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Fibromyalgia syndrome

This is an update of a previous How to Treat on fibromyalgia syndrome, published 6 June 2008.

Background

CHRONIC or persistent musculoskeletal pain, out of proportion to any easily demonstrable peripheral pathology, is a common presentation in general practice. It can have a devastating impact on quality of life, and can be highly frustrating both for the patient and GP to manage. Such pain is characteristically associated with deep soft tissue (especially muscle) tenderness, whether regional or more widespread, and may occur in the complete absence of any locally definable 'organic' lesion.

Fibromyalgia syndrome occupies the severe end of the spectrum of this type of pain and pressure sensitivity. It is the third most prevalent musculoskeletal disorder, twice as common as rheumatoid arthritis and with at least comparable impact on quality of life. It is recognised by the WHO as a medical disorder (ICD-10, Other soft tissue disorders, M79.7).

While traditionally all 'medically unexplained' musculoskeletal pain has been interpreted as having a psychological origin, including hypochondriasis, 'masked' depression or somatisation, advances in pain science indicate that these interpretations are incomplete.

Considerable indirect scientific evidence now strongly suggests that much persistent pain has a primarily neurological basis, with disordered processing by pain neural pathways, and that this is variably modulated by genetic, peripheral tissue (nociceptive) and supraspinal (psychological) factors.

Importantly, these insights have led to the continuing development of scientifically validated management strategies for fibromyalgia syndrome, with increasing benefits for patients.

Together with the growing recognition in the community of the need for early diagnosis and intervention, increased consumer expectations for management are therefore resulting in more fibromyalgia-related presentations to, and hence challenges for, Australian general practice.[1]

In response, this article updates and complements the How to Treat article from 6 June 2008 on fibromyalgia syndrome.

In particular, it emphasises the primary role of general practice in managing these complex, often multidimensional, chronic illness patients, and the increasing practical resources that are now available to assist GPs.

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Epidemiology

DESPITE fibromyalgia syndrome being defined by its hallmark symptom of pain and the related physical examination finding of pressure sensitivity, it is a multisystem complaint that overlaps with many functional pain or somatic syndromes. These related syndromes occur with increased frequency within fibromyalgia syndrome patients and/or relatives.

Lifetime and current stress-related psychiatric disorders are also increased within patients and/or relatives. Additionally, cross-sectional studies consistently show that up to 80% of patients with the syndrome are psychologically distressed, but much of this is may be a reaction to physical symptomatology. Consistent with this, premorbid psychological distress does not occur clearly in the majority of fibromyalgia syndrome cases in prospective studies.[2]

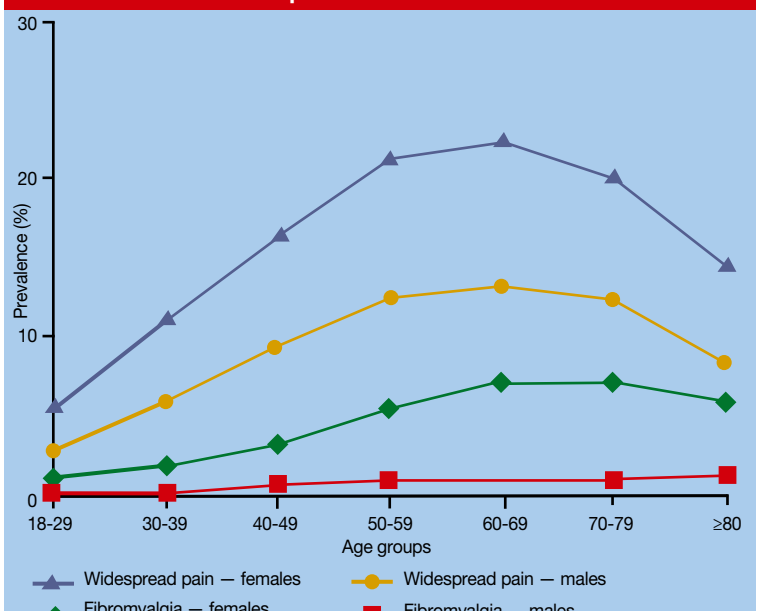
Overseas studies suggest that fibromyalgia syndrome afflicts 2% of the population, the great majority being female with a still-to-be explained peak incidence in middle life (figure 1).

Epidemiological studies indicate that there exist both genetic and environmental risk factors for the development of fibromyalgia syndrome. First-degree relatives of individuals with fibromyalgia have an eightfold increased risk of developing the condition, but only a twofold risk of having a lifetime psychiatric disorder. In general terms, environmental risk factors comprise physical and/or psychological stressors. These include cold or humid weather, weather changes, poor sleep, emotional stress, physical overactivity or physical inactivity, and flare-ups in response to noise and smell.

It is notable, however, that fibromyalgia syndrome often stems from the cumulative effects of multiple stressors to which individuals have been exposed over time, and that the syndrome's phenotype may, at best, only partially resolve with the removal of such stressors.

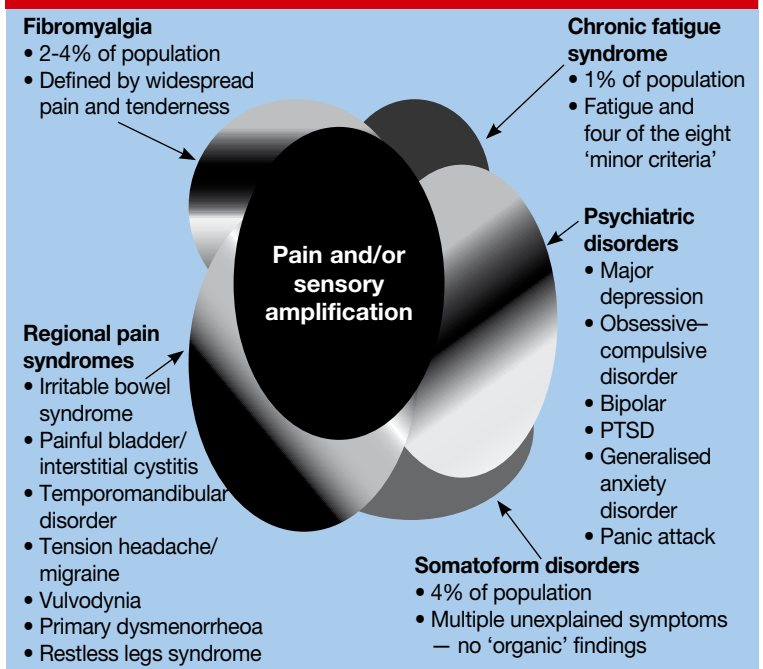
Twin studies have demonstrated that these associations (between functional somatic syndromes themselves, psychiatric disorders themselves and between functional and psychiatric disorders) may be explained by two independent sets of genetic traits that partially overlap: one potentially predisposing to the (often polymodal) sensory sensitivities of these syndromes, and the other to their affective components, thereby explaining the frequent co-occurrence of all these disorders (see figure 2), but implying that functional somatic syndromes are not psychiatric disorders.[3] A unifying grouping as 'central sensitivity syndromes' has therefore been suggested for all these conditions.

Figure 1: Prevalence rates for chronic widespread pain and fibromyalgia by age and sex across the adult life span.



Source: McBeth J, Mulvey MR. Fibromyalgia: mechanisms and potential impact of the ACR 2010 classification criteria *Nature Reviews, Rheumatology* 2012; 8:108-16.

Figure 2: Central sensitivity syndrome.



Adapted from: *Rheumatic Disease Clinics of North America* 2009; 35:233-51.

Fibromyalgia syndrome often stems from the cumulative effects of multiple stressors to which individuals have been exposed over time.

Pathogenesis

DESPITE evolving scientific investigations, a precise mechanistic understanding of the fibromyalgia syndrome presentation remains incomplete, and so it remains a syndromic diagnosis. Furthermore, pathophysiological heterogeneity under the fibromyalgia syndrome diagnostic label may be confounding scientific efforts to elucidate the disorder.

However, there continues to be consensus that the pain of fibromyalgia derives in large part from combined facilitation of ascending excitatory pain neural pathways and dysfunction of descending pain modulatory pathways with a net overactivity of pain excitatory neural mechanisms. Experiments have not found a link between psychological hypervigilance and the multiple sensory complaints of fibromyalgia patients.[4]

Nociception (the biological neural encoding and processing of noxious stimuli) comprises a dynamic physiological process extending from peripheral tissues to the cerebral cortex, probably involving multiple feedback loops. One well-studied node in this system, which dynamically integrates ascending (from the periphery) and descending (supraspinal) neural information, is the dorsal horn of the spinal cord. The dorsal horn participates in facilitatory and inhibitory feedback loops with the brainstem–limbic system.

Current evidence strongly suggests that, at least at the dorsal horn level, the nociceptive system in fibromyalgia syndrome is augmented with an overall excitatory integrated output ascending to the brain, a state that is called central sensitisation.

Extrapolating from animal and human neurophysiological studies, the widely distributed, deep tissue, spontaneous pain and evoked pain (the latter manifesting as 'allodynia' to normally non-noxious stimulation, and 'hyperalgesia', or pain amplification, to noxious stimulation), which characterise the syndrome, can therefore be explained.

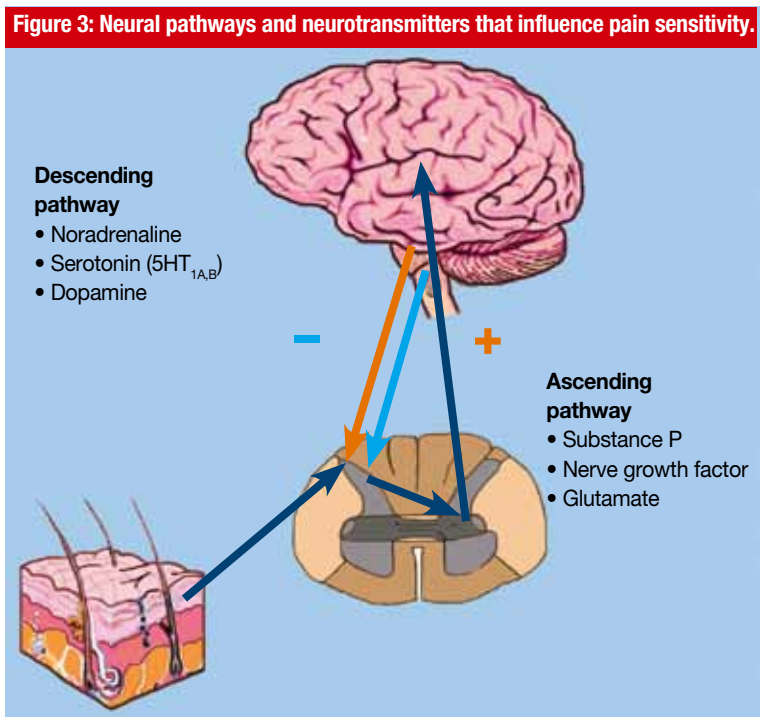
Also, and most importantly, the seemingly unique tendency of fibromyalgia patients to have protracted flares of pain after physical activity, potentially for days, has one possible explanation, as the dorsal horn processes of central sensitisation include prolonged reverberation of neural circuitry after stimulation by noxious or non-noxious stimuli.

Additionally, the prominent tendency for psychosocial stress to exacerbate the pain of fibromyalgia can be partially explained by dysfunction of descending pain modulatory pathways.

Evidence consistent with such dorsal horn dysregulation is accumulating. Enhanced spinal cord reactivity to painful stimulation occurs in a significant proportion of fibromyalgia patients using the objective electrophysiological nociceptive withdrawal reflex. Sub-anaesthetic ketamine, which blocks nociceptive pathway sensitisation at the dorsal horn and brainstem, can suppress characteristic psychophysical indicators of spinal sensitisation in most fibromyalgia patients. Functional neuroimaging findings of increased cortical and subcortical responses to standardised painful stimuli are congruent with enhanced nociception in fibromyalgia arising caudal to the forebrain.

Also, descending supraspinal inhibitory modulatory influences on dorsal horn nociception have been shown in psychophysical experiments to be deficient. Consistent with this, depressed cerebrospinal fluid levels of metabolites of dorsal horn inhibitory neurochemicals noradrenaline, serotonin and dopamine have been demonstrated in cross-sectional studies of fibromyalgia syndrome, and levels of facilitatory substance P, glutamate and nerve growth factor are increased (figure 3).

Figure 3: Neural pathways and neurotransmitters that influence pain sensitivity.



Furthermore, medications that correct CNS levels of these neurochemicals — for example SSRI/

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SNRIs and alpha2-delta ligands, such as gabapentin and pregabalin (see figure 4) — ameliorate pain in subgroups of patients with fibromyalgia syndrome.

Therefore, a viable hypothesis for understanding the pain of fibromyalgia is that it is causally associated with increased dorsal horn excitability along the entire length of the spinal cord. This sensitisation results from increased excitability of the integrating neural circuitry of the dorsal horn, partly due to decreased descending inhibition.

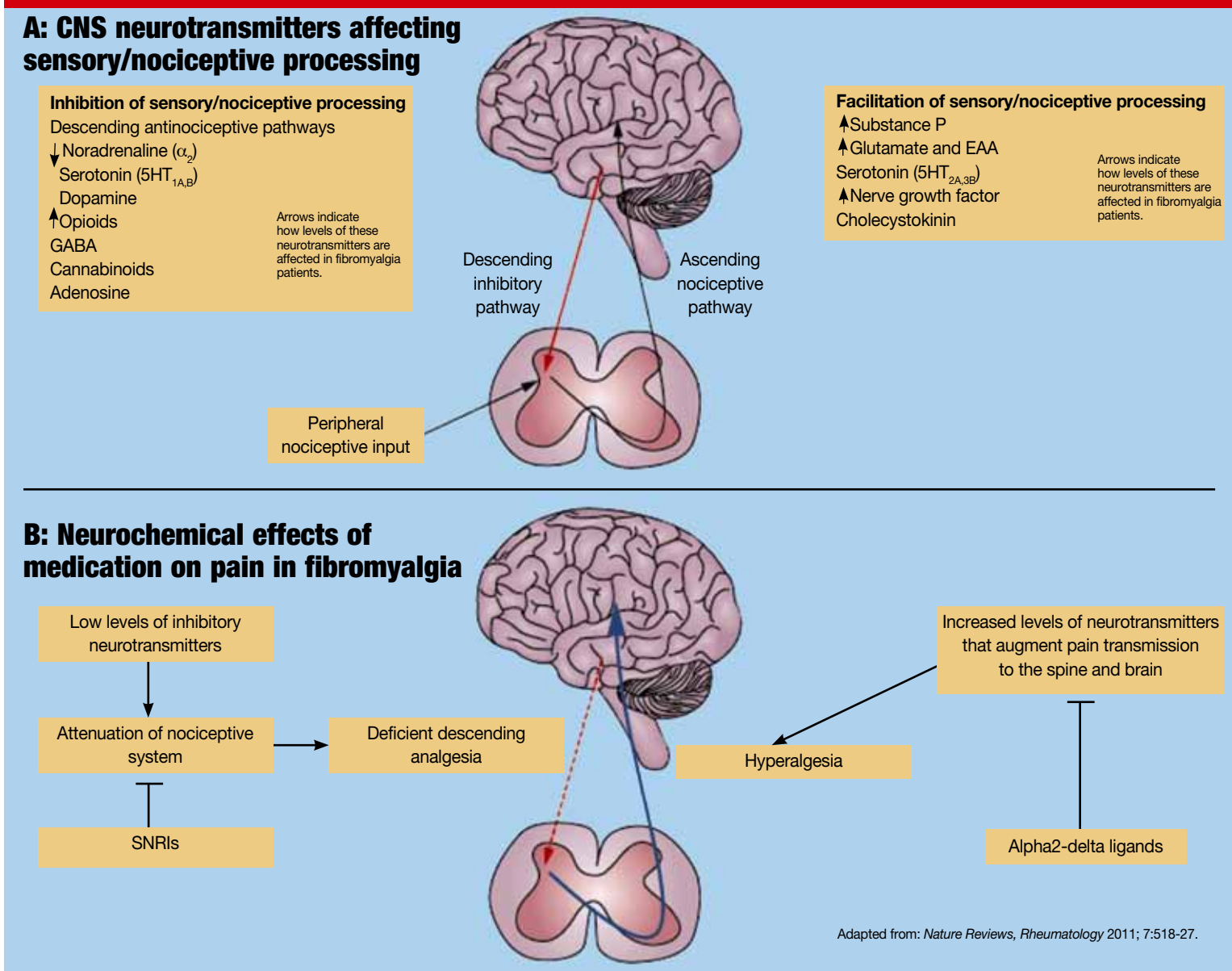
From animal studies, however, this dynamic model requires continuing nociceptive afferent input from the periphery to generate an output to ascending nociceptive pathways, but in primary fibromyalgia syndrome no peripheral source of afferent input is readily apparent. However, growing evidence suggests irritative foci within skeletal muscle (such as myofascial trigger points) may provide at least some of this input in the syndrome, and might do so in a positive feedback loop.

There exists preliminary confirmatory evidence that successful management of fibromyalgia will therefore require optimisation of all descending supraspinal and peripheral afferent influences on the dorsal horn nociceptive system.[5,6]

Compatibility of this central sensitisation model with the traditional biopsychosocial model of chronic pain is therefore also confirmed.

Although persistent pain no doubt contributes mechanistically to the remaining multisystem complaints of fibromyalgia syndrome, it is clinically apparent that amelioration of pain often does not lead to their resolution, implying that central sensitisation theory may not completely explain the syndrome. Also, it remains unclear which of the major non-pain symptoms are unique to the syndrome, or which of those may arise in any persistent pain condition.

Figure 4: Pain-processing pathways in fibromyalgia syndrome.



Adapted from: *Nature Reviews, Rheumatology* 2011; 7:518-27.

Diagnosis

WHILE fibromyalgia syndrome is characterised by persistent widespread pain in the presence of widespread pressure sensitivity (mechanical allodynia), it is generally accompanied by multiple somatic symptoms, of which fatigue, non-restorative sleep, cognitive dysfunction and psychological distress are the most frequent.

Paradoxically, the disorder's multiregional pain is frequently described as mixed mechanical and inflammatory pain, with prominent complaints of stiffness, despite the disorder traditionally being considered non-inflammatory. Although pain in most cases is reported as predominantly involving the trunk, the syndrome frequently presents with complaints of extremity pain alone.

The diagnosis is essentially a clinical one, and can be suspected from a carefully taken history alone, given its core symptoms of longstanding, widely distributed, muscular deep-tissue pain, daytime fatigue and non-restorative sleep.

Its presence can be confirmed by the physical examination finding of widespread (periaxial and peripheral) muscle group tenderness to a standardised pressure, calibrated at around 4kg. However, consistency of digital pressure is probably more important than its precise measure, and specific examination of tender point sites as determined by the American College of Rheumatology (ACR) is not critical in routine clinical practice.

Table 1: Pain types

	Peripheral (nociceptive)	Neuropathic	Central (non-nociceptive)
Aetiology	Primarily due to inflammation or mechanical damage in periphery	Damage or entrapment of peripheral nerves	Primarily due to a central disturbance in pain processing
Management	Responds to NSAIDs, opioids, procedures (eg, surgery)	Responds to both peripheral and central pharmacological therapy	Tricyclic, neuroactive compounds most effective
Behavioural factors	Behavioural factors minor	—	Behavioural factors more prominent
Examples	Osteoarthritis, rheumatoid arthritis, cancer pain	—	Fibromyalgia, irritable bowel syndrome, tension headache, idiopathic low back pain

Other causes of widespread pain should always be excluded when making the diagnosis. However, if fibromyalgia syndrome is interpreted as a dysregulation of (central) pain processing, it is conceivable that the condition can co-occur with widely distributed peripheral pathology causing widespread pain per se, and indeed may be triggered by the same. If fibromyalgia syndrome is defined as the combination of chronic widespread somatic pain and tenderness, it remains unclear if any pathologically well-defined medical illness is able to have a similar presentation.

An important part of the diagnostic process is always to determine if complaints of somatic pain are nociceptive, neuropathic, and/or non-nociceptive (table 1). Indeed, most persistent pain patients have more than one pain-generating mechanism operating, and it has been suggested that 20-30% of all patients with chronic nociceptive pain will additionally have centrally mediated enhanced nociception, presumably as a secondary somatic response.

Important conditions to be excluded in fibromyalgia

- Hypothyroidism
- Polymyalgia rheumatica
- Multiple sclerosis
- Statin myopathy
- Hypovitaminosis D
- Hepatitis C infection
- Obstructive sleep apnoea
- Inflammatory myopathies
- Connective tissue diseases (especially inflammatory arthritis)
- Opioid-induced hyperalgesia

Predisposing conditions that may be aggravating the underlying nociceptive disturbance of fibromyalgia syndrome also need to be elucidated (see box, page 24).

Importantly, comorbid regional functional pain syndromes (see figure 2, page 20) may also drive fibromyalgia syndrome and need to be specifically addressed.

Medical disorders that can mimic fibromyalgia are important to exclude also, at least clinically (see box above), but confusion can arise as possibly all can predispose to concomitant fibromyalgia syn-

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drome. A reasonable initial laboratory screen therefore comprises an FBC, full biochemical screen, thyroid function tests, creatine kinase, CRP and ESR.

While in otherwise-well adult women with longstanding symptoms the diagnosis of fibromyalgia can be very straightforward, the long differential diagnostic list and the frequent co-occurrence of multiple pain-causing pathologies can make diagnosis challenging. Therefore, referral to a rheumatologist or experienced pain physician can certainly be useful for advice on both diagnosis and management.

The ACR 1990 classification criteria for clinical diagnosis of fibromyalgia have long been criticised, in part because the tender point count has been shown to be influenced by not only physiologically based sensitivity to pressure but psychological distress.

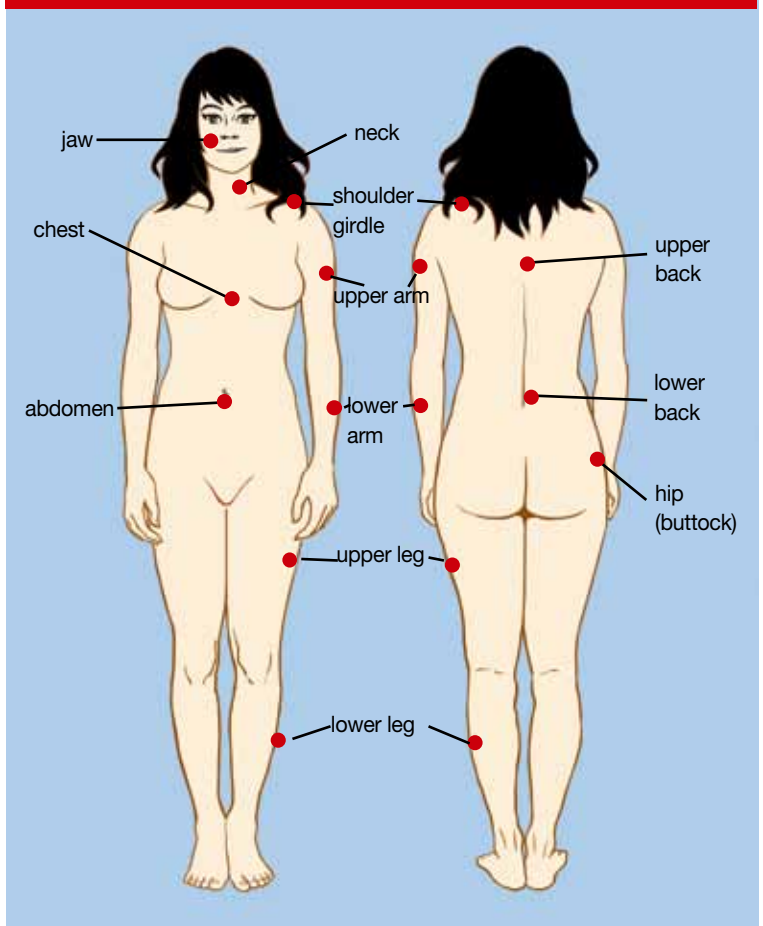
In response, in 2010 the ACR published provisional diagnostic criteria (see Online resources), which do not require a clinical assessment of mechanical allodynia, but do include a weighted evaluation of relevant concomitant multisystem symptoms. Figure 5 shows the ACR's pain sites, used in the classification criteria to calculate the widespread pain index.

However, the ACR 2010 preliminary diagnostic criteria have not been validated against other systemic rheumatic diseases but have been validated against regional non-inflammatory disorders, where the criteria appear to concordantly diagnose 88% of patients meeting ACR 1990 classification criteria.

Importantly, according to the ACR 2010 criteria, a diagnosis of fibromyalgia syndrome cannot now be made in the presence of a concomitant medical illness that can cause widespread pain. Therefore, the ACR 2010 criteria can only be used when the practitioner has excluded other possible causes of multiregional pain.

Therefore, the ACR 2010 criteria cannot be regarded as a diagnostic instrument that can differentiate between other systemic disorders. Utilisation of questionnaires based on the ACR 2010 criteria, however, may prove useful as a screening tool (see Online resources), but ultimately the diagnosis of fibromyalgia remains clinically based.

Figure 5: Visual aid for patients to identify their pain sites over the past week.



Predisposing conditions that may aggravate fibromyalgia

- Spinal mechanical pain syndromes (including post trauma)
- Hypermobility syndromes
- Inflammatory arthritis (especially rheumatoid arthritis)
- Connective tissue disorders (SLE, Sjogren's syndrome)
- Systemic inflammatory states (polymyalgia rheumatica, obesity, chronic infections, especially neurotrophic HIV and hepatitis C)
- Post-infectious fatigue syndromes
- Neuropathies
- Primary sleep disorders (obstructive sleep apnoea and restless legs syndrome)
- Stress-related psychiatric disorders (anxiety and depression)

Management

DESPITE these continuing problems of definition, scientific application of the ACR 1990 classification criteria has resulted in concrete, increasingly evidence-based advances in the management of fibromyalgia syndrome, directed at the syndrome's pain neural pathway sensitisation and rehabilitation. Several evidence-based national and international clinical practice guidelines have been published, the most recent from Germany.[7]

Recent approaches are both pharmacological and non-pharmacological, and overall have a modest, although significant effect, even when combined. In general, only a minority of individuals will respond to any specific therapy used as monotherapy. A significant proportion of patients do not respond to any extent and consequently the syndrome remains a chronic disorder that does not remit in most patients.

Fibromyalgia is therefore best managed using chronic disease principles, with an emphasis on optimising function. For most patients with a relatively uncomplicated presentation, this is naturally and best conducted in the primary care setting facilitated in Australia by use of Medicare's chronic disease management programs.[8]

Management needs to be patient-centred and holistic, with integrated care planning emphasising the acquisition of self-management skills and evidence-based medical care, all promoting self-efficacy and an enhanced internal locus of control.[9] The role of the GP is therefore one of supportive partnership, assisting the patient to access community resources and relevantly skilled health practitioners and prescribing appropriate medication.

Importantly, collaboration will be the most productive if it is well appreciated that patients have the continuing challenge of managing not only the daily impact of multiple symptoms but the psychosocial issues that arise from having a long-term multisystem and pervasive disorder. An important aim of care will be to assist the patient in learning how to live constructively with their chronic condition.

Overall treatment goals in fibromyalgia management

Reduce pain and tenderness

Ameliorate multidimensional symptoms, including:

- Fatigue
- Cognitive impairment
- Disrupted sleep
- Mood and anxiety symptoms
- Stiffness

Restore function and improve quality of life

Notwithstanding the limitations of modern management of fibromyalgia syndrome, all patients have the potential to improve at least somewhat using this article's recommended approach, and a sizeable proportion will significantly improve, making involvement in the care of these patients very gratifying.

Early diagnosis of fibromyalgia is now strongly advocated, to maximise the potential effectiveness of treatments and avoid the self-perpetuating physical, psychological and socioeconomic consequences of untreated pain, thereby minimising chronicity. Early validation of symptomatology can play an important role in promoting patient engagement with consequent encouragement of active illness behaviour.

Successful management initially requires careful clinical assessment to clarify the diagnosis. This includes identifying the predisposing factors and comorbid conditions (see Diagnosis, page 22), which may be driving the pathophysiological disturbance of the syndrome and which would therefore require independent management.

Ranking of patient priorities with regard to symptoms, function and quality of life is critical, as this enables individualised, focused management. This can be facilitated using inventories such as the Revised Fibromyalgia Impact Questionnaire (FIQR) or Fibromyalgia Assessment Status (FAS) (see Online resources, page 25) and patient symptom diaries, which can be used repeatedly throughout management.

Overall, a semiformal iterative process using realistic goal-setting and outcome assessment can provide structure to continuing management, enabling the eventual discovery of the optimal individual mix of pharmacological and non-pharmacological management techniques for each patient (see figure 6).

Concentrating on the management of the most intrusive complaints (as determined by formal ranking) at each visit, will expedite stabilisation of the patient in the general practice setting.

Optimal management of fibromyalgia requires a multimodal (pharmacological and non-pharmacological) approach, tailored to each patient's unique presentation. While pharmacological therapies have the strongest evidence base, combinations of exercise and educational or psychological techniques may be more effective.[10] However, the scientific evaluation of treatment combinations, including pharmacological, remains in its infancy.

Features on presentation that might predict intolerance of and/or response to particular therapies unfortunately remain unclear, implying that trials of all interventions are empirical and may need to be performed very cautiously.

Four core principles of fibromyalgia syndrome management — formal self-management education, mechanism-specific neuromodulatory medication, exercise, and cognitive behavioural therapy — are the most evidence-based. However, additional, less formal, self-managed psychosocial and lifestyle adaptations, with skills acquired via experiential learning, can also be successful.

Non-pharmacological therapies

Education

At diagnosis, referral to resources that educate patients about the nature of fibromyalgia syndrome, its management, and the limitations of therapies is strongly recommended, and is fortunately now easier with improved online resources (for example the Fibromyalgia Australia website).

Approaches using experiential learning result in greater engagement than passive formal courses, and especially if performed in a group setting that includes interactions with peer patients. This helps to give patients an understanding of the need for active involvement in self-care and development of proactive self-management skills.

As management strategies for the syndrome are evolving, continuing interaction with educational resources should be encouraged. Patients also need to educate themselves continually about the unique, dynamic, often complex features of their illness and how they are responding to the management strategies that are being trialled. Self-monitoring by regularly recording symptoms in a diary (see Online resources) and discussing these with the patient's relevant health professional can be very productive and can increase patient autonomy in the management of their condition.

Psychosocial and lifestyle adaptations

Psychosocial stress, physical activity and/or poor quality sleep, frequently aggravate the symptoms of individuals with fibromyalgia syndrome, often in a vicious cycle. Cognitive-behavioural measures

Figure 6: Fibromyalgia management in primary care.

Confirm fibromyalgia diagnosis — Define remediable risk factors and aggravating comorbidities

Early intervention — validate, engage and educate (reduce chronicity)
- Provide information about fibromyalgia, pathophysiology, treatment, expectations, prognosis
- Refer to pain medicine specialist or rheumatologist, if required

Stabilise condition for rehabilitation and improving quality of life
- Utilise assessment tools to rank symptoms
- Manage risk factors and comorbidities
- Stabilise symptoms/functional problems — sleep, pain
- Introduce the importance of stress reduction to prevent pain wind-up; pacing, monitoring and feedback
- Referral to allied health, community education and activity programmes.

Community resources
www.fibromyalgiaaustralia.org.au
- Web-based information
- Web-based education programs
- Fibromyalgia self-management programs (group cognitive behavioural therapy)
- Pain management programs
- CBT with a community-based psychologist

Regularly review care guided by treatment outcomes — Ongoing fibromyalgia management

GP management plan	Team care arrangement	Community resources
Early referral to • Fibromyalgia syndrome self-management education program (group or web-based CBT) **Treatment plan** reflects evidence-based recommendations of an integrated combination of: • Education. • Psychological, lifestyle adaption. • Physical therapy • Pharmacological **Specialist referrals** • Sleep • Pain • Comorbidities	**Care plan, agreed treatment goals:** to include: • Physiotherapist • Psychologist • Allied health professionals who specialise in fibromyalgia syndrome • Community education and activity programs **Practice nurse reviews** • Monitor all interventions and self-management strategies **Referrals influenced by:** • Availability of local services • Patient's health fund chronic disease management items • Guided by outcomes, diary, records	• Web-based information (www.fibromyalgiaaustralia.org.au and and other sites) • Exercise, movement, mobility, pain management interventions • Stress reduction, pain management CBT programs • Diet and nutrition • Occupational therapy • Fibromyalgia self-management programs, CBT, group or web-based • Community preventive education, movement and life skills programs • Special Interest groups/networking groups to enhance quality of life: - hydrotherapy - exercise, movement, relaxation, massage - mindfulness meditation - fibromyalgia syndrome support groups

Patient's symptoms will cycle, maintain focus on progress and prevention over time vs daily ups and downs

Review treatment outcomes and adjust treatment plan at follow-up visits
- Use assessment tools, patient diary
- Medication efficacy and adverse effects
- Monitor comorbidities and referral outcomes
- Adjust treatment

A dynamic or cyclic stepwise process
As patient's situation improves or changes, treatment priorities and goals will change as well.

to ameliorate these interactions, including stress management, activity pacing and sleep hygiene techniques are frequently indicated to stabilise symptoms.

Formal cognitive behavioural therapy has a small effect on pain and health-related quality of life, and only appears to significantly help one-third of fibromyalgia sufferers.[7] Improved efficacy may occur if CBT is tailored to the psychological characteristics of individuals, for example persistence vs avoidance of activity styles.

Traditional CBT comprises the exploration of a medley of techniques, including stress management, goal-setting, activity pacing, problem solving and cognitive restructuring, all to promote cognitive and behavioural coping skills, and therefore self-efficacy.

Newer approaches such as emotional disclosure and acceptance–commitment therapy are being explored, and may be useful in complementing traditional coping skills. Functional improvement is therefore emphasised, with consequent improvement in quality of life, despite residual symptoms.

However, by using community resources, such skills can be acquired less formally (see figure 6) and at a lower cost. There is growing evidence that suggests small but useful effect sizes for sleep hygiene techniques, meditative movement therapies (tai chi, yoga), hypnosis/guided imagery, and mindfulness-based stress reduction (health-related quality of life only).[7] Stress management is critical for many. Simple reminder techniques, such as lists, can ameliorate memory dysfunction. Activity pacing can optimise productivity while managing pain and fatigue.

Physical therapies

Exercise, especially aerobic, is widely recommended in fibromyalgia management, but is often viewed as problematic by patients. Formal studies of aerobic exercise have shown significant drop-out rates and only modest effect sizes for pain, fatigue and health-related quality of life, which wane after study completion.[7] Early studies suggest equal efficacy of aerobic and isometric exercise, with potential for synergism. Preliminary investigations suggest increased lifestyle-associated physical activity levels can result in modest improvements, as can yoga, tai chi and Nordic walking.[11]

The mechanism of benefit from exercise in fibromyalgia syndrome is unclear. In part, improvement comes from physical reconditioning, implying that exercise, at the very least, is always needed in the syndrome to avoid deconditioning, which in itself exacerbates pain and fatigue. In healthy individuals and patients with arthritis, exercise has the additional benefit of reducing sensitivity of endogenous ascending pain pathways via increasing descending inhibition, thereby improving pain control.

Mechanistically this should be ideal for fibromyalgia sufferers, but it is now appreciated that exercise in the syndrome uniquely and paradoxically causes enhancement of ascending nociceptive pathways, often causing widespread pain. This may be a result of increased descending facilitation and/or increased peripheral input from sensitised peripheral nerves or nociceptive foci.[12]

Exercise in the syndrome therefore needs to be individually tailored and often commenced extremely cautiously. Pain control will often be necessary before exercise, and pre-exercise biomechanical assessment and treatment by a specialist physiotherapist may prove invaluable for the most deconditioned. Patients should aim for a goal of half an hour of mildly to moderately vigorous aerobic exercise — water- or land-based — three days a week. Exercising to an intensity that still allows conversation with others is a useful guide. Whether promotion of descending inhibition can eventually be achieved remains to be proven.

When establishing exercise therapy for a fibromyalgia patient, the GP should bear in mind the following:
- Exercise should be fun, not a burden.
- Include exercise of non-painful parts of the body.
- Modify exercise to allow increased pain during and shortly after exercise, but avoid continuously increasing pain intensity over time.
- Keep the exercise well within the capabilities of the patient's body.
- Monitor symptom flares — minor symptom flares are to be expected during the initial stages of therapy, but should ease off once a routine is established. During major symptom flares, do not grade the exercises.

The evidence base for efficacy of passive physical therapies, including acupuncture and massage, remains modest, and a time limit should be set for these therapies. Complicating regional musculoskeletal issues may, however, respond favourably to passive therapies.

Pharmacological therapies

Two broad groups of evidence-based approaches to medication exist, each directed against an assumed mechanistically driven neurochemical imbalance of fibromyalgia (see figure 4, page 22):
- Tricyclic and SNRI antidepressants, which centrally increase noradrenaline and serotonin levels.
- Alpha2-delta calcium-channel

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Online resources

- Fibromyalgia Australia: www.fibromyalgiaaustralia.org.au
- American College of Rheumatology 2010 Preliminary Diagnostic Criteria questionnaire: www.fibroknowledge.com/site/downloads/2010_ACR_CRITERIA.pdf
- Revised Fibromyalgia Impact Questionnaire (FIQR): www.fmmgmt.com/pdf/Quiz/FIQR.pdf
- FIQR validation and psychometric properties: www.ncbi.nlm.nih.gov/pmc/articles/PMC2787284
- Self-administered Fibromyalgia Assessment Status (FAS): www.aafplearninglink.org/Resources/Upload/File/AAFP-10-106-Assessment-09-07-10.pdf
- Development and validation of the self-administered Fibromyalgia Assessment Status: a disease-specific composite measure for evaluating treatment effect: www.ncbi.nlm.nih.gov/pmc/articles/PMC2745809
- Symptom diaries and explanatory notes on their use: www.cfidsselfhelp.org/files/symptom_log.pdf; www.cfidsselfhelp.org/library/7-records-and-worksheets

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modulators (gabapentinoids), which decrease glutamate and substance P levels centrally.

Low-dose amitriptyline has been shown in low-quality trials (three months' duration or less) to have a moderate effect on pain and sleep improvement in fibromyalgia, and has unrestricted use under the PBS. Tolerance to the analgesic effect and weight gain, however, are frequently observed.

Duloxetine has high-quality, six-month duration evidence of small overall effect size for durable pain relief, irrespective of depression status, but is Therapeutic Good Administration and PBS registered in Australia for major depression only. Risk of weight gain appears to be less for duloxetine.

Tramadol, a Schedule 4 weak opioid with two-thirds of its analgesic action mediated through balanced elevation of central noradrenaline and serotonin, can be used as an alternative, and has a modest evidence base with no potential for weight gain.

In high-quality studies of up to six months' duration, pregabalin has been shown to modestly improve pain and sleep overall, but has TGA approval for use in Australia for neuropathic pain only. It is only available to veterans under the PBS. After six months, one in three initial responders will have developed tolerance to its therapeutic effects.

Gabapentin in a single, three-month, modestly sized trial has been shown to improve pain and sleep in fibromyalgia to some degree. Weight gain can be a limiting side effect for both gabapentinoid drugs.

A practical approach to pharmacotherapy is summarised in the box, at right.

Use of pure mu-opioid receptor agonists in fibromyalgia syndrome is undesirable because of long-term side effects, the increased risk of opioid-induced hyperalgesia, and dependency and lack of evidence of durable effect. However, opioids other than tramadol that also potentially have pain modulatory actions, for example transdermal buprenorphine or low-dose methadone, may eventually prove useful in carefully selected circumstances.

Given that the randomised controlled trials already mentioned had a limit of six months' duration, and also given the possibility of deleterious side effects and/or development of drug tolerance, a systematic trial of medication withdrawal, or at least dose reduction, should be considered in all patients after six months of therapy.

In general, the efficacy of all medications can be evaluated within four weeks of commencement and non-pharmacological therapies within three months.

Standard pharmacological therapy options for associated sleep and mood disturbances need to be adapted to the recommendations mentioned above.

The gabapentinoids have a seemingly unique capacity to increase both slow-wave and REM sleep, and are appropriate hypnotics for fibromyalgia; benzodiazepines decrease slow-wave and REM sleep, and should be avoided, while tricyclics decrease REM sleep.

In summary, it is possible that all fibromyalgia syndrome patients, through skilled self-management techniques and judicious use of evidence-based medical care, can learn to live successfully with their chronic disorder.

Four cornerstones of modern management of fibromyalgia syndrome

Education
Psychosocial and lifestyle adaptations
Physical therapies
Pharmacological therapies

Tips for improving pain therapy

Individualise therapy
If exhaustion, mood dominate, start with duloxetine
If pain and sleep dominate, start with gabapentinoid, low dose tricyclic antidepressant or tramadol
Avoid pure mu-opioid receptor agonists
For any drug, start low and increase dose gradually
Recommended dose is often not achieved because of side effects
May be better to add second drug rather than switch
Non-pharmacological therapy is as important as drugs

Adapted from: *Best Practice and Research in Clinical Rheumatology* 2007; 21:499-511.

How to Treat Quiz

Fibromyalgia syndrome — 23 November 2012

INSTRUCTIONS

Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points. We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

ONLINE ONLY

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1. Which THREE statements regarding the epidemiology of fibromyalgia syndrome and environmental risk factors are correct?

a) The hallmark clinical features of fibromyalgia syndrome are pain and the related physical examination finding of pressure sensitivity
b) Studies suggest that fibromyalgia syndrome afflicts 25% of the population
c) First-degree relatives of individuals with fibromyalgia syndrome have an eightfold increased risk of developing the condition
d) Physical stressors such as weather changes, emotional stress and physical overactivity are some of the environmental risk factors for the development of fibromyalgia

2. Which THREE statements regarding the pathophysiology of fibromyalgia are correct?

a) The pain of fibromyalgia is considered to be due to a combined facilitation of ascending excitatory pain neural pathways and dysfunction of descending pain modulatory pathways with a net overactivity of pain excitatory neural mechanisms
b) Studies have been able to confirm that psychological hypervigilance wholly accounts for the multiple sensory complaints of fibromyalgia patients
c) The dorsal horn of the spinal cord integrates nociceptive afferent (from the periphery) and descending (supraspinal) neural information
d) The nociceptive system at the dorsal horn level in fibromyalgia syndrome is augmented with an overall excitatory integrated output ascending to the brain, a state that is called central sensitisation

3. Which TWO statements regarding pain, stress and neurotransmitters in fibromyalgia syndrome are correct?

a) Hyperalgesia is pain caused by normally non-noxious stimulation
b) A possible explanation for the tendency of fibromyalgia patients to have protracted flares of pain after physical activity may be that the dorsal horn processes of central sensitisation include prolonged reverberation of neural circuitry after stimulation by noxious or non-noxious stimuli
c) The tendency for psychosocial stress to exacerbate the pain of fibromyalgia syndrome is unrelated to the descending pain modulatory pathways
d) Depressed cerebrospinal fluid levels of metabolites of dorsal horn inhibitory neurochemicals noradrenaline, serotonin and dopamine have been demonstrated in fibromyalgia syndrome

4. Which TWO statements regarding pain in fibromyalgia syndrome are correct?

a) The persistent pain of fibromyalgia is rarely accompanied by other somatic symptoms
b) Fibromyalgia patients complain of stiffness despite the disorder traditionally being considered non-inflammatory
c) Fibromyalgia syndrome rarely presents with a patient complaining of pain in the extremities
d) The diagnosis of fibromyalgia syndrome can be suspected from a history of symptoms of longstanding, widely distributed, muscular deep-tissue pain, daytime fatigue and non-restorative sleep

5. Which TWO statements are correct regarding diagnosis of fibromyalgia syndrome?

a) Specific examination of tender point sites as determined by the American College of Rheumatology is essential in the diagnosis of the condition
b) Blood tests are unwarranted in the diagnosis of fibromyalgia syndrome
c) It is important to determine if complaints of somatic pain are nociceptive, neuropathic, and/or non-nociceptive
d) Conditions predisposing to fibromyalgia syndrome include spinal mechanical syndromes, inflammatory arthritis and connective tissues disorders

6. Which THREE statements are correct regarding central pain?

a) It is primarily due to a central disturbance in pain processing
b) Central pain is opioid responsive
c) Tricyclics and other neuroactive medications are most effective in treating central pain
d) Cancer pain is an example of central pain

7. Which THREE statements regarding management of fibromyalgia syndrome are correct?

a) Fibromyalgia patients have shown an excellent response to both pharmacological and non-pharmacological treatments
b) The most effective approach to management of fibromyalgia is to use chronic disease principles and emphasise optimisation of function
c) It is important for GPs managing patients with fibromyalgia to understand that patients have the continuing challenge of managing not only the daily impact of multiple symptoms but the psychosocial issues that arise from having a long-term, multisystem and pervasive disorder
d) Inventories such as the Revised Fibromyalgia Impact Questionnaire can be useful in the ranking of patient priorities with regard to symptoms, function and quality of life

8.Which TWO statements are correct regarding pharmacological therapies in fibromyalgia syndrome?

a) Tricyclic and SNRI antidepressants centrally increase noradrenaline and serotonin levels
b) Gabapentinoids increase glutamate and substance P levels centrally
c) There is evidence that duloxetine has a small overall effect size for durable pain relief, irrespective of depression status
d) Both duloxetine and pregabalin are available on the PBS for treatment of fibromyalgia syndrome

9. Which TWO statements regarding medications in fibromyalgia syndrome are correct?

a) Pure mu-opioid receptor agonists such as codeine and morphine are recommended for the treatment of pain in fibromyalgia
b) Weight gain can be a limiting side effect of gabapentinoid drugs
c) If exhaustion and mood are predominant symptoms, start pharmacological treatment with a gabapentinoid
d) The efficacy of all medications can be evaluated within four weeks of commencement

10. Which THREE statements regarding non-pharmacological treatments in fibromyalgia syndrome are correct?

a) Patients should be referred at diagnosis to educational resources about the nature of fibromyalgia syndrome, its management and the limitations of therapies
b) Recording symptoms in a diary is of little use in the management of fibromyalgia
c) Vigorous exercise in fibromyalgia syndrome uniquely and paradoxically causes enhancement of ascending nociceptive pathways, often causing widespread pain
d) Emotional disclosure and acceptance–commitment therapy are newer psychological approaches, which are currently being studied, and may be useful in complementing traditional coping skills

CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2011-13 triennium. You can complete this online along with the quiz at **www.australiandoctor.com.au.** Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.

Australian Doctor Education

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NEXT WEEK Australia's suicide rate peaked in 1997. Since then, GPs have been diagnosing and treating depression more often, and as a result, suicide rates have fallen. Even so, more than 40 people die from suicide every week in Australia. The next How to Treat examines ways to assess suicide risk and how to prevent suicide. The author is **Dr David Horgan**, Clinical Associate Professor of Psychiatry, University of Melbourne; honorary senior specialist psychiatrist, Royal Melbourne Hospital, Parkville; consultant psychiatrist in private practice, w, Victoria; and director, Australian Suicide Prevention Foundation.