CBT is not available to your patients or they are not interested in seeing a mental health provider, the clinician may wish to consider utilizing some aspects of CBT in their clinic-based management. The following measures may help to empower patients and prevent them from dwelling on their symptoms:

- Work with patients to find more effective coping mechanisms.
- Help patients understand how avoiding activity and staying in bed may exacerbate their symptoms, rather than improving them.

- Encourage patients to maintain diaries, initially recording such items as weight, diet, sleep, and other objective elements.
- Later, guide patients toward writing more about life events and feelings and emotions; help them to see connections between life events and emotions, and in turn, physical symptoms.
- Help patients understand how expressing their feelings, either verbally or in writing, may help to prevent manifestation as somatic symptoms.
- For creative or artistic patients, encourage creative writing, which has been shown to improve the health status of patients with asthma and rheumatoid arthritis, or artwork.

Patient and Family Education

Some patients want only to be told that their condition is non-progressive and not causing damage or inflammation to their body. These patients generally have milder symptoms that have been present for some time and possess adequate strategies for improving symptoms and maintaining function. Education may be the only necessary treatment for these patients.

Patient education is of paramount importance for ALL patients with CFS/FM. The clinician should describe the condition in terms comfortable to them, and then refer the patient to reputable sources for additional information. Several national patient support organizations (e.g., American Fibromyalgia Syndrome of America, National Fibromyalgia Research Association and Fibromyalgia Alliance of America) produce excellent materials to help patients with FM learn more about their illness. Patients should be warned about getting information from less reputable sources, particularly on the Internet, where there is a great deal of misinformation.

Internet-savvy patients may be interested in learning more from some of the information sources on the Internet. Patients should be warned about the lack of evidence for, and potential harm from, some suggested "cures" that may be espoused by Web sites or other sources (e.g., Internet Chat/Support Groups). The high rate of placebo responses in conditions such as CFS/FM allows some poorly controlled studies to indicate benefits when there are no true benefits and possibly harmful effects.

Helping patients to gain a clear understanding of the nature of their illness is an important element of care management. For example, some patients harbor fears that an infection or environmental pollutants may be causing irreversible damage. Others may have been led to believe that any physical activity at all could be harmful. Unwarranted concerns of this kind may lead to maladaptive attitudes and behaviors that may increase the disability and retard recovery.

Psychosocial Support

As with other chronic illnesses, managing patients with CFS/FM requires consideration of the psychological and social impacts of the illness. Patients may be unable to continue full-time work, so financial difficulties may rapidly develop.

A successful return to work or school after a prolonged illness with CFS/FM often requires a rehabilitation program that incorporates medical treatments, psychological support and occupational therapy. The clinician may need to coordinate the help of other health care and educational professionals to implement the appropriate program for the patient.

Consideration should also be given to the impact that the illness may be having on the patient's family. In some circumstances, it may be useful for the spouse or partner to accompany the patient with CFS/FM to a consultation, to help them better understand the illness and provide an opportunity to discuss any coping difficulties.

Joining a patient support group may be valuable for some patients. Support groups can offer individual and group support, education and advice (e.g., how to gain access to social welfare agencies). Patients may also benefit from the opportunity to exchange coping strategies for dealing with day-to-day difficulties common to those living with debilitating conditions. However, the quality of advice can vary and it is therefore useful for the clinician to be knowledgeable about the activities and attitudes of local support groups.

With early recognition, patient education and effective multi-modal management, most patients with CFS/FM can lead a fairly normal life. Clinicians should be prepared to act as advocates for their patients in negotiations with employers, educational institutions and social welfare organizations. For instance, the patient may need assistance in arranging part-time work or school alternatives or securing disability allowances.

The clinician should refocus the attention from symptoms to improving patient functioning. Potentially modifiable psychosocial barriers to patient functioning could include the following:

- Living environment—Homelessness can perpetuate chronic illness as the result of environmental exposure and virtually non-existent personal hygiene.
- Support systems—Negative support on the part of the spouse, family, or significant other can impair and even worsen functionality.
- Job—Work place factors have been associated with illness-related behavior.
- Finances—Disability compensation can perpetuate illness by requiring continuing symptoms and disability for the worker to be eligible for benefits.

FOLLOW-UP

Follow-Up Visits

- The goals of follow-up visits are to monitor the severity of symptoms, impact of the symptoms on activities, effects of treatments, and presence of adverse effects to treatments, and assess patients for new symptoms suggestive of other diagnoses.
- Scheduled visits are preferred over as-needed (PRN) revisits.
- The amount of time between visits will vary depending on a number of factors, including the following:
 - Quality of the provider/patient relationship (i.e., new or established patient)
 - Distress of the patient
 - Need for refinement of the treatment plan
 - Presence or absence of psychosocial stressors
- If symptoms remit, the interval between follow-up visits may gradually lengthen.
 - Initially, a revisit at two to three weeks would be appropriate.
 - As soon as the patient is doing well, revisits every 3 to 4 months would be recommended.
 - Visits at one to two-month intervals may be needed for patients on a graded exercise program or weight loss program to reinforce compliance.
- Continually re-evaluate the patient for worsening of chronic symptoms or presence of new symptoms suggestive of other diagnoses.

Reassess Symptoms Severity

The primary reason for assessing current symptom status is to compare to the baseline status and estimate the response to active treatment strategies. With the lack of objective findings, treatment response must be monitored using subjective patient reports of symptoms and their impact on functional status. Though the symptoms are subjective, it is possible, using standardized questioning, to obtain reproducible measurements of the patient's clinical status. The following standardized assessments are recommended:

For pain: "On a 0 to 10 scale, 0 being no pain and 10 being pain as bad as you can imagine, what number would you say your pain has been over the past week?"

For symptoms other than pain: "On a 0 to 10 scale, 0 being no (insert SYMPTOM) and 10 being (insert SYMPTOM) as bad as you can imagine, what number would you say your (insert SYMPTOM) has been over the past week?"

For symptom impact: "During the past week, how much have your symptoms interfered with your usual work or activities, 0 being does not interfere at all and 10 being completely interferes?"

The clinician should initiate a complete initial symptom assessment (e.g., symptom duration, onset, triggers, and severity for new symptoms not previously assessed).

Adjust Treatment; Encourage, Reinforce, and Monitor for Emerging Conditions

With patient consent, the clinician should become less involved as the patient is able to sustain lifestyle changes that have positive impact on functional ability and quality of life.

- Assure the patient that you believe their symptoms are real.
- Assess progress towards negotiated goals.
- Reevaluate the patient, with special concern for new symptoms or worsening chronic symptoms.
- Respond to the patient's desire to change the treatment plan or behavior that indicates a need to re-evaluate the treatment plan.
- Assess the patient's adherence to treatment and address any barriers to treatment.
- Assist the patient to take an active role in their recovery.

Consider Consultation

The PCM is not expected to directly provide treatment, but is expected to serve as the focal point for a multi-disciplinary approach to treatment that may span the continuum of care, beginning with self-management. The treatment team may include those from whom prior consults have been obtained, such as physical therapy, nutrition, social work, psychology, rheumatology, and significant others within the patient's social network. The PCM, with patient consent, may find it useful to involve the patient's employer/supervisor, spouse, and friends in the defined treatment team.

Mental health professionals should provide input into implementing psychotherapies and psychopharmacology in outpatient or partial hospitalization settings. Social workers should help build family and social support networks or recommend changes in the patient's living situation, in order to create a positive support network. Within the most intensive treatment setting within the continuum of care, residential treatment may be required to assure the presence of a support network.

Provide Symptomatic Treatment and Consider Consultation

For unexplained symptoms that are not CFS or FM:

- Continue time-contingent follow-up.
- Emphasize efforts to improve functioning.
- Monitor for treatable disease explanations for symptoms (including psychiatric disorders).
- Use rehabilitative psychosocial strategies (e.g., CBT, and gradual physical reactivation/exercise) and symptom-based pharmacologic therapies, as appropriate (see Annotation L).
- Reassess target symptoms and clinical status at each visit.