Resource utilisation and health care costs in patients diagnosed with fibromyalgia in Spain

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ABSTRACT

Objective. Fibromyalgia (FM) patients have been regarded as great utilisers of health resources, with important related costs. The aim of this study is to describe health care resource utilisation and related costs of FM from the perspective of the National Health System in Spain.

Patients and methods. A cross-sectional multicenter study was conducted on FM patients based on a patient interview. Data about demographic and clinical variables, physical examination, self-perceived health, psychosocial variables and health resource utilisation, were collected. Direct and indirect costs were calculated, and a correlational study between costs and clinical variables was performed.

Results. Three-hundred and one patients were studied. During the year 2006 the mean total cost per patient per year was 9,982 Euros, of which 3,245.8 (32.5%) corresponded to health care costs and 6,736.2 (67.5%) to indirect costs attributable to productivity losses. Non-drug therapies accounted for the largest proportion of the health care costs, three times greater than the drug treatment. Patients with higher total costs showed the greatest disease involvement. The variables associated to the total health care costs were functional capacity, depression, comorbidities and age. Patients with permanent working disability were the greatest resource utilisers.

Conclusion. FM patients with higher costs show the greatest disease involvement. Direct and indirect costs are well correlated to disease severity. The indirect costs account for most of the economic burden of FM and approximately double the health care costs. Patients with permanent working disability present more severe disease and generate greater health care costs.

Introduction

Patients with fibromyalgia (FM) have been regarded as great utilisers of health care resources, with important disease-related costs (1-7).

The health care costs derived from FM can triple those of the average patient attended by general practitioners and included in computerised database of national or private health systems of some countries (5); double those of in-flammatory disorders such as ankylosing spondylitis (6), and prove similar to other diseases considered to be first-order health problems, such as chronic low back pain (6), osteoarthritis (7) or generalised anxiety (8).

The total economical cost associated with a given disease depends on the direct health care costs and on the indirect costs. In relation to health care costs, medical visits, diagnostic complementary studies, drug and non-drug therapies, alternative therapies, and hospital admissions, can be analysed (9).

The indirect costs are fundamentally attributable to productivity losses associated with sick leave and disability subsidies. This category can also include productivity losses among housewives, the payment of other people needed to help the patient, the costs associated with patient transport due to limitations, adjustments in the home, etc (9). Thus, economical cost analyses can vary considerably from one study to another, depending on the concepts included, but also on the health care system of the country in which the study is made, private or public coverage, the origin of the patients (databases, primary or specialised care), etc.

To date, no precise assessment had been made in Spain on resource utilisation and costs in patients with FM. Here, we studied the economic burden of FM from the perspective of the National Health System, and analyze the variables associated with increased economical costs.

Patients and methods

Patients

The study population was primarily urban above 18 years of age with a diagnosis of FM according to American College of Rheumatology (ACR) criteria (10) recruited from 15 public rheumatologic clinics of the Spanish National Health System throughout the country. All those patients who signed the informed consent were consecutively included between January and April 2007.

Patients presenting other concomitant diseases with severely impaired functional capacity, rheumatic inflammatory diseases, cardiovascular or pulmonary diseases with poor aerobic capacity, uncontrolled psychiatric diseases or involved in litigation process, were excluded from the study.

Study design and data collection

A cross-sectional multicenter study was conducted based on a face-to-face patient interview. Data were obtained on the main sociodemographic variables, frequent clinical manifestations, their intensity (scored in a Likert scale where 1=unimportant, 2=scantly important, 3=moderately important, and 4=very important), the number of other comorbidities, and the use of health care and non-health care resources related to FM during the year 2006. Patients also completed questionnaires about self-perceived health and psychosocial variables.

The study protocol was approved by the Clinical Research Ethics Committee of Gregorio Marañón Hospital (Madrid, Spain).

Health care, non-health care resources and cost estimation

Health care resource utilisation comprised visits in primary care centers, referrals to specialists, pain clinic visits, complementary diagnostic tests, emergency room visits, hospitalisation stays and drug prescriptions. Non-drug therapies such as acupuncture, physical therapies, psychological counseling, etc., and required special food, were also documented. Health care resource utilisation and costs calculations were considered if it were directly related to FM. Non-health care resources were considered to represent days of sick leave and shorted work day in the active population, and early retirement because of permanent disability.

Different study concepts and their economic evaluation were as follows: a) complementary tests, including laboratory tests (mean expenses per procedure), conventional radiology (fee per requested test), and supporting tests (fee per requested test); b) ordinary or emergency referrals to specialists, pain clinics or hospitals (referral adapted fee); c) prescriptions (acute, chronic, or requested medical prescriptions; market price per container); d) workdays lost (professional average salary), and information regarding early retirement (in<65 years old) because of permanent disability.

Health care resource prices were obtained from the Drug Catalog of the Spanish General Council of Pharmacist Associations for prices of drugs (11); from the Oblikue Consulting cost database for complementary tests and medical visiting prices (12); from the patients themselves for special diets and/or foods; and from experts and public prices for non-drug therapies. We used public selling reference prices when available, and an average price for drugs with more than one commercial brand or generic presentation.

Indirect costs were calculated according to human capital methodology (9, 13). Two main components of these costs were computed; firstly, workdays lost due to sick leave in the active population, which were computed as the sum of the yearly number of workdays lost, multiplied by the daily average salary in active subjects. Secondly, we added the cost to society of those patients with early retirement before 65 years of age (permanent disability for usual working activity). These costs were computed as a whole year average salary, which is regarded as an opportunity cost. The yearly average professional salary in the year 2006 was Euros 18.714.

All costs were expressed in Euros of the year 2006, and are reported as mean cost per patient per year.

Patient-reported outcome questionnaires

Self-perceived health and emotional aspects were assessed in the validated Spanish versions by the following questionnaires:

Fibromyalgia Impact Questionnaire (FIQ) (14, 15) is a FM specific quality of life questionnaire. It contains 10 questions and the total score reflects the impact of FM in a range from 0 to 100 (maximum impact).

Brief Pain Inventory (BPI) (16, 17) measures pain severity, from 0 to 10 (pain as bad as you can imagine); and interference, from 0 to 10 (completely interferes).

Hospital Anxiety and Depression Scale (HADS) (18) contains 14 item designed to measure levels of anxiety and depression. Total score ranges from 0 to 21 (maximum levels).

Health Assessment Questionnaire (HAQ) (19, 20) contains 20 questions about activities of daily living. The final score is expressed in a 0-3 (worst ability) scale.

Fatigue Assessment Scale (FAS) (21) measures fatigue in a 10 item rating scale from 0 to 4. Total score ranges from 0 to 40 (maximum level).

Statistical analysis

Data were reviewed to study the distribution of frequencies, and checked for possible recording or codifying errors until the quality of computerised data was considered appropriate.

A descriptive statistical analysis was conducted and multiple regression analysis was performed to determine which set of variables was most closely related to the total costs. The model incorporated those variables showing significant correlation (p<0.05) to the total costs in a stepwise forward selection and adding variables that increased the multiple R² by the largest amount until there were no significant increases. The variables were introduced with the assumption that it could be of greatest relevance from the clinical perspective.

Results

Three hundred and one patients (women: 96.7%) were studied. There were no significant differences in clinical and Table I. Main demographic parameters and mean score of the self-administered questionnaires at the inclusion visit in the 301 patients with fibromyalgia studied.

	Mean	SD	Range
Demographic characteristics			
Age (yrs.)	48.7	8.5	26 - 74
Duration of pain (yrs.)	11.5	9.1	0.5 - 51.4
Number of comorbidities	3.0	2.2	0 - 14
Tender points	15.2	2.5	6 – 18
Self-administered questionnaires			
Mean BPI pain	6.4	1.5	2.2 - 10.0
Mean BPI interferences	6.6	1.9	0.2 - 9.8
FIQ	70.7	14.9	18.3 - 97.6
FAS	26.0	7.2	3.0 - 40.0
HAQ	1.4	0.5	0.0 - 2.7
HADS anxiety	12.2	4.3	2.0 - 21.0
HADS depression	9.8	4.8	0.0 - 21.0

demographical characteristics between sexes and there was similar distribution among centres. Demographical characteristics and mean score of the self-administered questionnaires can be seen in Table I.

Description of resource

utilisation and associated costs Total all type medical visits were 5,759 (mean 19.1±16.7 visits/patient), distributed as shown in Table II. The average cost of visits to specialised care was almost three-fold greater. A total of 1,913 explorations (mean 6.3±5.1 explorations/patient) were made. Magnetic resonance imaging (MRI) represented

Table II. Annual statistics per patient corresponding to utilisation of the different health care resource components and the mean costs.

	Resource utilisation			Costs (Euros)		
	Mean	SD	Range	Mean	SD	Range
Medical visits						
Primary care	8.9	10.3	0 - 62	182.2	210.9	0 - 1261.1
Specialists	8.4	9.6	0 - 99	489.0	560.3	0 - 5735.1
Emergency	1.3	2.7	0 - 20	156.1	311.5	0 - 2298.2
Pain unit	0.3	1.6	0 - 24	19.8	88.3	0 - 1262.6
Total medical visits	19.1	16.6	0 - 103	847.1	768.2	0 - 5911.0
Complementary tests						
Complete blood count + biochemistry	2.6	2.5	0 - 30	64.3	61.7	0 - 723.3
Plain x-rays	1.6	1.8	0 - 12	58.4	65.1	0 - 425.5
MRI	0.5	0.9	0 - 6	198.2	323.5	0 - 2117.6
Ultrasound	0.7	1.1	0 - 6	96.7	151.8	0 - 808.3
Other ^a	0.7	1.12	0 - 6	55.8	96.4	0 - 672.9
Total complementary tests	6.3	5.1	0 - 40	473.5	495.1	0 – 2755.9
Type of drug therapy b						
NSAIDs	0.8	0.8	0 - 5	47.0	78.8	0 - 452.7
Analgesics	1.1	1.1	0 - 6	80.4	170.7	0 - 2072.9
Antidepressants	0.9	0.8	0 - 4	161.8	292.1	0 - 1965.6
Hypnotics	0.1	0.2	0 - 1	1.8	7.6	0 – 39.6
Antiseizure drugs	0.2	0.4	0 - 2	129.9	345.6	0 - 2246.4
Benzodiazepines	0.6	0.7	0 - 4	18.3	38.0	0 - 388.8
Total type of drugs	3.9	1.8	0 – 7	439.2	561.1	0 - 4202.3
Non-drug therapy sessions						
Physiotherapy	8.6	18.5	0 - 100	488.9	954.5	0 - 6076.0
Hydrotherapy	2.9	12.3	0 - 100	34.5	144.2	0 - 1164.0
Massages	7.5	21.5	0 - 90	519.6	973.5	0 - 7200.0
Electrotherapy	4.4	14.2	0 - 60	19.4	50.8	0 - 306.0
Psychotherapy	1.4	6.7	0 - 80	59.7	272.7	0 - 3238.4
Relaxation	7.7	44.9	0 - 150	109.5	373.1	0 - 3834.0
Other ^c	3.1	10.3	0 - 99	136.5	448.2	0 - 3600.0
Total non-drug therapy sessions	35.8	66.5	0 - 723	1368.1	1874.3	0 - 8698.6

^a Includes: Computed tomography, mammography, electromyogram, bone densitometry, gammagraphy and endoscopy.

^b Number of the different type of drugs prescribed to the patient.

^c Includes: Acupuncture, chiropractic, osteopathy, ozone, mesotherapy, magnetotherapy, stretching, iontophoresis, fibromyalgia workshops, swimming, shiatsu, homeopathy, reiki, aquagym.

SD: Standard deviation.

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the most important cost in this chapter, with a mean of 0.6 ± 0.9 MRI/patient. Thirty patients (10.0%) had been admitted to hospital during 2006, with a total of 32 admissions (22 surgical, 10 medical). Only one of these admissions due to major depression was considered directly related to FM for cost calculation. The total cost of this admission was 20,856.6 Euros, representing a mean of 69.3±1202.1 Euros/patient. The mean number of different drugs used for treating FM was 3.9 ± 1.8 drugs being conventional analgesics (69.1% of the

patients) and antidepressants (63.5%)

the drugs most commonly used. Different non-drug therapies were used by 208 patients (69.1%). A total of 10,779 therapeutic sessions (mean 35.8±66.5 sessions/patient) were recorded (Table II). A total of 131 (43.2%) patients reported some special diet or paramedicinal product. The most frequently products were herbal remedies (22.3%) and dietary supplements (21.9%) with a mean frequency utilisation of 121.5 days per patient and year. Considering a mean cost of 0.4 Euros/day, the amount totalled 48.6±88.4 Euros/patient and year (range 0-436.8 Euros). The cost of special diets was difficult to establish and has not been calculated in this study.

Regarding the indirect costs of FM, patient's working status and associated costs can be seen in Table III. The total months of sick leave for working patients was 717 months, with a mean of 2.4 ± 3.8 months per patient (range 0-12 months).

The mean total cost per patient per year was 9,982.0 Euros, of which 32.5% corresponded to health care costs, and 67.5% to indirect costs (Table IV).

Comparison between high

and low total cost patients

The patients were divided into two groups: the 20% with the highest total costs, and the rest of patients. There was only one patient admitted to hospital by FM related depression. This patient had a sanitary cost of 27,005 Euros, while the second more costly patient was 12,499 Euros. We considered this hospital admission cost as marginal and the patient was discarded for the analysis. Table III. Patient's working status and indirect costs due to sick leave.

Working status	Patients		Indirect costs (Euros) ^a			
	n.	%	Mean	SD	Range	
Workers	207	68.7				
Active worker	171	56.8				
Some sick leave	116	67.8 ^b	3556.2	5813.3	0-18954.0	
No sick leave	55	32.2 ^b				
Permanent working disability	36	11.9	2266.9	6160.	70-18954.0	
Reduced working hours c	29		913.1	2801.0	0 - 9477.0	
Housewife	63	20.9				
Unemployed	18	6.0				
Other	13	4.4				
Total	301	100.0	6736.2	7521.3	0-18954.0	

^aAnnual statistics per patient; ^b Percentages with respect to total active workers; ^c Active workers with reduced working hours.

n: number of patients; SD: standard deviation.

Table IV. Relative	cost distribution	by	component.
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	Mean (Euros)	% Total	% Subtotal
Total costs	9982.0	100.0	_
Health care	3245.8	32.5	100.0
Medical visits	847.1	8.5	26.1
Complementary tests	473.5	4.7	14.6
Non-drug therapies	1368.1	13.7	42.2
Drug therapies	439.2	4.4	13.5
Other ^a	117.9	1.2	3.6
Indirect	6736.2	67.5	100.0
Reduced working hours	913.1	9.1	13.5
Sick leave	3556.2	35.7	52.8
Permanent disability	2266.9	22.7	33.7

^aIncludes: hospital admission costs and utilisation of paramedicinal products.

The drug costs, health care costs, and indirect costs were all significantly greater in the first group of patients. This group also showed the greatest disease involvement, as reflected by the following clinical variables: FIQ (77.5±11.6 vs. 69.0±15.3; p<0.0001), number of comorbidities $(3.8\pm2.5 \text{ vs. } 2.8\pm2.1;$ p < 0.004), BPI pain (6.9 \pm 1.5 vs. 6.3 \pm 1.6; p < 0.009), BPI interference (7.5±1.6 vs. 6.4±2.0; p<0.0001), FAS (30.2±5.8 vs. 25.0±7.2; p<0.0001), HAQ (1.8±0.5 vs. 1.3±0.6; p<0.0001), HADS anxiety (13.8±4.6 vs. 11.9±4.2; p<0.001) and HADS depression (12.5±4.5 vs. 9.2±4.6; p<0.0001). No significant differences were found in the demographic variables.

Analysis of the clinical variables associated with total costs

A weak yet significant negative correlation was observed (r=-0.122, p=0.035) between total costs and patient age in such a way that total cost being seen to decrease while increasing patient age. No correlation was found between total costs and the duration of FM.

The correlations between cost and the severity of FM were seen to be significant in all cost categories. Accordingly, the greater the severity of FM, the greater the costs generated by the disease. The mean number of clinical manifestations was 8.9±1.6, their degree of intensity was 3.2 ± 0.4 , and the mean number of comorbidities was 3.0±2.2. The correlation coefficients between total costs and these severity variables were as follow: total FIQ, r=0.329 (p<0.0001); clinical manifestations, r=0.194 (p<0.001); intensity, r=0.236 (p<0.0001); comorbidities, r=0.207 (p < 0.0001). The same significant correlations were found with the questionnaires that specifically assessed pain, anxiety, depression, general health, functional capacity and fatigue.

Table V. Multiple regression analysis.

	Unstandardised coefficient B	SD	Standardised coefficient Beta	t (95% CI)	<i>p</i> -value
Constant	7474.33	2821.71		2.649 (1921.16; 13027.51)	0.009
HAQ HADS (depression Comorbidities Age	3701.60 a) 371.77 708.17 -177.27	914.79 109.60 211.07 54.01	0.246 0.205 0.181 -0.174	4.046 (1901.28; 501,93) 3.392 (156.06; 587,48) 3.355 (292.77; 1123,56) -3.282 (-283.58; -70,96)	0.000 0.001 0.001 0.001

HAQ: Health Assessment Questionnaire; HADS depression: Hospital Anxiety and Depression Scale, subscale depression; SD: standard deviation.



Fig. 1. Cost comparisons of the different components of the health care costs for each of the working patient groups. *p*-value is calculated across all three groups using ANOVA

Non-drug therapy sessions cost was well correlated with comorbidities (r=0.216, p<0.0001), while drug therapy cost was well correlated with total FIQ ((r=0.295, p<0.0001) and intensity of clinical manifestations (r=0.218, p<0.0001).

Multiple regression analysis of the clinical variables associated with total costs

In the multiple regression model, the variables associated to total costs were the HAQ, HADS depression, comorbidities and younger patient age, with an adjusted dispersion coefficient R^2 =0.221 (Table V).

Analysis of occupational status and total costs

The comparative analysis of the health care cost, indirect costs and total costs among patients without sick leave, with sick leave, and permanent disability (see Table III), revealed significant differences (Fig. 1). From the clinical perspective, significant differences were also detected among the three groups in relation to the main clinical variables analyzed.

Comparison between patients with and without sick leave showed no differences in age, age at the time of diagnosis, or the time elapsed prior to diagnosis of the disease. However, there were significant differences between these two groups with a poorer clinical condition being found in the patients that required sick leave. Likewise, there were more medical visits, higher use of drugs, and significantly higher total health care costs among the patients requiring sick leave.

Comparing patients with sick leave versus those with permanent working disability, the latter were seen to yield poorer results in terms of certain clinical disease parameters, and also used more drugs. On the other hand, the patients with permanent disability were older.

Lastly, comparison of the 66 housewives and the workers without sick leave revealed no statistically significant differences in relation to most of the clinical parameters analyzed. Likewise, there were no differences in terms of health care costs.

Analyzing only the working population, males tended to use more drugs, fewer paramedical products and generated greater indirect costs, although significant differences versus women were not reached, probably as a result of the small proportion of men in the study sample.

Discussion

Patients with FM attended by the Spanish National Health System showed health care resource utilisation rates and total costs similar to those reported in other countries (3, 6, 22).

Almost two-thirds of the total costs of our patients were attributable to indirect costs resulting from sick leave, in coincidence with the observations of other authors (22). This was due to the fact that the average patient with FM is fully productive and working days lost have a great impact upon the total associated costs of the disease. In this context, almost two-thirds of our active workers patients had sick leaves in the previous year, accounting for over half of the indirect costs.

Only 11.9% of our working patients suffered permanent working disability. This figure is in contrast to the data published in other countries, where the mean working disability rate among FM patients was found to be about 25% (2, 23), and coincides with the results of a Spanish epidemiological study on the prevalence of rheumatic diseases, in which the permanent disability rate among FM patients was 11.5% (24).

FM was of increased severity among patients requiring sick leave and even greater among the patients with permanent working disability. These data suggest that the working days lost and the permanent working disability are

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directly related to the severity of the disease, as estimated in this study. Furthermore, we also found that the patients who were already permanently off work continued to be the greatest resource utilisers. The positive correlation between resource utilisation, work status and the severity of the disease has sense, but the reasons for this relationship cannot be answered with this correlational study.

Non-drug therapies accounted for the largest proportion of the health care costs, with an amount three times greater than the cost of drug treatment. This parameter is difficult to compare among different studies, since each study contemplates different treatment modalities.

Massages generated the greatest cost, though the published systematic reviews have shown little evidence of the efficacy of massages (25). Other treatment modalities that have shown little evidenced efficacy were also commonly used among our patients.

Surprisingly, although it is known the great importance that psychosocial factors play in FM as well as the good evidence about the efficacy that some psychological therapies have shown in the treatment of these patients (26), the number of sessions of psychological therapies in our study was very low.

It is necessary to stress that optimum resource utilisation requires the application of treatments of demonstrated efficacy, since among other considerations, the Spanish National Health System does not cover most of the nondrug therapies with the exceptions of physiotherapy, which is covered only in part, and psychotherapy, in which the low number of clinical psychologists makes very difficult the utilisation of this modality. This means that treatments of this kind must be paid by the own patient a situation that further worsens the personal economical burden of the disease. The fact that patients are using many non-pharmacological therapies of unproven efficacy may indicate that actual treatment for FM does not satisfy patients' expectations. What is needed is a new approach on treatment and resource utilisation.

A tendency towards increased health

care resources by FM patients was previously noted by Wolfe *et al.* (1), who reported a gradual increase in the direct costs over a period of 7 years. On comparing medical visiting rates in databases of other countries, patients with FM are seen to visit 2-4 times more often than average patients (2, 5).

The performance of complementary tests also increases the health care costs. In our study, such tests represented almost 15% of the total cost, being equivalent to approximately onehalf of the cost of the medical visits. Of note is the fact that over 40% of the costs resulting from complementary studies was due to magnetic resonance imaging, which in such patients only serves to discard other comorbidities. The important degree of discomfort and functional disability caused by FM leads patients to seek solutions that quite probably explain this large number of medical visits and tests. A greater implication in patient management on the part of primary care physicians would greatly reduce the health care costs of FM.

During the 10 years prior to the diagnosis of FM, the number of visits is seen to increase slowly, with a marked rise in the last three-year period (4). Once FM is diagnosed, the number of visits decreases, and subsequently returns to the previous levels after three years (4). The total cost is seen to decrease once the disease has been diagnosed showing the diagnosis of FM thus appears as a cost-effective procedure (27). A delay in the diagnosis of the disease therefore appears to be another factor contributing to the high health care costs of FM.

Clinical units with health care professionals trained in treating FM patients would reduce time of diagnosis using a lesser number of medical visits and diagnostic tests. Moreover, a multidisciplinary approach using a combination of the best evidenced efficacy therapy modalities may conduct to a best cost effective treatment of these patients saving direct costs for the health care system as well as for the patient. An early diagnosis of FM followed by the best treatment choice probably would also reduce productivity losses improving indirect costs, the most important chapter in the economic burden of FM. Specialised clinical units may play an important role in the consecution of this objective.

In our study we found a correlation between the economical costs and the severity of FM, whereby patients with a poorer clinical condition were the individuals with the greatest health care resource utilisation and costs. The factors that best predicted total economical cost were functional disability, depressive symptoms, other comorbidities, and younger age. Similar findings have been reported by other investigators (1, 22). The fact that comorbidities predict total costs suggests that not all costs may be directly attributable to FM.

The main limitation of our study is that the patients in this cohort were seen in specialised public rheumatology clinics, a fact that may imply increased severity compared with those patients seen in primary care, and therefore greater costs that could not be extrapolated to the global population of patients.

The way to obtain information about health care use resources and its associated costs should be cautiously considered in our study. The structured interview to the patient has some methodological limitations due to validity studies comparing with other forms of retrieving information have not been performed. This is especially certain for non-pharmacological treatments where its heterogeneity makes difficult its identification and cost quantification in some instances.

Another limitation derives from the Spanish Health System, which offers universal coverage; as a result, abusive patient utilisation of resources may contribute to increase the costs. Lastly, in our study we did not include the costs of productivity losses in housewives or their caregivers, the help required by some patients, more costly transport due to the limitations, or adjustments in the home, which may increase the computed costs.

In this work, resource use and costs were calculated specifically for FM. Hospital admissions and drug for any other comorbidity were excluded of the analysis. However, it is difficult to

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know how many of the medical visits and tests can be attributed to other comorbidities and how much may increase the economical costs associated to FM in our work.

Nevertheless, the results of a study such as ours are necessary to establish a health care strategy destined to improve the cost-effectiveness of FM management. Knowledge of the most important cost components helps define where specific intervention is needed.

In summary, patients with higher total costs showed the greatest disease involvement. The indirect costs accounted for most of the economic burden of FM. Both, direct and indirect costs are significantly correlated to disease severity, the degree of functional disability, the presence of depressive symptoms, the existence of comorbidities, and a younger patient age. Patients with permanent working disability present more severe disease.

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