Prospective study of the use of healthcare resources and economic costs in patients with fibromyalgia after treatment in routine medical practice

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**ICAF: Indice Combinado de Afectación de la Fibromialgia (Combined Index of Severity of Fibromyalgia).*

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ABSTRACT

Objective. *To estimate the burden and to prospectively analyse resources utilisation and costs in a cohort of treated patients with fibromyalgia (FM) in daily practice.*

Methods. *Prospective, observational, multicentre, 3-month study in 232 patients with FM according to the ACR criteria (98% women, 47 years), with no concomitant systemic diseases, followed in rheumatology units. The control group consisted of 110 subjects without FM or any other systemic condition, paired by age and gender. Clinical assessment, use of healthcare resources and treatments, out-of-pocket expenses, occupational status, days off work, and calculation of lost workdays equivalents were recorded.*

Results. *Patients had worse clinical status, four times the control group's healthcare costs, twelve times its indirect costs and six times its total costs. After the treatment, there was significant clinical improvement in the patient group, the healthcare costs were significantly reduced in all components except for drugs costs, which increased ($p<0.001$), and out-of-pocket expenses, which remained unaltered. Indirect costs were reduced ($p<0.05$) in the FM group only, mainly due to fewer days off work. The patient group presented a significantly greater variation in montly total costs than the controls; -€193.75 ± 781.9 vs. -€26.22 ± 402.7, $p=0.006$. The patients who most reduced their healthcare costs were actively employed.*

Conclusions. *Treated patients with FM in daily practice improved their clinical status and were accompanied by a significant reduction in the cost of the illness. The extra cost of drugs is substantially compensated for by less use of other healthcare resources and fewer days off work.*

Introduction

Fibromyalgia (FM) is a widespread disorder of unknown aetiology that affects an estimated 1–4% of the general population (1). It may occur in 2.1–5.7% of the general adult population, mainly women, representing 10-20% of all rheumatology consultations and 5–8% of all primary care consultations. It is the most common cause of general and chronic musculoskeletal pain (2). This condition has acquired greater significance in recent years, becoming a public health problem of the first order. There are several reasons for this situation, including the high prevalence rate, the lack of information regarding its origin and pathophysiology, the lack of curative therapeutic options and the high degree of patient and professional dissatisfaction with current medical interventions.

Patients with FM have been regarded as great users of healthcare resources, with considerable disease-related costs (3-12). The healthcare costs derived from this health disorder may triple those of the average patient attended by general practitioners and included in the computerised national or private health system databases in some countries (7), double those of inflammatory disorders such as ankylosing spondylitis (8), and prove similar to other diseases classified as health problems of the first order (8-10, 13).

The total economic cost associated with a given disease depends on both direct healthcare and indirect costs. The former include medical visits, diagnostic studies, drug and non-drug therapies, alternative therapies and hospital admissions (14). Indirect costs are essentially attributable to loss of productivity associated with sick leave and disability payments due to permanent work disability (PWD) as a con-

sequence of the disease. This category may also include loss of productivity among housewives, payment for caregivers, the costs associated with patient transport due to limitations in mobility, home adjustments, etc. (14).

The scientific literature contains numerous publications about the cost of FM, most of which are retrospective analyses with a cross-sectional design or no control group, thus failing to identify the impact of medical interventions for fibromyalgia on the use of healthcare resources, associated sick leave and related costs for both the National Health System and society. The objective of this study was to estimate the economic burden on the National Health System and society and to prospectively analyse resources utilisation and costs in a cohort of treated patients with fibromyalgia (FM) in routine clinical practice in Spain.

Methods

Study populations

The study population was primarily urban, over 18 years of age and with a diagnosis of FM according to the American College of Rheumatology (ACR) criteria (15). It was recruited from 15 public rheumatology clinics throughout Spain to whom were refered by their family physicians, general practitioners or other specialist. A total of 232 patients with FM were included in the study, 228 women and 4 men, with a mean age of 47.73 years (SD=8.61). Patients presenting other concomitant diseases with severely impaired performance status, rheumatic inflammatory diseases, cardiovascular or pulmonary diseases with poor aerobic capacity, uncontrolled psychiatric diseases or who were involved in litigation processes, were excluded from the study.

A sample of healthy subjects matched by gender and age was also studied as a control group. The control group subjects were selected from among healthcare personnel and the companions of patients who attended the clinic for reasons other than FM, chronic lower-back pain, or chronic pain due to other causes. The control group was selected with the same exclusion criteria as the FM patient group, plus they could not have clinical symptoms compatible with FM or any type of musculoskeletal pain. The control group included 110 subjects, 106 women and 4 men, with a mean age of 46.01 years (SD=9.35). There were no significant age or sex differences between the two groups. All the patients and controls who signed the informed consent form were consecutively included.

Study design and data collection

Prior to the study, the investigators from the 15 participating centres met to unify the inclusion criteria and study procedures. The study was designed as a prospective, observational, multicentre and comparative *versus* a control group of healthy subjects, with a 3-months follow up, and was conducted from 2008 to 2009. The control group was used to test the differential costs of patients with FM in comparison with healthy subjects, and test the hypothesis that FM is associated with incremental cost to the society. At the first visit, demographic data, clinical characteristics, utilisation of healthcare resources, days of sick leave and shortened working days in the active population, and information about early retirement for usual working activity before the age of 65 were collected for patients and controls. After the patients completed the evaluation, they were prescribed the treatment considered most appropriate by the rheumatologist according to routine clinical practice. A final visit with a further evaluation was carried out after 3 months. The study protocol was approved by the Independent Ethics Committee of Hospital Gregorio Marañón (Madrid, Spain).

Clinical evaluation

A clinical evaluation was carried out on patients and controls using the recently developed ICAF self-assessment questionnaire (16). ICAF evaluates emotional aspects (anxiety and depression) and their impact on social aspects. It also evaluates the patient's performance status, fatigue, sleep quality, pain, and the way in which patients cope with the disorder. It comprises four factors; Emotional, Physical, Active Coping and Passive Coping, as well as a global score. High scores in Emotional, Physical, Passive Coping and global score indicate a poorer clinical status. High scores in Active Coping indicate an improved clinical status.

Treatments used during the study

All the FM patients initiated treatment of their syndrome with a variety of drugs regularly used in such patients in routine medical practice. The participating rheumatologist were free to chose the medication they considered more appropriate in each case according with available drugs in the country that are usually prescribed for such condition. These, included anti-depressants, relaxant drugs, benzodiazepines, analgesics non-narcotics, anticonvulsants, non-steroidal anti-inflammatory drugs (NSAIDs), or minor opioids, and they could be prescribed alone or in combination using standard doses. The control group received no treatment but continued to take any medication prescribed for other reasons.

Use of healthcare and non-healthcare resources and work productivity

Information regarding the use of healthcare resources in the last month was obtained from centre records and a personal interview with the patients. Visits or appointments in primary healthcare centres, referrals to specialists, pain clinic visits, investigations and diagnostic tests, visits to emergency rooms, hospitalisations and drug prescriptions were recorded. Information about non-pharmacological therapies such as acupuncture, physiotherapy, psychological therapy, relaxation techniques etc., and out-of-pocket expenses (special food because of their illness, transportation to visit physician or medical facilities, in-house devices for rehabilitation exercises) was also collected. Healthcare costs and out-of-pocket expenses (which are non healthcare costs) are the two components of direct costs.

Patients were also interviewed about the impact of their illness on their productivity at work in the last month. Information was collected about the number of days off, days working with symptoms/pain, and their average self-

perceived work productivity on these occasions (determined as 0% to 100% productivity). From these data, calculations were made of the number of lost-workday equivalents (LWDE), by applying the following formula: LWDE=W1 + W2 (1- P), where W1 is the number of days they were unable to work or perform everyday activities due to pain in the last month, W2 is the number of days working with FM symptoms in the same period, (1-P) is percentage of labour disability at work, and P the percentage of self-perceived effectiveness at work (17).

Estimation of costs

Calculation of the total cost per patient included direct costs (healthcare and non-healthcare costs) and indirect costs derived from LWDE. Different study concepts and their economic evaluation were as follows: a) complementary tests, including laboratory tests (mean cost per application), conventional radiology (fee per ordered test), and support tests (fee per ordered test); b) medical visits to primary care physicians, ordinary or urgent referrals to specialists, pain clinics or hospitals (adapted referral fee), and visits to emergency rooms; c) prescriptions (short-term, long-term, or requested medical prescriptions; market price per item), and d) non pharmacological treatments including number of sessions or times used. All of these accounted for the healthcare direct component of cost. The other component of direct cost corresponded to the out-of-pocket cost as they were declared by patients or subjects included in the study. The indirect component of costs corresponded to the lost-workdays equivalents as calculated before in case of labour active subjects. Also, subjects with permanent work disability (PWD) as a consequence of the disease were recorded (Table I).

Healthcare resource prices were obtained from the Drug Catalogue of the General Council of the Spanish College of Pharmacists for prices of drugs (18), from the Oblikue Consulting cost database for complementary tests and medical visit prices (19), and from experts and public prices in the case of non-drug therapies. We used public-sale recommended retail prices + VAT when available, matching the cheapest generic medications, or the cheapest branded pharmaceutical products in the absence of generic medication or a reference price. Indirect costs were calculated according to human capital methodology (14, 20, 21). Two main components of these costs were computed. The first were the LWDE due to sick leave in the active population, computed as the sum of the number of LWDE per month multiplied by average daily salary. Secondly, we added the social cost of patients with PWD. These costs were computed as a whole month's average salary (classified as opportunity cost). All costs were expressed in year 2010 euros and shown as mean monthly cost per patient.

Table I. Unit costs in year 2010.

Resource	Unit cost (€)	Source
Productivity		
Day off work	60.07	INE (Ref. 20)
Non-pharmacological treatment (per session)		
Physiotherapy	32.26	APTN[1]
Massage	42.47	APTN[1]
Electrotherapy	2.71	e-SALUD (Ref.19)
Relaxation techniques	13.57	APTN[1]
Hydrotherapy	6.18	e-SALUD (Ref.19)
Psychotherapy	21.49	GCCPS[2]
Acupuncture	37.16	APTN[1]
Osteopathy	53.09	e-SALUD (Ref.19)
Chiropractic	47.78	APTN[1]
Messotherapy	42.47	APTN[1]
Ozone therapy/oxygen therapy	2.63	e-SALUD (Ref.19)
Medical visits		
Primary care visit	21.22	e-SALUD (Ref.19)
Pain Unit visit	54.89	e-SALUD (Ref.19)
Visit to specialist	60.44	e-SALUD (Ref.19)
Emergency room	119.90	e-SALUD (Ref.19)
Complementary tests		
Blood test	25.16	e-SALUD (Ref.19)
X-ray	18.50	e-SALUD (Ref.19)
Doppler ultrasound scan	140.57	e-SALUD (Ref.19)
Magnetic resonance imaging	368.26	e-SALUD (Ref.19)
Mammography	52.61	e-SALUD (Ref.19)
CT scan	155.68	e-SALUD (Ref.19)
Electromyogram	135.57	e-SALUD (Ref.19)
Endoscopy	60.73	e-SALUD (Ref.19)
Bone densitometry	82.77	e-SALUD (Ref.19)
Bone scan	142.79	e-SALUD (Ref.19)

All costs are fees except days off work from the INE source. [1]APTN: Spanish Federation of Natural Therapies and Unconventional Therapies; [2]General Council of Colleges of Psychology of Spain.

Statistical analysis

Prior to analysis, the data were carefully reviewed to study the distribution of frequencies and check possible recording or encoding errors. The quality of the computerised data obtained was considered to be appropriate, and the legal confidentiality of the information was maintained. The statistical analysis compared FM patients with the control group as the primary endpoint. A second analysis evaluated the effect of grouping the FM patients into three occupational categories (active, PWD because of the disease and inactive (unemployed, housewives, students, retired, etc.) on how the use of healthcare resources and costs evolved. Missing data were imputed following two strategies; the vertical mean in its group for baseline visit missing values, and last observation carried forward (in this case the baseline value wich correspond to the worst-observation carried forward) for missing values in end-of-study visit, which was considered the most conservative procedure.

A descriptive univariate statistical analysis was conducted including analysis

of correlation between costs and clinical variables as well as differences between the initial and final visits in ICAF scores. To compare means, *t*-tests were used for continuous variables and non-parametric tests for categorical variables. For comparing means between more than two groups, an ANOVA test was employed. All tests used data from the baseline visits to test group homogeneity. A 2-factor ANOVA model was used to analyse the differences between the groups during the study, one with repeated measures (time) to compare both the mean monthly values of healthcare and non-healthcare resource use and overall and disaggregate costs at the baseline and final visits between the controls and FM patients (22-24). The Bonferroni correction was used to adjust for multiple comparisons. The monthly variations in the cost per patient between the baseline and final visit were analysed by a univariate general linear model (ANCOVA) with the baseline value as a covariable to analyse how costs evolved in FM patients according to occupational status (active, PWD and inactive). The gender effect was not analysed as most of the patients were women (98% of the sample). Age was also not included as a covariable as there were no significant differences in this variable between the FM patients and controls; 47.73 (SD=8.61) years *versus* 46.01 (SD=9.35) years.

The SPSSWIN statistical package, version 17.0 was used to carry out the statistical analysis and a $p<0.05$ level of statistical significance was established.

Results

On average, the FM patients received 3.33 (SD=1.95) drug substances from 6 different therapeutic groups, distributed as follows: antidepressants (60.3%), non-narcotic analgesics (45.7%), anticonvulsant agents (45.3%), NSAIDs (44.4%), opiates (35.3%) and benzodiazepines (33.6%).

The initial clinical evaluation showed significant differences in terms of a higher score, and therefore poorer status, in the patient group compared to the controls in all individual ICAF factors and overall scores. After three months of treatment, only the patient group showed a significant improvement in emotional, physical and active coping factors, as well as global ICAF score. There was no significant difference between the two visits in the passive coping factor (Table II).

Table II. Mean (± standard deviation) overall ICAF and factors (T scores) in the Fibromyalgia group (n = 213) at baseline and final visit.

Factors	Baseline	Final visit	*p*-values
Emotional	49.95 (9.14)	46.88 (7.11)	0.0001
Physical	50.64 (9.49)	45.77 (12.76)	0.0001
Active coping	48.78 (9.65)	50.14 (10.07)	0.038
Passive coping	51.68 (10.54)	52.46 (10.65)	0.287
Overall ICAF	51.03 (9.51)	47.41 (9.95)	0.0001

p-values correspond to between baseline and final visits comparisons using a paired *t*-test.

Use of resources and associated healthcare costs

Of the FM patients, 131 (56.4%) were actively employed, while 31 (13.4%) were classified as permanently disabled because of the condition. The rest were not actively employed (retired, students, housewives, etc.). Of the 131 actively employed patients, 49 (37.5%) had not had days off and worked full-time, while 82 (62.5%) had been on sick leave at some point in the last month. The mean monthly number of LWDEs decreased significantly during the study in the FM patients, from 12.7 (SD=12.3) to 11.7 (SD=12.7) days, $p=0.023$; while this was not observed in the control group, who went from 0.2 (SD=0.7) to 1.0 (SD=3.8) days, $p=0.273$. Tables III and IV compare the mean monthly use and associated costs of the healthcare, out-of-pocket expenses and indirect costs (loss of work productivity) in the FM patients to those in the controls, both at baseline and after starting specific disease-treatment for FM.

The patient group showed a higher frequency of resource use in most of the analysed components, both at baseline and after the 3-month follow-up. The differences were particularly significant in the number of medical visits, number of complementary tests and number of sessions of non-pharmacological therapies (Table III). While subjects in the control group did show negiglible variations in the use of healthcare resources or costs, patients with FM showed significant mean reductions in medical visits; -0.7 (2.9), $p<0.001$, particularly to specialists, number of diagnostis tests; -0.2 (0.7), $p<0.05$, and sessions of non-pharmacological therapies; -1.8 (14.5), $p<0.05$. On the other hand, pharmacological costs did not vary in the control subjects during the study. Nevertheless, FM patients showed changes in their baseline treatment, adding more specific drugs for the treatment of their condition. This was associated with a significant increase in the cost of this component of €27.8 (43.0), from approximately €32 per month to €60 ($p<0.001$, Table IV). However, the extra pharmacological cost derived from specific treatment of the disorder was clearly compensated for by significant reductions in the costs of the other components [non-pharmacological therapies and medical visits of -€44.2 (302.7) and -€49.0 (176.7), respectively $p<0.05$ and $p<0.01$], which gave rise to a significant decrease in total direct costs of -€92.3 (519.0), from €492 to €401/month, $p<0.01$. No significant variations in any of the cost components were found in the control subjects. It was also interesting to find that, despite the specific treatment, there was no change in the FM patients' monthly out-of-pocket expenses, although the significant reduction in the number of their LWDEs gave rise to a significant decrease in the indirect cost component, close to €80/month (Table IV), this not being found in the controls. Lastly, the reduction in the monthly cost of different FM cost components not only compensated for the greater pharmacological expenditure but also gave rise to a statistically significant reduction in the total monthly costs of the disorder at the final study visit by

Table III. Mean (± standard deviation) monthly use of healthcare resources per study group.

Resource	FM (n=232)		Control (n=110)		*p* between groups	
	Baseline	Final	Baseline	Final	Baseline	Final
No. of drugs	3.06 (1.65)	3.33 (1.95)	0.59 (1.15)	0.67 (1.14)	0.001	<0.001
Medical visits	2.98 (3.01)	2.29 (2.72)‡	0.53 (0.95)	0.50 (0.81)	<0.001	<0.001
Primary care	1.20 (1.80)	1.03 (1.63)	0.30 (0.52)	0.26 (0.50)	<0.001	<0.001
Specialists	1.49 (1.21)	0.87 (1.21)‡	0.0	0.18 (0.43)	<0.001	<0.001
Emergency room	0.31 (1.21)	0.20 (0.64)	0.0	0.04 (0.20)	0.009	0.013
Pain unit	0.05 (0.24)	0.11 (0.74)	0.44 (0.72)	0.0 0.024	0.151	
Investigations	0.49 (0.62)	0.38 (0.60)≠	0.27 (0.45)	0.15 (0.36)	0.001	<0.001
Plain x-ray	0.35 (0.55)	0.11 (0.39)‡	0.08 (0.28)	0.04 (0.20)	0.059	0.009
MRI	0.09 (0.29)	0.07 (0.35)	0.0	0.0 0.001	0.042	
Ultrasound scan	0.13 (0.50)	0.06 (0.32)≠	0.11 (0.32)	0.01 (0.10)	0.647	0.412
Others [a]	0.13 (0.50)	0.66 (1.26)≠	0.08 (0.39)	0.18 (0.48)	0.482	0.078
Sessions of non-pharmacological therapies	8.06 (12.99)	6.17 (11.56)≠	2.41 (7.66)	2.18 (6.77)	<0.001	0.001
Physiotherapy	2.06 (4.75)	1.40 (4.29)	0.55 (0.90)	0.69 (3.24)	0.011	0.140
Hydrotherapy	0.91 (3.39)	0.53 (2.21)	0.62 (2.75)	0.11 (0.99)	0.013	0.069
Massage	1.41 (3.41)	1.02 (2.07)≠	0.17 (0.57)	0.08 (0.36)	<0.001	<0.001
Electrotherapy	0.89 (3.33)	0.50 (2.77)≠	0.0	0.1 (0.10)	0.007	0.074
Psychotherapy	0.28 (0.97)	0.30 (1.02)	0.04 (0.38)	0.06 (0.44)	0.012	0.025
Relaxation	1.87 (6.16)	1.66 (5.63)	0.55 (3.20)	0.75 (3.69)	0.044	0.143
Acupuncture	0.08 (0.48)	0.09 (0.57)	0.05 (0.43)	0.04 (0.40)	0.640	0.458
Chiropractic	0.02 (3.33)	0.01 (0.21)	0.0	0.0	0.486	0.486
Osteopathy	0.09 (0.51)	0.02 (0.25)	0.01 (0.010	0.0	0.167	0.333
Ozone	0.05 (0.48)	0.0†	0.0	0.0	0.253	-
Mesotherapy	0.03 (0.37)	0.01 (0.14)	0.0	0.0	0.323	0.487
Homeopathy	0.28 (2.78)	0.17 (2.09)	0.0	0.0	0.293	0.419
Others [b]	0.46 (3.43)	0.42 (3.05)	0.07 (0.76)	0.0	0.237	0.165

[a]Other tests such as densitometry, CT scan, colonoscopy, cytology, biopsy, etc.; [b]Other sessions such as laughter therapy, ocular therapy, etc.; Values expressed as mean (standard deviation). ‡ $p<0.001$, † $p<0.01$, ≠ $p<0.05$ *vs*. baseline value in the intragroup comparison for variables showing statistical significant differences. *p*-values calculated by a 2-factor ANOVA with one repeated factor (time).

Table IV. Mean monthly costs (euros) in year 2010 associated with the use of healthcare and non-healthcare resources by study group.

Cost (euros)	FM (n=232)		Control (n=110)		*p* between groups	
	Baseline	Final	Baseline	Final	Baseline	Final
Direct healthcare costs	423.1 (414.8)	335.1 (381.4)†	114.9 (235.2)	81.9 (175.5)	<0.001	<0.001
Medical visits	150.8 (181.4)	101.7 (136.3)¶	28.0 (60.5)	25.3 (49.9)	<0.001	<0.001
Investigations	69.6 (155.7)	46.7 (192.6)	36.0 (108.0)	12.2 (61.5)	0.042	0.067
Pharmacological treatments	32.0 (39.7)	59.7 (50.2)¶	0.4 (1.1)	0.7 (2.3)	<0.001	<0.001
Non-pharmacological therapies	170.7 (283.4)	126.9 (222.1)≠	50.6 (143.5)	43.7 (122.2)	<0.001	<0.001
Direct non-healthcare costs (out-of-pocket)	68.9 (139.6)	65.9 (121.6)	19.4 (57.4)	13.4 (45.6)	<0.001	<0.001
Total direct costs	492.1 (483.0)	400.9 (450.5)†	134.3 (277.6)	95.3 (192.0)	<0.001	<0.001
Indirect costs	742.4 (735.1)	662.8 (759.7)≠	59.6 (295.7)	56.5 (227.6)	<0.001	<0.001
Total costs	1,234.5 (943.6)	1,063.7 (949.8)‡	193.8 (470.0)	151.8 (317.1)	<0.001	<0.001

Values expressed as mean (standard deviation). ¶ $p<0.001$, † $p<0.01$, ≠ $p<0.05$ *vs*. baseline value intragroup. Not significant when not specified. *p*-values calculated by a 2-factor ANOVA with one repeated factor (time).

approximately €167/month ($p<0.05$, Table IV).

The correlation analysis showed a weak, although significant, correlation between clinical (ICAF scoring) improvement after treatment and reduction in total costs (r=0.160, $p<0.02$). Of the different cost components, only the reduction in indirect costs showed a significant correlation with clinical improvement.

Analysis according to occupational status

When the actively employed patients are compared with those with PWD and the other inactive patients (retired, housewives, unemployed or others), statistically significant differences were observed in most of the healthcare cost parameters analysed and in the total costs variations at end of the study (Fig. 1A, B), with the exception of the cost of drugs and those paid by the own patient (direct non-healthcare costs). Figure 1A shows that these three groups had modest but significant increments in cost of drugs (mean increase of -€19.1±38.3, -€28.8±55.8, -€15.0±28.7, in actives, PWD and inactives respectively, $p<0.05$ in all cases *versus* baseline visit), although differences between each other could not be observed from an statistical standpoint. Cost variations at

the end of the study were statistically significant in the active group only in most of the analysed parameters; medical visits: -€39.7±149.4 (p<0.001), diagnostic tests: -€36.7±150.8 (p<0.01), non-pharmacological therapies: -€33.2 ±220.8 (p<0.05), total healthcare costs: -€90.0 ±366.9 (p<0.01), indirect costs: -€116.8 ±580.3 (p<0.01), and total costs: -€215.5±725.1 (p<0.001) (Fig. 1). Similarly, the active FM patients show significant reduction in indirect costs at the end of the study (Fig. 1B). Together with the reduction in healthcare costs, this gives rise to a significant and very considerable reduction in total costs (p<0.001, Fig. 1B), despite a significant increase in the cost of drugs. The patients with PWD showed similar reductions to the actively employed in terms of figures but the differences were not significant, probably because of the small number of patients in this situation. The inactive patients however did not show this cost reduction trend.

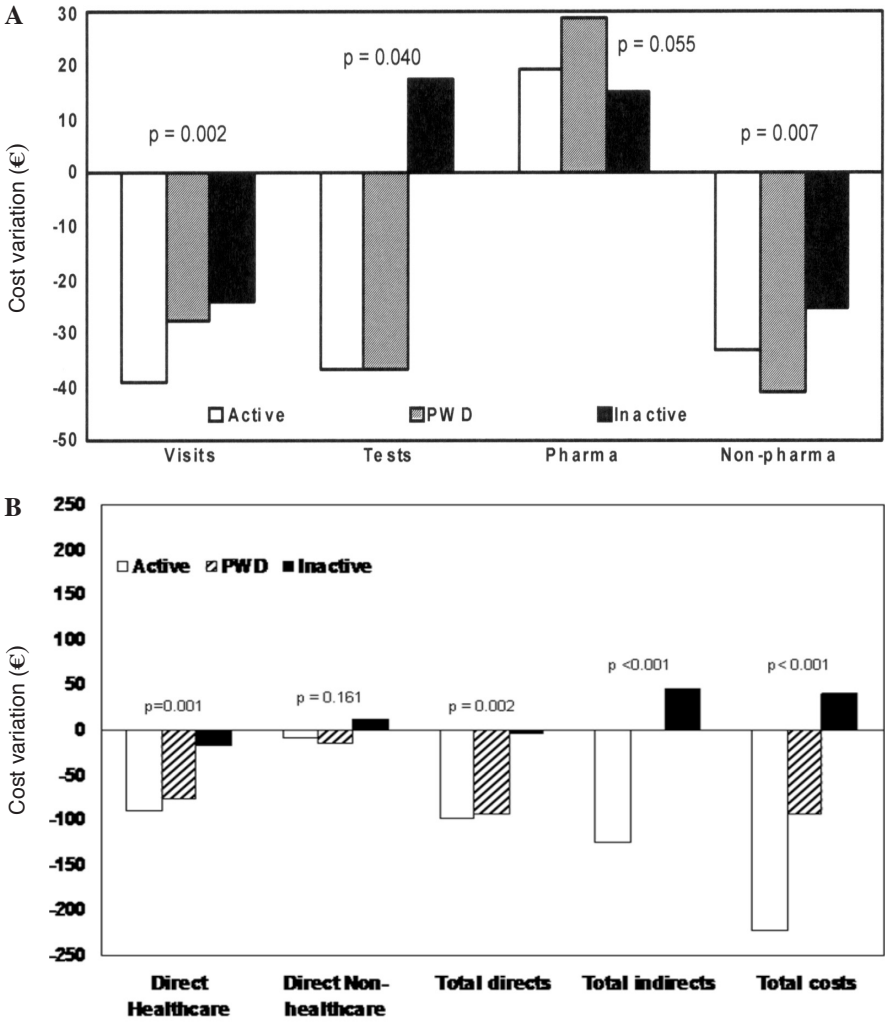

Fig. 1. Total monthly costs (Euros) variation during treatment broken down into the different components of healthcare costs (**A**) and overall costs (**B**). Comparisons are showed according to occupational status of patients with Fibromyalgia; Active, Permanent Work Disability (PWD) and Inactive.
Pharma: pharmacological treatments; Non-pharma: non-pharmacological treatments (massage, physiotherapy, etc.); PWD: permanent work disability.

Discussion

The results concerning the utilisation of resources and total healthcare costs in the patients in this study are similar to those obtained by us previously in a different patient sample (12). Basically, the direct costs in FM patients represent a third of the total costs. The most costly area is non-pharmacological therapies and the least costly is pharmacological treatment. Approximately two thirds of the actively employed patients show a loss of work productivity, which is the most costly area for indirect costs. These findings are also consistent with other publications (11, 25). It has been found that FM patients incur higher costs in all areas compared with other disorders. In studies on patients included in health insurance company databases, their healthcare costs are approximately double those of patients with other disorders (5, 7, 9, 11, 26). In our study, healthcare costs are four times higher, indirect costs are multiplied by 12 and the total cost is six times higher in FM patients than in our controls. These differences can be explained if we consider that studies conducted with healthcare databases use code ICD-9 for patient selection, although this code is not specific for FM and include other diagnostic possibilities such as chronic muscle or subcutaneous tissue pain, muscular degeneration and a common non-articular rheumatic condition that is characterised by muscle pain, tenderness, and stiffness. Patient selection according to this code could introduce considerable bias in the sample and, in this respect, we should note that the percentage of women in many of these studies ranges from 60% to 80%, and is even only 50% in some cases (9).

In most studies in FM patients using the ACR criteria for selection purposes, the percentage of women is always higher, close to 95%. In this study, the FM diagnosis was confirmed by a rheumatologist, the patients met the ACR criteria, 98% of them were women and they were therefore representative of the type of FM patient visiting rheumatologists in routine clinical practice. We therefore believe that the economic costs found in the study are closer to the reality of this disorder.

One of the study's most interesting findings was that the treatment of FM patients in routine practice is capable of improving their clinical status. This clinical improvement is accompanied by fewer medical visits, examinations, non-pharmacological therapies and days off work. The only cost increase is found in pharmaceutical costs, which grew from 2.6% to 5.6%, with a slight increase in the number of drugs used.

This increase in cost is probably because the drugs used are more expensive and not because more drugs are used to treat these patients. In our study, this increase in pharmaceutical cost is substantially compensated for by less use of other resources, leading to a significant reduction of up to 14% in total costs.

Other authors have also found that the diagnosis of FM significantly reduces the use of resources (27), although there are signs that in 2 to 3 years, said use grows again to its original level (6). This is still a controversial issue, as a recent study found that resource and drug use is higher a year after diagnosis than before diagnosis, although it is not known whether there was a clinical improvement with the treatment in question (28). It is easy then to conclude that the first step in the strategy for controlling spending in these patients is that FM should be diagnosed as early as possible. Control of the pharmaceutical costs, one of the most important areas of all economic healthcare studies as it is usually one of the most costly components, is not so important in FM, as it only represents 5.6% of the total cost of the disorder, equivalent to 14.9% of its healthcare costs. In FM, the most costly components are the indirect costs derived from days off work, which represent up to 62% of the total cost, followed by non-pharmacological therapies with 11.9%, medical visits and complementary tests. Therefore, a strategy aimed at reducing the most costly areas will always be more effective.

Out-of-pocket expenses are not often studied in FM patients. This study calculated that they represent approximately 6% of the total cost. It was recently found that the out-of-pocket expenses of patients with rheumatic conditions grow by 7% per year (29). In FM patients, on whom the economic impact of the disease is already significant due to losing or having to leave their jobs (9), such an increase would represent an additional burden, increasing the negative impact of the disorder and reducing the possibility of other treatments not financed by the National Health System which depend exclusively on the patients.

Some studies have shown that the severity of FM is greater in patients with permanent working disabilities than in the actively employed (12). There is also a correlation between economic costs and severity; the poorer the patient's clinical status, the higher the associated costs (3, 12, 25). This study showed that the actively employed patients had the greatest reduction in resource use, direct, indirect and total costs after the treatment, unlike the patients with permanent working disabilities, suggesting that the early treatment of patients before the disorder has progressed could achieve better results in terms of use of resources and economic cost.

The main advantage of our study is that it is a prospective study conducted in routine clinical practice in patients diagnosed with FM who are treated with the drugs normally used in this type of disorder. Its main limitation is the short time between the two visits, making it difficult to extrapolate our results for longer periods of time. We need to know whether the effect of the pharmacological treatment applied remains or whether the clinical change and cost reduction is a temporary response linked to the introduction of a new treatment. It is therefore important to measure the impact of the treatment on consumption and total costs in the longer term. Another possible limitation is the way that information about healthcare resource use and associated costs was obtained. Structured patient interviews have some methodological limitations, as validity studies comparing them with other forms of retrieving information have not been conducted. We were unable to find some unit costs, including the cost of smoking cannabis, dance, laughter therapy and homeopathy in general although the number of patients is low and with small comsumption so we do not believe that this introduces significant bias. Finally, the representativity of the control group included here merit some comments. The group of healthy subjects was formed with age and sex matched subjects among companions' persons of the patients attending clinic of rheumatology. Even this approach is common in other studies, certain bias could not be completely ruled out. Nevertheless, controls were enrolled all over the country in participating centres meeting representativity to some extent. In addition, we enrolled near one control per two cases completing more than one hundred controls that guaranteed enough size for comparison purposes, and to test the differential costs of patients with FM in comparison with healthy subjects.

Conclusion

To sum up, despite these limitations, the treatment of patients with FM in routine clinical practice in rheumatology departments improves their clinical status and is accompanied with a significant reduction in the cost of the disorder, at least, in the short term. The extra pharmacological cost is substantially compensated for by the reduced use of other healthcare resources and the reduction in number of days off work.

Authors' contributions

JR, MAV and JEV conceived the study. JR, JRG , MAV and MSC participated in the statistical analysis and interpretation of the data. JR, JRG, MSC and MAV revised the data obtained and drafted the manuscript. All the authors read and approved the final manuscript. ICAF Group authors contributed only in the data acquisition.

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