

English Version of "Definition, Diagnostik und Therapie von chronischen Schmerzen in mehreren Körperregionen und des sogenannten Fibromyalgiesyndroms bei Kindern und Jugendlichen. Systematische Literaturübersicht und Leitlinie". DOI 10.1007/s00482-012-1168-y © Deutsche Schmerzgesellschaft e.V. Published by Springer-Verlag - all rights reserved 2012

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Definition, diagnosis and therapy of chronic widespread pain and so-called fibromyalgia syndrome in children and adolescents

Systematic literature review and guideline

Epidemiologic studies reveal a high prevalence (between 25% and 46%) of chronic pain in children and adolescents, an increased prevalence with age and a higher prevalence in girls [14, 32, 58, 68]. The most common locations of pain—in order of descending frequency—are head, abdomen and musculoskeletal system; some of the children and adolescents report pain in several regions [14, 32, 58, 67]. About 3% of children and adolescents develop severe, disabling chronic pain with negative effects on school attendance, recreational activities, contact with peers and family and emotional distress, such as anxiety and depression [32, 55]. A subset of these children and adolescents suffer from additional symptoms, for example disordered sleep [45, 57] or fatigue [19]. In children and adolescents who suffer from generalized pain of the musculoskeletal system, additional symptoms and muscle tenderness, the diagnosis juvenile fibromyalgia syndrome (JFMS) is used. The definitions of JFMS, however, have substantial operationalizational problems. The authors of the update of these guide-

lines therefore chose to use the term “so-called JFMS”.

For the planned update of the guidelines, the following research questions were addressed by use of a comprehensive literature review:

1. What are the core symptoms of the so-called JFMS?
2. What differences/overlap exist between so-called JFMS and somatoform pain disorder?
3. According to which criteria should the so-called JFMS be diagnosed?
4. Which diagnostic examinations are required to rule out alternative diagnoses?
5. When is a psychological evaluation reasonable?
6. Are there different courses or degrees of severity of the so-called JFMS?
7. Which information about symptoms, therapeutic goals and treatment opportunities should be made available at the time of diagnosis?
8. Is patient education useful?
9. Which subspecialty should coordinate the care of the so-called JFMS?

10. Is a graded treatment approach useful?
11. Which physical, physical therapeutic, psychotherapeutic, pharmacologic and complementary approaches are useful in the so-called JFMS?
12. Which physical, physical therapeutic, psychotherapeutic, pharmacologic and complementary approaches should be advised against in the so-called JFMS?
13. When is an inpatient multimodal treatment indicated?

Materials and methods

The methods of literature search and preparation of recommendations are presented in the article “Methodological fundamentals used in developing the guidelines”.

Results

The literature search yielded 265 hits. Due to the low number of high quality studies, there was no gradation of the level of evi-

dence according to the quantity or quality of the evidence.

Definition and classification

Clinical consensus

For children and adolescents there are currently no standardized and validated criteria for defining chronic pain in multiple body regions leading to clinically significant impairment in everyday life and that does not occur within a defined somatic disease. Strong consensus

Comment. In childhood and adolescence, pain, regardless of its location, is defined as chronic if it lasts for at least 3 months or is recurrent over this time period [33, 47, 54]. Persistent or recurrent pain may fluctuate greatly in intensity, quality, frequency, predictability and may occur either in single or multiple body regions. The focus on the temporal dimension of chronic pain has recently been criticized. Studies indicate that children, who suffer from shorter-lasting pain, are often significantly impaired in their daily lives and require treatment [28, 33]. The aspect of pain-related impairment has only recently been explicitly considered in the context of epidemiological and clinical studies [29, 30, 54]. Rief et al. [64] included the issue of impairment as a central criterion within a new diagnostic category of “chronic pain disorder with somatic and psychological factors” (ICD-10 F45.41). Studies on the incidence of this diagnosis in childhood and adolescence are lacking.

According to Sherry [46, 73], in the case of chronic pain in children and adolescents with mostly musculoskeletal pain, “diffuse” and “idiopathic localized” musculoskeletal pain can be defined. Another commonly used term is “chronic widespread (musculoskeletal) pain (CWP)” [15, 50]. For further consideration, it is important to note that not all CWP goes along with pain-related impairment in everyday life, distress or a subjective sense of illness. However, this is described for the so-called juvenile fibromyalgia syndrome (JFMS).

Traditionally, the so-called JFMS is defined according to the Yunus criteria [83]:

- a) generalized musculoskeletal aching at ≥ 3 sites,
- b) duration for at least 3 months,
- c) normal laboratory test results,
- d) at least 5 of 11 tender points,
- e) at least 3 of the following 10 features:
 1. chronic anxiety or tension,
 2. fatigue,
 3. poor sleep,
 4. chronic headaches,
 5. irritable bowel syndrome,
 6. subjective soft tissue swelling,
 7. numbness,
 8. pain modulation of physical activity,
 9. pain modulation by weather factors,
 10. pain modulation by anxiety and/or stress.

Other publications on JFMS used the definition of the American College of Rheumatology (ACR) in 1990 for adults. The specificity and sensitivity of the Yunus criteria and the ACR criteria have rarely been investigated in children and adolescents. In a study by Reid [61], only 75% of pediatric patients fulfilled both the Yunus as well as the 1990 ACR criteria. The pain is typically highly variable; therefore, the Yunus criteria are met only irregularly. Both the Yunus and the 1990 ACR criteria have substantial problems in their operationalization:

1. The so-called tender points are problematic for the following reasons:
 - a) From studies on quantitative sensory testing (QST) in children and adolescents it is known that the pressure pain threshold when using a pressure gauge device (FDN 100, Wagner Instruments, USA) depends on the age and sex of the child and the location tested [3]. Fifty percent of healthy children report pain at a pressure ranging from 163–1,039 kPa (100 kPa=1 kg/cm²), whereas the upper and lower 95% confidence interval (95% CI) vary according to age, sex and location of pressure application between 82–1,890 kPa. The testing of tender points using thumb pressure or technical devices with a pressure independent of the age, sex and loca-

tion of pressure application may not lead to valid results, since the pressure–pain threshold in healthy children is influenced by these factors. Tenderness thresholds from about 3 kg/cm² (300 kPa/cm²) or 3 kg/1.5 cm² (depending on the study and thumb size) or even 5 kg/1.5 cm² were considered as pathologic [7]. Depending on age, gender and location of pressure application, many healthy children report pain at these pressures.

- b) In the published studies, the so-called tender points were generally not standardized, often only examined by thumb pressure and not examined in a double-blind fashion. However, for the thumb pressure not only the compressive force, but also the support surface is critical.
 - c) When two pediatric rheumatologists examined tender points in the same child, their agreement was around 44%, not better than chance [9].
 - d) Some studies show that children with juvenile idiopathic arthritis (JIA) have identical tender point pain thresholds as children with so-called JFMS [62].
 - e) If tender points are positive, so-called control points are often positive as well [72]. Häfner et al. [21] found that tender points were variable and fluctuated.
2. The so-called minor symptoms of the Yunus criteria have not been defined. Headaches should be classified according to the International Headache Society (IHS) criteria, e.g., chronic tension headache, episodic tension headache, migraine, medication-induced headache. The same is true for the diagnosis irritable bowel syndrome, for which the Rome criteria should be required [20].
 3. For psychological symptoms such as anxiety and depression and functional impairment due to chronic pain, a standardized survey with established instruments should be implemented (see below).

Due to these limitations of operationalization, the term JFMS has been rejected by leading rheumatologists and researchers since it is not scientifically established or clinically helpful [73]. The guideline committee agrees to this opinion.

Based on the work by Rief et al. the authors of the present guidelines suggest, that, in the future, the diagnosis “chronic pain disorder in several body regions with somatic and psychological factors” should be used for children with chronic widespread pain (CWP), who also suffer from other symptoms such as headache or abdominal pain, non-restorative sleep, muscle tenderness, fatigue, irritable bowel syndrome, anxiety, depression and a strong pain-related impairment in everyday life.

In adults, Rief et al. [64] suggested to optimize the classification of chronic pain in ICD-10 (section F) according to the biopsychosocial model. Thus far, chronic pain has been classified as “somatic pain disorder” (F 45.4). For this diagnosis, psychologic factors were considered to trigger the pain. Since this relationship could not always be confirmed in studies, a new proposal for the diagnosis “chronic pain disorder with somatic and psychological factors” (F45.41) was created [64]. The clinical picture is dominated by pain lasting for at least 6 months in one or more anatomical regions. This pain is assumed to have been triggered either by psychological processes or a physical disorder. Psychological factors are considered to play an important role in the degree of severity, exacerbation or maintenance of pain, but to a minor degree a causative role. The pain causes clinically significant distress and impairment in social, occupational or other important areas of functioning. The pain is not voluntarily produced or pretended (as in factitious disorder or simulation). For children and adolescents, the pain disorder should last for at least 3 months (for reasoning, see above).

In this guideline we will use the term of the “so-called JFMS”, because the cited studies describe JFMS patients even though the diagnosis JFMS cannot be operationalized (see above). The authors of these guidelines agree that the diagnosis JFMS is neither scientifically established,

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Definition, diagnosis and therapy of chronic widespread pain and so-called fibromyalgia syndrome in children and adolescents. Systematic literature review and guideline

Abstract

Background. The scheduled update to the German S3 guidelines on fibromyalgia syndrome (FMS) by the Association of the Scientific Medical Societies (“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 diagnosis FMS in children and adolescents is not established. In so-called juvenile FMS (JFMS), multidimensional diagnostics with validated measures should be performed. Multimodal therapy is warranted. In the case of severe pain-related disability, therapy should be primarily performed on an inpatient basis. The English full-text version of this article is available at SpringerLink (under “Supplemental”).

Keywords

Chronic pain · Fibromyalgia syndrome · Review, systematic · Guideline · Children and adolescents

Definition, Diagnostik und Therapie von chronischen Schmerzen in mehreren Körperregionen und des sogenannten Fibromyalgiesyndroms bei Kindern und Jugendlichen. Systematische Literaturübersicht und Leitlinie

Zusammenfassung

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

Material und Methoden. Die Leitlinie wurde unter Koordination der Deutschen Interdisziplinären Vereinigung für Schmerztherapie (DIVS) von 9 wissenschaftlichen Fachgesellschaften und 2 Patientenselbsthilfeorganisationen entwickelt. Acht Arbeitsgruppen mit insgesamt 50 Mitgliedern wurden ausgewogen in Bezug auf Geschlecht, medizinischen Versorgungsbereich, potenzielle Interessenkonflikte und hierarchische Position im medizinischen bzw. wissenschaftlichen System besetzt. Die Literaturrecherche erfolgte über die Datenbanken Medline, PsycInfo, Scopus und Cochrane Library (bis Dezember 2010). Die Graduierung der Evidenzstärke erfolgte nach dem Schema des Oxford Center

for Evidence Based Medicine. Die Formulierung und Graduierung der Empfehlungen erfolgte in einem mehrstufigen, formalisierten Konsensusverfahren. Die Leitlinie wurde von den Vorständen der beteiligten Fachgesellschaften begutachtet.

Ergebnisse und Schlussfolgerung. Die Diagnose eines juvenilen FMS (JFMS) wurde als wissenschaftlich nicht etabliert eingestuft. Beim sog. JFMS wird eine multidimensionale Diagnostik mit validierten Instrumenten gefordert. Die Therapie sollte multimodal erfolgen, bei starker schmerzbedingter Beeinträchtigung auch primär stationär.

Schlüsselwörter

Chronische Schmerzen · Fibromyalgiesyndrom · Systematische Übersicht · Leitlinie · Kinder und Jugendliche

nor helpful. Therefore, they propose to use the term “chronic pain disorder in several body regions with somatic and psychological factors” instead.

Clinical diagnosis

Clinical consensus

In children and adolescents with chronic pain in multiple body regions (CWP) a multidimensional diagnosis of pain and other physical and psychological symptoms is recommended. Validated tools and methods should be used. Strong consensus

Comment. As no pathognomonic individual diagnostic findings for so-called JFMS are available, the diagnosis is based on the presence or absence of a characteristic constellation of symptoms and signs after exclusion of all other diseases that may also have such a constellation of symptoms and signs. Therefore, the differential diagnosis and exclusion of other diagnoses is of particular importance. The differential diagnosis itself depends on the clinical picture. Various organic diseases have to be considered: (systemic) inflammatory conditions such as juvenile idiopathic arthritis, malignant conditions such as leukemias [8, 77] and endocrine-metabolic diseases [42, 49]. Psychological problems/disorders should be considered since they are even more common, e.g., depression (subtypes according to DSM-IV, see below), anxiety disorders (subtypes according to DSM-IV, see below), post-traumatic stress disorders (PTSD) and dissociative disorders with or without self-injurious behavior. There is also the possibility of mental illness of parents, as seen in Munchhausen by proxy syndrome.

In a study by Degotardi et al. [11] 2 of 77 children, all of whom met the Yunus criteria and all of whom were diagnosed by pediatric rheumatologists as JFMS, were eventually diagnosed with severe psychiatric disorders (“schizoaffective disorder” and “depression with suicidal ideation”) during further psychological evaluations. In the course of the study an additional 3% of the enrolled children had a “need for psychiatric referral.” Kashikar-Zuck et al. studied 102 adolescents with the diagnosis of so-called JFMS regard-

ing psychiatric disorders using standardized tests and an extensive psychological exploration: 19% suffered from depression according to DMS-IV criteria [major depression (n=7), dysthymic disorder (n=8), depressive disorder not otherwise specified (NOS) (n=5)], 55% an anxiety disorder [panic disorder (n=6), agoraphobia (n=4), specific phobia (n=0), social phobia (n=11), obsessive-compulsive disorder (n=3), posttraumatic stress disorder (n=5), generalized anxiety disorder (n=17), or separation anxiety disorder (n=3)] and 24% suffered from attention deficit hyperactivity disorder (ADHD) [37, 38]. Therefore, the clinical assessment should include a profound medical and psychological examination, preferably by use of validated tools such as the German Paediatric Pain Questionnaire (“Deutscher Schmerzfragebogen für Kinder und Jugendliche”, DSF-KJ) [71]. Specifically, the following examinations should be conducted:

- basic laboratory diagnostic, e.g., erythrocyte sedimentation rate, complete blood count with differential count, C-reactive protein, creatine kinase. Further diagnostic studies (e.g., antinuclear antibodies, rheumatoid factor, imaging, electroencephalography, electrocardiography, genetic studies, biopsy) are indicated if there is a clinical suspicion for an alternative cause of the pain, and
- psychological standard diagnostics such as the “Depressionsinventar für Kinder- und Jugendliche (DIKJ)” (depression inventory for children and adolescents), “Angstfragebogen für Schüler (AFS)” (fear questionnaire for students).

If applicable, polysomnography

Epidemiology

Evidence-based observation

The prevalence of CWP is strongly age-dependent and ranges between 1 and 15% in children and adolescents. Diffuse musculoskeletal pain in combination with other physical or psychological symptoms such as tension-type headaches, fatigue, sleep disturbance and emotional distress is present in <1% of

children and adolescents between the ages of 8–15 years in international studies. There is a female predominance.

Strong consensus

Comment. When reviewing epidemiological studies, distinction must be made with regard to the sample studied—specifically, between studies that examined only the presence of CWP [15, 50] and studies that studied children who also suffered from other symptoms indicative of the diagnosis of so-called JFMS.

Epidemiological studies in school children focused on children between 10 and 12 years and reported prevalences of CWP of 1% [50], 7.5% [52] and 9.9% [51]. In a follow-up study by Mikkelsen et al. [50], adolescents between the ages of 14 and 16 years had a prevalence of CWP of 15%.

In a German representative population sample, 302 adolescents were in the age group between 14 and 24 years; none of them fulfilled the FMS criteria according to the survey criteria [22]. Since the diagnosis of adult FMS by means of tender points was abandoned in the latest ACR criteria [81], epidemiological studies of the prevalence of so-called JFMS need to be re-evaluated. Of the 7 children who were classified as having so-called JFMS (prevalence approximately 1% among school children 9–15 years) in the study by Clark et al. in 1998 [9], there was only one child who fulfilled all examined additional criteria (sleep disturbances, morning stiffness, fatigue, sadness). Three children fulfilled only one criterion each; neither the severity of symptoms nor the impairment of the children by the symptoms was reported. Other studies that found a significantly higher prevalence of so-called JFMS of 6.2% for 9- to 15-year-old school children based their diagnosis mainly on muscle tenderness [7], which, due to the methodological difficulties described above, can be criticized.

Disease course

Evidence-based observation

In most patients with CWP, or so-called JFMS, the disease course is variable with alternating episodes of increased, decreased or absent symptoms. Evidence level 2b, strong consensus

Comment. In a study on the course of CWP in childhood and adolescence, only 10% of children who had CWP at baseline complained of persistent symptoms after 1 and 4 years [50].

The evaluation of studies on the course of the so-called JFMS is complicated by the fact that the diagnosis itself is not valid, due to the methodological problems described in detail above. Moreover, in most studies, the study population was not assessed with standardized instruments. Essentially, children and adolescents with a pain disorder diagnosed in a non-standard fashion were examined in a non-standard fashion, and described by the authors as having so-called JFMS.

In clinical studies, the persistence of long-term symptoms is described in a subset of patients. Malleson et al. [46] conducted a retrospective survey based on medical records. Twenty-eight of 35 patients diagnosed with JFMS had more than one appointment in the rheumatology clinic. After a variable observation period between 1 and 48 months, 17 of 28 patients with so-called JFMS had persistent symptoms after an average of 27 months [46]. In a retrospective study, Siegel et al. [74] assessed 44 patients over 6 years with so-called JFMS. Subsequent phone interviews, on average 2.6 years (range 0.1–7.6 years) after diagnosis, demonstrated an increase in the number of reported symptoms. On a visual analog scale (VAS) from 1–10 (1=complete disability; 10=no disability), the patients assessed their current impairment as being less pronounced than in the previous year (previous year 5.1 ± 3.1 vs. currently 6.9 ± 1.6). The patients received a standard outpatient treatment (tricyclic antidepressants, non-opioid analgesics, exercise program) [74]. The study results are promising; however, there is a core critical point: the authors changed their study methods between the time of outpatient treatment (unstructured survey) and the telephone interview (structured survey). In addition, no standardized instrument to assess pain-related disability was used, e.g., the Functional Disability Inventory [36, 79]. Gedalia et al. [18] conducted a retrospective study over a period of 4 years. Fifty of 59 patients with so-called JFMS were seen more than once in the

outpatient clinic. At an average follow-up of 18 months (range 3–65 months), 60% of the children improved, 36% experienced no change and 4% experienced a worsening of pain symptoms. The therapy consisted of a combination of pharmacological and nonpharmacological interventions; at the time of follow-up 74% of children were taking medications [18].

Of 48 U.S. American children and adolescents diagnosed with JFMS, after an average of 3.7 years, 62.5% suffered from CWP, and 60.4% fulfilled criteria for so-called JFMS [40].

Population-based studies in children and adolescents reveal a more favorable disease course: In a population of Israeli school age children, Buskila et al. [6] diagnosed so-called JFMS in 21 of 337 patients (6.2%) according to the ACR criteria; after 30 months of follow-up, the ACR criteria were met by only 4 of 21 children. In the Finnish study by Mikkelsen et al. [52], only 4 of 16 school age children with so-called JFMS fulfilled the ACR criteria of so-called JFMS after a follow-up of 1 year.

Exacerbating factors for CWP include the following: daily hassles, pain-related catastrophizing, lack of self-efficacy and lack of positive family support [43]

Etiology

Somatic complaints (headache and abdominal pain), behavioral problems and increased physical activity

Evidence-based observation
Somatic complaints (headache and abdominal pain), behavioral problems and increased physical activity frequently occur prior to CWP. There are no studies on the relationship of these factors to so-called JFMS. Evidence level 2b, strong consensus

Psychosocial problems

Evidence-based observation
Studies regarding psychosocial problems in patients with so-called JFMS demonstrate controversial findings. Evidence level 3b, strong consensus

Comment. A biopsychosocial perspective is necessary to understand the origin and maintenance of chronic pain [78]. Chronic pain in children is the result of a dynamic process of biological factors (e.g., an underlying somatic disease), physical components (e.g., a lowered threshold of pain), psychological factors (e.g., pain-related fears, dealing with pain and pain coping) and sociocultural conditions (e.g., pain-related parenting, social attitudes, gender roles, social interactions in dealing with pain). All of these factors interact with each other.

Risk factors for the development of a so-called JFMS or chronic pain disorder of the musculoskeletal system have not been investigated to date.

In an English population-based prospective follow-up study over a study period of 12 months, 1,440 school children were examined for risk factors for the development of CWP. These risk factors included physical symptoms such as headache on more than 7 of 30 days [relative risk (RR) 2.50, 95% CI 1.16–5.39], abdominal pain at 1–7, but not less than one or more than 7 days per month (RR 1.8, 95% CI 1.1–2.9), as well as increased physical activity of more than 6 h per week (RR 2.03, 95% CI 1.05–3.94). Prosocial behavior was identified as a protective factor for CWP (RR 0.50; 95% CI 0.28–0.90) [34].

In a case control study, no significant differences in psychological distress were observed between patients with a so-called JFMS and JIA [60]. In contrast, Conte et al. [10] reported a higher incidence of anxiety and depression in patients with so-called JFMS compared to healthy subjects and patients with JIA. In a case control study of a private psychiatric hospital, 32 adolescents who met the criteria of so-called JFMS reported more physical and emotional problems than the control group of 30 adolescents with other mental disorders [44].

A case-control study of 55 patients with so-called JFMS and 55 healthy controls showed that adolescent patients with so-called JFMS described themselves as more withdrawn and less popular and, thus, were more likely than their peers to be socially isolated [39]. This was not the case for patients with JIA.

Family history

Evidence-based observation

So-called JFMS and adult FMS occur together in families. Evidence level 2b, strong consensus

Comment. The increased joined occurrence of adult FMS and so-called JFMS in first-degree relatives has consistently been reported in several studies [1, 6, 53, 65, 76]. In an Israeli study of 37 families with FMS (at least 2 relatives), 74% of siblings and 53% of parents were diagnosed with FMS according to the ACR criteria [5]. The studies on familial clustering, however, do not provide evidence that the increased incidence of adult FMS and so-called JFMS is genetically determined. The results of an American study of over 40 families with FMS (at least 2 first-degree relatives) were consistent with a genetic linkage to the HLA region [82]. A Finnish longitudinal cohort study of 11-year-old twins (583 monozygotic pairs, 588 same-sex dizygotic and 618 different-sex dizygotic pairs) demonstrated a CWP prevalence of 9.9% and mostly discordance; a genetic basis could not be shown [51].

Non-genetic, psychological factors for the increased incidence of chronic pain in children of adult chronic pain patients are much more likely to play a role than genetic models (role modeling etc.) [2, 56].

Parental factors

Evidence-based observation

Parents of patients with so-called JFMS frequently show increased anxiety, a history of chronic pain, depressive symptoms and chronic diseases. Evidence level 3b, strong consensus

Comment. Parents of children and adolescents with so-called JFMS:

- more frequently report chronic pain [35, 70],
- tend to show increased anxiety [10],
- more frequently demonstrate depressive symptoms [10, 35], and
- suffer from more somatic symptoms [10].

Pathophysiology

Evidence-based observation

Due to the lack of studies, no comment can be made on the pathophysiology of so-called JFMS. Strong consensus

Coordination of care

Evidence-based recommendation

Children and adolescents with CWP should be presented to a clinical specialist familiar with chronic pain in childhood on an outpatient basis. In the case of long school absences, severe limitations in activities of daily living, physical inactivity or increasing social isolation, inpatient treatment in a facility that offers a special treatment program for children and adolescents with chronic pain, should be recommended. Evidence level 4, strong consensus

Comment. In a study by Hechler et al. [28] on the stratification of therapy in a sample of children and adolescents with chronic pain (headaches, abdominal pain or musculoskeletal pain), the criteria for stratification of therapy were studied. The intensity of initial therapy (outpatient therapy, outpatient group therapy, inpatient therapy) turned out to be correct for the majority of children. An intensification of therapy was rarely needed. In this study, children were assigned to multimodal inpatient treatment based on the following criteria: chronic pain for at least 3 months, no successful therapy in the previous setting, high pain-related impairment [Pain Disability Index (PDI) >36] and the presence of 3 of the following 4 criteria:

- pain duration >6 months,
- average pain intensity in the last 7 days ≥ 5 [visual analog scale (NRS) 0–10],
- pain peaks ≥ 8 (NRS 0–10) at least twice a week, and
- at least 5 school days of absence during the last 20 school days.

Children and adolescents with so-called JFMS who do not (yet) express this level of severe impairment, should initially be treated as outpatients. Local or part-time inpatient multimodal treatment is rarely

offered for children and adolescents with chronic pain of the musculoskeletal system in Germany. Therefore, for the less severely affected children, an individual multimodal program should be planned based on the existing facilities in Germany (e.g., outpatient psychotherapy, physical therapy, regular visits to the pediatrician). There are only a few centers offering multimodal inpatient therapy; thus, treatment often takes place remote from the hometown. Even though only studies with a level of evidence grade 4 are available, the authors agreed in a unanimous consensus to recommend this modality with a strength level B given the following criteria are met: low risk, high acceptance rate among patients (adherence to therapy between 95% [13] and 98% [16]) and ethical necessity, since normal childhood development is endangered.

General principles of treatment

Therapeutic goals

Evidence-based recommendation

Goals of treatment should be pain relief, restoration of functioning, reduction of school absenteeism, dissolving social isolation, strengthening self-awareness, mobilizing domestic resources and the development of strategies for coping with pain. The inclusion of the family, the training of strategies in everyday life and the treatment of mental co-morbidities are also important. Evidence level 2c, strong consensus

Comment. The general principles of therapy have been formulated comprehensively in prospective outcome trials [12, 13, 16, 23, 24, 25, 26].

Patient education

Clinical consensus

Patient and parent education and self-help groups for children, adolescents and parents may be offered. Strong consensus

Psychotherapy

Clinical consensus

Scientifically established methods of psychotherapy should be used for children and adolescents with so-called JFMS part of a multimodal pain therapy. Strong consensus

Comment. A U.S. randomized study in cross-over compared active coping with pain to self-monitoring in 30 adolescents; at the end of the study both groups demonstrated a reduction of functional limitations and depression [41]. A significant reduction of pain could not be demonstrated. This study had major methodological problems; neither the sample size was calculated nor was a primary outcome measure predetermined.

The authors believe that, according to experts and studies about multimodal pain therapy, scientifically established psychotherapies (cognitive behavioral therapy, trauma therapy, systemic family therapy, analytical therapy) in children with so-called JFMS should only be carried out as part of a multimodal pain therapy or for treatment of psychiatric co-morbidity. The content of the therapy should be adjusted to the individual child or adolescent and his/her situation. Local outpatient psychotherapy should be considered on a case-by-case basis.

Physical therapy and physical measures

Clinical consensus

Physical therapy should be used as part of multimodal pain therapy. Strong consensus

Comment. In a randomized-controlled trial (RCT), 14 patients with so-called JFMS were treated with aerobic exercise of moderate intensity and 16 were treated with Qi-Gong. At the end of therapy, the group performing aerobic training reported a greater reduction in pain, fatigue and impairment in quality of life than the group performing Qi-Gong. In the Qi-Gong group, there was significant change in pain, fatigue and impairment in quality of life [75]. A recent study by Kashikar-Zuck [37] showed that adoles-

cents who suffered from so-called JFMS and who were physically active (“high activity” as measured by actigraphy), had less pain, were judged by their parents as being less depressed and were functionally less impaired as compared to adolescents who were moving less (“low activity”). However, the cross-sectional design did not allow establishing a cause-effect relationship.

Studies on the efficacy of other methods of physical therapy and physical measures are not available. Nevertheless, these therapies are recommended by the authors with a level of recommendation grade B since they are preferred by the patients, are accompanied by a high level of adherence and have low risk of potential adverse effects, and since they are easy to implement in Germany, both on an outpatient and on an inpatient basis.

Pharmacologic therapy

Evidence-based recommendation

Pharmacologic therapy should not be performed in children with CWP or so-called JFMS. Co-morbidities (e.g., depression in adolescence) should be treated according to the available guidelines. Evidence level 4, consensus

Comment. Controlled drug studies are not available. In a U.S. case series of 15 patients, it was reported that aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) were not effective; 73% of children responded to cyclobenzaprine 5–25 mg/day [66]. Two observational studies reported on the use of NSAIDs and/or psychotropics in combination with exercise therapy [74] or a complex multimodal treatment [63]. Saccomani et al. [69] described a clinical improvement with trazodone or amitriptyline in 2 Italian patients. Children and adolescents were generally excluded from drug trials in adult FMS patients.

Tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRI) are not approved for the treatment of children and adolescents in Germany (off-label therapy). Clinical experience suggests that there can be a role for drug therapy in the treatment of comorbidities of the individual multimodal therapy concept.

However, focusing on medications must be avoided. The potential risks of drug therapy, the lack of approval of most drugs used as well as the failure to show a benefit for the individual patient justify, according to the authors’ opinion, a recommendation against drug therapy.

Multimodal therapy

Clinical consensus

In patients with so-called JFMS, multimodal pain management should be performed. In cases of severe impairment or unsuccessful other approaches, this should be pursued in an inpatient unit, in case of less severe impairment, initially in an outpatient unit. Strong consensus

Comment. Multimodal pain therapy, in the context of these guidelines, is understood to be a combination of at least one method of activating physical therapy with at least one method of psychotherapy, as described by the working group multimodal therapy [4]. In the case of outpatient multimodal pain therapy, the pediatric rheumatologist or pediatric pain specialist assumes the coordination of care. Stipulations of inpatient multimodal pain therapy for children in Germany are described in the OPS (“Operationen- und Prozedurenschlüssel”) under paragraph 8–918.x.

There are no RCTs on the efficacy of multimodal therapies in so-called JFMS.

In pediatric studies on the effectiveness of multimodal treatment programs (outcome studies, level of evidence 2c), there was always a more or less large proportion of children and adolescents with CWP and additional psychosomatic/psychological complaints/abnormalities. The proportion of these children was 40% (n=23) in the study by Eccleston et al. [17], and in the study by Hechler and Dobe [25], the proportion of children with predominant musculoskeletal pain was 14% (n=28). In the latter work, the chronically ill children and adolescents in 40% of cases reported pain in more than one region (n=61). Three months after completion of inpatient multimodal pain therapy, 75% of children reported significant positive changes in pain intensity, 63% a significant improvement in pain-related

disability and 45% significant changes in the days absent from school (30% of the children had no significantly increased school absenteeism at baseline). Clinically significant changes in the emotional impairment were exhibited in 13–26% of patients, whereby 50–60% had no emotional distress at baseline. More than half of the children (55%) demonstrated overall improvement 3 months following treatment [25].

In their recent analysis of 200 children and adolescents with chronic pain, Dobe et al. [13] showed that the success of the multimodal inpatient program was independent of the site of pain.

It is recommended children and parents receive instructions for home therapy during multimodal inpatient treatment. The continuation of parts of the multimodal program in everyday life is crucial for the prognosis. Relaxation techniques and physical therapy, exercise therapy and other athletic activities, physical activities and the coping with stressors and psychological problems (e.g., by use of social support) are important tasks to take home [12, 23, 25, 27].

Contraindications for multimodal inpatient treatment are serious psychiatric illnesses such as the presence of psychosis or anorexia nervosa [13]. Suicidal ideation in adolescents with chronic pain or depression—a frequently described comorbidity in children with chronic pain in multiple body regions—has been reported. Therefore, the diagnosis and treatment of children and adolescents with so-called JFMS should always be conducted by a multidisciplinary team, involving child and adolescent psychologists or psychiatrists.

Discussion

The first version of the guideline for so-called JFMS was substantially revised [48]. It has been shown that the diagnosis of JFMS is not yet scientifically established, so that the concept of so-called JFMS was implemented in this paper. The question of how children and adolescents with chronic pain in several body regions accompanied by other symptoms should be diagnosed and classified is an urgent question for future research. This raises

the question of whether the clinical picture of JFMS exists or whether the children and adolescents with these symptoms suffer from other specified diseases. A second new feature of the guidelines is the requirement for a standardized diagnostic procedure, which also includes validated psychological assessments. Since it is known that the so-called JFMS does not represent a well-established disease, it is even more important to recognize defined organic and mental diseases, such as posttraumatic stress disorder in order to identify and deliver appropriate therapy. As in the first version of the guideline, multimodal treatment approaches are warranted for affected children. In addition to the general principle of “outpatient before inpatient care”, we present criteria that, when present, suggest assignment to multimodal inpatient treatment. These criteria do not relate primarily to pain intensity or duration of the disease, but in particular to pain-related adverse effects such as school absenteeism, a marked reduction of the activities of daily living or social withdrawal. As in the first version of the guidelines, drug therapy is not recommended for the treatment of the so-called JFMS. Co-morbid mental disorders should be treated according to the respective guidelines.

In summary, the revised and updated second version of this guideline clearly recommends a comprehensive reassessment of the so-called JFMS taking into account current work on quantitative sensory testing (QST), psychological assessment of chronic pain as well as the success of multimodal pain management programs in children and adolescents. Controlled studies for the diagnosis of children who present with a symptom complex that reminds of adult FMS, and RCTs of children suffering from chronic musculoskeletal pain and other physical and mental symptoms, are urgently needed to clarify the diagnosis of JFMS and to provide evidence for multimodal pain treatment for these children.

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Conflict of interest. See [Tab. 5](#) in “Methodological fundamentals used in developing the guidelines” by W. Häuser, K. Bernardy, H. Wang, and I. Kopp in this issue.

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