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**A diagnostic accuracy study**

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## Clinical Pain Research

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# Performance of the 2016 diagnostic criteria for fibromyalgia in a tertiary care pain rehabilitation setting: a diagnostic accuracy study

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### Abstract

**Objectives:** With the International Classification of Diseases 11th revision (classifying fibromyalgia as a primary pain disorder) soon to be implemented, the importance of pain physicians being able to identify patients with fibromyalgia is emphasized. The diagnostic criteria proposed in 2016 are based on self-reported pain distribution and symptom severity. The study aimed to evaluate the diagnostic accuracy of the 2016 diagnostic criteria for fibromyalgia applied in a population of patients with high impact chronic pain referred for pain rehabilitation.

**Methods:** The study was performed as a diagnostic accuracy study at two Danish interdisciplinary pain rehabilitation centers, including 215 participants. All participants

were evaluated clinically to identify patients with fibromyalgia. The diagnosis was based on expert opinion, but the minimum requirements were: (1) pain in all four body quadrants and axially for at least three months and (2) minimum 8 of 18 positive tender points. Participants filled in the fibromyalgia survey questionnaire, the patient version of the 2016 diagnostic criteria. Sensitivity, specificity, likelihood ratios, and positive and negative post-test probabilities were calculated using a clinical diagnosis of fibromyalgia as the reference standard.

**Results:** Based on clinical diagnosis 45% of the participants were diagnosed with fibromyalgia; of these, only 19% had been diagnosed previously. The 2016 diagnostic criteria demonstrated a sensitivity of 88.5%, a specificity of 81.5%, a positive likelihood ratio of 4.79, a negative likelihood ratio of 0.14, a positive post-test probability of 79.4%, and a negative post-test probability of 10.2%.

**Conclusions:** Fibromyalgia was severely under-diagnosed among patients with high impact chronic pain referred to tertiary care in two pain rehabilitation centers in Denmark. The 2016 diagnostic criteria showed sufficient discriminatory properties suggesting that the fibromyalgia survey questionnaire can be used as a screening tool assisting the identification of fibromyalgia in this patient population.

**Keywords:** diagnostic accuracy; diagnostic criteria; fibromyalgia; sensitivity; specificity.

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## Introduction

Fibromyalgia (FM) is a pain disorder characterized by chronic widespread pain (CWP) and generalized mechanical hyperalgesia. Other significant symptoms include insomnia, fatigue, and cognitive dysfunction [1]. Patients with FM represent a subgroup of CWP presenting with a higher symptom burden and lower functional ability [2, 3]. In Denmark, a rheumatologist traditionally diagnoses patients with FM, but daily care is provided by primary care practitioners, who can choose to refer severely affected

patients (high-impact chronic pain [4–7]) to a tertiary care pain rehabilitation center. When the new International Classification of Diseases 11th revision (ICD-11) is implemented in 2022, fibromyalgia will be classified as a primary pain disorder (a subtype of CWP) instead of a rheumatological disease [8]. Consequently, in the future, specialists working with chronic non-malignant pain (CNMP) patients should be able to identify individuals with fibromyalgia.

No objective biological markers can validate a diagnosis of fibromyalgia, and several criteria for the classification and diagnosis of fibromyalgia have been suggested over the years. The purpose of classification criteria is to identify well-defined homogeneous groups of patients for research purposes, requiring high specificity. In contrast, diagnostic criteria strive to capture as many cases as possible and must perform with high sensitivity [9]. However, the utilization of diagnostic tests in patient care settings must be guided by evidence, and predictive values are greatly influenced by the prevalence of the disease and should not be generalized beyond the studied population.

The most widely used fibromyalgia research criteria are the dual 1990 American College of Rheumatology (ACR) classification criteria requiring both anamnestic widespread pain and widespread mechanical hyperalgesia assessed by manual tender point examination [10]. When developing these criteria, tender point count was the most powerful discriminator separating fibromyalgia from other painful rheumatic disorders [10]. The ACR 1990 uses 11 positive tender points as cut-off, but later studies have shown that a shift in disease severity in patients with CWP occurs at eight tender points [11]. In the clinical context, the ACR1990 classification criteria have been criticized for placing the diagnosis at the far end of a severity spectrum and ignoring other important key symptoms [12, 13]. This led to the proposal of diagnostic symptom-based criteria in 2010, and the definition of fibromyalgia expanded to include symptoms other than pain [14]. For the 2010 diagnostic criteria, three pain sites were sufficient for the definition. With a revision of the criteria in 2016 a generalized pain criterion was added, requiring pain in four out of five body regions with a minimum of four pain sites [15]; these criteria are referred to as the 2016 diagnostic criteria. The 2016 diagnostic criteria have been validated in populations with rheumatic disorders [16–18] and in a Norwegian population of CNMP patients [19], showing acceptable internal consistency and good construct validity.

To our knowledge, only one study has investigated the diagnostic accuracy of the 2016 diagnostic criteria in a tertiary care pain rehabilitation setting, using the ACR1990 criteria as the reference standard [20]. Only patients with CWP were included, and the 2016 diagnostic criteria demonstrated both

low sensitivity and specificity. However, as diagnostic and classification criteria have been developed for different purposes, using classification criteria as a reference standard for the diagnostic accuracy of diagnostic criteria is questionable.

This study aimed to investigate the diagnostic accuracy of the 2016 diagnostic criteria for fibromyalgia in a cross-sectional sample of patients with mixed CNMP disorders referred to tertiary care, using a clinical diagnosis of fibromyalgia by expert opinion as the reference standard.

## Materials and methods

### Study design

The study was designed as a prospective diagnostic accuracy study. The performance of the 2016 diagnostic criteria for fibromyalgia was investigated in a cross-sectional sample of patients with mixed chronic pain conditions referred to tertiary care. The reference standard was a clinical diagnosis of fibromyalgia by expert opinion. The study was performed according to Standards for Reporting Diagnostic accuracy studies (STARD) 2015 guidelines [21].

### Participants

Participants were recruited from two Danish public interdisciplinary pain rehabilitation centers. One was a university hospital unit (Center 1) and the other a general hospital unit (Center 2). Both centers received patients with different CNMP disorders referred by primary care practitioners. Patients referred to pain rehabilitation in Denmark must be sufficiently examined for diseases accessible to causal treatment before referral. Most patients referred will suffer from primary chronic pain conditions displaying nociplastic pain features [22]. Only a minor group consists of patients with rheumatological or neurological diseases, where disabling pain is still present despite successful causal treatment.

A specific chief consultant at each pain center recruited the study participants. From December 10th, 2017, patients were invited to participate at their first appointment with one of the two responsible consultants for two consecutive years. As one of the consultants changed employment during the study period, inclusion was terminated earlier in Center 2 (end of August 2019). Inclusion criteria were patients aged 18 years or above who could read and understand Danish. Patients who were not able to complete questionnaires due to poor somatic or mental status were excluded.

### The 2016 diagnostic criteria

The 2016 diagnostic criteria consist of a Widespread Pain Index (WPI), a Symptom Severity Score (SSS), and a generalized pain criterion [15]. The questionnaire can be completed by a physician or patient. The patient version used in this study is referred to as the fibromyalgia survey questionnaire (FSQ) [23]. To fulfill the 2016 criteria, the patient had to have a WPI of at least seven and a SSS of at least five or a WPI of 4–6 and a SSS of at least nine. Furthermore, a generalized pain

criterion had to be satisfied, defined as pain in a minimum of four of five regions.

### Translation procedure

The FSQ was translated to Danish according to standardized guidelines [24]. The questionnaire was initially translated independently from English to Danish by a panel of two researchers and one nonprofessional. Based on these three translations, the panel agreed on a Danish version. A new panel of two researchers and one nonprofessional then translated the Danish version back to English. Finally, all six members of the two panels collectively evaluated the Danish version and the reverse English translation and agreed on a final Danish version. Members of both panels had to be fluent in both Danish and English. The final version was pilot tested in six patients with FM or other CNMP conditions. The patients were asked to fill in the questionnaire and were consecutively interviewed regarding comprehensibility. Approval was obtained from the developers to use and translate the instrument. The Danish version is presented in the Supplementary Material.

### Assessment of widespread pain and tender point examination

Information about pain distribution was obtained both from interviews and pain drawings (body chart). In this study, CWP was defined as persistent or recurrent pain during the past three months located both axially and in all four body quadrants (representing five pain regions). The presence of widespread tenderness was evaluated based on examination of the 18 tender points defined by the ACR1990 criteria [10]. The tender point examination was carried out using a handheld spring-based pressure algometer with a probe area of 1 cm<sup>2</sup>. At each point, increasing pressure was slowly applied until a maximum of 4 kg/cm<sup>2</sup>. If a pain reaction was observed (vocalized, grimace or flinch) before or at a pressure of 4 kg/cm<sup>2</sup>, the point was considered a positive tender point. The two consultants trained the procedure together before and during the trial to secure a high and identical quality of testing [25]. Consultants were blinded to the responses on the fibromyalgia survey during the interview and the tender point examination.

### Reference standard

The reference standard was a clinical diagnosis of FM by expert opinion based on full history and clinical examination. To be diagnosed with FM the patients had to fulfill the criteria for CWP as described above. Furthermore, they were required to have symptoms of widespread pressure hyperalgesia, demanding a minimum of eight positive tender points (moderate pain = vocalized, grimace, or flinch) located both over and below the waist.

Both consultants had long-term experience in evaluating pain patients and received training from a senior rheumatologist and fibromyalgia expert to ensure a uniform evaluation of the clinical diagnosis of fibromyalgia. Continuous consensus in diagnosing was made between the two pain specialists throughout the study, and in complicated cases, the senior rheumatologist was consulted.

### Other assessments

Demographic data were collected about age, gender; body mass index, work status, medication, comorbidity, and existing FM diagnosis. Comorbid diseases were required to be in a stable and inactive state. Disease activity was evaluated using information from the patients' file only, and we did not perform new laboratory testing. To evaluate the level of pain and the intensity of common pain-related symptoms, the participants were asked to complete the symptom domain of the symptom impact questionnaire-revised (SIQR) [26, 27].

### Statistical analyses

Our study group previously estimated the prevalence of FM in the target population to be 37% based on the 2016 diagnostic criteria [28]. However, the diagnostic accuracy of the 2016 criteria was unknown, and we suspected the true prevalence to be lower. With an estimated prevalence of FM set at 30%, a minimum sample size of 103 subjects (including 31 subjects with FM) would be required to achieve a minimum power of 80% to detect a change in the percentage value of sensitivity from 70.0 to 90.0 based on a target significance level of 0.05 [29]. A minimum sample of 44 subjects (including 13 subjects with FM) is required to detect a change in the percentage value of specificity from 70.0 to 90.0. As the prevalence estimate was uncertain, it was decided to include patients over two consecutive years, approximately 200 patients.

Data were collected in paper format, entered into a database, and transferred to the statistical program Stata 16 for analysis. Descriptive statistics were used to describe the population, using numbers and percent to present categorical variables and median and interquartile ranges to present continuous and numerical variables. Comparative analyses were performed to investigate any differences in demographic data, pain characteristics, and level of pain-related symptoms between patients with and without FM based on the clinical diagnosis. Comparative analyses were also made between FM patients with and without an existing diagnose. The chi-square test, Fisher's exact test, or the Wilcoxon rank-sum test was used according to data type. A p-value < 0.05 was considered significant.

To analyze performance characteristics of the 2016 diagnostic criteria, contingency tables were made using the clinical diagnosis as the reference standard. Data were derived from the tables to calculate sensitivity, specificity, and positive and negative likelihood ratios. Furthermore, we have examined the positive post-test probability (PPTP) and the negative post-test probability (NPTP). PPTP is the probability of having the disease if the test is positive. PPTP has the same value as the positive predictive value (PPV). The negative post-test probability (NPTP) is the probability of having the disease if the test is negative. NPTP equals one minus the negative predictive value (NPV).

## Results

### Study participation

Of the 297 patients screened for eligibility, 275 met the inclusion criteria, and 215 patients were included in the

study, giving an overall participation rate of 78% (Figure 1). Of these, 163 (76%) were included at the university hospital unit and 52 (24%) at the general hospital unit, with 76 and 87% participation rates, respectively. Patient characteristics are presented in Table 1.

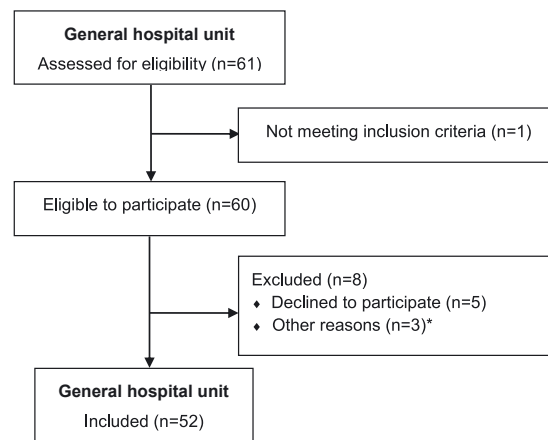
## Diagnose of FM based on expert opinion

Among the 215 participants evaluated by the two expert pain physicians, 96 were diagnosed with FM equivalent with 45% of this sample (Table 2). In this study population, 15% of the men and 55% of the women were diagnosed with FM.

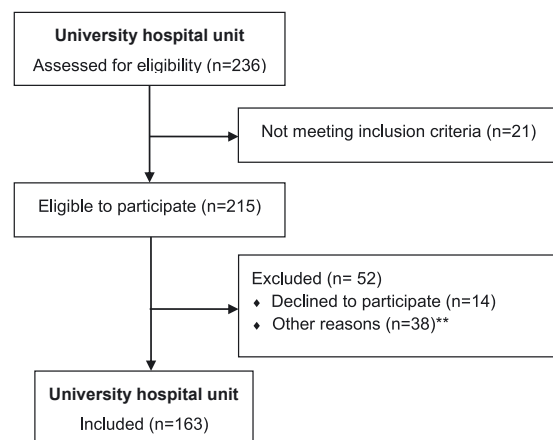
## Performance of the 2016 diagnostic criteria

The contingency table and performance characteristics for the 2016 diagnostic criteria using a clinical diagnosis as the reference standard are presented in Tables 2 and 3. The criteria demonstrated a sensitivity of 88.5%, a specificity of 81.5%, a positive likelihood ratio of 4.79, a negative likelihood ratio of 0.14, a positive post-test probability of 79.4%, and a negative post-test probability of 10.2%.

Contingency table and performance characteristics showing how the criteria would perform if the 1990ACR classification criteria had been used as the reference standard instead are presented in Supplementary Tables 1 and 2.



\*Other reasons: treatment ended before second visit (n=2), excluded because of very poor somatic or mental status (n=1)



\*\*Other reasons: treatment ended before second visit (n=27), excluded because of very poor somatic or mental status (n=11)

**Figure 1:** Overview of participant flow.  
\*Other reasons: Treatment ended before the second visit (n=2); excluded due to very poor somatic or mental status (n=1).  
\*\*Other reasons: Treatment ended before the second visit (n=27); excluded due to very poor somatic or mental status (n=11).

**Table 1:** Patient characteristics showing the distribution for the entire cohort and each pain center.

Variable	Total (n=215)	Centre 1 (n=163)	Centre 2 (n=52)
Women n, %	160 (74)	123 (76)	37 (71)
Age in years (median, quartiles)	49 (38, 58)	50 (38, 58)	45 (38, 53.5)
BMI kg/m <sup>2</sup> (median, quartiles)	26.8 (24, 32)	28.2 (24, 33)	25.6 (23, 29)
Pain duration in years (median, quartiles)	10 (5, 20)	11 (6, 20)	7 (4, 19)
Employment situation <sup>a</sup> :			
Working on ordinary conditions n, %	30 (14)	18 (11)	12 (23)
Subsidized job n, %	46 (21)	40 (25)	6 (12)
Sick leave n, %	52 (24)	40 (25)	12 (23)
Disability pension n, %	40 (19)	30 (18)	10 (19)
Retired n, %	23 (11)	17 (10)	6 (12)
Studying n, %	15 (7)	13 (8)	2 (4)
Fibromyalgia diagnosed before referral n, %	40 (19)	32 (20)	8 (16)
Fibromyalgia diagnosed after referral n, %	96 (45)	73 (45)	23 (44)

<sup>a</sup>Different n due to missing data.

**Table 2:** 2 × 2 contingency table for the 2016 diagnostic criteria vs. a clinical diagnose of fibromyalgia based on expert opinion.

2016 diagnostic criteria	Clinical diagnose of fibromyalgia		Total
	Yes	No	
Positive	85	22	107
Negative	11	97	108
Total	96	119	215

### Differences in characteristics between patients with and without FM

Differences regarding demographics and pain characteristics are shown in Tables 4 and 5. There were significantly more women in the FM group, and FM patients were more often in a subsidized job, on sick leave, or disability pension. Longer duration of pain, higher intensity of both pain, and all other SIQR items, including the symptom domain score, were observed for the FM group. FM patients used opioids less frequently and low dose naltrexone more regularly.

### Differences in characteristics between FM patients with and without an existing diagnose

Among the 96 participants diagnosed with FM in this study, 40 (19%) had been diagnosed before referral (Table 1). There were no men with an existing FM diagnosis, but eight male FM patients were identified in the study. The group with an existing FM diagnose (FM-E) was compared to the group diagnosed only in the study (FM-S) (Tables 4 and 5). The number of tender points was significantly higher in the FM-E group. Otherwise, no differences were found regarding demographics, pain characteristics, or level of symptoms. The number of patients who fulfilled the ACR1990 criteria was comparable between the FM-E and FM-S groups.

The expert pain physicians confirmed all patients with an existing FM diagnosis to have FM. Among the 56 patients from the FM-S group, the referral diagnoses were CWP (n=15), rheumatological disease (n=6), back pain (n=13), neck pain (n=7), other localized pain (n=7), or unspecified pain (n=8).

**Table 3:** Performance characteristics of the 2016 diagnostic criteria for fibromyalgia, using a clinical diagnosis as the reference standard.

Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Positive post-test probability	Negative post-test probability
0.885 (0.822–0.949) <sup>a</sup>	0.815 (0.745–0.885) <sup>a</sup>	4.789 (3.262–7.032) <sup>a</sup>	0.141 (0.080–0.247) <sup>a</sup>	0.794 (0.718–0.871) <sup>a</sup>	0.102 (0.045–0.159) <sup>a</sup>

<sup>a</sup>95% confidence interval.

**Table 4:** Differences in demographic data between patients with and without fibromyalgia and between patients with fibromyalgia diagnosed before and after referral.

Variable	No fibromyalgia (n=119)	Fibromyalgia (n=96)	p-Value <sup>a</sup>	Fibromyalgia previously diagnosed (n=40)	Fibromyalgia not previously diagnosed (n=56)	p-Value <sup>a</sup>
Women n, %	72 (61)	88 (92)	<0.001	40 (100)	48 (85)	<0.05
Age in years (median, quartiles)	49 (37, 61)	48.5 (41, 55)	0.42	49.5 (43, 55.5)	48.5 (37.5, 53)	0.23
Pain duration in years (median, quartiles)	8 (4, 17)	13 (8, 21)	<0.001	15 (9, 25)	11 (6, 20)	0.06
Employment status: <sup>b</sup>			<0.05			0.12
Working on ordinary conditions n, %	22 (18)	8 (8)		4 (11)	4 (7)	
Subsidized job n, %	22 (18)	24 (25)		11 (30)	13 (23)	
Sick leave n, %	26 (22)	26 (27)		6 (16)	20 (36)	
Disability pension n, %	19 (16)	21 (22)		13 (35)	8 (14)	
Retired n, %	19 (16)	4 (4)		1 (3)	3 (5)	
Studying n, %	8 (7)	7 (7)		2 (5)	5 (9)	
Comorbidity:						
Inflammatory rheumatic disease n, %	7 (6)	9 (9)	0.33	2 (5)	7 (13)	0.21
Polyneuropathy or multiple sclerosis n, %	9 (8)	1 (1)	<0.05	0 (0)	1 (2)	0.40
Pain medication:						
Paracetamol n, %	41 (34)	26 (27)	0.25	12 (30)	14 (25)	0.59
NSAIDs n, %	13 (11)	12 (13)	0.72	5 (13)	7 (13)	1.00
Tricyclic antidepressants n, %	18 (15)	11 (11)	0.43	5 (13)	6 (11)	0.79
Gabapentin n, %	19 (16)	10 (10)	0.24	4 (10)	6 (11)	0.91
Pregabalin n, %	15 (13)	8 (8)	0.31	4 (10)	4 (7)	0.62
SNRIs n, %	24 (20)	20 (21)	0.90	11 (28)	9 (16)	0.17
Low dose naltrexone n, %	5 (4)	13 (14)	<0.05	8 (20)	5 (9)	0.12
Opioids n, %	43 (36)	22 (23)	<0.05	8 (20)	14 (25)	0.57

<sup>a</sup>Chi-square test or Fisher's Exact test for categorical data and Wilcoxon rank-sum test for continuous or numerical data. <sup>b</sup>Different n due to missing data.

## Discussion

To our knowledge, this is the first study to investigate the diagnostic accuracy of the 2016 diagnostic criteria for fibromyalgia using clinical diagnosis as the reference standard in a CNMP tertiary care pain rehabilitation setting. The 2016 diagnostic criteria were translated to Danish according to standardized guidelines [24], and the Danish version is provided in the Supplementary Material and is freely available for other purposes. The 2016 diagnostic criteria showed acceptable discriminatory properties for the identification of fibromyalgia in the population examined.

### Diagnosing FM in the clinic

There is an ongoing debate whether to regard fibromyalgia as a primary pain disorder or as part of a functional

somatic syndrome [8, 30, 31]. However, as experts working with pain rehabilitation, pain medicine, and pain research (e.g. clinical trials investigating the effect of new pain treatments), we welcome the new ICD-11 revision, which acknowledges widespread pain to be the core symptom in fibromyalgia. The presence of widespread pain is a key symptom in both the ACR1990 classification criteria, the 2016 diagnostic criteria, and other later proposed diagnostic criteria [32–35]. Some criteria have focused on mechanical hyperalgesia as another important key symptom. In contrast, others focus more on the level of somatic symptoms. A diagnosis of FM in the clinical setting will always be based on an expert's opinion, taking symptoms, objective signs, comorbidity, medication, and the ruling out of other possible causes of the symptoms into consideration. However, a systematic approach using well-validated diagnostic criteria can be a valuable aid in identifying patients with FM.

**Table 5:** Differences in pain characteristics and level of symptoms between patients with and without fibromyalgia and between patients with fibromyalgia diagnosed before and after referral.

Variable	No fibromyalgia (n=119)	Fibromyalgia (n=96)	p- Value <sup>a</sup>	Fibromyalgia previously diagnosed (n=40)	Fibromyalgia not previ- ously diagnosed (n=56)	p- Value <sup>a</sup>
Widespread pain index (WPI) <sup>b</sup> (median, quartiles)	5 (3, 7)	11 (9, 15)	<0.001	10.5 (9, 16)	12 (9, 14)	0.89
Symptom severity score (SSS) <sup>c</sup> (median, quartiles)	7 (4, 9)	10 (8, 11)	<0.001	10 (8, 11)	10 (9, 11)	0.32
Tender point count <sup>d</sup> (median, quartiles)	6 (2, 11)	16 (13, 18)	<0.001	17 (15, 18)	15.5 (12, 18)	<0.05
Full fills ACR1990 criteria <sup>e</sup> n, % Items from the SIQR symptom domain <sup>f</sup>	0 (0)	88 (92)	<0.001	37 (93)	51 (91)	0.80
Pain (median, quartiles)	6 (5, 8)	7 (6, 8)	<0.05	7 (6, 8)	7 (6, 8)	0.69
Energy (median, quartiles)	6 (4, 8)	7 (5, 8)	<0.05	7 (5, 8)	7 (5, 8.5)	0.67
Stiffness (median, quartiles)	5 (2, 7)	7 (5, 8)	<0.001	7 (5, 8)	7 (5, 8)	0.54
Sleep quality (median quartiles)	6 (2, 8)	8 (6, 9)	<0.001	8.5 (6.5, 10)	8 (6, 9)	0.38
Depression (median quartiles)	2 (0, 5)	5 (1, 7)	<0.001	5 (1, 7)	5 (1.5, 6.5)	0.99
Memory problems (median, quartiles)	5 (2, 7)	7 (5, 8.5)	<0.001	7 (6, 8)	7 (5, 9)	0.72
Anxiety (median quartiles)	0 (0, 2)	2 (0, 5)	<0.001	1 (0, 3.5)	3 (0, 6.5)	0.09
Tenderness to touch (median, quartiles)	4 (0, 7)	7 (5.5, 9)	<0.001	7 (5, 9)	7 (6, 9)	0.62
Balance problems (median, quartiles)	2 (0, 5)	5 (2, 7)	<0.001	5 (3, 7)	5 (1, 7)	0.39
Sensitivity to sensory inputs (median, quartiles)	2 (0, 7)	7 (4.5, 8)	<0.001	8 (5, 9)	7 (3, 8)	0.12
FIQR symptom domain sum score <sup>g</sup> (median, quartiles)	38 (28, 51)	61 (49, 70.5)	<0.001	60.5 (50.5, 69)	61 (48.5, 71)	0.94

<sup>a</sup>Chi-square test or Fisher's Exact test for categorical data and Wilcoxon rank-sum test for continuous or numerical data. <sup>b</sup>Widespread Pain Index (WPI) from the 2016 diagnostic criteria. The WPI counts the number of painful body parts during the past 7 days, giving rise to a score between 0 and 19. <sup>c</sup>Symptom Severity Score (SSS) from the 2016 diagnostic criteria. SSS is ranging from 0–12. <sup>d</sup>Tender point examination was carried out using a handheld pressure algometer. Each tender point was examined applying a slowly increased pressure until 4 kg/cm<sup>2</sup>. If the threshold for pain was reached, the tender point was considered positive. The number of positive tender points is ranging from 0–18. <sup>e</sup>All participants were classified according to the American College of Rheumatology classification criteria from 1990 (ACR1990). The participants full filled the criteria if they reported having had widespread pain (pain in all four body quadrant plus axially) during the last 3 months and had a minimum of 11 out of 18 positive tender points. <sup>f</sup>Level of pain and the intensity of nine common pain-related symptoms, were evaluated using the 10 items from the symptom part of the Symptom Impact Questionnaire-Revised (SIQR). Each item evaluates the average severity of the symptom during the last 7 days on a 0–10 numeric rating scale (NRS), 0 indicating “no problem” and 10 indicating “severe problems.” <sup>g</sup>The SIQR symptom domain sum score is calculated as the sum of the 10 items (range 0–100).

## Diagnosing FM in the study population

In this study, we diagnosed FM based on expert opinion, considering both full history and clinical examination. To secure homogeneity and transparency of the diagnosis, some minimum requirements were agreed on (1) pain located in all four body quadrants plus axially for at least three months, and (2) the presence of a minimum 8 of 18 positive tender points. This was based on a previous study showing that a shift in severity of disease in CWP patients occurs at eight positive tender points [11]. The tender point

examination is a quick, easy to learn, and reliable instrument in the clinic [25, 36]. Most of the patients diagnosed with FM in the study also fulfilled the ACR1990 criteria.

That fibromyalgia is more prevalent among women, with a male to female ratio of 1:3 found in the general population [37], was observed in our present sample with a ratio of 1:3.7. Only 19% of the patients diagnosed with FM had an established diagnosis, and notably, none of them were men. Patients diagnosed with FM only in the study did not differ from patients with an existing FM diagnosis, except they had a lower tender point count.



In our study population, 45% were diagnosed with FM based on expert opinion, 41% fulfilled the ACR1990 criteria, and 50% fulfilled the ACR2016 criteria. In a previous study, including 1,343 patients from Center 1, only 37% fulfilled the ACR2016 criteria [28]. The demographic characteristics for the two study populations are comparable except regarding gender, showing a higher ratio of women in our present sample (74 vs. 66%), which could explain the observed differences in FM frequency. In a recent study including more than 12,000 patients from all tertiary pain centers in Denmark, 68% were women [22].

## Performance of the 2016 diagnostic criteria

Even though the diagnostic accuracy of the 2016 diagnostic criteria has previously been shown to be acceptable in the general population and populations of patients with different rheumatic diseases [15], they might perform differently in CNMP populations. In our mixed CNMP tertiary care sample, the 2016 diagnostic criteria demonstrated high sensitivity and acceptable specificity. Thus, in this study population, the 2016 diagnostic criteria showed sufficient discriminatory properties, indicating that the FSQ can be used as an easily applied tool to assist systematic screening for FM in patients referred for tertiary pain rehabilitation.

In a previous diagnostic accuracy study of the 2016 diagnostic criteria in a tertiary care pain rehabilitation setting, only patients with CWP were included. Using the ACR1990 criteria as reference standard they found the 2016 criteria to perform poorly [20]. This finding suggests that the 2016 diagnostic criteria might not be helpful in discriminating FM from CWP with lower severity in populations with high impact pain.

## Implications of diagnosing FM

It is well known that patients with fibromyalgia have a higher symptom burden and lower functional ability compared to patients with other chronic pain disorders, including patients with CWP who do not fulfill the ACR1990 criteria [3, 38]. In accordance with this, we found that patients diagnosed with FM had a significantly longer duration of pain, higher symptom burden, and were more work incapacitated than the non-FM group.

We found FM to be severely under-diagnosed in this cross-sectional sample of patients with mixed high-impact chronic pain conditions referred to pain rehabilitation. Only 15 of the 56 patients not previously recognized to have FM were referred with a diagnosis of CWP, whereas the remaining

41 were referred with localized or unspecified pain diagnoses. Despite rapidly increasing insight into pathophysiological mechanisms [39, 40], fibromyalgia remains a controversial diagnosis due to limited knowledge about the disease among many healthcare professionals [41, 42], and the diagnosis is often delayed by several years [43]. A correct and timely diagnosis is of great value to patients as it encourages better self-management [44] and helps healthcare providers to offer appropriate care [42]. We suggest that a systematic approach, including the use of the FSQ, could easily be implemented as a routine to assist the identification of FM among patients with chronic pain referred to tertiary care.

## Strengths and limitations

To secure an accurate reference standard and to limit interrater variability, patients were recruited by two senior pain specialists who were trained in diagnosing fibromyalgia and performing tender point examination. Secretaries otherwise not involved in the study allocated all referred patients randomly to all the specialists working at the centers, striving to secure a valid cross-sectional sample of the total population from the two pain centers. However, this cross-sectional sample had a high frequency of women, explaining the relatively high frequency of FM found in the present study. With a fibromyalgia prevalence of 45% in this population, the sample size was sufficient to estimate the diagnostic accuracy with acceptable power [29]. To reduce bias the investigators were blinded regarding the FSQ and the participants were not informed whether they were diagnosed with FM in the study until after they had completed the FSQ.

As the study was performed at two pain centers in Denmark, our results might not be generalizable to other tertiary care chronic pain populations in Denmark or other countries. In Denmark, all patients referred to pain rehabilitation receive the diagnose “chronic complex non-malignant pain.” We did not collect data about the history of trauma, surgery, or previous cancer treatment in the present study. The implementation of the ICD-11 will secure diagnosis of primary and secondary pain in future trials.

## Conclusions

The 2016 diagnostic criteria showed high sensitivity and acceptable specificity in the study population and were able to capture the spectrum of the disease, but also included some false positives. Our results suggest that the FSQ might be useful as an easily applied screening tool to

assist the identification of patients with fibromyalgia in tertiary care chronic pain settings. However, more studies investigating the diagnostic accuracy of the 2016 criteria in larger CNMP populations and other settings and countries are warranted.

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**Informed consent:** Informed consent was obtained from all individuals included in this study.

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