Determining the PASS cut-off points for the FIQR, FASmod and PSD in patients with fibromyalgia: a registry-based study

F. Salaffi[1], M. Di Carlo[1], M. Di Franco[2], G. Bianchi[3], L. Bazzichi[4], R. Tirri[5], S. Guiducci[6], R. Gorla[7], F. Atzeni[8], R. Giacomelli[9], E. Di Donato[10], G. Guggino[11], F. Fischetti[12], E. Tirri[13], G. Biasi[14], R. Foti[15], L. Dagna[16], F. Carubbi[17], E. Gremese[18], M. Govoni[19], M. Cutolo[20], F. Iannone[21], I. Lippolis[22], F. Conti[2], G. Tramontano[3], V. Marino[5], S. Farah[1], P. Sarzi-Puttini[23]
on behalf of the Società Italiana di Reumatologia (SIR)

[1]Rheumatology Clinic, Dipartimento di Scienze Cliniche e Molecolari, Università Politecnica delle Marche, Jesi; [2]Department of Clinical Internal Medicine, Anaesthesiology and Cardiovascular Sciences, Rheumatology Unit, Policlinico Umberto I, Sapienza University of Rome; [3]Department of Medical Specialties, Division of Rheumatology Asl 3, Genova; [4]Rheumatology Unit, AOU Pisana, Pisa; [5]Rheumatology Unit, Department of Precision Medicine, University of Campania L. Vanvitelli, Naples; [6]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, AOU Careggi, Florence; [7]Unit of Rheumatology and Clinical Immunology, ASST Spedali Civili, Brescia; [8]Rheumatology Unit, Department of Experimental and Internal Medicine, University of Messina; [9]Unit of Allergology, Clinical Immunology and Rheumatology, Università Campus Bio-Medico di Roma; [10]Internal Medicine and Rheumatology Unit, Azienda Ospedaliero-Universitaria di Parma;[11]Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties, University of Palermo; [12]Department of Medical Sciences, University of Trieste, UCO Medicina Clinica (SSD Reumatologia), Trieste; [13]U.O. Reumatologia, Ospedale S. Giovanni Bosco, Napoli;[14]Rheumatology Unit, Department of Medical Sciences, Azienda Ospedaliero-Universitaria Senese and University of Siena;[15]Rheumatology Unit, AOU Policlinico San Marco, Catania; [16]Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), IRCCS San Raffaele Scientific Institute and Vita-Salute San Raffaele University, Milan;[17]Department of Medicine, ASL 1 Avezzano-Sulmona-L'Aquila, San Salvatore Hospital, L'Aquila; [18]UOC Reumatologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome; [19]Rheumatology Unit, Department of Medical Sciences, University of Ferrara and Azienda Ospedaliera-Universitaria di Ferrara; [20]Laboratory of Experimental Rheumatology and Division of Clinical Rheumatology, Department of Internal Medicine DiMI, University of Genova, IRCCS San Martino Polyclinic, Genova; [21]Rheumatology Unit, Dipartimento di Medicina di Precisione e Rigenerativa e Area Jonica-DiMePRe-J, University of Bari; [22]Rheumatology Unit, Azienda Ospedaliera Universitaria Integrata di Verona; [23]Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Milan, Italy.

Abstract

Objective

To determine the cut-off values of Patient Acceptable Symptom State (PASS) for the revised Fibromyalgia Impact Questionnaire (FIQR), the modified Fibromyalgia Assessment Scale (FASmod), and the Polysymptomatic Distress scale (PSD) and to determine the predictors of PASS in patients with fibromyalgia (FM).

Methods

FM patients belonging to the Italian Fibromyalgia Registry (IFR) completed the FIQR, the FASmod and the PSD. The PASS was assessed using a dichotomous answer. The cut-off values were obtained through the receiver operating characteristic curve (ROC) analyses. A multivariate logistic regression analysis was performed to determine predictors of achieving the PASS.

Results

5545 women (93.7%) and 369 males (6.3%) were included in the study. The 27.8% of patients reported an acceptable symptom state. Patients in PASS differed in all patient-reported outcome measures ($p < 0.001$). The FIQR PASS threshold was ≤58 (area under the ROC curve [AUC] =0.819). The FASmod PASS threshold was ≤23 (AUC = 0.805) and the PSD PASS threshold was ≤16 (AUC=0.773). In the pairwise AUC comparison, the discriminatory power of the FIQR PASS outperforms both FASmod PASS ($p=0.0124$) and PSD PASS ($p<0.0001$). Multivariate logistic analysis showed that FIQR items related to memory and pain were the only predictors of PASS.

Conclusion

The FIQR, FASmod and PSD PASS cut-off points for FM patients have never been determined before. This study provides additional information to facilitate interpretation of the severity assessment scales in daily practice and clinical research related to FM patients.

Key words

fibromyalgia, Patient Acceptable Symptom State, revised Fibromyalgia Impact Questionnaire, modified Fibromyalgia Assessment Status, Polysymptomatic Distress scale

Fausto Salaffi, MD, PhD
Marco Di Carlo, MD
Manuela Di Franco, MD
Gerolamo Bianchi, MD
Laura Bazzichi, MD
Rosella Tirri, MD
Serena Guiducci, MD
Roberto Gorla, MD
Fabiola Atzeni, MD
Roberto Giacomelli, MD
Eleonora Di Donato
Giuliana Guggino, MD
Fabio Fischetti, MD
Enrico Tirri, MD
Giovanni Biasi, MD
Rosario Foti, MD
Lorenzo Dagna, MD
Francesco Carubbi, MD
Elisa Gremese, MD
Marcello Govoni, MD
Maurizio Cutolo, MD
Florenzo Iannone, MD
Irma Lippolis, MD
Fabrizio Conti, MD, PhD
Giuseppina Tramontano, MD
Valentina Marino, MD
Sonia Farah, Eng
Piercarlo Sarzi-Puttini, MD

Please address correspondence to:
Marco Di Carlo
Rheumatologia,
Università Politecnica delle Marche,
Ospedale Carlo Urbani,
Via Aldo Moro 25,
60035 Jesi (AN), Italy.
E-mail: dica.marco@yahoo.it

Received on December 22, 2022; accepted in revised form on February 9, 2023.

Competing interests: F. Iannone has received consultancies from Abbvie, Eli Lilly, Galapagos, Pfizer and Janssen, not related to the present work. The other authors have declared no competing interests.

Introduction

Fibromyalgia (FM), with a 2.2% estimated incidence in Western countries (1), is a condition characterised by chronic widespread pain, tenderness, and somatic symptoms, such as fatigue, cognitive impairment, and non-restorative sleep (2-4). Suffering from fibromyalgia results in a heavy impact on psychological health, affective and cognitive domains, with major repercussions on patients' ability to work and important costs for health care systems (5, 6).

The clinical picture, however, might vary significantly within a patient, over time, and from patient to patient. One of the most difficult aspects of FM diagnosis and clinimetry has been determining how severe the symptoms are. On the other hand, assessing and quantifying the severity of FM would be helpful in a number of ways, such as the choice of patients to participate in trials, the recognition of treatment responders at different levels (clinical practice, observational studies, clinical trials), and the identification of non-responders (7).

The severity of the disease is evaluated using fully patient-reported outcome measures (PROMs) disease specific like the revised Fibromyalgia Impact Questionnaire (FIQR) (8), the Fibromyalgia Assessment Status (FAS) or its modified version FAS (FASmod) (9, 10), and the Polysymptomatic Distress scale (PSD), as there are currently no reliable biomarkers to assess FM severity in daily clinical practice (11, 12).

When evaluating the effectiveness of rheumatological therapy choices for common musculoskeletal diseases, the patients' perspective, assessed by PROMs, has become important (13, 14). It is common practice to evaluate results using a variety of classic outcome tools (15). The fact that most outcome scores are expressed as continuous data is a common constraint of these measures. Due to this, it might be challenging to interpret the response in a way that is relevant to a specific patient. Among the cut-offs recognised as valid and informative of a numerical scale is Patient-Acceptable Symptom State (PASS), described as the highest degree of symptom beyond which patients regard themselves to be in good health (16, 17). PASS is in all purposes a PROM that includes a single dichotomously answered question about how satisfied the patient is with the severity of his or her symptoms (18, 19). PASS was created to improve the arbitrary interpretation of assessments derived from other outcome measures. In chronic inflammatory joint disease and connective tissue disease, PASS has been shown to be significantly correlated with disease activity (20-23). The robustness of PASS cut-off points has also been studied. It appears that the PASS cut-off values are consistent over time, and are not significantly modified by age, disease duration, and gender of the patient (21). There is a paucity of information on the potential use of PASS in FM patients.

Taking these considerations as a starting point, the objectives of this study are (i) to identify the PASS cut-off points for the principal PROMs used to monitor FM severity (FIQR, FASmod, and the PSD), and (ii) to establish the variables capable of determining PASS in patients with FM.

Materials and methods

Patients

The data of this study were retrospectively extracted from a large database of patients with FM belonging to the Italian Fibromyalgia Registry (IFR) (24). The patients included in the IFR were recruited from November 2018 to October 2022, in 23 Italian rheumatology centres, with FM diagnosed according to the American College of Rheumatology (ACR) 2010/2011/2016 criteria (10, 25). A rheumatologist with at least 10 years of experience made the diagnoses of FM in each of the IFR centres. The data of patients included in the IFR were collected in a naturalistic manner, based solely on the clinical and clinimetric examination of patients with FM, in the absence of therapeutic interventions under study. Patients were therefore included regardless of current therapies or disease severity. All patients underwent a diagnostic work-up including a complete physical examination and laboratory tests specified in the recommendations of the European Alliance of Associations for Rheumatology

(EULAR) for the management of FM (26). Patients with major concomitant psychological illnesses, including severe depression, connective tissue diseases, or inflammatory arthropathies that interfered with the metric assessment of FM were excluded. Patients with incomplete IFR data were excluded. Each patient provided the written informed consent for the anonymous data collection. The ethics committee of the coordinating centre (Marche Regional Ethics Committee - CERM) approved the study (no. 1970/AV2), and this approval was endorsed by the ethics committees of all the other IFR centres.

Measurements and instruments

A series of questionnaires including sociodemographic information, disease duration, quality of life, and disease-related characteristics were given to the patients to complete. The IFR's variables were selected with the intention of producing a coherent minimalistic needs-based data set. Age, sex, body mass index (BMI), marital status (single, married, divorced/separated), and level of formal education (primary school, middle school, high school/university) are the essential sociodemographic variables.

Clinimetric assessment

The questionnaires considered for clinical evaluation were the FIQR (8), the FASmod (10), the PSD (11, 12) and the PASS (18, 19).

The FIQR is the updated version of the Fibromyalgia Impact Questionnaire (FIQ) (27), realised to overcome the limitations of the original instrument. FIQR consists of twenty-one 0–10 numerical rating scales (NRS, with 10 being the "worst") investigating three main health domains, respectively function, overall impact, and symptoms. All of the questions refer to the previous seven days. The final score (range 0-100, with greater values indicating greater disease severity) is calculated as follows: the algebraic sum of the 9-item function domain (range 0–90) is divided by three, the algebraic sum of the 2-item overall impact domain (range 0–20) is considered as it is, and the algebraic sum of the 10-item symptom domain (range 0–100) is divided by two (8). These three sub-scores are then added together. The proposed cut-off points for disease severity are: 0–23 for remission, 24-40 for mild disease, 41–63 for moderate disease, 64–82 for severe disease, and 83–100 for very severe disease (7).

The FASmod is composed of two sections (10). The first consists of two questions about fatigue and unrefreshing sleep over the preceding week. Each item is graded using a 0-10 NRS and the maximum subscore of the first section is 20. The second section is a front-back mannequin with 19 body areas and patients are asked to choose the painful areas. Each painful area is scored 1. The final FASmod score is between 0 and 39, with the cut-off points for disease severity: 0–12 for remission, 13–20 for mild disease, 21–28 for moderate disease, 29–33 for severe disease, and 34–39 for very severe disease (7).

The PSD is derived from the variables used in the 2010/2011 ACR criteria as modified for surveys and clinical research (11, 12), and the widespread pain index (WPI) and the symptom severity scale (SSS) are added to determine it. The WPI is a 0-19 count of painful non-articular body regions (the 19 body areas assessed by FASmod correspond to those of the WPI), and the SSS is a 0–12 measure of the severity of these symptoms: the presence of fatigue, sleep, and cognitive problems over the past week, scored on 0-3 scales (where 0 indicates no problem and 3 severe problem), and the presence of headache, pain or cramps in the lower abdomen and depression over the past six months, scored in 0 or 1 fashion. PSD severity cut-off points include: 0–5 for remission, 6–15 for mild disease, 16–20 for moderate disease, 21–25 for severe disease, and 26–31 for very severe disease (7).

Finally, the question assessing PASS was formulated as the following: "Taking into account all the activities you have during your daily life, your level of pain, fatigue and also your functional impairment, do you consider that your current state is satisfactory?". The yes/no response was used as an external indicator of the patient's satisfaction with the current symptoms state (28).

Statistical analysis

Patient demographics and disease characteristics were compared between those who reported being in PASS and those who did not, using descriptive statistics (mean and standard deviation [SD], median and interquartile range [IQR]), Student's t-test for continuous data, or the Mann-Whitney U-test for non-Gaussian variables. Where appropriate, the 2 test or Fisher's test was used to perform univariate comparisons between nominal variables. Two-tailed *p*-values were reported, and *p*-values less than 0.05 were considered significant (28, 29).

PASS thresholds of FIQR, FASmod, and PSD were measured using the optimal point on the receiver operating characteristic (ROC) curve, in which the cut-off was measured using the Youden index. An adequate discriminatory test is one with an area under the curve of >0.7, and an outstanding test is one with an area under the curve of >0.8 (28, 29). The general PASS question served as an external anchor, categorising patients between those who considered their symptoms to be acceptable (PASS-Y) versus those who considered their symptoms to be unacceptable (PASS-N). According to Hanley and McNeil, the areas under the ROC curves (AUC-ROCs) were compared using the non-parametric Wilcoxon's signed ranks test (30).

A secondary analysis was conducted to identify the patient-related characteristics influencing the PASS. To identify determinants of achieving the PASS, a multivariate logistic regressions analysis was performed applying the 21 items of FIQR, age, disease duration, and BMI as independent variables.

MedCalc for Windows XP, v. 19.5.1, was used for all analyses.

Results

Sociodemographic characteristics and descriptive statistics

The study sample included 5914 FM patients, 5545 women (93.7%) and 369 men (6.3%), with a mean age of 53.4 (SD 12.2) years and a mean disease duration of 7.5 (SD 5.2) years. 75.3% of patients were married, and the majority held college degrees (high school edu-

Table I. Sociodemographic and disease-related characteristics of study sample (n=5914).

Variable	Mean	Median	SD	IQR
Age, years	53.43	54.00	12.16	47.00 - 61.00
Gender, n (%)				
Male			369 (6.26)	
Female			5545 (93.74)	
Disease duration, years	7.49	7.033	5.15	2.00 - 10.00
BMI, kg/m^2	28.54	25.00	4.84	22.00 - 29.00
Marital status, n (%)				
Single			855 (14.46)	
Married			4456 (75.34)	
Divorced/separated			465 (7.86)	
Widowed			138 (2.34)	
Educational level, n (%)				
Primary school			268 (4.57)	
Secondary school			1414 (23.90)	
High school/university			4232 (71.54)	
FIQR				
Physical function (0-30)	17.25	18.00	7.39	12.00 - 23.00
Overall impact (0-20)	11.84	13.00	5.82	8.00 - 17.00
Symptoms (0-50)	32.92	35.00	10.29	27.00 - 41.00
Total score (0-100)	61.98	65.00	21.61	48.00 - 79.00
FASmod				
Fatigue (0-10)	7.64	8.00	2.39	7.00 - 10.00
Sleep (0-10)	7.26	8.00	2.70	6.00 - 10.00
WPI (0-19)	11.47	11.00	4.78	8.00 - 15.00
Total score (0-39)	26.37	27.00	7.99	22.00 - 32.00
PSD				
SSS (0-12)	8.23	9.00	2.96	7.00 - 11.00
WPI (0-19)	11.47	11.00	4.78	8.00 - 15.00
Total score (0-31)	19.70	20.00	6.72	16.00 - 25.00

SD: standard deviation; IQR: interquartile range; BMI: body mass index; FIQR: revised Fibromyalgia Impact Questionnaire; FASmod: modified Fibromyalgia Assessment Status; WPI: Widespread Pain Index; PSD: Polysymptomatic Distress scale; SSS: Symptom Severity Scale.

cation or above). They were all moderately overweight, with a mean BMI of 28.5 (SD 4.8) kg/m^2.

The median value of FIQR was 65.0 (IQR 48.0–79.0), of FASmod was 27.0 (IQR 22.0–32.0), and of PSD was 20.0 (IQR 16.0–25.0) (Table I).

Discriminative ability

Patients who reported an unacceptable symptoms state (PASS-N) are compared with patients who reported an acceptable symptoms state in Table II (PASS-Y). The minority of participants (27.8%) reported their status as acceptable (PASS-Y). In comparison to patients PASS-N, PASS-Y patients showed a significantly better overall mean FIQR, FASmod and PSD scores and subscores (p<0.001) (Table II). The mean score of each of the 21 items of the FIQR was significantly lower in PASS-Y patients than in PASS-N patients (Fig. 1, Table III).

PASS cut-off points of FIQR, FASmod and PSD

All the three indices clearly distinguished PASS-Y *versus* PASS-N patients (Fig. 2). The FIQR PASS cut-off point was ≤58 (AUC=0.819; 95% confidence interval [CI] 0.806–0.831, sen-

Table II. Demographics and disease characteristics according to the PASS categorisation.

	PASS-N (4272 patients, 72.2%)				PASS-Y (1642 patients, 27.8%)				
Variable	Mean	Median	SD	IQR	Mean	Median	SD	IQR	p*
Age, years	53.56	54.00	12.29	47.00 - 61.00	53.09	54.00	11.80	46.00 - 60.25	ns
Disease duration, years	7.233	6.89	5.08	2.20 - 11.00	7.66	7.12	5.98	2.50 - 11.50	ns
BMI, kg/m^2	29.10	25.00	51.17	22.00 - 29.00	27.91	25.00	4.48	22.00 - 29.00	ns
FIQR									
Physical function (0-30)	19.36	20.00	6.33	15.00 - 24.00	11.74	11.00	7.12	6.00 - 17.00	<0.001
Overall impact (0-20)	13.50	14.00	5.01	10.00 - 18.00	7.51	7.00	5.57	2.00 - 12.00	<0.001
Symptoms (0-50)	36.19	37.00	7.94	31.00 - 42.00	24.41	24.00	10.82	16.00 - 32.00	<0.001
Total score (0-100)	69.02	71.00	17.11	59.00 - 82.00	43.62	43.00	21.33	26.00 - 59.00	<0.001
FASmod									
Fatigue (0-10)	8.37	9.00	1.73	8.00 - 10.00	5.74	6.00	2.81	4.00 - 8.00	<0.001
Sleep (0-10)	7.97	9.00	2.21	7.00 - 10.00	5.41	5.00	2.99	3.00 - 8.00	<0.001
WPI (0-19)	12.54	13.00	4.43	9.00 - 16.00	8.67	8.00	4.51	5.00 - 12.00	<0.001
Total score (0-39)	28.88	29.00	6.27	25.0 - 34.000	19.81	20.00	8.29	13.75 - 26.00	<0.001
PSD									
SSS (0-12)	9.03	9.00	2.36	8.00 - 11.00	6.17	6.00	3.37	3.00 - 9.00	<0.001
WPI (0-19)	12.54	13.00	4.43	9.00 - 16.00	8.67	8.00	4.51	5.00 - 12.00	<0.001
Total score (0-31)	21.56	22.00	5.68	18.00 - 26.00	14.84	15.00	6.79	9.00 - 20.00	<0.001

PASS: Patient Acceptable Symptom State; SD: standard deviation; IQR: interquartile range; BMI: body mass index; FIQR: revised Fibromyalgia Impact Questionnaire; FASmod: modified Fibromyalgia Assessment Status; WPI: Widespread Pain Index; PSD: Polysymptomatic Distress scale; SSS: Symptom Severity Scale.
*Mann-Whitney test for unpaired samples.

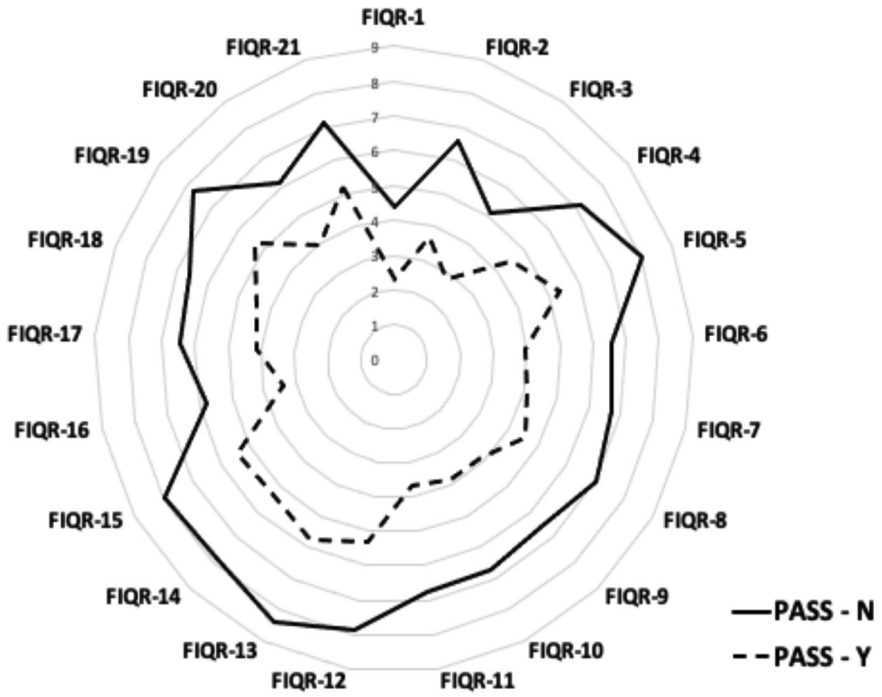

Fig. 1. Spydergrams of the FIQR domains according with the answer to PASS. The domain scores are plotted from 0 (best, at the centre) to 10 (worst, at the outside). FIQR function (items 1 to 9); FIQR overall impact (items 10 and 11); FIQR symptoms (items 12 to 21).
FIQR: revised Fibromyalgia Impact Questionnaire; FIQR1: brush or comb hair; FIQR2: walk continuously for 20 minutes; FIQR3: prepare a homemade meal; FIQR4: vacuum, scrub or sweep floors; FIQR5: lift and carry a bag full of groceries; FIQR6: climb one flight of stairs; FIQR7: change bed sheets; FIQR8: sit in a chair for 45 minutes; FIQR9: go shopping for groceries; FIQR10: cannot achieve goals; FIQR11: feel overwhelmed; FIQR12: pain rating; FIQR13: fatigue rating; FIQR14: stiffness rating; FIQR15: sleep quality; FIQR16: depression level; FIQR17: memory problems; FIQR18: anxiety level; FIQR19: tenderness level; FIQR20: balance problems; FIQR21: environmental sensitivity.

sitivity=74.83%, specificity=75.05%, positive likelihood ratio [LR+] =3.00) (Supplementary Table S1). The cut-off point for FASmod PASS was ≤23 (AUC=0.805; 95% CI 0.792–0.818, sensitivity=66.73%, specificity=81.13%, LR+=3.54) (Suppl. Table S2), and for PSD PASS was ≤16 (AUC=0.773; 95% CI 0.759–0.787, sensitivity=58.99%, specificity=81.96%, LR+ =3.27) (Suppl. Table S3).
In the pairwise AUC comparison, the FIQR PASS outperforms both FASmod PASS (differences between areas =0.0138; p=0.0124) and PSD PASS (differences between areas = 0.0459; p<0.0001) in terms of discriminatory power (Suppl. Table S4).

PASS predictors
Lower FIQR pain rating (FIQR item 12) (p=0.0048) and lower FIQR memory difficulties score (FIQR item 17) (p=0.0468) were the independent variables linked with being in PASS (Table IV). Age, sex, disease duration, and BMI were not PASS predictors (Table IV).

Discussion

To the best of our knowledge, this is the first study to establish PASS cut-

Table III. FIQR characteristics according to the PASS categorisation.

	PASS-N (4272 patients, 72.2%)				PASS-Y (1642 patients, 27.8%)				
FIQR items	Mean	Median	SD	IQR	Mean	Median	SD	IQR	p*
FIQR1	4.41	5.00	3.15	1.00 - 7.00	2.30	1.00	2.91	0.00 - 4.00	<0.001
FIQR2	6.56	7.00	2.93	5.00 - 9.00	3.69	3.00	3.14	1.00 - 6.00	<0.001
FIQR3	5.11	5.00	2.93	3.00 - 7.00	2.78	2.00	2.71	0.00 - 5.00	0.0021
FIQR4	7.16	8.00	2.58	6.00 - 9.00	4.55	5.00	3.00	2.00 - 7.00	<0.001
FIQR5	8.00	9.00	2.62	7.00 - 10.00	5.37	6.00	3.07	2.00 - 8.00	<0.001
FIQR6	6.57	7.00	2.85	5.00 - 9.00	3.95	4.00	3.06	1.00 - 6.00	<0.001
FIQR7	6.73	7.00	2.91	5.00 - 9.00	4.11	4.00	3.01	1.00 - 7.00	<0.001
FIQR8	7.01	8.00	2.79	5.00 - 9.00	4.54	5.00	3.18	1.00 - 7.00	<0.001
FIQR9	6.53	7.00	2.89	5.00 - 9.00	3.88	4.00	3.07	1.00 - 6.00	<0.001
FIQR10	6.74	7.00	2.64	5.00 - 9.00	3.84	4.00	2.92	1.00 - 6.00	<0.001
FIQR11	6.75	7.00	2.74	5.00 - 9.00	3.65	3.00	2.98	1.00 - 6.00	<0.001
FIQR12	7.84	8.00	1.77	7.00 - 9.00	5.32	5.00	2.64	3.00 - 7.00	<0.001
FIQR13	7.12	8.00	2.65	6.00 - 9.00	5.16	5.00	3.07	2.00 - 8.00	<0.001
FIQR14	8.37	9.00	1.73	8.00 - 10.00	5.73	6.00	2.81	4.00 - 8.00	<0.001
FIQR15	7.82	8.00	2.01	7.00 - 9.00	5.34	5.00	2.80	3.00 - 8.00	<0.001
FIQR16	7.97	9.00	2.21	7.00 - 10.00	5.41	5.00	2.98	3.00 - 8.00	0.0027
FIQR17	5.80	6.00	3.05	4.00 - 8.00	3.38	3.00	2.92	1.00 - 5.25	<0.001
FIQR18	6.47	7.00	2.73	5.00 - 8.00	4.15	4.00	2.93	1.00 - 7.00	<0.001
FIQR19	6.58	7.00	2.79	5.00 - 9.00	4.45	4.00	2.97	2.00 - 7.00	<0.001
FIQR20	7.74	8.00	2.17	7.00 - 9.00	5.37	6.00	2.85	3.00 - 8.00	<0.001
FIQR21	6.14	7.00	2.80	5.00 - 8.00	3.98	4.00	3.21	1.00 - 6.00	<0.001

FIQR: revised Fibromyalgia Impact Questionnaire; PASS: Patient Acceptable Symptom State; SD: standard deviation; IQR: interquartile range.
*Mann-Whitney test for unpaired samples.

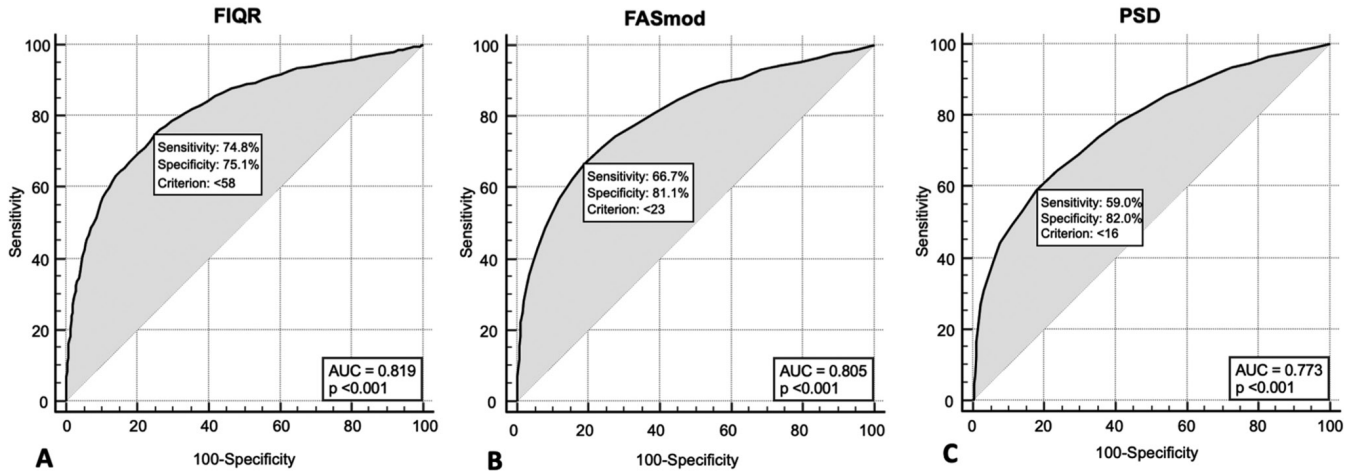

Fig. 2. ROC curves for the PASS prediction for FIQR (**A**), FASmod (**B**), and PSD (**C**).
ROC: receiver operating characteristic; FIQR: revised Fibromyalgia Impact Questionnaire; FASmod: modified Fibromyalgia Assessment Status; PSD: Polysymptomatic Distress scale; AUC: area under the curve.

off points in FM patients for the main PROMs used as indicators of disease severity in FM. These cut-off points, obtained from a large multicentre study, may represent useful information that can be used in daily clinical practice as well as in research.

As was underlined by the Outcome Measures in Rheumatology (OMERACT), evaluating the patients' point of view is crucial for conducting a thorough assessment and may have an impact on clinical decision-making (3). In this context, PASS is a simple, accurate and valid measure of well-being that could easily be incorporated into rheumatology practice. PASS has so far been used in patients with various rheumatic diseases, inflammatory and non-inflammatory, demonstrating a significant relationship with disease activity (20-23). Building on these previous experiences, this study evaluated the validity of PASS in a large group of FM patients. These results essentially translate into a clinimetric simplification (31), that may be useful for FM, a condition for which there is a certain redundancy of indices. As was somewhat expected, a minority of patients described their symptoms as acceptable.

All questionnaires showed a substantial difference between PASS-Y and PASS-N. Interestingly, the cut-off points obtained for PASS correspond, for all three clinimetric indices studied, to a state of moderate disease severity (7). Between them, FIQR, FASmod and PSD are rather different instruments, in particular the FIQR differs from FASmod and PSD due to the lack of a bodily pain location and extension. However, this work confirms the correlation between the indices and, to a certain extent, their interchangeability (32). The cut-off point of 58 for the FIQR, although it may be considered relatively high for a scale ranging from 0 to 100, would seem to reflect the severity of the condition in clinical practice. A previous study of a multidisciplinary treatment approach using the FIQ as one of the outcome measures revealed that, despite improvements, no patient scored below 39 (33).

The definition of PASS raises potential

Table IV. Logistic regression analysis of the variables determining the PASS (dependent variable).

Variable	coefficient	standard error	wald	*p*
FIQR1	-0.0006	0.0992	0.0000	0.9946
FIQR2	0.0540	0.1111	0.2365	0.6268
FIQR3	0.0484	0.1283	0.1426	0.7057
FIQR4	-0.1489	0.1567	0.9033	0.3419
FIQR5	-0.0645	0.1152	0.3132	0.5757
FIQR6	0.0495	0.1366	0.1315	0.7168
FIQR7	0.0343	0.0938	0.1335	0.7148
FIQR8	0.0259	0.1179	0.0484	0.8258
FIQR9	-0.0006	0.0992	0.0000	0.9946
FIQR10	-0.0741	0.1465	0.2563	0.6127
FIQR11	0.0313	0.1184	0.0699	0.7914
FIQR12*	-0.5278	0.1869	7.9669	0.0048
FIQR13	0.1090	0.1792	0.3700	0.5430
FIQR14	0.0563	0.1477	0.1453	0.7031
FIQR15	-0.1358	0.1061	1.6399	0.2003
FIQR16	-0.0730	0.1086	0.4519	0.5014
FIQR17*	-0.2977	0.1280	4.1315	0.0468
FIQR18	0.0450	0.1123	0.1610	0.6882
FIQR19	0.0257	0.1358	0.0359	0.8497
FIQR20	-0.0337	0.1256	0.0723	0.7880
FIQR21	-0.0668	0.0929	0.5175	0.4719
Age (years)	-0.0025	0.0175	0.0214	0.8837
Disease duration (years)	0.1017	0.1071	1.6385	0.2051
BMI (kg/m^2)	0.0002	0.0095	0.0005	0.9813
Constant	4.2653	1.3521	9.9513	0.0016

PASS: Patient Acceptable Symptom State; FIQR: revised Fibromyalgia Impact Questionnaire; BMI: body mass index.
*significative variable (FIQR12: pain, FIQR17: memory problems).

problems in a condition as complex as FM. There may be numerous confounding factors that go beyond the definition of symptom severity in the strict sense. These factors include how patients perceive their illnesses, the nature of their interactions with their physicians, psychological and cultural factors, chance events, and other systematic discrepancies between how patients and physicians assess the severity or activity of their illnesses. In this regard, an interesting result of this study is the fact that pain and depressive symptoms are predictors of PASS. This could be consistent with the previous theory that the acceptability of a particular disease state does not only depend on the absolute degree of the complaints, but also on other elements, in this case the patient's mood and experience of pain. If further studies confirm this conclusion, it could lead to new thinking on how to treat FM patients who fail to reach a desirable level of symptoms. Age, disease duration and BMI had no impact in the PASS definition. If for the first two variables the result might have been predictable (34), given the relationship between BMI and disease severity (35), some influence of the variable on PASS might have been expected.

Although the PASS includes a variety of disease domains, it is not considered comprehensive enough to replace other process and outcome indicators in FM. Indeed, it is a single-item assessment with little validity for a comprehensive definition of disease severity. However, based on the results of this study, the PASS could be a reasonable substitute for determining the disease state from the patient's perspective. Of course, the basic character of the PASS question, in which an 'acceptable' status does not completely fit the concept of remission, could explain the low concordance obtained with more comprehensive measures of disease severity.

Other disadvantages of PASS lie in the fact that there is no universally accepted method for establishing the concept of an acceptable state, the question used in previous studies varied, as did the time frame of its determination. If PASS is to be adopted worldwide, it is necessary to develop a common anchor question defining the duration of an acceptable state to allow for meaningful comparison of results between groups. Finally, the methodology used to identify PASS may have an impact on cut-off points. It appears that, in general, the ROC approach produces slightly lower estimates than the cut-off points determined by the 75th percentile approach (20, 36).

The main limitation of the study to be mentioned is the cross-sectional design that did not allow the sensitivity to change to be assessed. Therefore, further research is needed, particularly to evaluate the performance of PASS during long-term follow-up. The use of PASS in FM presents a problem in that it may change with the course of the disease: clinical symptoms may change and PASS is known to change over time. In conclusion, PASS is a very rapid test that, if administered correctly, can reflect the global status of patients, simplifying some routine assessments. In daily clinical practice, PASS should not be applied as a substitute, but administered together with commonly used severity indices. More extensive investigations are needed to confirm these results and to establish its applicability in FM, which presents high clinical heterogeneity.

Take home messages

- Patient Acceptable Symptom State (PASS) is a yet unexplored outcome measure in fibromyalgia.
- The PASS cut-off points obtained were FIQR ≤58, FASmod ≤23 and PSD ≤16.
- The FIQR items related to pain and memory problems are the only two PASS predictors.

Acknowledgements

List of collaborators

Giulio Dolcini: Dept. of Clinical Internal Medicine, Anaesthesiology and Cardiovascular Sciences, Rheumatology Unit, Policlinico Umberto I, Sapienza University of Rome;

Maurizio Rossini: Rheumatology Unit, Azienda Ospedaliera Universitaria Integrata di Verona;

Luca Riccio: Rheumatology Unit, Dept. of Precision Medicine, University of Campania L. Vanvitelli, Naples;

Emanuela Gaggiano: Rheumatology Unit, Dept. of Precision Medicine, University of Campania L. Vanvitelli, Naples;

Alberto Batticciotto: Rheumatology Unit, Internal Medicine Department, ASST Settelaghi, Ospedale Di Circolo - Fondazione Macchi, Varese.

The authors are deeply grateful to the Italian Society for Rheumatology (SIR) for its support in the implementation and maintenance of the IFR and for providing meeting rooms and facilitating the production of educational material. We would also like to thank the 5914 FM patients who spent their valuable time and energy in helping us better understanding the severity of FM in Italy.

References

1. SARZI-PUTTINI P, GIORGI V, ATZENI F *et al.*: Fibromyalgia position paper. *Clin Exp Rheumatol* 2021; 39 (Suppl. 130): S186-93. https://doi.org/10.55563/clinexprheumatol/i19pig
2. SALAFFI F, MOZZANI F, DRAGHESSI A *et al.*: Identifying the symptom and functional domains in patients with fibromyalgia: results of a cross-sectional Internet-based survey in Italy. *J Pain Res* 2016; 9: 279-286. https://doi.org/10.2147/JPR.S100829
3. MEASE P, ARNOLD LM, CHOY EH *et al.*: Fibromyalgia syndrome module at OMERACT 9: domain construct. *J Rheumatol* 2009; 36: 2318-2329. https://doi.org/10.3899/jrheum.090367
4. WOLFE F, WALITT BT, KATZ RS, HÄUSER W: Symptoms, the nature of fibromyalgia, and diagnostic and statistical manual 5 (DSM-5) defined mental illness in patients with rheumatoid arthritis and fibromyalgia. *PLoS One* 2014; 9: e88740. https://doi.org/10.1371/journal.pone.0088740
5. D'ONGHIA M, CIAFFI J, RUSCITTI P *et al.*: The economic burden of fibromyalgia: a systematic literature review. *Semin Arthritis Rheum* 2022; 56: 152060. https://doi.org/10.1016/j.semarthrit.2022.152060
6. KNIGHT T, SCHAEFER C, CHANDRAN A, ZLATEVA G, WINKELMANN A, PERROT S: Health-resource use and costs associated with fibromyalgia in France, Germany, and the United States. *Clinicoecon Outcomes Res* 2013; 5: 171-180. https://doi.org/10.2147/ceor.s41111
7. SALAFFI F, DI CARLO M, BAZZICHI L *et al.*: Definition of fibromyalgia severity: findings from a cross-sectional survey of 2339 Italian patients. *Rheumatology* (Oxford) 2021; 60: 728-36. https://doi.org/10.1093/rheumatology/keaa355
8. BENNETT RM, FRIEND R, JONES KD, WARD R, HAN BK, ROSS RL: The Revised Fibromyalgia Impact Questionnaire (FIQR): valida-

tion and psychometric properties. *Arthritis Res Ther* 2009; 11: R120. https://doi.org/10.1186/ar2783
9. SALAFFI F, SARZI-PUTTINI P, GIROLIMETTI R, GASPARINI S, ATZENI F, GRASSI W: Development and validation of the self-administered Fibromyalgia Assessment Status: a disease-specific composite measure for evaluating treatment effect. *Arthritis Res Ther* 2009; 11: R125. https://doi.org/10.1186/ar2792
10. SALAFFI F, DI CARLO M, FARAH S *et al*.: Diagnosis of fibromyalgia: comparison of the 2011/2016 ACR and AAPT criteria and validation of the modified Fibromyalgia Assessment Status. *Rheumatology* (Oxford) 2020; 59: 3042-9. https://doi.org/10.1093/rheumatology/keaa061
11. WOLFE F, WALITT BT, RASKER JJ, KATZ RS, HÄUSER W: The Use of Polysymptomatic Distress Categories in the Evaluation of Fibromyalgia (FM) and FM Severity. *J Rheumatol* 2015; 42: 1494-501. https://doi.org/10.3899/jrheum.141519
12. WOLFE F, BRAHLER E, HINZ A, HAUSER W: Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. *Arthritis Care Res* 2013; 65: 777-85. https://doi.org/10.1002/acr.21931
13. ORBAI AM, BINGHAM CO 3RD: Patient reported outcomes in rheumatoid arthritis clinical trials. *Curr Rheumatol Rep* 2015; 17: 28. https://doi.org/10.1007/s11926-015-0501-8
14. CLIMENT-SANZ C, MARCO-MITJAVILA A, PASTELLS-PEIRÓ R, VALENZUELA-PASCUAL F, BLANCO-BLANCO J, GEA-SÁNCHEZ M: Patient reported outcome measures of sleep quality in fibromyalgia: A COSMIN systematic review. *Int J Environ Res Public Health* 2020; 17: 2992. https://doi.org/10.3390/ijerph17092992
15. SALAFFI F, SARZI-PUTTINI P, CIAPETTI A, ATZENI F: Assessment instruments for patients with fibromyalgia: properties, applications and interpretation. *Clin Exp Rheumatol* 2009; 27 (Suppl. 56): S92-S105.
16. MAKSYMOWYCH WP, RICHARDSON R, MALLON C, VAN DER HEIJDE D, BOONEN A: Evaluation and validation of the patient acceptable symptom state (PASS) in patients with ankylosing spondylitis. *Arthritis Care Res* (Hoboken) 2007; 57: 133-9. https://doi.org/10.1002/art.22469
17. MAKSYMOWYCH WP, GOOCH K, DOUGADOS M *et al*.: Thresholds of patient-reported outcomes that define the patient acceptable symptom state in ankylosing spondylitis vary over time and by treatment and patient characteristics. *Arthritis Care Res* (Hoboken) 2010; 62: 826-34. https://doi.org/10.1002/acr.20131
18. TUBACH F, DOUGADOS M, FALISSARD B, BARON G, LOGEART I, RAVAUD P: Feeling good rather than feeling better matters more to patients. *Arthritis Rheum* 2006; 55: 526-30. https://doi.org/10.1002/art.22110
19. TUBACH F, RAVAUD P, BEATON D *et al*.: Minimal clinically important improvement and patient acceptable symptom state for subjective outcome measures in rheumatic disorders. *J Rheumatol* 2007; 34: 1188-93
20. TUBACH F, RAVAUD P, BARON G *et al*.: Evaluation of clinically relevant states in patient reported outcomes in knee and hip osteoarthritis: the patient acceptable symptom state. *Ann Rheum Dis* 2005; 64: 34-7. https://doi.org/10.1136/ard.2004.023028
21. HEIBERG T, KVIEN TK, MOWINCKEL P, ALETAHA D, SMOLEN JS, HAGEN KB: Identification of disease activity and health status cut-off points for the symptom state acceptable to patients with rheumatoid arthritis. *Ann Rheum Dis* 2008; 67: 967-71. https://doi.org/10.1136/ard.2007.077503
22. KVAMME MK, KRISTIANSEN IS, LIE E, KVIEN TK: Identification of cutpoints for acceptable health status and important improvement in patient-reported outcomes, in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. *J Rheumatol* 2010; 37: 26-31. https://doi.org/10.3899/jrheum.090449
23. CONTI F, CECCARELLI F, MASSARO L *et al*.: Evaluation of the patient acceptable symptom state (PASS) in Italian patients affected by systemic lupus erythematosus: association with disease activity indices. *PLoS One* 2013; 8: e73517. https://doi.org/10.1371/journal.pone.0073517
24. SALAFFI F, FARAH S, DI CARLO M *et al*.: The Italian Fibromyalgia Registry: a new way of using routine real-world data concerning patient-reported disease status in healthcare research and clinical practice. *Clin Exp Rheumatol* 2020; 38 (Suppl. 123): S65-71
25. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al*.: 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum* 2016; 46: 319-29. https://doi.org/10.1016/j.semarthrit.2016.08.012
26. MACFARLANE GJ, KRONISCH C, DEAN LE *et al*.: EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017; 76: 318-28. https://doi.org/10.1136/annrheumdis-2016-209724
27. BENNETT R: The Fibromyalgia Impact Questionnaire (FIQ): a review of its development, current version, operating characteristics and uses. *Clin Exp Rheumatol* 2005; 23 (Suppl. 39): S154-S62.
28. KVIEN TK, HEIBERG T, HAGEN KB: Minimal clinically important improvement/difference (MCII/MCID) and patient acceptable symptom state (PASS): What do these concepts mean? *Ann Rheum Dis* 2007; 66 (Suppl. 3): iii40-1. https://doi.org/10.1136/ard.2007.079798
29. KATZ P, KANNOWSKI CL, SUN L, MICHAUD K: Estimation of minimally important differences and patient acceptable symptom state scores for the Patient-Reported Outcomes Measurement Information System Pain Interference Short Form in Rheumatoid Arthritis. *ACR Open Rheumatol* 2020; 2: 320-9. https://doi.org/10.1002/acr2.11141
30. HAULEY JA, MCNEIL BJ: A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983; 148: 839-43. https://doi.org/10.1148/radiology.148.3.6878708
31. DI CARLO M, SALAFFI F: Is it good to simplify clinimetry in chronic inflammatory joint diseases? *J Rheumatol* 2022; 49: 1079-81. https://doi.org/10.3899/jrheum.220543
32. SALAFFI F, DI CARLO M, FARAH S *et al*.: The measurement of fibromyalgia severity: converting scores between the FIQR, the PSD and the FASmod. *Clin Exp Rheumatol* 2023; 41(6): 1225-9. https://doi.org/10.55563/clinexprheumatol/31gsnd
33. VAN KOULIL S, KRAAIMAAT FW, VAN-LANKVELD W, VAN RIEL PL, EVERS AW: A patient's perspective on multidisciplinary treatment gain for fibromyalgia: an indicator for pre-post treatment effects? *Arthritis Rheum* 2009; 61: 1626-32. https://doi.org/10.1002/art.24792
34. DI CARLO M, FARAH S, BAZZICHI L *et al*.: Fibromyalgia severity according to age categories: results of a cross-sectional study from a large national database. *Clin Exp Rheumatol* 2022; 40: 1084-90. https://doi.org/10.55563/clinexprheumatol/od40pa
35. ATZENI F, ALCIATI A, SALAFFI F *et al*.: The association between body mass index and fibromyalgia severity: data from a cross-sectional survey of 2339 patients. *Rheumatol Adv Pract* 2021; 5: rkab015. https://doi.org/10.1093/rap/rkab015
36. SALAFFI F, CAROTTI M, GUTIERREZ M, DI CARLO M, DE ANGELIS R: Patient acceptable symptom state in self-report questionnaires and composite clinical disease index for assessing rheumatoid arthritis activity: identification of cut-off points for routine care. *Biomed Res Int* 2015; 2015: 930756. https://doi.org/10.1155/2015/930756