Design and validation of a predictive model for determining the risk of developing fibromyalgia

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Abstract

Objective
Fibromyalgia is a prevalent disease of unknown aetiology and is difficult to diagnose. Despite the availability of the American College of Rheumatology criteria for diagnosis, it continues to be a challenge in the field of primary health care in terms of identifying individuals with susceptibility to developing the disease. The aim of this study is to design and validate a predictive model of fibromyalgia in subjects with a history of chronic pain.

Methods
This multicentre observational retrospective cohort study was performed on patients aged >18 years, who visited four primary health centres between 2017 and 2020, with a diagnosis of fibromyalgia or arthritis. The Bootstrapping resampling method was used for the validation of the model.

Results
A total of 198 subjects with fibromyalgia (93 with osteoarthritis, 20 with other types of arthritis, 4 with rheumatoid arthritis) and 120 without fibromyalgia (116 with osteoarthritis, 23 with other types of arthritis, 7 with rheumatoid arthritis) participated in the study. The predictive factors of the final model were self-reported age at onset of symptoms, first-line family history of neurological diseases, exposure to levels of stress, history of post-traumatic acute emotional stress, and personal history of chronic widespread pain prior to diagnosis, comorbidity, and pharmacological prescription during the year of diagnostic confirmation. The predictive capacity adjusted by Bootstrapping was 0.972 (95% CI: 0.955–0.986).

Conclusion
The proposed model showed an excellent predictive capacity. The risk calculator designed from the predictive model allows health professionals to have a useful tool to identify subjects at risk of developing fibromyalgia.

Key words
chronic pain, fibromyalgia, predictive model, primary care, validation

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Introduction

Fibromyalgia is a disease of unknown aetiology, based on the presence of chronic generalised pain lasting for more than 3 months, with chronic fatigue, sleep disorders, and other functional symptoms, that is included within the central sensitisation syndrome (1-3).

In the absence of biological markers to diagnose the disease, the American College of Rheumatology (ACR) proposed a number of diagnostic criteria in 1990 (ACR 1990). The pain is experienced in the four quadrants of the body, on both sides, above and below the waist, and in the axial skeleton, with pain upon palpation in 11 of the 18 tender points when exerting a pressure of 4 kg/cm (4-6).

Years later, the ACR would propose new diagnostic criteria for fibromyalgia. This is how ACR 2010, ACR 2010 modified, ACR 2011, and ACR 2016 were incorporated (7, 8).

Fibromyalgia has a worldwide prevalence of 2.7% (9), was recognised by the World Health Organisation in 1992 (10), and is currently included in the ICD-11 in the group "Chronic widespread pain". Nevertheless, a large percentage of health professionals, especially in primary health care, continue to attribute the symptoms to problems of a mental nature and not as a disease caused by an alteration of the neurotransmitters of the nervous system that causes the symptomatology.

This position causes serious problems for the patient and the health care system, by slowing down diagnostic confirmation, increasing the consumption of health care resources by patients, leading to non-recognition of the degree of disability, and increasing the potential biopsychosocial deterioration caused by this disease (11-15).

Being aware of this scenario and of the great controversies surrounding fibromyalgia (2, 16, 17), several investigations have been performed to find new information that provides a greater understanding of the disease (18-22).

In this context, validation studies have focused on the creation of tools that facilitate the identification of patients with fibromyalgia (23-26) from primary care consultations. Even so, its percentages of sensitivity, specificity, and correct classification, added to the comorbidities of osteoarticular diseases that share similar symptoms and its low use in daily practice, continue to make it difficult to identify patients at risk of suffering from the disease (27). On the other hand, other authors have demonstrated the effectiveness of predictive models as an alternative tool to identify populations at risk (28, 29). In the case of fibromyalgia, a validation study of a predictive model to be used as a screening tool to identify the population at risk of having fibromyalgia has not yet been developed. Considering the above, the purpose of our study was to design and validate a predictive formula (risk calculator), easy to use from the primary care consultation to quantify the risk of suffering from the disease and thereby reduce the average time of diagnosis confirmation. The proposed tool does not complicate the diagnosis, on the contrary, it better approximates its suspicion.

Materials and methods

Design, setting, study population and inclusion and exclusion criteria

This is a multicentre observational retrospective cohort study in patients >18 years of age, who visited four primary health centres in Barcelona, between 2017-2020, and considering that fibromyalgia is one of the most common causes of chronic widespread pain, the sample was selected from the population with a history of chronic pain equal to or greater than three months duration, with a confirmed diagnosis of fibromyalgia according to the criteria of the ACR 1990 and diagnosis arthritis (chronic disease that occurs with a process of inflammation of the joints, for example: rheumatic arthritis, osteoarthritis, or other types of arthritis such as psoriatic arthritis). A Rheumatologist specialist made the both the diagnoses of fibromyalgia and of arthritis.

We excluded patients with severe cognitive impairment, a serious mental illness, or in the form of an acute process that, in the investigator's opinion, could interfere with the reliability of the information. Patients not previously
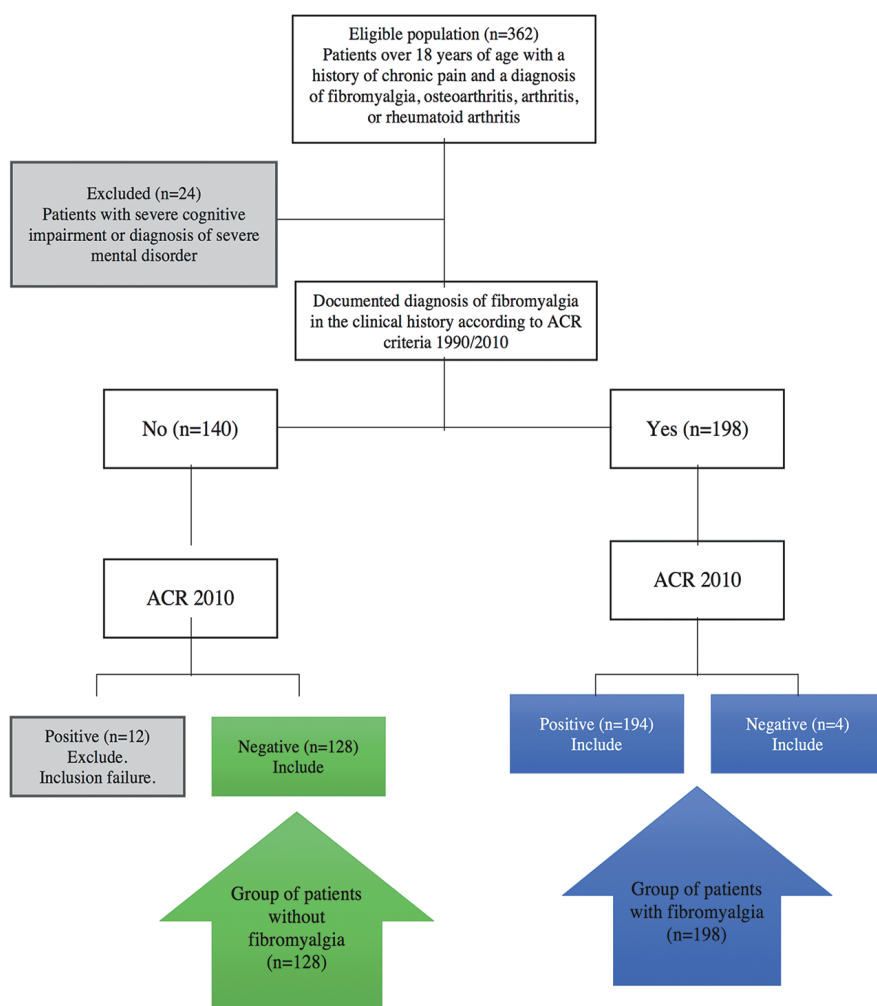
Fig. 1. Inclusion of study participants.
ACR: American College of Rheumatology. Source: ceated by author.

diagnosed with fibromyalgia and who obtained a positive score for fibromyalgia during the interview according to the ACR 2010 criteria were considered inclusion failures.

Sample
Assuming the classic Freeman formula (30): $[n = 10 * (k + 1)]$, where k represented the number of variables included in the multiple model and, considering for study purposes the maximum inclusion of 19 variables in the predictive model, in addition to an adjustment of 20% for losses, the minimum sample necessary to fulfill the purpose of the study was 297 subjects. Among the 362 included initially, 24 were excluded for not meeting the selection criteria and 12 were inclusion failures; thus, leaving a final sample of 326. Figure 1 shows the inclusion of the participants.

Development of the patient questionnaire
The research team conducted a review of the literature in the databases: PubMed, BioMed Central, Cochrane Library, Science Direct, Scopus and LILACS to collect information on the epidemiological characteristics that characterise patients with fibromyalgia. The research team used the results of the literature review to develop the patient questionnaire. Two fibromyalgia experts reviewed the questionnaire and evaluated the items for clarity, coherence, and relevance of the items in the established groupings.

Subsequently, the research team conducted a cognitive interview with two people with similar characteristics to the sample, to assess the comprehension of the items.

In those items that presented difficulty in understanding the question or selecting the answer options, the research team conducted a deeper investigation to facilitate the process of analysis and adjustment of the items.

Based on the comments of the patients, the research team developed a second version of the questionnaire. The experts evaluated the second version and after approving it, the research team conducted a pilot test to verify the content validity of the definitive version.

Figure 2 shows the conceptual model for the development of the patient questionnaire.

Variables and data collection questionnaires
Sociodemographic variables to characterise the study population were sex, current age, years since diagnosis, and personal history of osteoarthritis, rheumatoid arthritis, and other types of arthritis.

The dependent variable was fibromyalgia. Patients with fibromyalgia were considered those who had a documented diagnosis in clinical history according to the ACR 1990 criteria and patients without fibromyalgia who reported a negative ACR 2010 during the interview. In the group with fibromyalgia, some cases had the presence of osteoarthritis, rheumatoid arthritis, or other types of arthritis. In the group without fibromyalgia, all patients had the presence of osteoarthritis, rheumatoid arthritis, or other types of arthritis as comorbidity.

The independent variables to establish the predictive model were grouped into predisposing factors, triggers, and other variables of interest.

The questionnaires used for data collection were: 1) ACR 2010 questionnaire, validated by the American College of Rheumatology for the diagnosis of fibromyalgia, administered to identify cases of fibromyalgia not diagnosed at the time of inclusion in the study; 2) The patient questionnaire was prepared by the research team to collect information related to the study variables; 3) The clinical records audit questionnaire was prepared by the research team to collect data related to comorbidity (ICD-10 diagnoses: Internation-
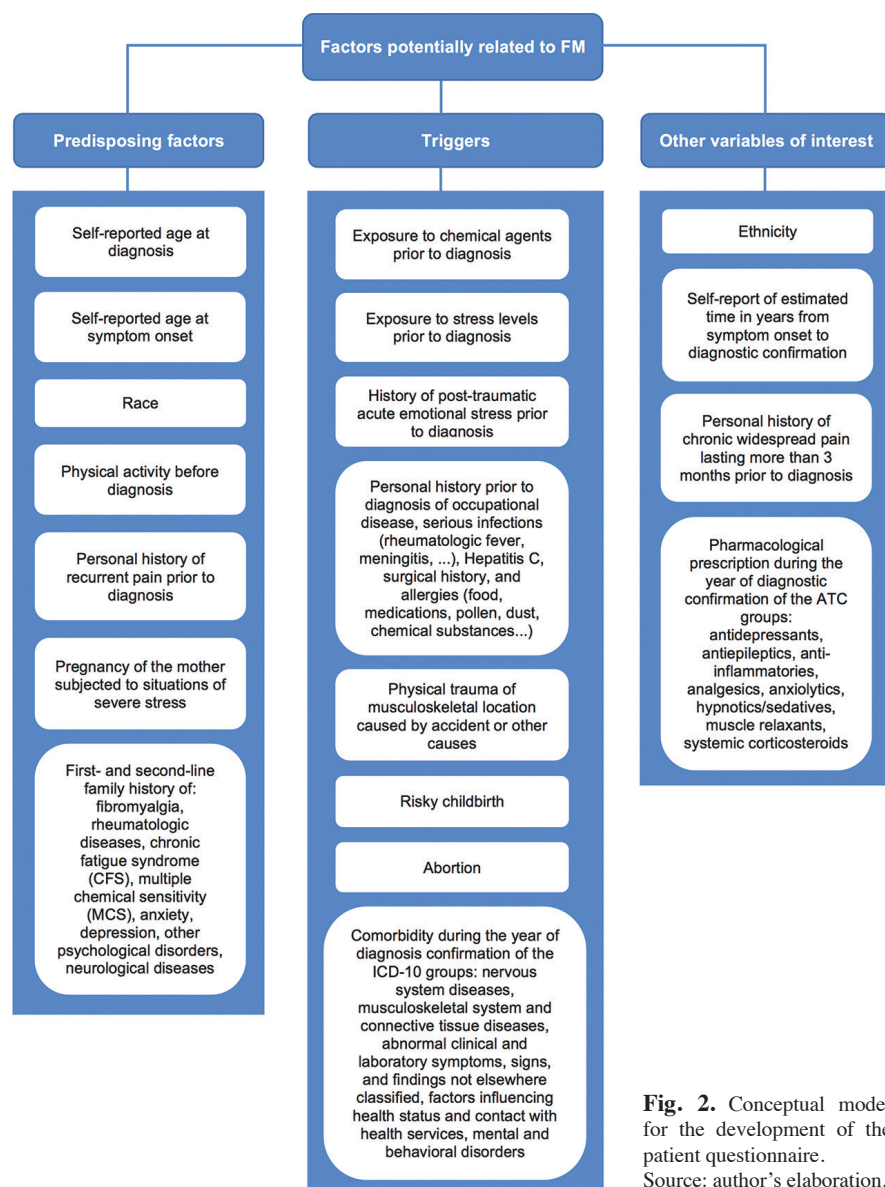
Fig. 2. Conceptual model for the development of the patient questionnaire. Source: author's elaboration.

al Classification of Diseases, 10th edition) and pharmacological prescription (ATC groups: Anatomical Therapeutic Chemical Classification Code).

Selection of items included in the predictive model

The patient questionnaire allowed the research team to collect information on the preselected variables.

Afterwards, the research team conducted an exploratory analysis, and the variables with a $p<0.20$ in the bivariate analysis were included in the multiple regression for each factor (predisposing, triggering, other variables of interest) (31).

Statistical analysis

Univariate analysis was performed using absolute and relative frequencies for categorical variables and the median and interquartile range (IQR) for continuous variables.

Bivariate analysis of potential predictive factors was conducted using Chi-squared or Fisher's exact test for categorical variables and Mann-Whitney U for quantitative variables.

Multivariate logistic regression was performed using the backward elimination method and variables with a p-value <0.05 were included.

The goodness of fit and predictive characteristics of the model were evaluated. The analysis of the ROC curve (receiver operating characteristic curve) was

Table I. Validation statistics of the prespecified and final models.

		Prespecified model						Final model using the backward model					
		Apparent performance			Bootstrap performance (Optimism adjusted) *			Apparent performance			Bootstrap performance (Optimism adjusted) **		
			95% CI			95% CI			95% CI			95% CI	
		Statistical	Inf	Sup	Statistical	Inf	Sup	Statistical	Inf	Sup	Statistical	Inf	Sup
Overall	*Brier scaled*	84.60%			75.20%			82.00%			73.50%		
Discrimination	*C-Statistic*	0.990	0.982	0.997	0.977	0.963	0.987	0.986	0.977	0.996	0.972	0.955	0.986
Calibration	*E:O ratio*	1.000			0.987	0.906	1.038	1.000			0.998	0.933	1.041
	Calibration-in-the-large	-0.000	-0.566	0.566	-0.061	-0.846	0.853	0.000	-0.521	0.521	0.003	-0.758	1.092
	(CITL) Slope	1.000	0.731	1.269	0.544	0.002	0.889	1.000	0.744	1.256	0.596	0.004	0.923
Shrinkage factors	*Heuristic Shrinkage*				0.946						0.946		
	Bootstrap shrinkage				0.544						0.596		

*50 Bootstrap samples of which 3 did not converge; **100 Bootstrap samples of which 9 did not converge.
Source: created by author.

the statistical method used to identify the optimal cut-off point to classify patients, guaranteeing a greater probability of being correctly classified, that is, differentiating the patient with fibromyalgia from the one who does not have it, considering "positive or at risk of having fibromyalgia" those values greater than or equal to the cut-off point and "negative or without risk of having fibromyalgia" those values below the cut-off point (32).

Scale validation
The Bootstrapping resampling method (33) was then performed in the model. Initially, a regression was performed with all the potential predictors. Subsequently, 50 Bootstrap samples were generated with replacements from the original sample and of the same size to perform the Bootstrap validation of the prespecified model.
Then, a multiple logistic regression was performed using the backward method for the selection of variables ($p<0.05$). With the variables not included in the model, 100 Bootstrap samples were generated with replacements from the original sample and of the same size as the latter to perform the Bootstrap validation of the final model.
The validation included measures of global performance measured through the Brier Scaled statistic, discrimination measured through the C-Statistic concordance statistic or area under the curve (AUC), and calibration measured through the ratio of E and O (E:O), calibration-in-the-large (CITL) and slope statistics.
Reliability of the predictors was measured through analysis of the frequency of inclusion of the variables in the model, with those that presented a percentage of appearance of >50% in the Bootstrap samples being significant.
The estimation of the adjustment factor or correction Shrinkage Factor was determined through Shrinkage Heuristic statistics and Bootstrap shrinkage.
The results of the final model adjusted by Bootstrap shrinkage were used to design the fibromyalgia risk calculator to provide health professionals with an easy-to-apply tool for clinical purposes (Supplementary Table S1).

For data collection, forms were created in the ACCESS version 15 programme and statistical analysis was carried out using STATA v. 16 and SPSS® v. 16.

Ethical approval
The study was approved by the Ethics Committee of the Hospital Clínic (registration: HCB/2016/0469) and the Ethics Committee of the Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAP Jordi Gol) (registration: 19/023-P). All patients gave their informed consent to participate before performing any study procedure.

Results
Sociodemographic characteristics of the study population
Of the 100% (n=326) of patients included in the study, 96.32% were women (with fibromyalgia = 97.47% *vs*. without fibromyalgia = 94.53%, $p=0.229$), with a median age of 65 years [IQR=57–71] (with fibromyalgia=61 years [IQR=55–67] *vs*. without fibromyalgia = 71 years [IQR=64.5–75], $p<0.001$) and median diagnostic progress of 10 years (IQR=5–15) (with fibromyalgia = 10 years [IQR=6–14] *vs*. without fibromyalgia = 9.5 years [IQR=4–15], $p=0.682$).
Regarding the personal history of osteoarticular diseases, 64.11% reported having osteoarthritis (with fibromyalgia = 46.97% *vs*. without fibromyalgia = 90.63%, $p<0.001$), 13.19% other types of arthritis (with fibromyalgia = 10, 10% *vs*. without fibromyalgia = 17.97%, $p=0.040$) and 3.37% rheumatoid arthritis (with fibromyalgia = 2.02% *vs*. without fibromyalgia = 5.47%, $p=0.087$).

Predisposing factors, triggers and other variables of interest related to fibromyalgia
Supplementary Table S2 shows the bivariate analysis of the potential predictors of fibromyalgia, which made up the prespecified model ($p<0.20$).
In the logistic regression of the prespecified model, the 19 variables potentially predictive of the risk of having fibromyalgia were included. This model provided an 80.89% explana-

tion for the event (no. of observations =324; LR χ^2 (19) = 350.98; Prob >χ^2 = <0.001; Log likelihood = –41.47).
In the logistic regression of the final model, variables with a *p*-value <0.05 were retained. This model was made up of 10 variables, providing a 77.60% explanation for the event (no. of observations = 324; LR χ^2 (10) = 336.73; Prob >χ^2 = <0.001; Log likelihood = 48.59). Supplementary Table S3 shows the logistic regression statistics of the prespecified model and final model using the backward method.
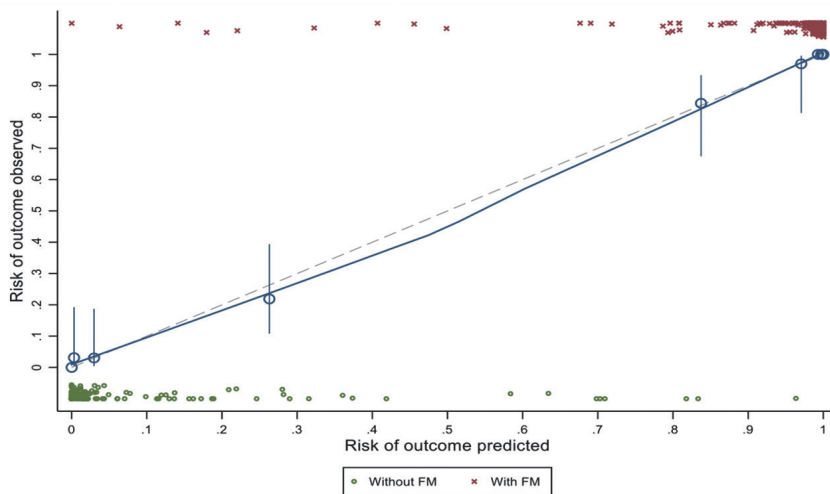
Goodness of fit and predictive characteristics of the models
When comparing the goodness-of-fit statistics of the prespecified model versus the final model, the Hosmer-Lemeshow goodness-of-fit test showed that both models fit the sample adequately. For its part, the Log-Lik Full Model or logarithm of the likelihood was significantly higher than the Log-Lik Intercept Only, which only included the constant, and showed that the independent variables included in the models influenced the dependent variable. This was reaffirmed when comparing the measures of likelihood using the LR test (test of the likelihood ratio) and its *p*-value (Prob>LR), which indicated that at least one of the coefficients was significantly different from zero.
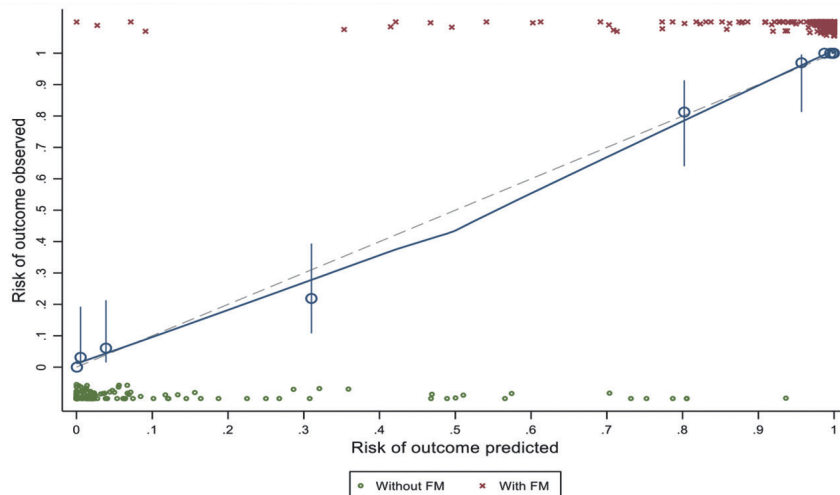The Pseudo R or McFadden's R2 was 81% for the prespecified model and 78% for the final model. When adjusting the statistic, the explanatory percentage decreased to 72 and 73%, respectively. The AIC of 119.19 and the BIC of –278.92 confirmed the final model as the best fit.
The proposed predictive formula showed a probability of occurrence of the event on a continuous scale of 0 to 1 (equivalent to 0% to 100%), and through the analysis of the area under the curve, the results showed that the cut-off point of 0.5 (50%) had better discrimination (AUC=0.986; CI 95%: 0.977-0.996), so values equal to or greater than 0.5 (50%) corresponded to patients with a probability of having fibromyalgia and values less than 0.5 (<50%) to patients without the probability of having the disease.
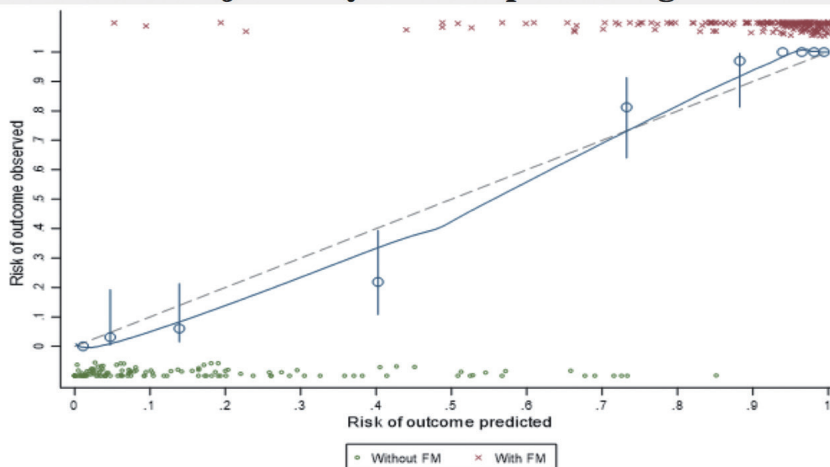
Prespecified model

Final model

Final model adjusted by Bootstrap Shrinkage

Fig. 3. Calibration plots for Bootstrap samples. Source: author's elaboration.

The goodness-of-fit statistics and the predictive characteristics are shown in Supplementary Table S4.

Bootstrap validation
Bootstrap validation of the prespecified model and the final model was performed after the regression analysis, which was the analysis best adjusted to the Bootstrap samples.

The unadjusted area under the curve for the prespecified model was 0.990 (95% CI=0.982–0.997) and for the final model, it was 0.986 (95% CI=0.977–0.996). When adjusting for Bootstrap samples, the predictive capacity decreased for the prespecified model to 0.977 (95% CI=0.963–0.987) and for the final model to 0.972 (95% CI=0.955–0.986).

Table I shows the validation statistics and Figure 3 shows the calibration plots for the prespecified and final models.

The reliability of the predictors is shown in Table II.

The final model coefficients were adjusted using a uniform shrinkage based on Bootstrapping estimation to correct for overfitting (Bootstrap shrinkage=0.596).

Table III shows the final model adjusted by Bootstrap shrinkage, which is information necessary to calculate the predictions of the risk of having fibromyalgia.

The predictive formula was evaluated in two patients with a history of chronic pain without a diagnosis of fibromyalgia. They were first given the 2010 ACR criteria and obtained a positive score for the disease. When evaluated by the rheumatologist using the ACR 1990 (Gold Standard), one patient was diagnosed with fibromyalgia and in the other, the disease was ruled out. The rheumatologist's criteria in both cases coincided with the result obtained through the predictive formula, demonstrating the effectiveness of this new screening tool.

Discussion

Some authors have designed and validated risk calculators to predict the appearance of an event (34). In the case of fibromyalgia, our study was possibly the first one to design and validate

Table II. Reliability of the predictors. Frequency of appearance of the variables in the Bootstrap samples using the backward method.

Variables	Frequency	Percentage
Predisposing factors		
Self-reported age at symptom onset	80	87.90%
Self-reported age at diagnosis	36	39.60%
Pregnancy of the mother subjected to situations of severe stress	30	33.00%
Personal history of recurrent pain prior to diagnosis	32	35.20%
First-line family history of neurological diseases	77	84.60%
First-line family history of depression	33	36.30%
First-line family history of chronic fatigue	22	24.20%
Triggers		
Exposure to chemical agents prior to diagnosis	28	30.80%
Exposure to levels of stress prior to diagnosis	91	100.00%
History of post-traumatic acute emotional stress prior to diagnosis	65	71.40%
Comorbidity during the year of diagnostic confirmation: ICD-10 group diseases of the nervous system	64	70.30%
Comorbidity during the year of diagnostic confirmation: ICD-10 group diseases of the musculoskeletal system and connective tissue	87	95.60%
Comorbidity during the year of diagnostic confirmation: ICD-10 group symptoms, signs, and abnormal clinical and laboratory findings not elsewhere classified	62	68.10%
Comorbidity during the year of diagnostic confirmation: ICD-10 group factors influencing health status and contact with health services	64	70.30%
Other variables of interest		
Personal history of chronic widespread pain lasting more than 3 months prior to diagnosis	100	109.90%
Self-report of the estimated time in years from the onset of symptoms to diagnostic confirmation	25	27.50%
Pharmacological prescription during the year of diagnostic confirmation: anti-inflammatory ATC group	82	90.10%
Pharmacological prescription during the year of diagnostic confirmation: antiepileptic ATC group	69	75.80%
Pharmacological prescription during the year of diagnostic confirmation: antidepressants ATC group	46	50.50%

Source: created by author.

Table III. Final model adjusted via Bootstrap shrinkage.

VARIABLES	Coef.	95% CI Inf	95% CI Sup	Std. Err.	z	*p*>z
Predisposing factors						
Self-reported age at symptom onset	-0.065	-0.09	-0.04	0.013	-4.93	<0.001
First-line family history of neurological diseases	1.434	0.40	2.47	0.528	2.72	0.007
Triggers						
Exposure to levels of stress prior to diagnosis	1.449	0.54	2.36	0.464	3.13	0.002
History of post-traumatic acute emotional stress prior to diagnosis	1.056	0.34	1.77	0.366	2.88	0.004
Comorbidity during the year of diagnostic confirmation: ICD-10 group diseases of the nervous system	0.642	0.10	1.18	0.276	2.33	0.020
Comorbidity during the year of diagnostic confirmation: ICD-10 group diseases of the musculoskeletal system and connective tissue	1.279	0.31	2.25	0.494	2.59	0.010
Comorbidity during the year of diagnostic confirmation: ICD-10 group symptoms, signs, and abnormal clinical and laboratory findings not elsewhere classified	-0.579	-1.06	-0.10	0.245	-2.37	0.018
Other variables of interest						
Personal history of chronic widespread pain lasting more than 3 months prior to diagnosis	3.819	2.72	4.92	0.562	6.8	<0.001
Pharmacological prescription during the year of diagnostic confirmation: anti-inflammatory ATC group	-0.682	-1.19	-0.18	0.258	-2.64	0.008
Pharmacological prescription during the year of diagnostic confirmation: antiepileptic ATC group	1.552	0.26	2.85	0.661	2.35	0.019
_cons	-2.998	-3.38	-2.61	0.196	-15.33	<0.001

Source: created by author.

a risk calculator based on the analysis of objective and quantifiable epidemiological predictors (Suppl. Table S1). This is how the fibromyalgia risk calculator has been created to facilitate primary care professionals the rapid identification of patients likely to have the disease. Which, in other words, translates into a screening test and in no case is intended to replace the ACR 1990 criteria.

The fibromyalgia risk calculator showed a strong influence of the predictor variable "history of chronic widespread pain"; it also highlighted the predictive value of other epidemiological variables as potential predictors of the disease. It is not limited to subjective items such as the presence and intensity of symptoms, but also includes objective items related to diagnoses of ICD-10 groups (1. diseases of the nervous system, 2. diseases of the musculoskeletal system and connective tissue, 3. symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified) and pharmaco-

logical prescription of the ATC groups (anti-inflammatory and antiepileptics) recorded in the patient's medical history in the last year. This may explain the greater sensitivity and specificity of the predictive model with respect to previously developed questionnaires, such as the FiRTS, FibroDetect or SI-FIS (24-26, 35).

In relation to the predisposing factors included in the predictive model, the self-reported age at onset of symptoms behaved as a protective factor against the risk of having fibromyalgia (OR=0.90; CI 95%=0.86–0.94; $p<0.001$). That could indicate that the symptoms of fibromyalgia tend to appear at younger ages compared to the appearance of symptoms associated with other rheumatological diseases such as osteoarthritis, rheumatoid arthritis or other types of arthritis (36). First-line family history of neurological diseases (diseases affecting the central nervous system and peripheral nervous system, for example: dementia, stroke, epilepsy, Parkinson's, multiple sclerosis, migraine) acts as a risk factor (OR=11.08; CI 95%=1.95–62.8; $p=0.007$), consistent with the findings of Moukaddem et al. (37).

About the triggering factors, the following predictors behaved as a risk factor for fibromyalgia: exposure to levels of stress prior to diagnosis (OR=11.37; CI 95%=2.48–52.23; $p=0.002$), history of post-traumatic acute emotional stress prior to diagnosis (OR=5.88; 95% CI=1.76–19.61; $p=0.004$), comorbidities during the year of diagnostic confirmation of the ICD-10 diseases group of the nervous system (OR=2.94; CI 95%=1.19–7.27; $p=0.020$), and group ICD-10 diseases of the musculoskeletal system and connective tissue (OR=8.55; CI 95%=1.68–43.44, $p=0.010$).

Comorbidity during the year of diagnostic confirmation of the ICD-10 group symptoms, signs, and abnormal clinical and laboratory findings not elsewhere classified (OR=0.38; 95% CI=0.17–0.85; $p=0.018$) act as a protective factor against the risk of having fibromyalgia.

Similar to the present study, some researchers consider fibromyalgia to be a disorder caused by stress-related

problems in the autonomic nervous system and propose that psychological stress, physical trauma, different types of infections or other stressors lead to uninhibited sympathetic hyperactivity in susceptible individuals with a maladaptive autonomic nervous system (13), so exposure to stress levels should be considered as a variable of interest involved in the process of triggering the disease (38, 39).

Regarding the other variables of interest, the pharmacological prescription during the year of diagnostic confirmation of the anti-inflammatory ATC group (OR=0.32; 95% CI=0.14-0.74; $p=0.008$) behaved as a protective factor. Contrary to what was found by Gendelman et al., difference probably attributed to the comparison group which, in Gendelman's study, was the general population (40).

However, the pharmacological prescription during the year of the diagnostic confirmation of the antiepileptic ATC group (OR=13.52; CI 95%=1.54–118.76; $p=0.019$) and the personal history of chronic widespread pain lasting more than 3 months prior to diagnosis (OR=606.98; 95% CI=95.60–3853.67; $p<0.001$), behaved as risk factors (4, 13, 18).

The limitations of the study were related to the measurement of variables that could be affected by the possible inaccuracy in the recall of previous events or experiences. To control it, the variable "years of diagnostic progress" was measured in both groups, verifying that the behavior of this variable did not vary between groups. Similarly, before starting the interview, patients were given some prior explanations about the objectives of the questionnaires, and the questions were contextualised chronologically with the occurrence of the events to be evaluated.

A standard operating procedure was designed to have greater control over the research processes, in order to control the presence of possible information or interviewer bias.

Although exploratory analysis showed that there were no differences in mean age between groups, in our study we did not match by age.

Another limitation was related to the

similarity of the symptoms of the diseases under study (fibromyalgia, osteoarthritis, rheumatoid arthritis, other types of arthritis) and the presence of two or more of them in the same patient. This favoured that sometimes the patient had difficulty chronologically contextualising the degree of exposure to some potential predictive factors. To overcome this limitation and collect the information in a clear and precise way, the researcher told the patient before starting the interview that the questions had to be answered using the date of the diagnostic confirmation of fibromyalgia as a point of reference. Accordingly, patients without fibromyalgia were asked to answer the questions based on the diagnostic confirmation of the oldest disease or the one that generated the greatest impact on the perception of their health status (osteoarthritis, rheumatoid arthritis, other types of arthritis).

Finally, despite the reliability of the internal Bootstrap validation for predictive model validation, it is recommended that the risk calculator be tested in the future in a prospective cohort of patients with a history of chronic pain in whom the cause of pain has not yet been diagnosed.

Conclusions

The fibromyalgia risk calculator is presented as an easy-to-apply detection tool, with a high predictive capacity (AUC adjusted by Bootstrap samples = 0.972): a sensitivity of 95.94%, specificity of 91.34%, and 94.14% correctly classified. Using the risk calculator, prediction percentages >50% identified the population at risk of having the disease. Its regular use in health care could reduce the average time to diagnostic confirmation through the ACR 1990 criteria.

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