

# Definition of fibromyalgia severity: findings from a cross-sectional survey of 2339 Italian patients

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## Abstract

**Objective.** To establish optimal cut-off values for the scores of the revised Fibromyalgia Impact Questionnaire (FIQR), the modified Fibromyalgia Assessment Scale (FAS 2019mod), and the Polysymptomatic Distress Scale (PDS) in order to distinguish five levels of FM disease severity.

**Methods.** Consecutive FM patients were evaluated with the three clinimetric indices, and each patient was required to answer the anchor question: ‘In general, would you say your health is 1 = very good, 2 = good, 3 = fair, 4 = poor, or 5 = very poor?’—which represented the external criterion. Cut-off points were established through the interquartile reconciliation approach.

**Results.** The study sample consisted of 2181 women (93.2%) and 158 men (6.8%), with a mean age of 51.9 (11.5) years, and mean disease duration was 7.3 (6.9) years. The overall median FIQR, FAS 2019 mod and PDS scores (25th–75th percentiles) were respectively 61.16 (41.16–77.00), 27.00 (19.00–32.00) and 19.0 (13.00–24.00). Reconciliation of the mean 75th and 25th percentiles of adjacent categories defined the severity states for FIQR: 0–23 for remission, 24–40 for mild disease, 41–63 for moderate disease, 64–82 for severe disease and >83 for very severe disease; FAS 2019 mod: 0–12 for remission, 13–20 for mild disease, 21–28 for moderate disease, 29–33 for severe disease and >33 for very severe disease; PDS: 0–5 for remission, 6–15 for mild disease, 16–20 for moderate disease, 21–25 for severe disease and >25 for very severe disease.

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**Conclusions.** Disease severity cut-offs can represent an important improvement in interpreting FM.

**Key words:** fibromyalgia; severity; cut-off points; revised Fibromyalgia Impact Questionnaire; modified; Fibromyalgia Assessment Status; polysymptomatic distress scale

### Rheumatology key messages

- FM severity should be measured using instruments with validated cut-offs.
- FM severity assessment can improve our understanding of the natural history of the condition.
- Determining FM severity can identify the clinical effectiveness and long-term outcomes of targeted interventions.

## Introduction

Fibromyalgia (FM), whose estimated prevalence is 2.2% in Western countries [1], is a complex disease characterized by chronic widespread pain, tenderness and somatic symptoms, including fatigue, cognitive dysfunction and non-restorative sleep. The burden of such a complex clinical picture results in an increased prevalence of depression, anxiety, stiffness and functional disability [2]. These clinical manifestations fall within the domains recognized by OMERACT as being important when assessing FM patients [3].

A large number of studies have described the negative effects of FM on physical and cognitive function, emotional and psychological status, and personal and social relationships [4]. FM may impair working ability, leading to reduced productivity and high healthcare costs [5]. The direct and indirect costs related to FM are higher among patients with more severe disease [6]. However, the clinical picture may fluctuate widely in the same patient, at different time intervals, and between patients. Measuring the severity of symptoms has been one of the greatest challenges in both diagnosis and clinimetry of FM.

Nevertheless, evaluating and measuring the severity of FM would be beneficial in a number of ways, including the selection of patients to participate in trials, the identification of treatment responders at different levels (clinical practice, observational studies, clinical trials), the recognition of non-responders.

Up to now reliable and easy to use biomarkers to assess FM in daily clinical practice are lacking; the severity of the disease is assessed through fully patient-reported instruments such as the Fibromyalgia Impact Questionnaire (FIQ) or the revised FIQ (FIQR) [7, 8], the Fibromyalgia Assessment Status (FAS) or the modified FAS (FAS 2019mod) [9, 10], and the Polysymptomatic Distress Scale (PDS) [11].

It is widely accepted that the measurement of the severity of the disease, in the field of chronic pain, should be performed through patient-reported instruments [12]. However, in order to provide information on the severity of a given condition in the results of the self-assessment

questionnaires, it is necessary to establish interpretative cut-offs [13, 14]. Currently, cut-offs have been proposed for FIQR, but based on a single monocentric study [15], and for PDS, whose main limit is represented by a single distinction, respectively in severe or very severe disease in diagnosed patients (PDS >12) [16]. Taking these considerations into account, the objective of this study was to establish optimal cut-off values for total FIQR, FAS 2019mod and PDS scores to distinguish remission, mild, moderate, severe and very severe FM, investigating data coming from a large multicentric cohort.

## Materials and methods

### Patient recruitment

The patients who participated in this study were recruited from November 2018 to April 2019 in 19 Italian rheumatology centres. Patients of adult age with a diagnosis of FM for at least 3 months based on the criteria of the ACR of 2010/2011 were included [11]. For each centre the diagnosis was made by an experienced rheumatologist with at least 10 years of experience. All of the patients underwent a diagnostic work-up including a complete physical examination and the laboratory tests specified in the revised EULAR recommendations for the management of FM [17]. Patients with comorbid conditions (i.e. inflammatory arthropathies, connective tissue diseases or significant psychiatric conditions, including severe depression) that would interfere with FM assessment were excluded.

All of the participants gave their written informed consent to the study. The protocol, patient information sheet and consent form were approved by the Ethics Committee of the Università Politecnica delle Marche, Ancona, Italy (Comitato Unico Regionale—ASUR Marche, No. 1970/AV2), and the review boards of all of the study centres. The study protocol did not require any medical intervention.

### Questionnaires

The patients filled in a comprehensive package of questionnaires related to demographic data (age, sex, marital

status, and education), disease variables, as well as the three disease-specific questionnaires (FIQR, FAS 2019mod, PDS). Below is a brief description of the three specific clinimetric instruments for FM.

The FIQR is composed of 11-points numerical rating scales (NRS) that investigate, referring to the last week, different health domains. In particular, Ten items explore the symptoms, nine items the physical function and two items the overall impact. The final score, ranging from 0 to 100 (higher scores indicate a more severe disease), is obtained from the algebraic sum of the symptoms domain divided by 2, plus the physical function domain divided by 3, plus the two items of the overall impact domain that are considered as they are [18].

The FAS 2019mod is a recent revised version of the FAS, which is easier to use than the previous instrument. It is composed of two sections that investigate the symptoms of the last seven days. The first section is two 11-point NRS that investigate fatigue and unrefreshing sleep, while the second section is the front and back of a manikin with 19 body areas that analyse widespread pain. The final score (from 0 to 39) is the sum of the two scales plus the score obtained on the manikin [10].

Finally, the PDS is based on the variables used in the ACR FM 2010/2011 diagnostic criteria, and is the algebraic sum of widespread pain index (WPI, range 0–19) and symptom severity scale (SSS, range 0–12). In addition to diagnostic purposes, the PDS (range 0–31) allows assessment of the severity of the disease because higher scores mean a more severe and pervasive disease [11].

### Statistical analysis

Normal data distribution was verified using the Shapiro–Wilk test (the data were generally not normally distributed), and the data are presented as median values and interquartile range (IQR) or mean values and s.d. as appropriate.

The correlations between the FIQR, FAS 2019mod and PDS scores were analysed using Spearman's correlation coefficient.

The interpretability of each tool was determined by dividing the patients into five disease severity categories (remission, mild, moderate, severe and very severe disease). A five-state severity scale was chosen because, from previous work [15], it emerged that many patients ended up in the highest category, and therefore a further clarification of the high severity of the disease was possible. Moreover, the distinction in five severity states was already in use for PDS [16]. The external criterion used to make this distinction was the answer to the question 'In general, would you say your overall health is 1 = very good, 2 = good, 3 = fair, 4 = poor, 5 = very poor?', attributing the state of remission for very good, mild severity for good, moderate severity for fair, severe for poor and very severe for very poor. Arithmetic mean values with their s.d. and median values with their 25th and 75th percentiles were calculated for each disease severity status, and the 75th–25th percentiles of adjacent disease severity

states (75th of the lower and 25th of the upper) were reconciled to define the cut-off values distinguishing them. Briefly, the cut-off value between remission and mild disease was obtained by calculating the arithmetic mean value between the mean 75th percentile of remission and the mean 25th percentile of mild disease, and, if necessary, rounding it to the first decimal place. The same method was used to define the cut-off values separating the other adjacent states of severity. Reconciling the mean 75th percentile of a lower category and the mean 25th percentile of a higher category is considered a valid means of determining cut-off values, and has been previously adopted in rheumatology [14, 19, 20]. The non-parametric Kruskal–Wallis test was used to assess the level of significance of the different disease severity categories in individual patients.

In addition, receiver operating characteristic (ROC) curve analysis was used to explore the discriminative accuracy of the three questionnaires in distinguishing patients with different levels of disease severity. The external anchor was the 'yes' or 'no' answer to a general question concerning the patient acceptable symptom state (PASS), defined as the value beyond which patients consider themselves well: 'Considering all the different ways your disease is affecting you, if you were to stay in this state for the next few months, do you consider your current state satisfactory?' [21]. As ROC curve analysis requires dichotomous external criteria, the patients in remission and those with mild or moderate disease were considered to be in a state of 'low severity', and those with severe or very severe disease were considered to be in a state of 'high severity'. Area under the ROC curve (AUC-ROC) values between 0.7 and 0.8 indicate reasonable discrimination, and those exceeding 0.8 indicate good discrimination. The best cut-off values for the FIQR, FAS 2019mod and PSD were obtained considering Youden's index [22]. Wilcoxon's non-parametric signed ranks test was used to compare the areas under the AUC-ROCs as suggested by Hanley and McNeil [23].

The study data were entered in a pre-constructed Microsoft Excel spreadsheet by a study assistant, checked by two of the authors (at random and on the basis of plausibility during the descriptive data analysis), and analysed using MedCalc 18.6 statistical software for Windows XP. Patients were excluded from the analysis if they failed to answer one or more of the items of the questionnaires.

## Results

### Demographic characteristics and descriptive statistics

The study sample consisted of 2339 FM patients, with 2181 women (93.2%) and 158 men (6.8%), with a mean age of 51.9 years (s.d. 11.5), and mean disease duration of 7.3 years (s.d. 6.9). The majority of the patients were married (71.3%) and generally well educated (high school education or above). Overall they were

moderately overweight (mean BMI 25.9 kg/m<sup>2</sup>, s.d. 4.20): 68 patients (2.9%) were underweight (BMI <18.5 Kg/m<sup>2</sup>), 1059 (45.3%) were normal weight (BMI 18.5-24.9 Kg/m<sup>2</sup>), 891 (38.1%) were overweight (BMI 25-29.9 Kg/m<sup>2</sup>), and 321 (13.7%) were obese (BMI 30 Kg/m<sup>2</sup>).

The median FIQR, FAS 2019mod and PDS scores (25th–75th percentiles) were respectively 61.16 (41.16–77.00), 27.00 (19.00–32.00) and 19.0 (13.00–24.00) (Table 1).

### Central tendency, distribution and correlations of FIQR, FAS 2019mod and PDS scores

None of the three clinimetric indices were normally distributed (Shapiro–Wilk test). The coefficients of skewness (degree of symmetry) were respectively  $-0.3913$  ( $P < 0.0001$ ),  $-0.5295$  ( $P < 0.0001$ ) and  $-0.3492$  ( $P < 0.0001$ ), whereas the coefficients of kurtosis (the degree of peakedness/flatness) were respectively  $-0.8071$  ( $P < 0.0001$ ),  $-0.5295$  ( $P < 0.0001$ ) and  $-0.7568$  ( $P < 0.0001$ ) (Table 2).

Pain (FIQR12), fatigue (FIQR13), stiffness (FIQR14) and sleep quality (FIQR15) were ranked the top four symptoms by the highest proportion of patients, and were ranked significantly higher among the female patients ( $P = 0.010$ ,  $P = 0.004$ ,  $P = 0.006$  and  $P = 0.003$ ,

respectively). The impact of the disease on functional domains such as personal care (FIQR1) and activities of daily living was also greater among women, but the differences were not significant except for FIQR4 and FIQR5 ( $P < 0.001$  for both).

There was a very high degree of correlation (Spearman's rank correlation coefficient) between FIQR and the FAS 2019mod ( $\rho = 0.810$ ;  $P < 0.0001$ ) and the PDS ( $\rho = 0.728$ ;  $P < 0.0001$ ), and between the FAS 2019mod and the PDS ( $\rho = 0.899$ ;  $P < 0.0001$ ).

### Interpretability

Reconciling the mean 75th and 25th percentiles of adjacent severity states in order to define cut-off FIQR values, the numbers considered for the transition from remission to mild disease were 22 (mean 75th percentile of remission) and 24 (mean 25th percentile of mild severity). The arithmetic mean of these two values was 23 (no need for rounding in this case), which therefore became the FIQR cut-off value for remission. Likewise, the FIQR cut-off value between mild and moderate severity was 40 (the arithmetic mean of the mean values of the 75th percentile of mild severity and the 25th percentile of moderate severity was 40.4, which was rounded down to 40); that between moderate and severe disease

**TABLE 1** Demographic characteristics of the study population

Clinical or demographic characteristic	Mean	Median	s.d.	25th–75th percentiles
Age, years	51.91	53.01	11.52	45.0–59.0
Disease duration, years	7.34	6.93	5.00	2.00–10.00
BMI, kg/m <sup>2</sup>	25.90	25.51	4.20	22.86–27.70
Marital status, <i>n</i> (%)				
Single	413 (17.7)			
Married	1667 (71.3)			
Divorced/separated	200 (8.6)			
Widowed	59 (2.5)			
Educational level, <i>n</i> (%)				
Primary school	155 (6.6)			
Secondary school	660 (28.2)			
High school/university	1524 (65.2)			
FIQR				
Total score (0–100)	57.86	61.16	23.37	41.16–77.00
Physical function (0–30)	16.06	16.16	7.73	10.00–22.33
Overall impact (0–20)	11.06	12.00	6.04	6.00–16.00
Symptoms (0–50)	30.74	33.00	11.45	23.00–40.00
FAS 2019mod				
Total score (0–39)	25.13	27.00	8.92	19.00–32.00
Fatigue (0–10)	7.18	8.00	2.80	4.00–8.00
Sleep (0–10)	6.87	8.00	2.93	4.00–9.00
WPI (0–19)	11.08	11.00	4.89	8.00–15.00
PDS				
Total score (0–31)	18.59	19.00	7.36	13.00–24.00
WPI (0–19)	11.08	11.00	4.89	8.00–15.00
SSS (0–12)	7.51	8.00	3.48	5.00–10.00

FAS 2019mod: modified Fibromyalgia Assessment Status; FIQR: revised Fibromyalgia Impact Questionnaire; PDS: Polysymptomatic Distress Scale; SSS: symptom severity scale; WPI: widespread pain index.

**TABLE 2** Descriptive statistics of FIQR, FAS 2019mod and PDS

	FIQR	FAS 2019mod	PDS
Lowest value	2.00	0.00	0.00
Highest value	100.00	39.00	31.00
Arithmetic mean	57.86	25.01	18.59
95% CI of arithmetic mean	56.91, 58.81	24.65, 25.37	18.29, 18.89
Median value	61.16	27.00	19.00
95% CI of median value	59.50, 62.50	26.00, 27.00	19.00, 20.00
Variance	546.52	79.33	54.30
S.D.	23.37	8.90	7.36
Relative S.D.	0.40 (40.40%)	0.35 (35.61%)	0.39 (39.63%)
Standard error of the mean	0.48	0.18	0.15
Coefficient of skewness	-0.391 ( $P < 0.0001$ )	-0.525 ( $P < 0.0001$ )	-0.349 ( $P < 0.0001$ )
Coefficient of kurtosis	-0.807 ( $P < 0.0001$ )	-0.529 ( $P < 0.0001$ )	-0.756 ( $P < 0.0001$ )
Shapiro-Wilk test of normal distribution	$W = 0.962$ Reject normality ( $P < 0.0001$ )	$W = 0.958$ Reject normality ( $P < 0.0001$ )	$W = 0.966$ Reject normality ( $P < 0.0001$ )

FAS 2019mod: modified Fibromyalgia Assessment Status; FIQR: revised Fibromyalgia Impact Questionnaire; PDS: Polysymptomatic Distress Scale.

**TABLE 3** FIQR, FAS 2019mod and PDS cut-off values for FM severity states

FM severity state	Cut-off values		
	FIQR	FAS 2019mod	PDS
Remission	≤23	≤12	≤5
Mild	>23 and ≤40	>12 and ≤20	>5 and ≤15
Moderate	>40 and ≤63	>20 and ≤28	>15 and ≤20
Severe	>63 and ≤82	>28 and ≤33	>20 and ≤25
Very severe	>82	>33	>25

FAS 2019mod: modified Fibromyalgia Assessment Status; FIQR: revised Fibromyalgia Impact Questionnaire; PDS: Polysymptomatic Distress Scale.

was 63 (the arithmetic mean of the mean values of the 75th percentile of moderate disease and the 25th percentile of severe disease was 63.4, which was rounded down to 63); and that between severe and very severe disease was 82 (the arithmetic mean of the mean values of the 75th percentile of severe disease and the 25th percentile of very severe disease was 81.7, which was rounded up to 82).

Using the same method, the FAS 2019mod scores obtained were 0–12 for remission, 13–20 for mild disease, 21–28 for moderate disease, 29–33 for severe disease and >33 for very severe disease.

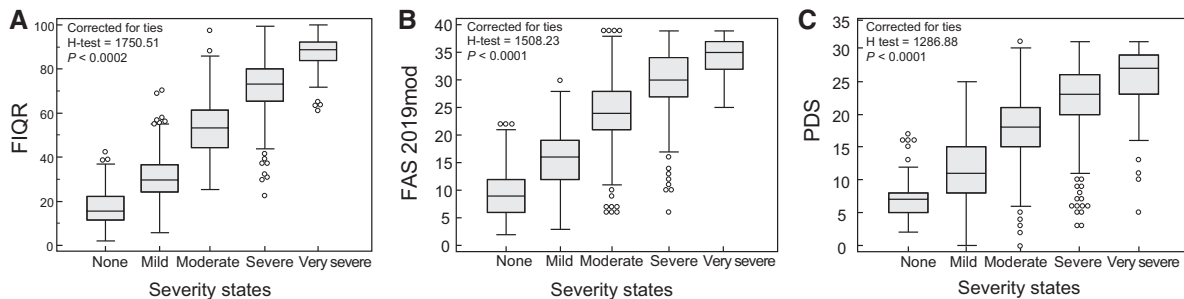
In the same way, the PDS scores were 0–5 for remission, 6–15 for mild disease, 16–20 for moderate disease, 21–25 for severe disease and >25 for very severe disease (Table 3).

The overall median (25th–75th percentiles) FIQR, FAS 2019mod and PDS values were respectively 15.50 (11.51–22.21), 9.00 (6.00–12.00) and 7.00 (5.00–8.00) for

remission; 29.58 (24.17–36.50), 16.00 (12.00–19.00) and 11.00 (8.00–15.00) for mild disease; 53.33 (44.33–61.50), 24.00 (21.00–28.00) and 18.00 (15.00–21.00) for moderate disease; 73.33 (65.33–80.00), 30.00 (27.00–34.00) and 23.00 (20.00–26.00) for severe disease; and 88.66 (83.83–92.33), 35.00 (32.00–37.00) and 27.00 (23.00–29.00) for very severe disease. Figure 1 shows the statistically significant stepwise increase in the severity scores (Kruskal–Wallis test,  $P < 0.0001$ ), indicating that these categories adequately distinguish the different degrees of severity.

Using the calculated FIQR, FAS 2019mod and PDS cut-off values, respectively 11.0%, 12.3% and 4.5% of the patients were in remission; 12.6%, 15.8% and 24.4% had a mild disease, 28.6%, 32.3% and 24.1% had a moderate disease; 31.2%, 21.2% and 25.7% had a severe disease; and 16.2%, 18.4% and 19.2% had very severe disease. On the basis of the FIQR cut-off values, 47.4% of the patients had severe or very

**Fig. 1** Box-and-whisker plots of FIQR (A), FAS 2019mod (B) and PDS severity states (C)



The boxes represent the interquartile range of each state, and the lines inside the boxes represent the median values. FAS 2019mod: modified Fibromyalgia Assessment Status; FIQR: revised Fibromyalgia Impact Questionnaire; Ht: Kruskal-Wallis test; PDS: Polysymptomatic Distress Scale.

severe disease, whereas the FAS 2019mod and PDS cut-off values respectively indicated that 39.6% and 44.9% of the patients fell into these categories (Fig. 2).

Considering low severity patients, 40.31% of subjects met the criteria for this category according to all three clinical scales studied (Supplementary Fig. S1, available at *Rheumatology* online).

#### Receiver operating characteristic curve analysis

Figure 3 shows the ROC curves of FIQR, FAS 2019mod and PDS. All three indices clearly distinguished patients in the 'low severity' group from those in the 'high severity' group. The FIQR area under the ROC curve (AUC) was 0.937 (95% CI: 0.927, 0.947); the FAS 2019mod AUC was 0.921 (95% CI: 0.910, 0.932); and the PDS AUC was 0.874 (95% CI: 0.860, 0.887). The pairwise comparisons of the FAS 2019mod vs PDS and the FIQR vs FAS 2019mod ROC curves were significant (differences between AUCs respectively of 0.019, 95% CI: 0.008, 0.003,  $P=0.0004$ , and 0.022, 95% CI: 0.001, 0.003,  $P=0.0002$ ).

## Discussion

This study determined the severity cut-offs of the main indices dedicated to the evaluation of FM using vast and solid data derived from a large multicentric cohort.

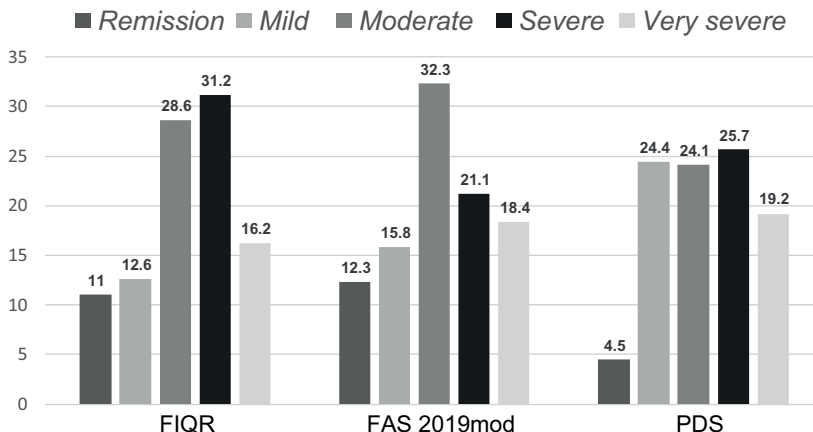
FM is a complex multi-system syndrome difficult to assess in terms of severity due to the lack of disease biomarkers and gold standard outcome measures [3]. Recent evidence-based guidelines for the management of FM recommended a graduated, severity-based approach to treatment, which is important when evaluating alternative treatments, the use of medical resources, costs and quality of life adjustments [14, 24, 25]. The definition of disease severity categories for FM can primarily serve to establish realistic goals that can be achieved in the individual patient by tailoring the

treatment strategy. This strategy can only be implemented through the measurement of disease severity using well-coded instruments [26]. In the case of patients with severe FM, it seems to be logical to intensify treatment using non-pharmacological therapeutic approaches such as physical exercise and psychological interventions. The clinical criteria defining severity are based on somatic and psychological distress levels, disability and the use of healthcare resources [24, 25, 27]; however, the lack of internationally accepted indices of grading severity can be considered a major obstacle.

Patient self-reporting is being increasingly used to evaluate disease status and management strategies in clinical trials, especially in the case of chronic pain conditions [12]. In FM, a classification of severity based solely on the criterion of pain would have a clear bias because most patients would be classified as severe. Therefore, it is important to use multidimensional tools that explore all the expressiveness of disease. Among them, the FIQ and, more recently, the FIQR are the most widely used disease-specific questionnaires for assessing the health status of FM patients as they capture FM-related symptoms and their impact on physical functioning [8]. A previous work has proposed severity categories for FIQR, whose main limitation is monocentric validation and categorization in only four disease severity states [15].

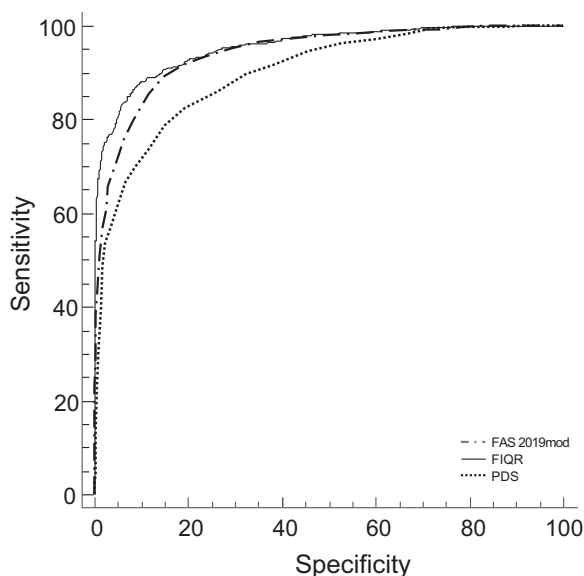
In recent years, PDS has also gained ground as a measure of 'fibromyalginess'. PDS has been considered as a good identifier of FM-related symptoms and higher scores are also associated with increased risk of cardiovascular disorders, hospitalization, working disability and death [28]. The scale can be applied directly to measure the severity of FM [11]. For PDS, severity criteria already existed [16]; however, as mentioned above, these cut-offs distinguished only two severity states in diagnosed cases and three degrees of severity in non-cases, probably making PDS somewhat uninformative in diagnosed patients. Recently, we have modified and validated the FAS as a means of

**Fig. 2** Percentage distribution of disease severity states for FIQR, FAS 2019mod and PDS



FAS 2019mod: modified Fibromyalgia Assessment Status; FIQR: revised Fibromyalgia Impact Questionnaire; PDS: Polysymptomatic Distress Scale.

**Fig. 3** ROC curves distinguishing patients in the 'low severity' state from those in the 'high severity' state



Receiver operating characteristic curves for FIQR (continuous thin line), FAS 2019mod (alternating dot-dash line), and PDS (dotted line) realized using patient acceptable symptom state as external indicator. Group A, patients considering their state satisfactory,  $n = 902$ ; group B, patients considering their state unsatisfactory,  $n = 1437$ . FAS 2019mod: modified Fibromyalgia Assessment Status; FIQR: revised Fibromyalgia Impact Questionnaire; PDS: Polysymptomatic Distress Scale.

evaluating the severity of FM, through questions investigating fatigue, unrefreshing sleep and widespread pain [10].

In this study we provided severity cut-offs for these three indices based on five severity states, easily applicable in clinical practice, trying to overcome the limitations present in previous validations.

Our findings are consistent with those of previous qualitative studies, and underline the need for a patient-centred approach and a comprehensive assessment of the multi-dimensional aspects of the disease in order to capture the full picture of the burden of FM. The essential difference among the three tools is that the PDS and FAS 2019mod give more weight to pain (as measured by means of a WPI) than is given by the FIQR. Consequently, although our use of multiple questionnaires may not be suitable for routine clinical care, and as it has been suggested that the severity of FM could be stratified in busy clinical practices using a single instrument [29], we believe that the FAS 2019mod or PDS could be used as a rapid means of assessing both severity and the constellation of FM symptoms.

The strong point of this study is that its classification of severity was obtained using data coming from a large multicentre cohort of FM patients, but it has some methodological limitations. First of all, as there is no gold standard for evaluating the severity of FM, it was not possible to assess the criterion validity of the FIQR, FAS 2019mod and PDS. The patients were asked to rate their overall health status on a five-point scale and a general PASS question was used as a common standard for the assessment of convergent validity (external anchor). Previous studies attempted to develop a severity model using patient-reported anchors [30, 31].

In the second instance, a cross-sectional evaluation was carried out, without a validation of the proposed cut-offs in a time interval in order to assess the responsiveness. On the other hand, FM symptoms tend to have a certain stability over time without major changes [32, 33].

Thirdly, no data concerning the medications and other treatment modalities that the patients may have used during the study were available. This is a limitation of the data collection system, but it was not feasible to collect information at this level of detail, and patients' recall of medication regimens are frequently inaccurate [34].

In the fourth instance, the disproportionate number of female participants raises the risk that gender bias may have skewed the data. Gender differences could affect the perception and reporting of pain and the determinants contributing to self-rated health status [35]. However, the sex ratio in this study reflects that observed in clinical practice.

Finally, as the study only involved adults with FM, it is possible that our findings cannot be generalized to community samples of adolescents with FM.

In conclusion, this large, cross-sectional, multicentre study is one of the first attempts to characterize the disease severity experienced by FM patients. The possibility of measuring the severity of FM is likely to lead to a number of benefits, including the identification of treatment responders in clinical trials and clinical practice. The characterization of severity levels may also be used to establishing a prospective web-based registry [36]. This can help clinicians to plan patient management, facilitates research-study patient recruitment, and provides the participating pain clinics with statistics based on real-world data.

Equally important, quantification of the impact of FM on multiple domains might also equip patients with a tool to accurately assess the clinical evolution of the response to clinical interventions, thus facilitating patient engagement in the therapeutic process.

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## Supplementary data

Supplementary data are available at *Rheumatology* online.

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