Fibromyalgia syndrome
Definition, classification, clinical diagnosis and prognosis

Das Fibromyalgiesyndrom. 
Background and questions
The fibromyalgia syndrome (FMS), its definition, classification and diagnosis among various medical associations, doctors, psychologists and patients is controversial [61]. The definition, classification and diagnosis of chronic pain in multiple areas of the body (chronic widespread pain, CWP) has been partially determined by the political claims of professional medical societies and the pension rights of the patients.

The working group focused on the following key questions:
1. What are the core symptoms of FMS?
2. What differences and overlapping symptoms exist between FMS and somatoform and depressive disorders?
3. What criteria should be used to diagnose FMS?
4. What exclusion diagnostics are necessary?
5. When are professional psychotherapeutic diagnostics meaningful?
6. Are there different courses and severities of FMS?
7. What is the prognosis (including life expectancy) of patients with FMS?

Materials and methods
The parameters of the literature search and analysis and the preparation of the recommendations are described in the article “Methodological fundamentals used in developing the guideline”.

Results
Preliminary remarks
The following findings apply to adults. For the definition, classification, clinical diagnosis and prognosis of chronic pain in multiple areas of the body in children and adolescents, see the article titled “Definition, diagnosis and treatment therapy of chronic widespread pain and so-called fibromyalgia syndrome in children and adolescents”. Key recommendations are italicized.

Definition of chronic pain in multiple areas of the body

Consensus-based statement
Definition of chronic widespread pain (CWP): CWP can be defined according to the American College of Rheumatology (ACR) 1990 criteria and the modified provisional ACR 2010 criteria. EL 5, strong consensus

Comment. Pain can be categorized according to clinical criteria into monolocular pain (e.g., in one part of the body), regional pain (e.g., in one specific area of the body, such as the shoulder or arm) and pain in multiple areas of the body. Population-based studies have shown that most people with musculoskeletal pain have more than one pain location [18, 45].

The ACR classification criteria from 1990 defines CWP in multiple body regions [58] as pain >3 months of continuous pain in the following areas:
- axial skeleton (i.e., cervical spine, anterior chest, thoracic or lumbar spine)
- right and left halves of the body
- above and below the waist.

Widespread pain may also be an indication of at least 7–19 of the predefined types of pain described in the Widespread Pain Index (WPI; modified preliminary ACR 2010 criteria [20, 64]).
Widespread pain can have specific causes (e.g., inflammatory rheumatic disease and diffuse bone metastases). In most patients affected with CWP, there are no specific causes of somatic disease [45].

Definition of FMS

Evidence-based statement
FMS was defined in the ACR 1990 classification criteria by CWP and painful pressure in at least 11 out of 18 tender points. EL 2b, strong consensus

Comment. People with chronic pain, sleep disorders and fatigue have been described since biblical times. Smythe [51] provided a historical overview of examples of famous people, such as Florence Nightingale and Charles Darwin, who were “lifelong invalids, yet lived to a ripe old age”. In the rheumatology literature, the symptom complex is known as soft tissue rheumatism or fibrositis. According to Smythe [50], fibrositis has an imprecise symptomatology with multicellular pain and stiffness lasting for more than 3 months with distinctive local hyperalgesia, chronic fatigue and sleep disorders. Additionally, a depressive mood is often involved. The term fibromyalgia was first used by Hench (1976) [25]. In 1990, the ACR defined specific criteria for fibromyalgia that are distinct from inflammatory rheumatic diseases and arthritis. The ACR classification criteria of FMS represents a consensus definition based on clinicians’ descriptions of the clinical picture of the disorder. The combination of the above-mentioned criteria distinguished patients with primary (no organic disease) and secondary (co-morbidity inflammatory rheumatic disease) fibromyalgia from control patients with inflammatory rheumatic diseases and regional pain syndromes (e.g., osteoarthritis) with a sensitivity of 88% and a specificity of 81% [58]. These classification criteria were not conceptualized by the ACR authors as diagnostic criteria [61].

Symptom complex of FMS

Evidence-based statement
People with CWP are described in population-based studies and are present in facilities that treat all of the stages of clinical care. Widespread pain is associated with other physical and mental complaints. EL 2b, strong consensus

Comment. Patients with CWP differ from patients with local and regional pain syndromes that are caused by an increase in the severity of physical and mental symptoms (distress). According to the ACR 1990 criteria, patients with CWP and FMS are different from patients with CWP without FMS because their physical and mental symptoms are more severe [7, 19, 56], and their tender points are markers of distress [60]. In a representative German population sample of 2,504 individuals in 2009, an asymptotic distribution of pain locations and physical and mental complaints were described. In a cluster analysis, four groups of individuals were identified: pain-free individuals without physical or mental discomfort (“healthy cluster”), individuals with oligolocular pain and mild physical or psychological symptoms (“regional pain cluster”), individuals with widespread pain, mild physical pain symptoms and no mental discomfort (“CWP cluster”) and individuals with widespread pain and severe physical and mental symptoms (“FMS cluster”) [19]. On the basis of a continuum representing the severity of physical (including the number of pain locations) and psychological symptoms, individuals with CWP were located on the outer region of the continuum, and people with FMS were at the end of the continuum [60].

Core symptoms of FMS

Evidence-based statement
In addition to CWP, the other core symptoms of FMS include sleep disorders (non-restorative sleep) and fatigue or exhaustion (physical or mental). EL 3b, strong consensus

Comment. All of the members of a German FMS self-help organization reported numerous physical and mental complaints as a result of a symptom questionnaire developed by the organization. The primary symptoms (in >97% of those affected) were muscle pain in various locations, back pain, fatigue, joint pain in various locations, poor sleep quality, morning stiffness, exhaustion in the morning, weak concentration, lack of stimulation, reduced performance and forgetfulness [16]. These complaints were also indicated as the most common by patients with FMS from various German clinical facilities who were diagnosed based on the ACR 1990 classification criteria [17], patients with FMS who were diagnosed based on the clinical criteria from the United States (US) database for rheumatic diseases [63] and patient and expert consensuses on the “key domains of FMS” [41].

Classification of FMS as a functional somatic syndrome

Consensus-based statement
FMS can be classified as a functional somatic syndrome. EL 5, majority

Comment. Functional somatic syndromes are defined by a clinical complex of physical symptoms, a defined time period and the absence of the causative somatic disease factors that explain the symptoms (e.g., structural tissue damage, biochemical disorder or specific laboratory findings). The individual medical societies define functional somatic syndromes associated with their respective symptoms and do not consider additional physical and mental complaints [40] associated with other disciplines in the definition. Fibromyalgia is described in the International Classification of Diseases in the German version of the World Health Organization (WHO) in the chapter titled “Diseases of the musculoskeletal system and connective tissue” and the subsection titled “Other soft tissue diseases not classified elsewhere” (M79.70) [8].

Definition/overlap of FMS with persistent somatoform pain disorder (F45.40) and chronic pain disorder with psychological and somatic factors (F45.41)

Evidence-based statement
The criteria for FMS (ICD-10 M79.70), persistent somatoform pain disorder (F45.40) and chronic pain disorder with psychological and somatic factors
(F45.41) overlap and include different clinical characteristics in individuals with CWP without specific somatic disease factors. FMS is not synonymous with a persistent somatoform pain disorder or a chronic pain disorder with psychological and somatic factors. EL 3a, strong consensus

Comment. The International Classification of Diseases published by the WHO includes the possibility of classifying chronic physical discomfort without somatic disease factors in the chapters on somatic diseases and in the chapter titled “Psychological and behavioral disorders” under somatoform disorders (F45). As a result, patients in Germany with fibromyalgia-like symptoms are not coded as M79.70 but as a persistent somatoform pain disorder (F45.40) or somatization disorder (F45.1) by many doctors and psychologists.

There is an intensive debate regarding the classification of physical ailments without somatic disease factors in the latest revision of the International Classification of Diseases [32]. The following are the opposing positions:

- elimination of the somatoform disorder diagnostic category and classification of physical complaints without somatic disease factors only for physical diseases [33] and
- preservation of the somatoform disorder category in the “Psychological and behavioral disorders” chapter with clarification of the criteria [37].

Persistent somatoform pain disorders are not clearly defined by the ICD-10 criteria. The diagnostic criteria of persistent somatoform pain disorders are not listed with respect to the primary criteria of a somatoform disorder that must be met for accurate classification and how many criteria must be met.

Overall criteria for somatoform disorders:

- Medical findings do not explain the type and the extent of the symptoms or the suffering or emotional involvement of the patient (e.g., a discrepancy between how the patient feels and the medical findings).

Keywords

Fibromyalgia syndrome · Definition · Classification · Diagnosis, clinical · Guideline

Das Fibromyalgiesyndrom. Definition, Klassifikation, klinische Diagnose und Prognose

Zusammenfassung

Hintergrund. Die planmäßige Aktualisierung der S3-Leitlinie zum Fibromyalgiesyndrom (FMS; AWMF-Registernummer 041/004) wurde ab März 2011 vorgenommen.


Schlüsselwörter

Fibromyalgiesyndrom · Definition · Klassifikation · Klinische Diagnose · Leitlinie

Abstract · Zusammenfassung

Fibromyalgia syndrome. Definition, classification, clinical diagnosis and prognosis

Abstract

Background. The updated German S guidelines for managing patients with fibromyalgia syndrome (FMS) published by the Association of the Scientific Medical Societies in Germany ("Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften", AWMF; registration number 041/004) was planned starting in March 2011.

Materials and methods. The development of the guidelines was coordinated by the German Interdisciplinary Association for Pain Therapy ("Deutsche Interdisziplinäre Vereinigung für Schmerztherapie", DIVS), 9 scientific medical societies and 2 patient self-help organizations. Eight working groups with a total of 50 members were evenly balanced in terms of gender, medical field, potential conflicts of interest and hierarchical position in the medical and scientific fields. Literature searches were performed using the Medline, PsycINFO, Scopus and Cochrane Library databases (until December 2010). The grading of the strength of the evidence followed the scheme of the Oxford Centre for Evidence Based Medicine. The formulation and grading of recommendations was accomplished using a multi-step, formal consensus process. The guidelines were reviewed by the boards of the participating scientific medical societies.

Results and conclusion. The clinical diagnosis of FMS should be based on the 1990 American College of Rheumatology (ACR) classification criteria (with the examination of tender points), the modified diagnostic criteria from the ACR 2010 (without the examination of tender points) or the criteria published in the German AWMF guidelines for FMS. The English full-text version of this article is available at SpringerLink (under “Supplemental”).

Keywords

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Abstract · Zusammenfassung

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even when the beginning and duration of the symptoms are closely related to unpleasant life events, difficulties or conflicts (somatic fixation).

- The understanding reached regarding the physical or psychological cause of the symptoms is often disappointing to the patients and doctors (dysfunctional relationship behavior).

- The attention-seeking (histrionic) behavior of patients, as listed in the “Etiology and pathophysiology of fibromyalgia syndrome” chapter [49], is not sufficiently explained by the physical symptoms of FMS through somatic disease factors. This criterion applies to most FMS patients. No studies were identified demonstrating that patients with FMS took the initiative to request another organic diagnosis by exclusion after they had been diagnosed with FMS.

Case studies from clinical facilities [15] and cohort studies by FMS self-help organizations [1] report that the majority of those affected by the question of subjective causes of the disease indicate that both physical and psychological factors are involved. A somatic fixation was determined in these samples in only a few patients with FMS. Studies on dysfunctional patient–physician behavior and attention-seeking relationship behavior in patients with FMS were not found. A multicenter German study evaluating the utilization of medical services showed that only a fraction of patients with FMS had an increased number of medical consultations compared to the entire German population [33].

Criteria for persistent somatoform pain disorder:

a) severe excruciating pain >6 months,
b) no sufficient evidence obtained from adequately conducted somatic testing to explain the symptoms,
c) occurs in conjunction with emotional conflicts or psychosocial problems that are important causal factors due to their severity and
d) exclusion of

- psychogenic pain during the course of a depressive disorder or schizophrenia and

- pain due to known or psychophysiological mechanisms, such as muscle tension pain or migraine.

Criteria a and b apply to patients with FMS. Criterion c applies to many, but not all, patients with FMS. Case studies from clinical facilities have shown that relevant psychosocial stress was temporally related to the development of or increase in CWP in 60–80% of patients with FMS [15]. Psychosocial stressors are associated with an increased risk of FMS [49]. Regarding criterion d, systematic review articles showed that co-morbid depressive disorders occur in 30–80% of patients with FMS [11]. The psychophysiological mechanisms of pain in FMS are described in the “Pathophysiology” chapter [49]. Longitudinal studies from the Swedish twin register have provided evidence of a common factor using path analysis (determined more by environmental factors than by genetic factors), which can affect both functional somatic disorders (e.g., FMS, irritable bowel syndrome, headaches and chronic fatigue syndrome) and psychological disorders (e.g., depression and generalized anxiety disorder) [28, 29]. A dimensional analysis of the FMS symptom complex based on physical and psychological complaints, psychosocial stressors, availability of medical services and subjective beliefs regarding the cause of the illness is more appropriate than the categorical classification of FMS as a persistent somatoform pain disorder [24].

The criteria of a chronic pain disorder with somatic and psychological factors (F 45.41) are as follows: pain that is present for at least 6 months in one or more anatomical regions, which originated due to a physiological process or a physical disorder. Although psychological factors play an important role in the severity, exacerbation or continuation of the pain, they are not the direct cause. The pain induces clinically significant distress and impairment in social, occupational or other important functional areas. Pain disorders that are specifically associated with mood, anxiety, somatization or psychotic disorders should not be considered in this context [8]. This diagnostic category can be used for patients with symptoms of CWP that originated due to inflammatory rheumatic disease or arthritis and because the current extent of their pain symptoms (i.e., number of pain sites, impairments) can be explained by psychosocial processes instead of inflammatory processes in cases of remission or mild clinical courses of the inflammatory symptoms.

Definition/overlap of FMS with depressive disorders

Evidence-based statement

FMS can be associated with depressive disorders (EL1b). However, FMS is not to be classified as a depressive disorder. (EL 3a), strong consensus

Comment. Population-based and clinical studies reveal an association between CWP, FMS and depressive disorders. However, not every patient with a depressive disorder reports pain, and not every patient with FMS is depressed [43].

The main symptoms of FMS, including pain and fatigue, are also possible symptoms of depressive disorders. Among patients with depressive disorders, 30–60% reported pain [2]. The most common physical symptom in patients with major depression disorders in pharmacological studies was fatigue [53]. Six percent of the patients in these studies reported ≥6 pain localizations [54]. The association rates of multilocular (>2) pain and mood disorders were between 2.8–19.6% in the World Mental Health Survey [13]. In a clinical study, 13% of patients with major depression fulfilled the ACR 1990 criteria for FMS [55]. In a German study, 38% of patients with depressive disorders (F32–34, F43.2) fulfilled the survey criteria for FMS (≥7/19 pain sites and fatigue ≥6/10 using the visual analogue scale) [20]. A subgroup of patients who were diagnosed as depressed also showed fibromyalgia-like symptoms.

In a representative sample of the German population in 2009, 12.5% of individuals with FMS met the survey criteria for major depression and 12.5% met the criteria for another depression syndrome, as measured using the depression module of the health questionnaire for patients [18]. A systematic review of clinical studies showed a prevalence rate of 30–70%
for depressive disorders in patients with FMS [11]. The symptomatology of a percentage of patients diagnosed with FMS also meets the criteria for depressive disorders (e.g., major or minor depression or atypical depression).

Despite a partial overlap in the symptoms and neuroendocrine mechanisms, one review article concluded that major depressive disorders and FMS should not be regarded as variants of the same disease [44].

Fibromyalgia versus fibromyalgia syndrome

Consensus-based statement
Because symptomatology is defined by a symptom complex, the term “fibromyalgia syndrome” is more appropriate than the term “fibromyalgia”: EL 5, consensus

Comment. Functional somatic syndromes do not exhibit a distinctive clinical picture (such as myocardial infarction). The basis for the definition of functional somatic syndromes is a continuum of complaints. The definition of a disease pattern results from the establishment of a threshold by an expert consensus and/or by clinical studies. The same approach is used to describe pronounced continuous biological variables, such as the degree of constriction of the coronary vessels and blood sugar levels. The authors are aware that the term “syndrome” is not used consistently in the medical literature. The concept of a syndrome is understood in these guidelines as “the aggregation of symptoms, which by themselves are not characteristic of the disease, to form a characteristic disease pattern”. Other functional somatic syndromes include irritable bowel syndrome or urethra syndrome. FMS is classified as a first-order syndrome or a symptom complex with unknown or unclear etiology, heterogeneous pathogenesis and a defined phenotype (see statement “Core symptoms of FMS”). Second-order syndromes (sequences) are defined by unknown etiologies, homogeneous pathogenesis and defined phenotypes (e.g., Cushing’s syndrome). Third-order syndromes are defined by homogeneous etiologies, unknown or insignificant pathogenesis and defined phenotypes (e.g., Down syndrome and Marfan syndrome) [34].

Progression of FMS

Evidence-based statement
Different forms of FMS progression with varying severity can be distinguished based on clinical characteristics. However, a generally accepted classification of the degree of severity does not exist. EL 5, strong consensus

Comment. Because the conditions that define FMS are distributed in the general population and clinical populations within a continuum (see statement “Symptom complex of FMS”), any classification of severity depends on the criteria and thresholds used. There is no generally accepted classification for the degree of severity of functional disorders in general and for FMS in particular. The German Guideline “Non-specific, functional and somatoform physical symptoms” differentiates between mild and severe manifestations ([14], Tab. 1).

In clinical populations of FMS, different clusters of patient groups or severity levels have been distinguished. An increase in physical distress and subjective disturbances were associated with increased drug consumption and physical and mental health comorbidities [6, 48]. In clinical trials, a severity level classification for FMS can be obtained using the Fibromyalgia Impact Questionnaire (FIQ) [46].

Case study of a patient with mild FMS:
A 37-year-old female patient reported recurring back pain starting at the age of 11 without radiation to other areas. However, the pain began to extend to her entire back and to all of her extremities 2.5 years ago. Since that time, she reported experiencing pain almost every day of the year. However, in the summer months or during vacations to Mediterranean countries, she experienced little or no pain. For 2 years, she experienced a constant pain level, with an average pain intensity of 6/10, ranging from the lowest pain intensity of 2/10 to the maximum pain intensity of 9/10 on an 11-point numerical scale (NRS). Additional physical discomforts included an increased stiff feeling in her hands and an increased cold sensitivity with no autonomic symptoms. Carrying heavy loads (such as hot boxes) was no longer possible, and the patient could walk but was unable to jog. There were no restrictions on domestic work. The patient had unobtrusive biographical anamnesis. At the time of the case study, the patient was married, had a self-employed husband and did not have any children. She had no current mental complaints or emotional disorders, and there were no reports of psychiatric and psychotherapeutic treatments in her patient history.

Case study of a patient with a severe history of FMS:
A 54-year-old female patient experienced recurring hip pain as a child and reported recurrent joint and back pain beginning in early adulthood. However, 8 years prior to the case study, the pain expanded to her entire back and to both of her arms and legs. At that time, the patient experienced continuous pain with an average pain intensity of 8/10, with the lowest pain intensity of 7/10 and the maximum pain intensity of 10/10 on the NRS, with no pain-free or low-pain intervals. For approximately 5 years, the patient has experienced mostly non-restorative sleep and increased daytime sleepiness with rapid exhaustion, limited physical or mental stress, increased feelings of stiffness in the hands, increased cold sensitivity, recurrent abdominal pain in alternating locations, an increase in the frequency of feces by 3–10 movements, the imperative and urgent need to urinate and defecate (gastroenterological and urological clarification without pathological findings) and arrhythmia (cardiological investigation without pathological findings and therapy with a β-blocker). She could only do light household chores, such as cooking and putting the dishes away; other domestic duties, including cleaning and laundry, were assumed by a housekeeper or her daughter. She gave up on her painting hobby 1 year ago due to pain in her arms and has been unable to work for the past 2 years but receives steady unemployment benefits. Regarding biographical anamnesis, the patient experienced physical trauma perpetrated by an alcoholic father as a
Schwerpunkt

Tab. 1 Clinical characteristics of mild and severe manifestations of fibromyalgia syndrome (transitional, no mandatory criteria) (modified after the AWMF guideline entitled “Non-specific, functional and somatoform physical symptoms” [14])

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Mild manifestation</th>
<th>Severe manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical symptoms</td>
<td>Predominant musculoskeletal discomfort</td>
<td>Numerous complaints, including musculoskeletal and other organ systems</td>
</tr>
<tr>
<td>Duration of physical symptoms</td>
<td>Relapsing, minor or discomfort-free intervals</td>
<td>Persistent, none or rare low or discomfort-free intervals</td>
</tr>
<tr>
<td>Psychological symptoms</td>
<td>Limited</td>
<td>Pronounced</td>
</tr>
<tr>
<td>Subjective disease diagnosis</td>
<td>Appropriate (e.g., dependent on stress and temperature)</td>
<td>Inappropriate (e.g., persistent fears of serious disease despite an exclusion diagnosis)</td>
</tr>
<tr>
<td>Subjective disturbances (e.g., profession, family and free time)</td>
<td>Missing or minor</td>
<td>High</td>
</tr>
<tr>
<td>Use of medical services</td>
<td>Minor</td>
<td>High (doctor-hopping)</td>
</tr>
<tr>
<td>Psychosocial stress</td>
<td>Few and mild stressors (family, profession)</td>
<td>Numerous and/or severe stressors (family, profession)</td>
</tr>
<tr>
<td>Practitioner–patient relationship</td>
<td>Cooperative</td>
<td>“Difficult”, frustrating</td>
</tr>
</tbody>
</table>

Tab. 2 Criteria for the clinical diagnosis of FMS

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Obligate core symptom</td>
<td>CWP according to the ACR 1990 criteria (see statement “Definition of chronic pain in multiple areas of the body”)</td>
<td>Regional pain index at ≥7/19 pain locations on the regional pain scale</td>
</tr>
<tr>
<td>Other obligate symptoms</td>
<td>None</td>
<td>Symptom intensity score ≥5*</td>
</tr>
<tr>
<td>Diagnostic exclusions</td>
<td>None</td>
<td>Exclusion of a physical illness that would sufficiently explain the typical pattern of symptoms</td>
</tr>
</tbody>
</table>

*Symptom severity score: sum of fatigue, non-restorative sleep and cognitive problems (0: not available to 3: extremely pronounced); headache, abdominal pain and depression (0: absent; 1: present; range of total scores: 0–12). According to the modified ACR 2010 provisional diagnostic criteria, FMS can be diagnosed in 3–6 pain locations on the regional pain scale and can have a symptom severity score ≥5 [64]. However, this diagnostic criterion is incompatible with the primary symptoms of FMS, which include CWP. Regional pain, such as in the neck, upper arm or forearm, may also occur at three pain locations on the regional pain scale. Therefore, the use of this diagnostic criterion is not recommended. The rate of agreement between the 1990 ACR criteria and the diagnostic criteria of the German AWMF guidelines for FMS was 87% [21] in a multicenter study. ACR American College of Rheumatology, AWMF Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, CWP chronic widespread pain, FMS fibromyalgia syndrome.

Evidence-based statement

The prevalence of FMS in Germany is approximately 3.5%. EL 2c, consensus

Comment. In a summary of 10 studies representing the general adult population from various countries, the prevalence of FMS was between 0.7% and 3.3%. The prevalence was between 1.0% and 4.9% in women and between 0.0% and 1.6% in men. The female-to-male ratio was between 2–21:1 [12].

In Germany, the prevalence of FMS based on the ACR criteria of 1990 in a population of 35- to 74-year-old women was 5.5% [46]. In a representative sample of the population in Germany, the point prevalence of widespread pain (backache and pain in all four extremities) was 8.6%. The point prevalence of FMS (according to the survey criteria of ≥7/19 pain locations and fatigue of ≥6/10 on the visual analog scale) was 3.8% [95% confidence interval (95% CI) 3.6–4.0]. The ratio of women to men was 1.2:1 [18]. In a European study (including Germany), the point prevalence of CWP was determined based on the pain criteria from the London Fibromyalgia Epidemiology Study Screening Questionnaire. The point prevalence of FMS was estimated based on the frequency of FMS in rheumatology practices using the CWP criterion from the London Fibromyalgia Epidemiology Study Screening Questionnaire. The point prevalence of CWP in Germany was 11%, and the point prevalence of FMS was 3.2% (95% CI 2.1–4.3). The female-to-male ratio for FMS was 1.6:1 [5].

In clinical settings, the female-to-male ratio is 8–12:1 [21]. The higher prevalence rates among men in recent epidemiolog-
Degenerative myopathy
Myopathy and neuropathy
Clofibrate
Enalapril
Cyclosporin
Heroin
Myalgia in rare diseases (e.g., stiff person syndrome)
Cromoglycate
Toxic myalgia
ACTH
L-Tryptophan
Myalgia by alteration to the central and peripheral nervous system
Interferon
Neurological diseases
Other myopathies
Amiodarone
Endocrinal myopathy
Carbimazole
Vincristine
HMG-CoA reductase inhibitor
Ezetimibe
Colchicine
Inflammatory myopathy

### Tab. 3  Important differential diagnostics of chronic widespread pain in multiple body regions (modified from [30])

<table>
<thead>
<tr>
<th>Internal diseases</th>
<th>Neurological diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic inflammatory rheumatic disease</td>
<td>Inflammatory myopathy</td>
</tr>
<tr>
<td>Chronic hepatitis C</td>
<td>Metabolic myopathy</td>
</tr>
<tr>
<td>Chronic inflammatory bowel disease</td>
<td>Degenerative myopathy</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Endocrinal myopathy</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Myotonia</td>
</tr>
<tr>
<td>Hyper-/hypoparathyroidism</td>
<td>Toxic myalgia</td>
</tr>
<tr>
<td>Hyper-/hypothyreosis</td>
<td>Myalgia in rare diseases (e.g., stiff person syndrome)</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>Myalgia by alteration to the central and peripheral nervous system</td>
</tr>
</tbody>
</table>

### Tab. 4  Painful myopathy triggered by medications and drugs (modified from [4])

<table>
<thead>
<tr>
<th>Inflammatory myopathy</th>
<th>Other myopathies</th>
<th>Myopathy and neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td>ACTH</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>D-Penicillamine</td>
<td>Carbimazole</td>
<td>Colchicine</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Clofibrate</td>
<td>Heroin</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Cromoglycate</td>
<td>Interferon</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Cyclosporin</td>
<td>L-Tryptophan</td>
</tr>
<tr>
<td>Procainamide</td>
<td>Enalapril</td>
<td>Vincristine</td>
</tr>
<tr>
<td>Sulfonamide</td>
<td>Ezetimibe</td>
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</tr>
<tr>
<td>Zidovudine</td>
<td>HMG-CoA reductase inhibitor</td>
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<tr>
<td></td>
<td>Metoprolol</td>
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<tr>
<td></td>
<td>Minoxidil</td>
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<tr>
<td></td>
<td>Proton pump inhibitor</td>
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<tr>
<td></td>
<td>Salbutamol</td>
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</tbody>
</table>


### Clinical diagnosis

**Clinical consensus point**

The clinical diagnosis of FMS can be determined according to the ACR 1990 classification criteria, the symptom-based criteria of the German FMS S3 guidelines or the current modified ACR 2010 criteria. The clinical diagnosis is based on the anamnesis of a typical symptom complex, clinical examination and the exclusion of physical diseases, which could satisfactorily explain this symptom complex. **Strong consensus**

**Comment.** Although the ACR 1990 classification criteria for FMS [58] were designed as classification criteria and not as diagnostic criteria, they were subsequently used for diagnosis in daily clinical routines and studies. The use of the tender point examination was criticized due to the lack of acceptance by non-rheumatologists, lack of objectivity in implementation, missing data on the reliability of the results outside of rheumatology settings and the lack of validity [21, 61].

Based on patient surveys, comparisons between patients with arthritis and rheumatoid arthritis and expert consensus [61], the tentative diagnostic criteria for FMS were developed by a group of experts from the ACR. In the modified preliminary ACR 2010 criteria, the medical assessment of the physical symptoms was replaced by a patient self-assessment using a questionnaire [64]. In the consensus conference of the German S3 guidelines for FMS [10], the AWMF criteria were developed for the clinical diagnosis of FMS ([21, Tab. 2). The historically described symptom triad of CWP, fatigue and sleep disorders is a required diagnostic criterion, and these symptoms are considered core symptoms in the diagnosis of FMS.

**Obligatory somatic diagnosis at the initial evaluation**

**Clinical consensus point**

If the initial assessment indicates possible CWP, the following measures are recommended:

- completion of a sketch of the pain or the regional pain scale by the patient,
- targeted exploration of other core symptoms, such as fatigue or sleep disorders,
- complete medical anamnesis, including drug history,
- complete physical examination, including skin, neurological and orthopedic findings
- basic laboratory tests:
  - erythrocyte sedimentation rate,
  - C-reactive protein and full blood count (e.g., polymyalgia rheumatica, rheumatoid arthritis),
  - creatine kinase (CK) (e.g., muscular disorders),
  - calcium (e.g., hypercalcemia),
  - basal thyroid-stimulating hormone (e.g., hypothyroidism),
- for indications of somatic causes of the symptoms, further diagnostics may be necessary depending on the suspected diagnosis.

**Strong consensus**

**Comment.** CWP and fatigue can be symptoms of several internal and neurological disorders (Tab. 3, 4). Muscle and joint pain in multiple body regions without evidence of a neuropathy or myopathy can be caused by many drugs. Statins are frequently prescribed, and 10–15% of the patients receiving statin therapy develop myalgia of varying degrees with and with-
out an increase in CK [38]. Arthralgias and myalgias are side effects of aromatase inhibitors [57] and interferons [42].

Additional technical diagnostics

Clinical consensus point
In a typical symptom complex and the absence of clinical references to internal, orthopedic or neurological diseases (anamnesis and clinical examination without reference to other diseases as causes of pain and fatigue, including unremarkable basic laboratory test results), additional technical diagnostics, such as follow-up laboratory tests, neurophysiology or imaging are not recommended. Strong consensus

Comment. A Norwegian longitudinal study in outpatient primary care indicated that radiological examination had a low diagnostic value in patients with CWP [35]. A Canadian study in outpatient primary and secondary care demonstrated that there was no diagnostic value gained from the determination of autoantibodies associated with inflammatory rheumatic diseases in the anamnestic indication of CWP, fatigue and the lack of ankle swelling or references to internal or organ diseases [52].

Screening for psychological stress symptoms

Clinical consensus point
In the initial evaluation of CWP, screening for increased mental workload of symptoms, such as anxiety and depression, is recommended. Strong consensus

Professional psychotherapeutic investigation

Clinical consensus point
A professional psychotherapeutic investigation by a specialist in psychiatry and psychotherapy, psychosomatic medicine, psychotherapy or a medical or psychological psychotherapist is recommended in the following cases:

- a) indications of increased psychological distress (e.g., anxiety or depression),
- b) anamnestic information on current severe psychosocial stressors,
- c) anamnestic information on current or previous psychiatric treatments,
- d) anamnestic information on serious biographical stress factors,
- e) maladaptive in coping with disease,
- f) subjective attributes of mental illness

Consensus

Mortality

Evidence-based statement
Mortality is not increased in FMS. EL 2b, strong consensus

Comment. In a retrospective case control study of 8,186 patients with FMS treated in rheumatology practices (US National Data Bank for Rheumatic Diseases) from 1974–2009, the death rate was not elevated compared to 12,329 patients with osteoarthritis (US National Death Index). The standardized risk of suicide was increased when compared to the US population [odds ratio (OR) 3.3, 95% CI 2.2–5.1] [65]. In a retrospective cohort study in Denmark, 1,361 patients with FMS were observed from 1984–1999. The mortality risk was not elevated, although the female patients had an increased risk of suicide (OR 10.5, 95% CI 4.5–20.7) [9].

Use of medical services

Evidence-based statement
FMS causes high direct and indirect medical expenses in Germany in terms of utilization of health care and health benefits, respectively. EL 2b, strong consensus

Comment. Only studies from Germany were considered. In “IMS Mediplus”, a database of 900 general medical practices in Germany, the use of outpatient services was compared for 4,983 patients with FMS and 4,983 age- and gender-matched controls from 2/2006–2/2007. Patients with FMS reported twice as many visits to general practitioners, transfers to specialists and sick leave compared to the control patients during the investigation period. The medical expenses for patients with FMS (e.g., doctor visits, medications, inpatient treatments and sick leave) were estimated to be $9,573 compared to $329 for the controls [3].

In a study of the former Barmer health insurance (Barmer Ersatzkasse, BEK) from 1 July 2008 to 30 June 2009 for 19,592 insured individuals (0.3% of the total insured in the population) diagnosed with FMS, the annual direct medical costs were calculated to be 3,160 € (outpatient and inpatient treatment), and the indirect medical costs were 721 € (sick pay). Data
from the control group were not reported [39].

**Conclusion**

The validation of the first version of the German S3 guidelines based on clinical consensus and symptom-based diagnostic criteria [22] and the participation of guideline group members toward the development of the modified provisional 2010 ACR diagnostic criteria [64], which provides a diagnosis of FMS without tender point examination, continues the efforts to facilitate the diagnosis of FMS by non-rheumatologists. By comparing the recommendations of the S3 guidelines to “non-specific/functional/somatiform disorders of the body” [24] for diagnostic labeling and treatment of the symptom complex, the working group hopes to end the debate of the classification of CWP without sufficient explanatory somatic disease factors. We hope to focus toward filling in the following research gaps:

- Development of reliable and internationally accepted degrees of severity for non-specific/functional/somatiform physical disorders in general and in FMS patients in particular and
- Prospective cohort studies on the importance of secondary disease gain, social factors, such as unemployment and pension loss, iatrogenic chronicification and diagnostic labels for patients with FMS.

**References**


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**Conflict of interest.** See Tab. S. in “Methodological fundamentals used in developing the guideline” by W. Häuser, K. Bernardy, H. Wang, and I. Kopp in this issue.