Fibromyalgia:

Clinical Pathophysiology, Epidemiology, Functional Impact and Evidence Based Management

Abstract

Fibromyalgia is a chronic pain disorder characterised by widespread musculoskeletal pain, fatigue, sleep disturbance and cognitive dysfunction. It affects approximately 2–4% of the global adult population and is more frequently diagnosed in women. The condition is associated with central sensitisation and altered pain modulation rather than peripheral inflammatory pathology. Diagnostic delay remains common, and epidemiological data suggest that a substantial proportion of individuals meeting diagnostic criteria remain undiagnosed. Fibromyalgia significantly impairs quality of life and is frequently associated with psychiatric and functional comorbidities. Management is multidisciplinary, incorporating pharmacological and non-pharmacological strategies. Continued research is required to refine mechanistic understanding and improve targeted treatment approaches.

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1. Definition and Classification

Fibromyalgia is defined as a chronic primary pain condition characterised by persistent widespread musculoskeletal pain accompanied by fatigue, sleep disturbance and cognitive symptoms[1]. The International Association for the Study of Pain classifies fibromyalgia as a nociplastic pain disorder, meaning that pain arises from altered nociceptive processing without clear evidence of ongoing tissue damage or inflammation[2]. Unlike inflammatory rheumatic diseases such as rheumatoid arthritis or systemic lupus erythematosus, fibromyalgia does not produce structural joint destruction or objective inflammatory markers on laboratory testing[3]. The disorder is therefore understood primarily as a condition of dysregulated pain processing within the central nervous system.

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2. Pathophysiology

The prevailing mechanistic model of fibromyalgia centres on central sensitisation, a phenomenon defined as increased excitability of neurons within the central nervous system that amplifies pain perception[3]. Functional neuroimaging studies demonstrate that individuals with fibromyalgia exhibit augmented activation of pain processing regions of the brain in response to stimuli that are non-painful in healthy controls[3]. Neurochemical analyses further reveal elevated concentrations of excitatory neurotransmitters such as substance P and glutamate in cerebrospinal fluid, alongside reduced levels of serotonin and norepinephrine, both of which are involved in descending inhibitory pain modulation[3]. These findings support the hypothesis that fibromyalgia represents a disorder of altered central pain regulation rather than peripheral nociceptive injury.

In addition to central sensitisation, neuroendocrine and autonomic dysfunction appear to contribute to symptom expression. Altered hypothalamic–pituitary–adrenal axis activity and abnormal cortisol secretion patterns have been observed in some patients[4]. Autonomic imbalance, particularly sympathetic overactivity, may contribute to fatigue, sleep disruption and orthostatic intolerance. Disturbances in sleep architecture, including reduced slow-wave sleep, further perpetuate pain amplification and fatigue[3]. Genetic predisposition has also been suggested, as familial aggregation studies demonstrate increased risk among first-degree relatives[4]. Environmental triggers such as trauma, infection or chronic psychological stress may precipitate symptom onset in susceptible individuals.

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3. Diagnostic Criteria

Fibromyalgia remains a clinical diagnosis based on symptom patterns rather than objective biomarkers. The 2016 revision of the American College of Rheumatology (ACR) diagnostic criteria specifies that patients must demonstrate widespread pain index and symptom severity scale thresholds, generalised pain in at least four of five body regions, and symptom duration of at least three months[5]. Laboratory investigations are performed primarily to exclude alternative diagnoses. Despite the availability of structured criteria, diagnostic delay is common and may extend from two to five years after symptom onset[6]. Contributing factors include symptom overlap with other chronic conditions, absence of confirmatory laboratory testing and variability in clinician familiarity with diagnostic standards.

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4. Epidemiology

Fibromyalgia is a common chronic pain condition worldwide. Systematic reviews estimate global prevalence between approximately 2% and 4% of the adult population[4,7]. In the United States, analysis of the National Health Interview Survey suggests a prevalence of 2.0–2.7%[8]. European estimates are broadly comparable at approximately 2.5%[4], although some regional surveys in the United Kingdom have reported prevalence rates as high as 5.4%[9]. Women are diagnosed approximately two to three times more frequently than men, though this disparity may partially reflect diagnostic bias[8]. Prevalence appears to increase with age until approximately the sixth decade of life[4].

Incidence data from UK primary care records suggest approximately 30–35 new cases per 100,000 person-years[10]. However, epidemiological interpretation is complicated by underdiagnosis. A population-based U.S. study demonstrated that only 34–40% of individuals meeting fibromyalgia criteria had received a formal clinical diagnosis[11]. This suggests that more than half of affected individuals may remain unrecognised within healthcare systems. Factors contributing to underdiagnosis include historical controversy regarding the condition, absence of objective diagnostic tests and misattribution of symptoms to psychiatric or somatic disorders.

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5. Clinical Presentation and Functional Impact

The clinical presentation of fibromyalgia is multisystemic. Patients typically report persistent widespread pain described as aching, burning or throbbing in quality[1]. Fatigue is often profound and disproportionate to physical exertion. Non-restorative sleep is nearly universal, and patients frequently describe cognitive impairment, colloquially referred to as “fibro-fog,” characterised by impaired concentration, slowed information processing and memory difficulties[1].

Health-related quality of life is markedly reduced. Comparative analyses demonstrate that fibromyalgia patients often exhibit physical functioning scores similar to or worse than those observed in rheumatoid arthritis or systemic lupus erythematosus[4]. Longitudinal studies indicate persistent impairment over extended follow-up periods[6]. Work participation is frequently compromised, and rates of work disability are significantly elevated compared to the general population[6].

Comorbidity is common. Major depressive disorder and anxiety disorders occur at substantially higher rates than in the general population[4]. Functional gastrointestinal disorders such as irritable bowel syndrome, migraine, temporomandibular disorders and chronic fatigue syndrome frequently coexist[4]. The presence of psychiatric comorbidity is associated with greater symptom severity and reduced functional capacity.

Qualitative research highlights the psychosocial burden of living with fibromyalgia. Patients often report feelings of invalidation due to the absence of objective diagnostic findings[12]. This

perceived stigma may contribute to social withdrawal, strained interpersonal relationships and psychological distress. The condition is frequently described as an “invisible illness,” reflecting the discrepancy between internal symptom severity and external appearance.

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6. Treatment and Management

There is no curative therapy for fibromyalgia, and management focuses on symptom control and functional improvement. Pharmacological treatments with moderate evidence of efficacy include serotonin–norepinephrine reuptake inhibitors such as duloxetine and milnacipran, the anticonvulsant pregabalin and low-dose tricyclic antidepressants such as amitriptyline[3][4]. These medications target central pain modulation pathways. Opioids are generally not recommended due to limited efficacy and potential harms[3].

In 2025, sublingual cyclobenzaprine (TNX-102 SL) received regulatory approval in the United States, representing the first new pharmacological option for fibromyalgia in over fifteen years[13]. Clinical trials demonstrated improvements in pain and symptom burden compared with placebo.

Non-pharmacological interventions constitute a cornerstone of management. Graded aerobic exercise and strength training have demonstrated consistent benefit in improving pain and physical function[4]. Cognitive behavioural therapy is effective in reducing pain-related disability and improving coping strategies[4]. The UK National Institute for Health and Care Excellence recommends personalised management plans that prioritise education, supervised exercise and psychological support[14].

Emerging investigational therapies include ketamine infusions, low-dose naltrexone, transcranial magnetic stimulation and cannabinoid-based treatments. While preliminary studies show potential benefit, evidence remains insufficient for routine clinical adoption.

Conclusion

Fibromyalgia is a chronic pain disorder characterised by central sensitisation and multisystem symptom burden. It affects approximately 2–4% of the global population, with a substantial proportion of cases remaining undiagnosed. The condition significantly impairs quality of life and is frequently associated with psychiatric and functional comorbidities. Management requires a multidisciplinary approach integrating pharmacological and non-pharmacological strategies. Ongoing research into neurobiological mechanisms may facilitate the development of more targeted therapeutic interventions.

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