Fibromyalgia: prevalence, course, and co-morbidities in hospitalised patients in the United States, 1999-2007

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ABSTRACT

Objectives. *To evaluate hospitalisation data for patients with a primary or secondary fibromyalgia (FM) diagnosis. We estimated the number of men and women with an FM diagnostic code and compared them across a number of demographic and hospitalisation characteristics; examined age-specific, population-based FM hospitalisation rates; and determined the most common co-morbid diagnoses when FM was either the primary or secondary diagnostic code.*

Method. *Hospital discharge data from the Nationwide Inpatient Sample (NIS) were used. Records were evaluated between 1999 and 2007 that contained the International Classification of Diseases, 9th Revision, Clinical Modification FM diagnostic code (729.1, Myositis and Myalgia, unspecified), the FM criterion used in large-scale health services studies.*

Results. *There were 1,727,765 discharges with a 729.1 diagnostic code (FM) during this nine-year span, 213,034 men (12.3%) and 1,513,995 women (87.6%). Discharges coded for FM increased steadily each year. The population-based rate of male FM discharges rose gradually across the lifespan; the rate for women rose sharply but then declined after age 64. Few differences between men and women across demographic and hospitalisation characteristics were evident. The most common co-morbidities with FM as the primary diagnosis were non-specific chest pain, mood disorders, and Spondylosis/intervertebral disc disorders/other back problems. Most common primary diagnoses, with FM as a secondary diagnosis, were essential hypertension, disorders of lipid metabolism, coronary atherosclerosis/other heart disease, and mental disorders.*

Conclusion. *A substantial number of U.S. residents with FM were hospitalised over the study period. Further analysis of hospitalisation data from patients with FM may provide guidance for both research and treatment, with the goal of improved care for FM patients.*

Introduction

In 1904, Gowers observed a cohort of patients who presented with diffuse musculoskeletal pain, and his description of these patients began the fibromyalgia (FM) saga (1). Gowers believed that the perceived pain reported by these patients resulted from inflammation and, therefore, used the term fibrositis to describe it (2). Fibrositis did not garner widespread attention until the 1970s when the term was superseded by its present name, fibromyalgia (3). As FM gained popularity, many began to question its existence (4, 5). Over the last two decades, FM has stimulated a dramatic increase in research that grows in both frequency and complexity (6).

Definition

Patients with FM report chronic, diffuse, widespread, pain; multiple tender points; and an assortment of associated symptoms and co-morbidities (7). Many authors question FM as a diagnosis because objective measures do not exist (8). In 1990, the American College of Rheumatology (ACR) proposed formal classification criteria for FM and classified it as widespread pain (≥ three months) in all four body quadrants in combination with excess pain to palpation in 11 of 18 predetermined tender points (9). This classification criterion originally was designed for experimental use but now often is applied for diagnostic purposes. Many experts believe that the ACR definition is not sufficient and that the multiple symptoms associated with FM should be included in the diagnosis (10). Still others believe that the 11 tender point criterion may not be necessary to confirm the diagnosis (11) because tender points often fluctuate as exacerbating factors change (12, 13). Others favour

creating subgroups of FM patients (14), and recently, Wolfe *et al*. (15) have proposed a new case definition for FM.

Fibromyalgia and co-morbid conditions

Very few large FM cohort studies exist in which co-morbid disease states are systematically evaluated, and there is sparse data on men. Most information has come from clinical and community studies with differing research aims, methods, and samples. Many researchers, however, have attempted to identify conditions that co-occur with FM (16, 17). These co-occurring conditions can be divided into medical, psychiatric, and functional subtypes. Some of the most commonly associated medical conditions are rheumatologic diseases such as osteoarthritis, osteoporosis, Crohn's disease, rheumatoid arthritis, ulcerative colitis, systemic lupus erythematosus, psoriatic arthritis, and Behçet's disease (18, 19). Approximately 27% of patients with inflammatory bowel disease have concurrent FM, which occurs more commonly in Crohn's disease than ulcerative colitis (20). As many as 65% of patients with systemic lupus erythematosus, 55% with rheumatoid arthritis, 24% with psoriatic arthritis, and 10% with Behçet's disease have co-morbid FM (21, 22). Other non-rheumatologic conditions such as hypertension, thyroid disorders, diabetes mellitus, sleep apnea, restless leg syndrome, and migraine headache have been reported (18, 19). Reported co-prevalence for some of these diseases varies from 25–67% for osteoarthritis, 10–42% for hypertension, 12–40% for osteoporosis and 4–23% for diabetes (19, 23, 24). Much of this variability may be due to sampling method (community *vs*. clinical), age of subjects, and a predominance of female study participants.

Many unique associations with FM also have been reported (25). Further, an increased prevalence in FM has been reported in patients with the HIV, hepatitis C viruses, and thyroid antibodies (26, 27). Moreover, many women with FM have co-occurring breasts cysts, ovarian cysts, dysmenorrheal, premenstrual syndrome, and endometriosis (28).

FM has a high co-occurrence with psychiatric disorders (29). The prevalence of major depressive disorder (present and in one's lifetime), in fact, has been reported to range from 30-86% in FM patients (30-32). FM commonly is associated with anxiety, eating, bipolar, and substance use disorders (30, 33). In general, psychiatric disorders are associated with worse pain and quality of life in FM patients (34). Interestingly, other conditions have been associated with a lower prevalence of co-morbid psychiatric disorders in FM (35). The high prevalence of psychiatric disorders with FM has led some researchers to explore factors common to both diagnoses (30).

Not surprisingly, FM is associated with other functional disorders (36, 37). Prevalence figures for some of these disorders range from 32-77% for irritable bowel syndrome to 2-40% for chronic fatigue syndrome (38). Like all functional disorders, these remain both difficult to treat and explain.

Epidemiology

The first attempt to determine the prevalence of FM in American adults – a survey of rheumatologists – was published in 1977. Interestingly, academic rheumatologists reported cases of FM much less frequently than did community rheumatologists (2.0% to 6.0%, respectively (39)). Reports taken from rheumatology practices show fairly dramatic differences: low estimates of 3.3% and 6.1% (40, 41) and high estimates of 10% to 25% (42, 43).

In the adult general population, the widely-reported FM prevalence estimates are from a single study done in Wichita, Kansas (44). The reported prevalence was 2.0% overall, 3.4% in women and 0.5% in men. In a recent United States cohort study (45), FM prevalence was reported to be 3.7% (4.8% women and 1.3% men). Although the figures from the two studies are roughly comparable, the more-recent data may reflect an actual increase in FM prevalence.

Natural history of fibromyalgia

FM is increasingly being diagnosed in all age groups (44, 46, 47), and its frequency increases with age. In the Wichita Kansas study, FM prevalence increased progressively through the eighth decade and thereafter declined. This can be contrasted with studies from London, Ontario (Canada) in which FM began to decline dramatically in the seventh decade (47) and from the U.S. in which FM declined at approximately age 61 (45).

FM and hospitalisations

In two small studies outside of the U.S., investigators have reported hospitalisation rates, co-morbidities, and dispositions in FM patients. In a study of 522 patients hospitalised on internal medicine wards in Israel, 62% complained of pain, and 15% were diagnosed with FM. Of those diagnosed with FM, 91% were female (48). In a study of FM prevalence in 122 Turkish patients hospitalised with cancer, 10.7% were diagnosed with FM (49). In this study, FM was associated with worse health and mental health status, including quality of life measures. Conclusions drawn from these studies must be considered preliminary, however, given the small numbers of patients and unique settings.

Study purposes

The present study was designed to evaluate hospitalisation data for patients admitted with either a primary or secondary FM diagnosis. The first objective was to document the number of men and women with an FM diagnosis and to compare men and women across a number of demographic and hospitalisation characteristics (*e.g*. age, race/ethnicity, length of stay, and disposition). Second, was to examine age-specific, population-based FM hospitalisation rates for men and women. Third, was to determine the most common primary and secondary diagnoses among patients with FM (total and by gender). Such information may help clarify FM's prevalence, natural history, and patterns in hospitalised patients.

Method

Data

Hospital discharge data from the Nationwide Inpatient Sample (NIS), which is the largest all-payer inpatient care database in the United States (Agency

for Healthcare Research and Quality [AHRQ]) (50) was used in this study. NIS is one of several datasets developed as part of the Healthcare Cost and Utilisation Project (HCUP), a Federal-State-Industry partnership sponsored by the AHRQ. NIS approximates a 20-percent stratified sample of U.S. community hospitals, with the sampling frame covering about 90 percent of all hospital discharges in the U.S. (50). Annual NIS databases contain roughly seven to eight million records representing discharges from approximately 1,000 hospitals, and the dataset has been used to address similar questions (51).

Subjects

Discharge records between 1999 and 2007 containing either a primary or secondary (out of 15 diagnosis fields) *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) FM diagnosis code (729.1, Myositis and Myalgia, unspecified) were selected. There is no specific ICD-9-CM diagnostic code for FM, and, thus, the 729.1 criterion is used to represent FM in many large health services research studies. As the Center for Disease Control cautions, however, hospitalisation rates based on this code may be overestimates for FM (http://www.cdc.gov/arthritis/basics/fibromyalgia.htm).

Analyses

Data processing and survey-adjusted statistical analyses of NIS data were conducted using SAS 9.2 (SAS Institute, Inc., Cary, NC). The first step was estimating the total number of discharges by a number of characteristics, such as race/ethnicity, year of discharge, and primary payor. Estimates for each of these variables were made for all subjects and separately for men and women.

Population-based rates were calculated and graphed by first estimating the total number of FM-related discharges by gender and five-year increments of age at time of discharge between 1999 and 2007. Those numbers then were divided by the total of annual Census gender by age estimates (also summarised into five year increments) over the same nine-year period. These were converted to gender/age rates per 100,000 population for ages 15-84. Population-based rates stop at 84 because annual gender by individual age population estimates are not released for individuals 85 years and older (http://www.cdc.gov/nchs/nvss/bridged_race/data_documentation.htm).

Diagnoses were evaluated two different ways. First we examined comorbidities (i.e., listed secondary diagnosis) among discharges having a primary diagnosis of FM (total and by gender). We used the Clinical Classification Software (CCS) schema developed as part of HCUP (http://www.hcup-us.ahrq.gov/toolssoftware/ccs/AppendixASingleDX.txt), which categorises thousands of individual ICD-9 diagnoses into approximately 270 mutually-exclusive and clinically meaningful cat-

Table I. Nationwide Inpatient Sample discharges with a Fibromyalgia Diagnosis Code (1999–2007).

ICD 9 = 729.1	Total survey n=353,766 estimated n=1,727,765 %	Men survey n=43,558 estimated n=213,034 %	Women survey n=310,056 estimated n=1,513,995 %
Age group			
0 to 21 years of age	1.5	4.8	1.0
22 to 44 years	23.9	26.0	23.6
45 to 64 years	49.1	41.8	50.1
65 and older	25.5	27.3	25.3
Race / ethnicity			
White	60.5	56.7	61.0
Black	5.8	8.5	5.4
Hispanic	3.8	6.0	3.5
Asian or Pacific Islander	0.5	1.0	0.4
Native American	0.3	0.3	0.2
Other	1.1	1.7	1.0
Missing*	28.1	25.7	28.4
Year of discharge			
1999	6.1	7.3	5.9
2000	7.4	8.1	7.3
2001	8.9	9.2	8.8
2002	10.4	10.5	10.4
2003	11.7	11.6	11.7
2004	12.5	12.1	12.5
2005	13.7	13.0	13.8
2006	14.2	13.7	14.3
2007	15.2	14.6	15.3
Primary payor			
Medicare	41.1	39.7	41.3
Medicaid	11.3	10.9	11.3
Private insurance	40.9	38.5	41.2
Self-pay	3.2	5.9	2.8
No charge	0.3	0.5	0.3
Other	3.1	4.4	3.1
Discharge status			
Routine	78.3	79.3	78.2
Transfer to hospital	2.1	2.7	2.0
Other transfer	9.4	8.4	9.5
Home health care	8.7	7.0	9.0
Against medical advice	0.9	1.6	0.8
Died	0.5	0.8	0.5
Other	0.0	0.0	0.0
Census region			
Northeast	15.0	16.1	14.9
Midwest	28.2	26.8	28.4
South	36.9	37.0	36.9
West	19.8	20.1	19.8

*Race/ethnicity is masked for approximately 25% of all NIS discharges as per individual state's policy.

egories. The CCS codes were updated in 2007 to provide greater specificity regarding mental and substance-related illnesses. A SAS program (http://www.hcup-us.ahrq.gov/toolssoftware/mhsa/mhsa.jsp) was used to update the mental illness related CCS codes provided in the 1999 through 2006 data. Examination of secondary diagnoses was done by determining the presence (yes/no) of all CCS categories across diagnoses 2 through 15. Because it was not practical to examine all CCS categories, only those present in at least 5% of total discharges are reported. We also evaluated discharges in which FM was the secondary diagnosis; CCS codes representing at least 1% of primary diagnoses are presented.

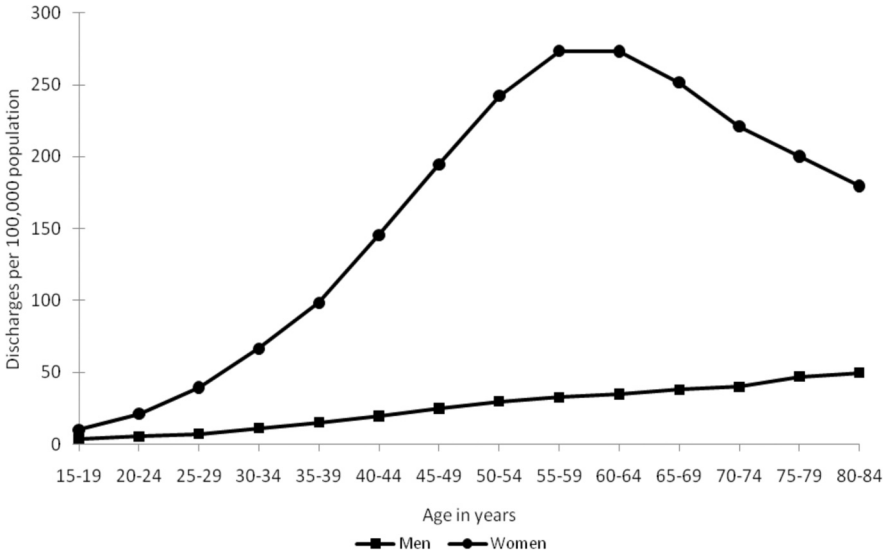

Fig. 1. Gender- and age-specific fibromyalgia-related discharges, 1999-2007.

Results

Personal and hospital characteristics

Based on NIS data, there were an estimated 341,915,364 hospital discharges in the U.S. between 1999 and 2007. As shown in Table I, there were 1,727,765 discharges with an FM diagnosis during this nine-year span, 213,034 men (12.3%) and 1,513,995 women (87.6%). Roughly half of all FM-related discharges were for individuals 45 to 64 years of age: one quarter of those were for those younger than age 45, and one quarter were for those older than age 64. Among FM-related discharges, 60.5% were White, 5.8% Black, and 3.8% Hispanic. Very few reported being Asian/Pacific Islander (0.5%) or Native American (0.3%), and 28.1% had missing data for this question. If one excludes the masked race/ethnicity data (some states, for example, Georgia, Illinois, Kentucky, Ohio, and Washington mask race/ethnicity), the figures are 83.4% for non-Hispanic Whites, 8.0% for non-Hispanic Black, and 5.2% for Hispanics.

Medicare and private insurance each funded approximately 41% of these FM-related hospitalisations/discharges and Medicaid 11.3%. Although 11.5% of FM discharges ended with a transfer to another hospital or facility and 8.7% in discharge to home health care, 78.3% ended in a routine discharge to home. The South accounted for 36.9% of FM discharges and the Midwest for 28.2%.

In general, differences between men and women are modest. Men were approximately two years younger than women on average, 52.8 (standard error 0.18) years *vs*. 54.7 (0.09) years and had a slightly longer length of stay; mean 4.6 days (0.04) compared to 4.3 (0.02) days for women. Just under 5% of the men were younger than 20 years of age compared to 1% of the women. Shown in Table I, a higher percentage of men were Black (8.5 male *vs*. 5.4% female) or Hispanic (6.0 *vs*. 3.5%), died (0.8 *vs*. 0.5%), left against medical advice (1.6 *vs*. 0.8%), and were self-pay (5.9 *vs*. 2.8%). In contrast, a lower percentage of men had private insurance (38.5 *vs*. 41.2%) and were in the 45 to 64 year age category (41.8 *vs*. 50.1%).

There was a steady increase in the percentage of FM-related discharges each year, rising from 6.1% (of all FM-related discharges) in 1999 to 15.2% in 2007 (number of discharges increasing from 105,451 to 262,188, respectively). Stratifying by gender, the percentages increased from 7.3 to 14.6% for men and from 5.9 to 15.5% for women.

Population-based hospitalisation rates

Shown in Figure 1 are the population-based rates of FM-related discharges between 1999 and 2007 (for men and women by specific age). The population-based rate of male FM-related discharges rose steadily from 3.8 per 100,000 among those 15 to 19 years of age to 49.7 per 100,000 among those 80 to 84 years of age. Among women, there was an inverted U-shaped curve, rising from 9.9 per 100,000 among those 15 to 19 years of age to 273.5 and 273.4 per 100,000, respectively, among those 55 to 59 and 60 to 64 years of age; then declining to 179.6 per 100,000 among those 80 to 84 years of age.

Secondary admitting diagnoses among patients with a primary diagnosis of fibromyalgia

Shown in Table II are the most frequent CCS categories for secondary diagnosis among an estimated 63,772 patients with a primary FM diagnosis. The most common comorbidities were essential hypertension (34.8%), disorders of lipid metabolism (17.8%), and coronary atherosclerosis and other heart disease (16.3%). The most common general categories were metabolic, cardiac, mental, and bone/tissue disorders. The figures for men and women, also shown in Table II, were similar for several diagnoses. Among these most common categories, men, however, had more coronary atherosclerosis/other heart disease (21.2 *vs*. 14.1%) and women more anxiety, mood, and miscellaneous mental disorders (approximately six percentage point differences for each disorder).

Table II. Most frequent Clinical Classification Software (CCS) categories for secondary diagnosis among patients with a primary diagnosis of fibromyalgia (estimated n=63,772).

CCS code and title		Men %	Women %	Total %
98	Essential hypertension	31.8	36.3	34.8
53	Disorders of lipid metabolism	19.5	17.2	17.8
101	Coronary atherosclerosis and other heart disease	21.2	14.1	16.3
49	Diabetes mellitus without complication	13.9	15.3	14.8
670	Miscellaneous mental disorders	8.8	14.7	14.0
661	Substance-related disorders	15.7	12.0	13.1
259	Residual codes; unclassified	12.3	13.2	12.9
205	Spondylosis; intervertebral disc disorders; other back problems	10.6	13.6	12.7
138	Esophageal disorders	7.3	13.3	11.4
211	Other connective tissue disease	12.1	10.5	11.0
58	Other nutritional; endocrine; and metabolic disorders	8.5	8.5	10.7
55	Fluid and electrolyte disorders	9.3	10.9	10.4
102	Non-specific chest pain	8.9	10.5	10.0
48	Thyroid disorders	3.8	12.8	9.9
204	Other non-traumatic joint disorders	9.4	10.1	9.9
657	Mood disorders	4.1	11.1	8.9
59	Deficiency and other anemia	7.3	9.5	8.8
95	Other nervous system disorders	8.0	8.6	8.4
651	Anxiety disorders	4.4	10.0	8.2
155	Other gastrointestinal disorders	5.4	9.2	8.0
203	Osteoarthritis	4.5	9.2	7.7
127	Chronic obstructive pulmonary disease and bronchiectasis	7.7	6.7	7.0
128	Asthma	4.3	8.1	6.9
212	Other bone disease and musculoskeletal deformities	6.5	7.0	6.9
106	Cardiac dysrhythmias	7.4	6.4	6.7
108	Congestive heart failure; non-hypertensive	5.2	5.3	5.3
84	Headache; including migraine	2.3	6.4	5.1
117	Other circulatory disease	4.5	5.3	5.1
159	Urinary tract infections	1.8	6.5	5.0
202	Rheumatoid arthritis and related disease	2.5	5.3	4.9

Primary admitting diagnoses among patients with a secondary diagnosis of fibromyalgia

Displayed in Table III are the most frequent CCS categories for primary diagnosis among the 1.6 million patients with a secondary FM diagnosis. The most common primary diagnoses were non-specific chest pain (6.2%), mood disorders (6.2%), and Spondylosis/intervertebral disc disorders/other back problems (4.3%). The 31 listed conditions accounted for roughly 60% of FM-related discharges. Summarising these 31 CCS categories, the most common general groups were cardiovascular (accounting for 14.2% of all discharges), bone and tissue related (9.6%), mental/neurological (9.5%), gastrointestinal (9.0%), and respiratory (7.4%). In general, the differences between men and women were not substantial (also shown in Table III). Men, again, had more coronary atherosclerosis/other heart disease (4.8 *vs*. 2.4%) and women osteoarthritis (3.9 *vs*. 1.4) and mood disorders (6.5 *vs*. 4.5%).

The 31 most common primary CCS categories among discharges where FM was a secondary diagnosis also were compared to the primary CCS categories for all discharges recorded in the NIS dataset between 1999 and 2007. Table III shows the ranking and frequency of those 31 conditions compared to all 278 CCS categories available in the NIS data. The 31 selected most common primary diagnosis categories among discharges having secondary FM accounted for 40.1% of all NIS discharges. We also looked at the most frequent 31 CCS categories in all NIS discharges (data not shown); the most common general groups were pregnancy and delivery (17.1%), cardiovascular (13.4%), respiratory (6.0%), bone and tissue related (5.3%), surgical/procedure related (3.9%), gastrointestinal (3.4%), and mental/neurological (3.0%). Thus, if one excludes pregnancy-related discharges, cardiovascular conditions are the most common reason for hospitalisation in general and for patients with FM. Patients with comorbid FM, however, were more likely to be admitted with bone and tissue, mental/neurological, and gastrointestinal conditions compared to those in the overall population.

Discussion

Personal and hospital characteristics

FM is a chronic, difficult to treat, often debilitating condition with many identified co-morbidities, which affects millions of Americans. There are, however, very few large cohort studies, with substantial numbers of men and racial/ethnic minorities, and very little information about patients who are admitted to the hospital with FM as either a primary or secondary diagnosis. The purpose of the present study was to bridge this gap in knowledge by examining FM-related discharges in the NIS from 1999 to 2007.

In our cohort of hospitalised patients in the United States, 0.51% had been given an FM diagnostic code. This figure is much lower than other estimated FM-related hospitalisation rates (7.5% in Germany and 5% in England) (52, 53). Our figure also differs from those in two studies where patients were systematically evaluated; on medical wards in Israel, 5% had FM (48) and on an oncology unit in Turkey, 10.7% had FM (49). The contrasting results likely are due to diagnostic method, sample size, and sample type; moreover, the higher figures are not from population studies.

The mean age of patients in our cohort was 54.5 years (52.8 for men and 54.7 for women), which differs from the Israeli study reporting a mean age of 63.5 (48). In the present study, many more women than men were admitted with FM (87.6% *vs*. 12.3%). This confirmed what has been shown in previous clinical (42, 43), community (44, 45), and hospital (48, 49) studies; that the prevalence of FM is much higher in women than in men. Although this has been a consistent finding, there are still no good explanations for the apparent gender preference. Similarly, this has been reported in rheumato-

Table III. Most frequent Clinical Classification Software (CCS) categories for primary diagnosis.

CCS code	CCS title	Discharges where FM is comorbidity (est. n=1,663,993) Men %	Women %	Total %	All discharges (est. n=341,915,364) Rank	Total %
102	Non-specific chest pain	6.5	6.2	6.2	5	2.2
657	Mood disorders	4.5	6.5	6.2	7	2.0
205	Spondylosis; intervertebral disc disorders; other back problems	4.0	4.4	4.3	11	1.6
203	Osteoarthritis	1.4	3.9	3.6	13	1.6
122	Pneumonia (except that caused by tuberculosis or sexually transmitted disease)	4.7	3.4	3.5	2	3.3
101	Coronary atherosclerosis and other heart disease	4.8	2.9	3.1	3	3.2
127	Chronic obstructive pulmonary disease and bronchiectasis	2.2	2.1	2.1	12	1.6
55	Fluid and electrolyte disorders	1.9	1.8	1.8	16	1.4
128	Asthma	0.8	1.9	1.8	26	1.1
197	Skin and subcutaneous tissue infections	3.0	1.5	1.7	19	1.3
106	Cardiac dysrhythmias	1.8	1.6	1.6	10	1.8
251	Abdominal pain	1.2	1.7	1.6	53	0.5
254	Rehabilitation care; fitting of prostheses; and adjustment of devices	1.5	1.6	1.6	20	1.2
149	Biliary tract disease	0.7	1.7	1.6	21	1.2
237	Complication of device; implant or graft	1.6	1.5	1.6	14	1.5
159	Urinary tract infections	1.0	1.5	1.4	17	1.3
108	Congestive heart failure; non-hypertensive	1.7	1.3	1.3	4	2.8
84	Headache; including migraine	0.7	1.3	1.2	109	0.2
145	Intestinal obstruction without hernia	0.8	1.2	1.2	32	0.8
146	Diverticulosis and diverticulitis	0.9	1.2	1.1	31	0.8
155	Other gastrointestinal disorders	0.6	1.2	1.1	51	0.5
100	Acute myocardial infarction	1.8	1.0	1.1	8	1.9
211	Other connective tissue disease	2.2	0.9	1.1	79	0.3
661	Substance-related disorders	1.4	1.0	1.1	47	0.6
152	Pancreatic disorders (not diabetes)	0.9	1.1	1.0	34	0.7
95	Other nervous system disorders	1.2	1.0	1.0	72	0.4
50	Diabetes mellitus with complications	1.6	0.9	1.0	18	1.3
138	Esophageal disorders	0.7	1.0	1.0	63	0.5
245	Syncope	0.9	0.9	0.9	37	0.7
109	Acute cerebrovascular disease	0.8	0.9	0.9	15	1.5
170	Prolapse of female genital organs	0.0	1.0	0.9	167	0.4
	Total explained variation:	57.8	60.0	59.7		40.1

logic diseases; for example, 89.4% of the patients with systemic lupus erythematosus in the 1993-2006 NIS datasets were female, as were 76.7% of patients with rheumatoid arthritis (54). For patients with systemic sclerosis in the 2002-2003 NIS datasets, the rates for women were 4.5 times higher than for men (55).

Although men accounted for only 12.3% of discharges in the present study, the corresponding number is 213,034 representing the largest male FM cohort reported to date. Some interesting differences emerged between men and women; for example, there was a much higher percentage of men than women admitted from the 0–21 year age group (4.8% *vs*. 1.0%), suggesting that FM may be diagnosed earlier in men or those in this age group are more ill and require hospitalisation. All other age group percentages are comparable. Moreover, the percentages of Black, Hispanic, Asian/Pacific Islander, and Native American men affected by FM were higher compared to women. These differences and similarities have not been previously reported in smaller clinical and community studies, and presage further investigation.

Race/ethnicity data are masked for approximately 25% of all NIS discharges (each state can restrict release of sensitive data), so one must be cautious when drawing inferences from these data. Despite this caveat, we compared our figures to U.S. Census data. Between 2000 and 2007, there were an estimated 292 million residents in the U.S. The estimated racial/ethnic percentages were: 68.8% non-Hispanic White, 12.7% non-Hispanic Black, and 13.9% Hispanic (U.S. Census Bureau (56)). Based on our percentages (84.3% White, 8.0% Black, and 5.2% Hispanic among discharges in which race was reported), it appears that, compared to the general population, Whites are over-represented in this FM hospital population, and racial/ethnic minorities (Hispanics, in particular) are under-represented. Such under-representation is evident in most community prevalence studies of FM (44, 45). Approximately half of all discharges in both the female and male groups were among patients 45-64 years of age, although a higher percentage of this age group was female. Approximately 25% of all discharges were from the 22–44 and 65 and greater age groups with relatively equal representation from females and males.

FM-related hospitalisations showed a steady increase each year from 1999 through 2007. In fact, the rates more than doubled over this time period. This is similar to data from clinical studies (8, 36). This may be due to an increase in awareness of FM by physicians, which manifests as an increase in both sub-specialists and primary care physicians diagnosing FM.

Medicare funded 41.1% of all discharges, and 25.5% of discharges were for patients 65 years of age and older. Assuming that Medicare funded all discharges among those 65 and older, that would suggest that private insurance paid for nearly 55% of all discharges among adults younger than 65. Approximately 21% of adult patients younger than 65 must have had a physician determined disability, which made them eligible for Medicare. Furthermore, Medicaid paid for 15.2% of all discharges, suggesting a substantial number of FM patients presumably were unemployed, had low income, or were disabled.

Approximately two-thirds of the FM-related discharges are from hospitals in the Midwest and the South. The reason for this finding remains unclear. We do know that the development of FM and the worst pain-related disability and

disease progression in FM patients is associated with low income/poverty, low education, and obesity (45, 57-59), which in turn, tend to be more prevalent in Midwest and Southern states.

Population-based hospitalisation rates

In various studies of women with FM, there is a steady increase in prevalence with age with a peak later in life and subsequent decline (8, 44, 45). In the present study, the curve's peak occurs between ages 55 and 64, which is similar to results from the Haviland *et al*. (45) study. There are, however, no satisfactory explanations for this decline. Given the progression of FM and its co-morbidities, increased mortality might explain these data; however, Wolfe *et al*. (60) failed to find increased mortality in FM. Moreover, there are few reports of FM remissions. Men in our study, showed a steady increase in FM throughout life with no apparent decline. There are no published comparative (age-related) data for men.

Co-morbid conditions

Patients are rarely admitted to hospital with FM as the primary diagnosis. The five most common primary diagnoses for which patients with FM in our cohort are admitted to the hospital are essential hypertension (34.8%), disorders of lipid metabolism (17.8%), coronary artherosclerosis and other heart disorders (16.3%), diabetes mellitus without complications (14.8%), and miscellaneous mental disorders (14%). In the FM hospitalisation study from Israel, hypertension was present in 9% of patients, whereas coronary artherosclerosis was present in 31% and diabetes mellitus in 4% (48). In community studies of patients with FM, hypertension is present in 12–40% of patients, whereas diabetes mellitus is present in 4–23% (18, 19, 23). Lipid disorders are an interesting finding; traditionally they are classified as those that result from rare variants in genes and those that result from poor diet or lifestyle (61). It is intriguing that the traditional risk factors for myocardial infarction (MI) include age, plasma lipid concentration, blood pressure, use of tobacco products, and diabetes mellitus II. Strikingly, these risk factors for coronary artery disease and MI are the top four admitting diagnoses for FM patients. This raises some interesting possibilities; for example, (a) do FM, MI, and related risk factors share common genetic predispositions, or (b) does one disease process precede and lead to the others as is the case with risk factors for MI, or (c) does the stress of being in pain lead to other stress related disorders? We recently have reported an increase in co-morbid medical and psychiatric diagnoses paralleling an increase in functional pain disorders (irritable bowel syndrome and FM), which may reflect the burden of chronic pain in general (62)). Pursuing answers to these questions may be useful areas of investigation.

That mental disorders commonly co-occurred in patients with both primary and secondary FM (and more commonly in the general hospital population) is not a surprising finding. This high prevalence has been shown in many studies; the most common are depression and bipolar disorder (30-32). In our cohort, mental disorders are more prevalent in women.

Particularly noteworthy, is that the five most common admitting diagnoses in the present study are treatable. Future studies could be designed to explore patterns of illnesses in this group and formulate interventions and prevention measures designed to avoid hospitalisations.

When FM is the primary diagnosis, the most common co-morbid diagnoses are non-specific chest pain, mood disorders, Spondylosis/intervertebral disc disorders/other back problems, osteoarthritis, and pneumonia. Non-specific chest pain is a functional disorder often presenting as acute coronary syndrome. Osteoarthritis and spondylosis and other back problems have been shown in clinical studies to be common in patients with FM (18, 19, 23). All of these disease processes are treatable and often can be managed effectively on an outpatient basis. Our finding sets the stage for future studies to explore the process by which these patients are admitted to the hospital and the development of interventions that serve to avoid unnecessary admissions.

Study strengths

One strength of our study is the large number of FM-related hospital discharges. To put this number in perspective, the Census Bureau estimates that there were 310 million individuals in the U.S. in 2010. If FM affects even 2% of the population, there presently are approximately 6.2 million Americans with FM. Our figure of 1,727,765 discharges over a nine-year period may not be representative of the 6.2 million individuals, but it does represent a substantial proportion of the entire U.S. FM population. Moreover, this FM group represents an even higher percentage of FM patients in the population who are sick enough to be hospitalised. This large sample size also allowed for a better description of men having FM, typically an understudied group. Finally, these results also describe a very costly form of treatment, hospitalisation.

Study limits

Hospitalisation discharge records may not adequately represent all patients, especially those being seen only in outpatient settings. Moreover, NIS does not include every single hospitalisation; Veterans Administration (VA) hospitals, for example, are excluded. Furthermore, our data are for discharges, not unique individuals. It is likely that these data represent the most clinically-severe subgroup of patients having FM. Thus, one must use caution in making prevalence estimates and drawing inferences from these data. Finally, as noted, data based on the ICD-9-CM diagnosis code 729.1 likely overestimates FM prevalence because it is not specific to FM. ICD-10, however, now includes an FM code, which may strengthen new studies of this kind. The ICD-9-CM code used in this study, however, has been the standard in many previously published large-scale cohort studies (*e.g*. 63).

Research and practice recommendations

Our hospitalisation data reveal some unexpected relationships between FM and co-morbid disorders. Many of the disorders that account for these hospitalisations could have been prevented

or treated with early interventions, such as lifestyle modifications. Therefore, studies should be undertaken to determine how these patients can be better managed as outpatients and how effective prevention strategies can be implemented.

Future FM studies could (a) determine risk factors that lead to these admissions, (b) design and implement strategies to alter the present trajectories of these disease processes to avoid admissions while better treating the disease process, and (c) begin to uncover a causal relationship between the development and progression of FM with the identified medical co-morbidities and cardiac risk factors.

We have identified a number of factors, many treatable and open to experimentation, that can be explored with the aim of further improving the care of patients with FM while extending our understanding of a very complex and difficult to manage disease. Although there are limits to the data presented here, we believe that this portrait of hospitalised FM patients will be useful in guiding both research and practice.

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