Financial and Clinical Characteristics of Fibromyalgia: A Case-Control Comparison

Ana Palacio, MD, MPH; Claudia L. Uribe, MD, MHA; Hua Li, MD, PhD; John Hanna, MBA; Michael Deminski, MS, RPh; Jose Alvir, DrPH; Arthi Chandran, MPH; and Robert Sanchez, RPh, MS

Abstract

Objective: To compare healthcare utilization and costs between subjects with and without fibromyalgia (FM) using claims data from a large health benefits company in the United States.

Study Design: Retrospective cohort.

Methods: We analyzed 24 months of medical and pharmacy claims data comparing healthcare utilization and costs among Humana members diagnosed with FM to a propensity score matched control group without a diagnosis for FM. FM cases were identified as members aged 18 years and older, with at least 2 medical claims for International Classification of Diseases, Ninth Revision, Clinical Modification codes 729.0 and/or 729.1. The first medical claim for FM was utilized as the index date.

Results: A total of 9988 FM cases and 9988 controls were included in the analysis. Compared with controls, the use of pain-related medications by FM cases was approximately 2 times higher with opioids being used most commonly. FM cases utilized a mean (SD) of 22.5 (23.9) and 31.1 (26.6) outpatient services per year in the prediagnosis and postdiagnosis periods, respectively, compared with 14.8 (20.5) and 16.3 (24.5) among controls (*P* <.01). Office visits, tests, and procedures represented the majority of utilization. During the postdiagnosis period, the mean per-patient per-month costs for outpatient services among FM cases was \$377 (\$760) and \$217 (\$740.87) among controls (*P* <.01).

Conclusion: FM cases had significantly higher utilization and costs compared with controls. Office visits, tests and procedures, and the use of pain-related medications accounted for the largest absolute differences between the 2 groups.

(Am J Manag Care. 2010;16:S118-S125)

For author information and disclosures, see end of text.

PBP00992C

ibromyalgia (FM) is characterized by widespread pain and is accompanied by a variety of comorbidities such as fatigue, abnormal sleep patterns, functional bowel disturbances, cognitive dysfunction, anxiety, depression, and genitourinary symptoms.1 Patients with FM experience disability and reduced health-related quality of life.² The prevalence of FM is 2% in the general population, with a higher frequency among females. In recent years, at least 3 sets of guidelines have been developed by different medical organizations in an attempt to standardize the treatment of this condition (American Pain Society, European League Against Rheumatism, Association of the Scientific Medical Societies of Germany). 3-5 The current recommendations suggest that treatment should be multimodal, stepwise, and inclusive of both nonpharmacologic components, such as exercise programs, cognitive behavior therapy, and spa therapy, 6 and pharmacologic components with medications. Therapies such as tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, and the newer generation antiepileptic drugs have been found to have a beneficial effect in randomized controlled trials.^{7,8} However, there is also evidence that the response to different therapies can vary significantly. A recent meta-analysis reported that only a few medications have shown clear benefits in randomized controlled trials, and many of these studies show only partial results in a subset of patients.9

Despite the availability of recommended therapies, diagnosing and managing FM remains challenging, thus many FM patients continue to suffer with chronic symptoms that generate high healthcare costs and indirect costs related to loss of revenue and absenteeism.^{4,8} In addition to high direct costs,¹⁰ FM is also associated with significant indirect disease-related costs.¹¹

Significantly higher total healthcare costs have been reported among patients with the diagnosis of FM when compared with the general population ^{12,13} and to costs associated with other painful conditions such as ankylosing spondylitis. ¹¹ Additionally, Silverman et al reported that the mean annual expenditures of FM were comparable to those of rheumatoid arthritis. ¹⁴ However, there continues to be a lack of a more detailed understanding in regard to the determinants of costs among patients with FM and how costs differ from those among the general population.

The purpose of this study was to compare healthcare utilization patterns and medical and pharmacy costs between subjects diagnosed with FM and subjects without FM of similar age, sex, and comorbidity burden. This study also examined pain management therapies comparing the FM group with the control group and identified potential opportunities for improvement in the management of FM.

METHODS

Data Source

Medical and prescription claims data from members in Humana's Commercial and Medicare populations were used in the analysis. Three electronic databases were merged: a member file containing demographic information for each member per encounter (age, sex, type of insurance, and geographical region); a medical file containing up to 9 recorded International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes per encounter, frequencies and costs per encounter, Current Procedural Terminology codes for procedures, J codes for in-office injections, and a pharmacy file containing all Generic Product Identifier numbers and National Drug Codes of pharmacy-dispensed medications per claim, frequencies, and costs per claim.

Study Population

Members were included in the study if they met the following criteria: 18 years or older, 2 or more medical claims for diagnosis ICD-9-CM codes 729.0 (fibrositis) and/or 729.1 (unspecified myalgia and myositis) between the dates of June 1, 2002, and March 1, 2007 (identification period), and at least 24 months of continuous enrollment (minimum 12 months prior and at least 12 months postindex date). The index date was defined as the first medical claim for FM.

A randomly selected propensity score matched non-FM control group was generated using age, sex, enrollment period, and the Deyo-Charlson modified comorbidity index (CCI), which includes 17 diseases that have been selected and weighted on the basis of the strength of their association with mortality.¹⁵

Study Period

A total of 24 months of data divided into a 12-month prediagnosis period (preindex) and a 12-month postdiagnosis period (postindex) was analyzed. For the purpose of analyses, the pre- and postdiagnosis periods were subdivided into 6-month blocks: 1 to 6 months preindex, 7 to 12 months preindex, 1 to 6 months postindex, and 7 to 12 months postindex.

Definitions

Pain-related medications were defined as analgesics or adjuvant medication based on the World Health Organization guidelines initially developed for cancer pain relief. ¹⁶ This category included opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), antimigraine, antidepressants, antiepileptics, benzodiazepines, muscle relaxants, steroids, and sedatives. All other medications were classified as non–pain-related.

Outcomes

Healthcare costs and utilization were categorized into 4 service categories as follows: outpatient, emergency department (ED), inpatient, and pharmacy. The outpatient category was subdivided into office visits (which included primary care visits and specialty visits [excluding psychiatry visits, which were evaluated separately]), tests and procedures, rehabilitation services and durable equipment, and psychiatry visits. The inpatient category was subdivided into hospitalization and long-term facility. The pharmacy category was subdivided into pain-related and non-pain-related. The ED category included exclusively ED visits. Healthcare utilization was measured as the number and percentage of subjects utilizing the service or medication (percentage utilization). Healthcare costs included net paid amount by Humana or a third party and the amount paid by the member, including copayments and deductibles. Reimbursed amounts were used in all analyses of healthcare costs. Comparisons were made between the pre- and postdiagnosis periods and between cases and controls.

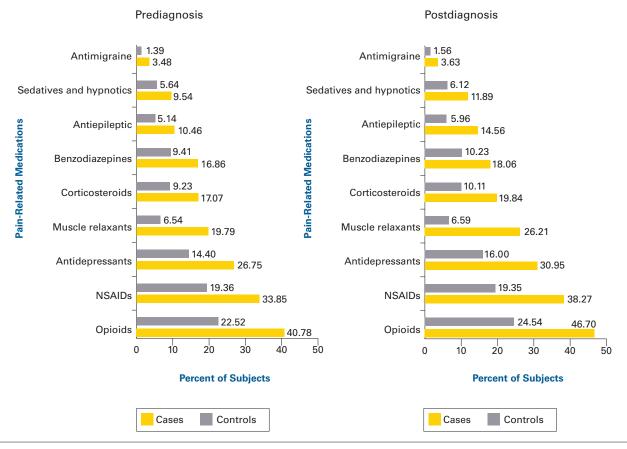
Statistical Analysis

Descriptive statistics were produced for each set of the study measures, with mean/standard deviation reported for continuous variables, and frequency counts for categorical variables. Statistical significance of differences pre- and postdiagnosis as well as for differences among cases and controls was calculated using paired t test for normally distributed continuous measures and a Wilcoxon signed-rank test for nonnormally distributed data. McNemar's test was used to determine the statistical significance of differences in categorical measures. SAS Version 9.1 (SAS Institute Inc, Cary, NC) was used for all statistical analyses.

RESULTS

A total of 9988 FM cases and 9988 propensity score matched controls were included in the analysis. Both cases and controls had a mean age of 55 years, were predominantly female (69.0% for cases and 68.4% for controls; P = .38), and were more commonly enrolled in a commercial health plan

■ Figure 1. Pain-Related Medication Use 1 Year Pre- and Postdiagnosis



NSAIDs indicates nonsteroidal anti-inflammatory drugs.

When compared with the controls, the cases were more likely to use all classes of pain-related medications, both pre- and postdiagnosis. The percentage of members utilizing opioids, NSAIDs, antidepressants, and antiepileptics was approximately 2 times higher among cases when compared with controls during the entire follow-up visit.

(66.2%). The mean CCI score was 0.66 for both cases and controls.

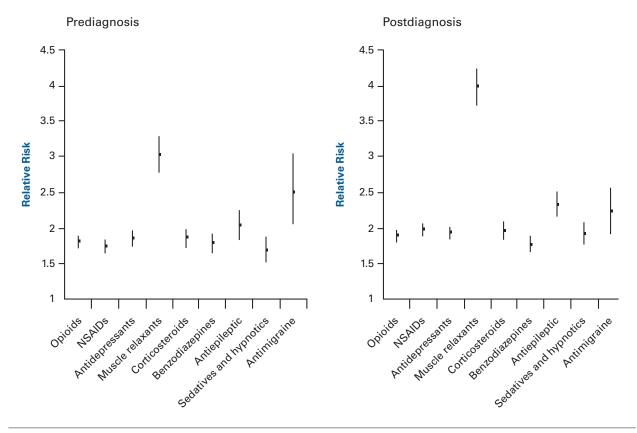
The most common primary diagnoses during the preindex period among the cases included spondylosis, intervertebral disc disorders, and other back problems (44.4%), other upper respiratory infections (34.6%), other connective tissue disease (34.6%), essential hypertension (34.2%), and other nontraumatic joint disorders (33.1%) (list of diagnoses available in **eAppendix A** at **www.ajmc.com**). Among the FM cases, a higher percent of subjects presented these comorbidities during the preindex period, as compared with the controls (*P* <.001).

Pain-Related Medication Utilization

The most frequently used pain-related medications among the FM cases before and after the diagnosis were opioids, followed by NSAIDs, antidepressants, muscle relaxants, corticosteroids, and benzodiazepines. The least frequently

used were antimigraine, sedatives and hypnotics, and antiepileptics (Figure 1). FM cases also experienced a statistically significant increase (P < .001) on the percent of subjects utilizing all classes of pain-related medications postdiagnosis, except for antimigraine medications. When compared with the controls, the cases were more likely to use all classes of pain-related medications, both pre- and postdiagnosis (Figure 1). During the prediagnosis period, FM patients were between 1.7 and 3 times more likely than the controls to use individual classes of pain-related medications. The relative risk was the highest for muscle relaxants and antimigraine medications, 3.0 and 2.5, respectively, although the absolute value of antimigraine medication use was very low (Figure 2). During the postdiagnosis period, the relative risks for the use of pain-related medications had minor variations when compared with the prediagnosis period. The percentage of members utilizing opioids, NSAIDs, antidepressants, and antiepileptics was approximately 2 times higher among cases

■ Figure 2. Relative Risk and 95% Confidence Intervals for Pain-Related Medication Use Among Cases Compared With Controls



NSAIDs indicates nonsteroidal anti-inflammatory drugs.

During the prediagnosis period, patients with fibromyalgia were between 1.7 and 3 times more likely than the controls to use any class of pain-related medications. The relative risk was the highest for muscle relaxants and antimigraine medications, 3.0 and 2.5, respectively.

when compared with controls during the entire follow-up period. Although the frequency of use of the different classes of pain-related medications was significantly higher among the cases, the distribution of the classes was similar between cases and controls.

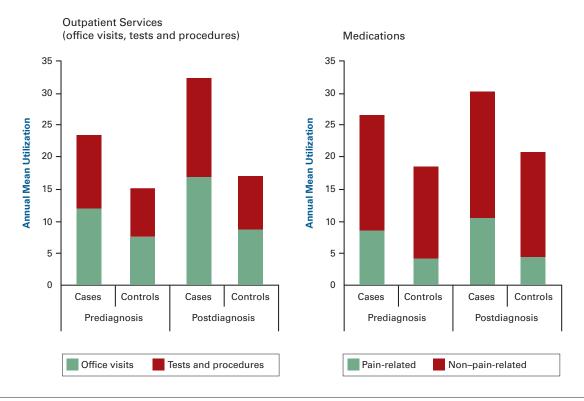
Healthcare Utilization and Costs

Overall, the mean annual utilization for all types of services was greater among FM cases when compared with controls, both before and after the FM diagnosis, with the exception of long-term care. The FM cases utilized a mean (SD) of 22.5 (23.9) and 31.1 (26.6) outpatient services (including office visits, tests and procedures, rehabilitation, durable equipment and psychiatric-related services) per year in the prediagnosis and postdiagnosis periods, respectively, compared with 14.8 (20.5) and 16.3 (24.5) among controls (P <.0001). Office visits, and tests and procedures represented the majority of utilization; however, statistically signifi-

cant differences were observed in all categories of outpatient services (Figure 3). Compared with controls, the FM cases were more likely to use ED services, inpatient hospitalization, and any type of medication in both the pre- (P < .05) and postdiagnosis (P < .0001) periods (eAppendix B available at www.ajmc.com).

Among the FM cases, there was an increasing trend in utilization of office visits, tests and procedures, rehabilitation, use of durable equipment, psychiatric, ED, and inpatient services, as well as use of pain-related medications. This trend was evident from 12 months prediagnosis through 6 months postdiagnosis of FM, with a subsequent drop in utilization after 6 months postdiagnosis (Figure 4). Conversely, a slight increasing trend was observed among controls for office visits, tests and procedures, rehabilitation, use of durable equipment, and pain-related medications throughout the entire study period (for comparison purposes, the graphs are labeled pre- and postdiagnosis although there was no index diagnosis

■ Figure 3. Healthcare Utilization by Type of Service: Annual Mean Utilization



The graphs show a greater annual mean utilization of office visits, tests and procedures, and medications (pain-related and non-pain-related) among the cases compared with the controls, both in the pre- and postdiagnosis periods.

Note: Graphs for emergency department, hospitalization, rehabilitation and durable equipment, and psychiatric visits are available online (eAppendix B at www.aimc.com).

among controls). Non–pain-related medications showed an increasing trend among cases and controls throughout the study period. Utilization of ED and inpatient services among controls had an inconsistent trend throughout the study, with very small variations by 6-month periods (eAppendix C available at www.aimc.com).

Healthcare costs of FM cases and controls followed the utilization patterns described above. During the preindex period, the mean (SD) per-patient per-month (PPPM) cost for outpatient services was 27.3% higher among the FM cases compared with the controls, \$261.23 (\$484.96) and \$189.92 (\$630.88), respectively (P < .0001). Likewise, during the postdiagnosis period, the mean (SD) PPPM cost for outpatient services was 42.4% higher among the cases compared with the controls, \$377.36 (\$760.75) and \$217.99 (\$740.87), respectively (P < .0001). PPPM costs among the cases were also higher in comparison to controls for ED, as well as for pain-related and non-pain-related medications, both pre- (P < .001) and post- (P < .0001) diagnosis (Table). Overall, medication costs were 29.6% (prediagnosis) and 32.3% (postdiagnosis) higher among the cases, with pain-

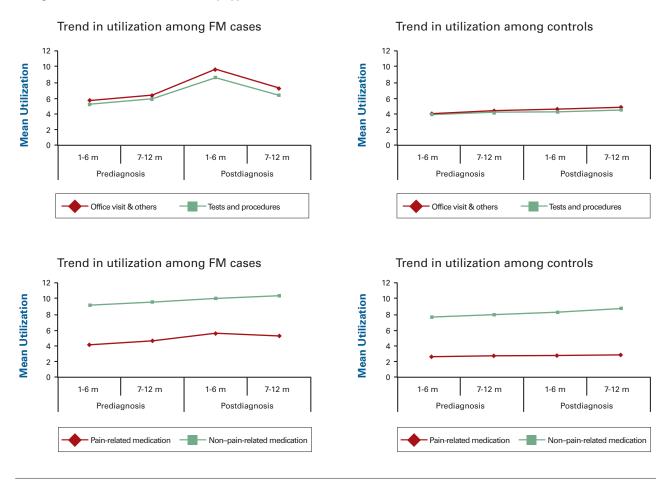
related medications accounting for most of the difference. Inpatient costs among the cases were slightly lower (0.6%) in the prediagnosis period and slightly higher (5.8%) in the postdiagnosis period when compared with the controls.

DISCUSSION

The FM cases used significantly more health services than the controls, particularly during the 12 months prediagnosis and the 6 months postdiagnosis. All categories of services were more common among the cases, with the exception of long-term care. Office visits, tests and procedures, and use of pain-related medications accounted for the largest absolute differences between the 2 groups. The significant increase in utilization during the 6 months before and the 6 months after the initial FM diagnosis may be due to additional office visits, tests, and procedures performed to confirm this diagnosis by excluding other possible causes for the symptoms.

Compared with the controls, the FM cases were associated with a greater prevalence of comorbid conditions, which

■ Figure 4. Healthcare Utilization by Type of Service: Trends in Mean Utilization



The graphs illustrate an increasing trend in utilization of office visits, tests and procedures, and pain-related medications from the first 6 months prediagnosis through the first 6 months postdiagnosis among the cases, while a slight increasing trend is observed throughout the study period among the controls. Non-pain-related medications have a slight increasing trend among cases and controls throughout the study period.

Note: Graphs for emergency department, hospitalization, rehabilitation and durable equipment, and psychiatric visits are available online (eAppendix C at

are not included in the CCI. The greater prevalence of comorbidities such as hypertension and dislipidemia among FM cases has been previously reported, 17,18 but the mechanisms for these associations are unknown. The increased prevalence may reflect a more intense medical-seeking behavior resulting in an increased opportunity to diagnose some conditions more often among the cases compared with the controls. However, the possibility of a common causal pathway, to our knowledge, has not been studied. Although it was not possible to evaluate the specific impact that these conditions may have in the overall costs among FM cases, the analysis revealed a similar increase in the utilization of non-painrelated medications for the cases and the controls during the follow-up period. In contrast, a significantly greater increase was noted in the use of pain-related medications among the cases, supporting a hypothesis that the increased rate of out-

patient visits was mainly directed at the management of the FM symptoms.

The most commonly filled pain medication prescriptions were similar between the cases and the controls both in the pre- and the post-FM diagnosis periods, although with significantly lower percentages of utilization among the controls. This finding is consistent with previously published studies¹⁷ and provides evidence about the preference among physicians for the use of opioids and NSAIDs for pain management (FM- and non–FM-related). An adequate dissemination of the FM treatment guidelines should generate a shift in the classes of medications used post-FM diagnosis, but this shift was not observed. The use of antidepressants is not only widely accepted as efficacious for general pain management, ^{19,20} but it is considered first line of treatment in FM.³ However, only 30% of the FM cases filled prescrip-

www.aimc.com).

■ Table. Per-Patient per-Month Costs (\$US) by Type of Service

	Prediagnosis			Postdiagnosis		
	FM (n = 9988)	Control (n = 9988	3)	FM (n = 9988)	Control (n = 9988)	
Characteristic	Mean (SD)	Mean (SD)	P	Mean (SD)	Mean (SD)	P
Outpatient						
Office visit & others	128.92 (309.51)	104.57 (485.63)	<.0001	190.89 (522.63)	126.42 (607.90	<.0001
Tests and procedures	112.33 (229.38)	74.06 (222.81)	<.0001	152.89 (345.35)	79.17 (211.39)	<.0001
Rehabilitation and durable equipment	12.18 (53.56)	6.85 (48.03)	<.0001	21.18 (67.55)	8.11 (51.72)	<.0001
Psychiatry	93.58 (572.89)	53.32 (540.54)	<.0001	150.04 (755.54)	51.72 (316.49)	<.0001
Any of above	261.23 (484.96)	189.92 (630.88)	<.0001	377.36 (760.75)	217.99 (740.87)	<.0001
Emergency department	17.38 (64.71)	10.43 (48.45)	<.0001	22.67 (76.06)	12.12 (52.39)	<.0001
Inpatient						
Hospitalization	89.07 (444.95)	89.43 (471.29)	.0004	127.22 (507.07)	118.09 (595.92)	<.0001
Long-term facility	3.03 (56.54)	3.23 (57.74)	.4704	6.69 (81.94)	8.04 (103.32)	.9457
Any of above	92.10 (454.96)	92.66 (484.62)	.0004	133.91 (531.95)	126.13 (633.34)	<.0001
Pharmacy						
Pain related	33.97 (104.99)	15.02 (70.17)	<.0001	47.11 (121.86)	17.95 (80.84)	<.0001
Non-pain-related	74.20 (134.62)	61.17 (131.16)	<.0001	86.59 (154.95)	72.61 (176.09)	<.0001
Any of above	108.17 (184.64)	76.19 (157.18)	<.0001	133.73 (215.01)	90.56 (201.00)	<.0001
Any of above	478.88 (878.6)	369.19 (1006.69)	<.0001	667.67 (1187.89)	446.79 (1241.31)	<.0001

tions for an antidepressant medication and only 15% filled prescriptions for an antiepileptic medication after the diagnosis of FM. Although FM cases were more likely to use these classes of medications than the controls, we expected a larger difference given the current guidelines for FM treatment.^{3,4,9}

In terms of healthcare utilization, there were statistically significant differences in mean annual utilization among the FM cases and the controls both before and after the diagnosis periods. Although the mean annual utilization among the cases was higher during the 12 months postdiagnosis, the trend showed a decline in services utilization during the second 6 months after the diagnosis was made, indicating a reduction in health-seeking behavior and work-up activities once the diagnosis has been confirmed. Further studies with a longer follow-up period are needed to investigate if this decreasing trend continues and if utilization stabilizes to prediagnosis levels or to levels similar to those among controls.

In this study, the diagnosis of FM was associated with higher healthcare costs as reported previously by other investigators. ^{14,17,21} Costs were significantly higher among the FM cases for all categories of care, but most of the costs were driven by excess outpatient visits, excess tests and proce-

dures, and excess use of pain medications with respect to the controls. A recent European study also revealed that primary care costs were significantly higher among subjects with FM.18 Although some of these studies have reported larger differences in costs, 17,18 they only matched the groups for age and sex. In contrast, our study incorporated a propensity score match of the comorbidity index with the intent to capture a more accurate measure of cost differences. One study described that the costs associated with FM were similar to those of rheumatoid arthritis, a known debilitating rheumatologic entity.14 In addition, Sicras-Mainar et al18 found correlations between pain, patient function, depression symptoms, and healthcare costs, suggesting that adequate management of pain and depressive symptoms could potentially reduce medical costs. Findings from this study suggest there is considerable opportunity for improvement in the treatment of FM.

The following limitations from our study are worth noting. The use of *ICD-9-CM* codes for the identification of subjects with FM has not been extensively validated, and the nature of claims data does not permit differentiation of pain-related medications prescribed specifically for FM from those prescribed to treat comorbid conditions. Another

potential limitation is the fact that the conditions that are not part of the CCI were not matched for and there were some conditions (eg, hypertension) that were more frequent among FM subjects and thus could potentially explain the higher utilization and costs found among FM cases. However, additional diseases were not included in the matching process to avoid risk of "overmatching," which could have masked the results in our study. The CCI is a validated tool to adjust for healthcare utilization and costs.¹⁵

CONCLUSION

Overall healthcare utilization and costs among insured FM cases were considerably higher than among matched non-FM controls, especially for outpatient services and pain-related medications. Pain management reflected the same class of preferences used for non-FM subjects and nonconcurrence with treatment guidelines. The study results suggest that the adoption of a more targeted and evidence-based approach to managing the disease once the diagnosis of FM is made potentially results in better control of FM symptoms. In theory, improved control of FM symptoms may also lead to cost reductions postindex.

Author Affiliations: From the Department of Internal Medicine Miller School of Medicine (AP), University of Miami, Miami, FL; Humana Inc, Health Services Research Center (CLU, HL, JH), Miami, FL; Pfizer, Inc. (MD, JA, AC, RS), New York, NY.

Funding Source: This study was funded by Pfizer, Inc. This supplement was funded by Pfizer, Inc.

Author Disclosures: Four authors (JA, MD, AC, RS) are employees as well as stockholders at Pfizer, Inc. Four of the authors (AP, CLU, JH, HL) served as paid consultants to Pfizer, Inc. during the conduct of this study and the development of this manuscript.

Authorship Information: Concept and design (AP, CLU, HL, JH, MD, JA, AC, RS); acquisition of data (HL); analysis and interpretation of data (AP, CLU, HL, JH, MD, JA, AC, RS); drafting of the manuscript (AP, CLU, JA, AC, RS); critical revision of the manuscript for important intellectual content (CLU, JH, MD, JA, AC, RS); statistical analysis (HL); obtaining funding (JH, RS); administrative, technical, or logistic support (CLU); and supervision (CLU, AC).

Address correspondence to: Ana Palacio, MD, MPH, Miller School of Medicine, University of Miami, 1120 NW 14th St, Ste 967, Miami, FL 33136. E-mail: apalacio2@med.miami.edu.

REFERENCES

- 1. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum.* 1990;33(2):160-172.
- 2. Wolfe F, Anderson J, Harkness D, et al. Work and disability

- status of persons with fibromyalgia. *J Rheumatol.* 1997;24(6): 1171-1178.
- **3. Carville SF, Arendt-Nielsen S, Bliddal H, et al.** EULAR evidence-based recommendations for the management of fibromyalgia syndrome. *Ann Rheum Dis.* 2008;67(4):536-541.
- **4. Goldenberg DL, Burckhardt C, Crofford L.** Management of fibromyalgia syndrome. *JAMA*. 2004;292(19):2388-2395.
- Klement A, Hauser W, Bruckle W, et al. [Principles of treatment, coordination of medical care and patient education in fibromyalgia syndrome and chronic widespread pain]. Schmerz. 2008;22(3):283-294.
- 6. Hauser W, Bernardy K, Arnold B, Offenbacher M, Schiltenwolf M. Efficacy of multicomponent treatment in fibromyalgia syndrome: a meta-analysis of randomized controlled clinical trials. *Arthritis Rheum*. 2009;61(2):216-224.
- 7. Hauser W, Bernardy K, Uceyler N, Sommer C. Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis. *JAMA*. 2009;301(2):198-209.
- 8. Hauser W, Bernardy K, Uceyler N, Sommer C. Treatment of fibromyalgia syndrome with gabapentin and pregabalin—a meta-analysis of randomized controlled trials. *Pain*. 2009;145(1-2):69-81.
- 9. Hauser W, Thieme K, Turk DC. Guidelines on the management of fibromyalgia syndrome—a systematic review. *Eur J Pain*. 2010:14(1):5-10.
- **10.** Rao SG, Clauw DJ. The management of fibromyalgia. *Drugs Today (Barc)*. 2004;40(6):539-554.
- 11. Boonen A, van den Heuvel R, van Tubergen A, et al. Large differences in cost of illness and wellbeing between patients with fibromyalgia, chronic low back pain, or ankylosing spondylitis. *Ann Rheum Dis.* 2005;64(3):396-402.
- 12. Henriksson CM, Liedberg GM, Gerdle B. Women with fibromyalgia: work and rehabilitation. *Disabil Rehabil*. 2005;27(12):685-694.
- 13. Robinson RL, Birnbaum HG, Morley MA, Sisitsky T, Greenberg PE, Claxton AJ. Economic cost and epidemiological characteristics of patients with fibromyalgia claims. *J Rheumatol*. 2003;30(6):1318-1325.
- 14. Silverman S, Dukes EM, Johnston SS, Brandenburg NA, Sadosky A, Huse DM. The economic burden of fibromyalgia: comparative analysis with rheumatoid arthritis. *Curr Med Res Opin.* 2009;25(4):829-840.
- **15. Deyo RA, Cherkin DC, Ciol MA**. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol.* 1992;45(6):613-619.
- **16. World Health Organization**. *Cancer Pain Relief*. Geneva, Switzerland: World Health Organization; 1996.
- 17. Berger A, Dukes E, Martin S, Edelsberg J, Oster G. Characteristics and healthcare costs of patients with fibromyalgia syndrome. *Int J Clin Pract.* 2007;61(9):1498-1508.
- **18. Sicras-Mainar A, Rejas J, Navarro R, et al.** Treating patients with fibromyalgia in primary care settings under routine medical practice: a claim database cost and burden of illness study. *Arthritis Res Ther.* 2009;11(2):R54.
- McCleane G. Antidepressants as analgesics. CNS Drugs. 2008;22(2):139-156.
- **20. Barkin RL, Fawcett J.** The management challenges of chronic pain: the role of antidepressants. *Am J Ther.* 2000;7(1):31-47.
- 21. Annemans L, Wessely S, Spaepen E, et al. Health economic consequences related to the diagnosis of fibromyalgia syndrome. *Arthritis Rheum.* 2008;58(3):895-902.