

Depression and Fibromyalgia: Treatment and Cost When Diagnosed Separately or Concurrently

REBECCA L. ROBINSON, HOWARD G. BIRNBAUM, MELISSA A. MORLEY, TAMAR SISITSKY, PAUL E. GREENBERG, and FREDERICK WOLFE

ABSTRACT. Objective. Depression and fibromyalgia (FM) are often coincident. Both syndromes share common symptoms and impose significant economic burdens. This study compared claims for treatment and costs of FM plus depression with those for FM or depression alone.

Methods. Administrative claims data from a national Fortune 100 manufacturer were used to identify 3 mutually exclusive patient cohorts based on claims with a diagnosis for: FM only, depression only, and FM plus depression. A fourth cohort comprised a random sample of 10% of the employer's overall beneficiary population. Cohorts were compared for demographics, comorbid conditions, and healthcare resources utilization. Mean direct (treatment) costs were calculated and indirect (work loss) costs imputed, and these were assessed using Student's *t* test and Bonferroni adjustments.

Results. Mean annual employer payments (direct plus indirect costs) per patient were \$5,163 for FM only, \$8,073 for depression only, \$11,899 for FM plus depression, and \$2,486 for the overall sample. Mean incremental employer payments (i.e., above those for the random sample) per patient with FM plus depression were \$9,413, an amount more than the sum of incremental costs for those with FM or depression alone (\$8,264). These costs are consistent with costs of other chronic diseases.

Conclusion. Patients with FM plus depression are high users of healthcare services. As in studies that established relationships between depression and other medical conditions, incremental costs for patients with FM plus depression were more than additive of costs for each condition alone. (J Rheumatol 2004;31:1621–9)

Key Indexing Terms:

PAIN DEPRESSION FIBROMYALGIA ECONOMIC IMPACT CLINICAL DIAGNOSIS

Exactly what constitutes an evidence-based clinical diagnosis of fibromyalgia (FM) is controversial, but physicians often report FM in administrative claims submitted for insurance reimbursement. It has been demonstrated that depression claims are often associated with high total healthcare costs including a large proportion of costs for general medical services¹⁻⁴. However, no definitive research has been published on the cost of combined depression and FM diagnoses, even though prevalence studies have indicated a strong link between these conditions. Prevalence of depression concurrent with FM was 22% to 45% for current depression in patient populations⁵⁻⁷ and 31.5% in a community sample⁸. Longterm prevalence in patients with FM was 48% for depression during a 7-year period⁶, and 68% for depression lifetime⁷.

Theoretically, FM and depression share common physiological, biological, and clinical etiologic elements⁹⁻¹⁴, including disturbance of serotonin and norepinephrine neurotransmitters in both syndromes^{15,16}. Mood disorders may exacerbate FM and complicate its management. Thus, information on the economic impact of FM and depression will be useful to clinicians, payers, and researchers.

Individuals diagnosed as having both FM and depression may experience more severe symptoms of FM^{6,8,17}. Patients with FM also often report physical complaints in addition to depression¹⁸, including muscle pain and tenderness, as well as comorbid conditions such as severe fatigue, insomnia, and irritable bowel syndrome¹⁹. Although in a large retrospective claims database, FM claimants were found to have higher rates of average claims for mental health services than the overall claimant sample (1.3 vs 0.4 claims per patient), only 9.2% of FM claimants versus 3.4% of the overall sample had any claim for depression²⁰. Whatever the cause of FM, patients do receive claims for this condition, and claims for either depression or FM alone add up to a considerable cost²⁰⁻²². We examined the similarities and differences in treatment and cost to employer of separate or concurrent claims for FM and depression.

MATERIALS AND METHODS

For the study period, 1996 through 1998, information was obtained from the large national administrative claims database of a Fortune 100 manu-

From Eli Lilly and Company, Indianapolis, Indiana; Analysis Group, Boston, Massachusetts; and the National Databank for Rheumatic Diseases, Wichita, Kansas, USA.

Dr. Birnbaum, Ms. Morley, Ms. Sisitsky, and Mr. Greenberg were supported by an unrestricted grant from Eli Lilly and Company. Ms. Robinson is a fulltime employee of Eli Lilly and Company. Dr. Wolfe has acted as a consultant to Eli Lilly and Company in other capacities.

R.L. Robinson, MS, Eli Lilly and Company; H.G. Birnbaum, PhD; M.A. Morley, MA; T. Sisitsky, MA; P.E. Greenberg, MA, MS, Analysis Group; F. Wolfe, MD, National Databank for Rheumatic Diseases.

Address reprint requests to R. Robinson, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285. E-mail: rrobinson@lilly.com
Submitted November 6, 2003; revision accepted February 5, 2004.

facturer (n > 100,000 beneficiaries). Data comprised healthcare (medical and prescription drug) claims for employees, spouses, dependants, and retirees (< 65 years of age) and employee disability claims. Diagnoses were based on International Classification of Diseases 9th Revision (ICD-9) codes and procedures on Current Procedural Terminology codes; prescription drugs were categorized by National Drug Codes for therapeutic classes.

Analyses included data on all beneficiaries continuously enrolled during the study period in the company's nationwide managed indemnity insurance plans. Beneficiaries of other managed care plans or > 65 years of age were excluded to avoid missing data from alternative payment sources. After eligible patients were identified, 3 specific, mutually exclusive cohorts were defined by diagnostic claims (Table 1): (1) the FM-only cohort: ≥ 1 medical or disability claim for FM throughout the study period, but no claim for depression in 1998; (2) the depression-only cohort: ≥ 1 claim for depression in 1998, but no claim for FM throughout the study period; and (3) the FM-depression cohort: claims for FM throughout the study period and for depression in 1998.

Disease cohorts were defined using distinct time periods (i.e., FM 3 years to represent its chronicity, and major depressive disorder one year to reflect current status). This methodology was used to more closely represent the natural course of these conditions. Persons with FM may not experience a claim for FM each year, yet the influence of FM symptoms still affects healthcare utilization indirectly. Although depression may be recurrent, a single year was used for analysis as depression in remission is more typical of a nondepressed group. Sensitivity analyses were performed to test this assumption.

For benchmarking purposes, a fourth cohort was derived, based on a random sample of 10% of the employer's overall beneficiary sample, including claimants with FM and depressive disorder. The overall beneficiary cohort allowed epidemiologic and cost-estimate comparisons among all cohorts.

The groups were compared for demographic data, 18 comorbid conditions derived from the literature as commonly comorbid with FM²⁰ (Table 1), amount and type of healthcare resources used, and medication use by therapeutic class. Disorders that were present in the literature, but that

occurred in less than 1% of this sample, were excluded from this category [i.e., temporomandibular joint (524.60), chronic tension headache (307.81), Raynaud's syndrome (443.0x), multi-somatiform disorder (300.8), and somatic reaction (306.9x)]. Healthcare costs were calculated using direct costs (actual employer payments for medical and pharmaceutical services) and indirect costs (disability payments and imputed costs of absenteeism). Costs (i.e., payments to providers or, in the case of work loss, to employees) were calculated for individuals (employees, retirees, spouses, and dependants). Analyses were calculated for 1998, the year of the most recent data.

Indirect costs were imputed using the approach of Burton and colleagues^{23,24}. Payments for sporadic illness-related absences were imputed based on days when medical care was provided. When employees not on disability received medical care during workdays, these days were considered illness-related work-loss days for hospital care, or half-day work losses for office visits. Because disability claims covered workdays missed due to illness for periods of ≥ 6 consecutive days for eligible workers, individuals with disability claims also were assigned 5 illness-related work-loss days. Work-loss costs were defined as employer payments for both disability claims and imputed sporadic illness-related absences. Our methodology for imputing payments for sporadic absenteeism was detailed by Barnett and colleagues²⁵.

Resources and associated costs were assessed by Student's t test. Given the multiple comparisons, p values are reported using Bonferroni adjustments. Standardized comparisons were represented by the incremental cost of a claimant in each sample, i.e., the excess of a claimant's cost in a disease-specific cohort above that of a claimant in the overall employer sample²⁶. Analyses Group (Boston, MA, USA), which specializes in health and economic outcomes studies, performed the analyses using SAS Version 8.

RESULTS

Demographics. In the employer sample of all patients, percentages of patients with a depression claim (3.4%) or a diagnosis of FM (2.8%) were consistent with previous

Table 1. ICD-9 codes for clinical diagnoses.

Diagnosis	ICD-9 Code
Fibromyalgia	729.1
Depression	296.2*; 296.3*; 300.4*; 309.0*; 311*
Abdominal pain	789.0
Allergic rhinitis	477*
Anxiety	300.0*
Back disorders	307.89; 724*; 839*; 846*-847*
Chronic fatigue syndrome	780.7*
Chronic sinusitis	437*
Hypertension	401*
Irritable bowel syndrome	564.1
Migraine	346*
Osteoarthritis	715*
Rheumatoid arthritis	714*
Sleep disturbances	307.4*; 780.5*
Symptoms involving head and neck	784.0*-784.3*
Chest pain	786*
Ulcer or stomach problem	531*-536*
Other musculoskeletal and connective tissue diseases	710*-713*; 716*-723*; 725*-729.0; 729.2*-739*
Other mental disorders	290*-295*; 296.0*-296.1*; 296.4-299*; 300.1*-300.3*; 300.5*-300.80; 300.83-306.8*; 307.0*-307.3*; 307.5*-307.80; 307.82-307.88; 307.9-308*; 309.2*-310*; 312*-319*

* Includes all other subcategories within the ICD-9 code.

reports^{17,27,28}. However, only 9.2% of FM claimants (0.3% of the 10% overall sample) also claimed depression, and only 7.6% (0.3% of the 10% overall sample) of depressed claimants also claimed FM. These percentages of diagnoses are much lower than previously reported estimates of current depression in patients with FM: 22% with major depressive disorder to 45% depressed according to validated scales⁵⁻⁸.

Women made up 59% of the FM-only cohort and 57% of the depression-only cohort, more women than men in comparison with the 49% women in the 10% overall sample (both $p < 0.0001$; Table 2). The FM-depression cohort had more women (72%) than either single-disease cohort ($p < 0.0001$). These findings confirm prior observations that FM and depression are more prevalent in women^{21,29,30}. In the FM-depression cohort, mean patient age was higher than in the 10% overall sample (44 vs 38 yrs; $p < 0.01$), consistent with reports of prevalence of FM increasing with age³¹.

The percentage of patients in each demographic category differed between the disease-specific groups and the overall 10% sample ($p < 0.01$, Bonferroni adjustment), except for percentage of spouses/dependants and percentage 18 to 35 years of age (Table 2). Percentage of FM-depression versus FM-only claimants differed for percentage retired, 36 to 45 years of age, and 56 to 64 years of age ($p < 0.01$, Bonferroni adjustment).

Treatment patterns. Claimants in the FM-depression cohort used more medical services than claimants in the other 3 cohorts (all $p < 0.01$; Figure 1). However, FM-specific and depression-specific claims accounted for a small share of care received overall (under 12% of total medical service utilization). FM-only and depression-only claimants used

about 3 times as many medical services as the overall 10% sample. Monthly, 62% of FM-depression claimants had 3 or more medical claims, versus 30% of FM-only or depression-only claimants. Twenty-three percent of FM-depression claimants averaged more than 4 claims per month, a rate roughly 4 times that of the FM-only or depression-only cohorts.

Primarily general practitioners and internists saw FM-only claimants, while mainly psychiatrists saw claimants with FM-depression. Only 5% of FM-only claimants saw a psychiatrist in 1998, compared to 17% of the FM-depression claimants. Compared with the overall 10% sample and FM-only claimants, FM-depression claimants used significantly more medical services provided by physicians practicing psychiatry, general medicine, radiology, surgery, neurology, anesthesiology, gastroenterology, and emergency medicine (all $p < 0.01$; Figure 2). Rheumatologists, often associated with treating FM claimants¹⁸, provided less care to the FM claimants than did other physician specialists.

Claims for emergency medical care differed across the cohorts. FM-only claimants were 60% more likely to receive medical treatment for an accident than the average beneficiary. Compared with the average beneficiary, claimants treated for depression-only were more than twice as likely, and claimants treated for both FM and depression were more than 3 times as likely to be treated for an accident. Thus, there was a more than additive relationship between the incremental risk of treatment for an accident of claimants treated for both FM and depression and the incremental risk of claimants treated for either condition alone.

The percentage of FM-depression claimants prescribed a drug from any of the selected drug categories associated with FM or depression^{17,28,31-35} was higher than for the overall beneficiary sample or for FM-only claimants, except in the case of antirheumatic agents (all $p < 0.017$; Table 3). No drug class was used by more than one-quarter of patients in the 10% overall sample, while more than one-third of claimants in the FM-depression cohort used narcotic analgesics, nonsteroidal antiinflammatory drugs, selective serotonin reuptake inhibitors or other antidepressants, anxiolytic drugs, antiallergy agents, proton pump inhibitors or H₂ blockers, or skeletal muscle relaxants.

Based on these claims data, patients in the FM-only or depression-only cohorts had claims with a mean of 4 comorbid conditions; those with FM-depression had claims with a mean of 6 comorbid conditions; and those in the overall 10% sample had claims with a mean of 2 such conditions. When comparing rates for each commonly comorbid condition, a significantly greater proportion of patients in the FM-depression and FM-only cohorts had at least one claim than in the overall sample (all $p < 0.017$, Bonferroni adjustment; Table 4). A greater proportion of patients in the FM-depression cohort than in the FM-only cohort had at least one claim for each comorbidity except hypertension

Table 2. Demographic characteristics, 1996–98 (see Results for statistically significant differences).

	All Patients			Employer Overall Sample
	FM Only	D Only	FM + D	
No.	4268	5211	431	10% Sample
% Female	59.4	56.6	71.9	48.9
Patient status				
% Employees	42.8	42.5	43.6	34.5
% Retired	3.7	5.0	1.2	6.5
% Spouses/Dependents	53.5	52.5	55.2	59.1
Age, yrs				
Mean	44.4	40.9	43.6	38.1
Median	47.0	45.0	45.0	44.0
Mode	51.0	49.0	47.0	51.0
< 18, %	5.4	11.6	3.0	21.4
18–35, %	16.8	17.6	14.9	15.1
36–45, %	21.5	23.9	34.5	17.5
46–55, %	36.3	33.1	36.0	28.7
56–64, %	20.0	13.8	11.6	17.3

FM: fibromyalgia; D: depression.

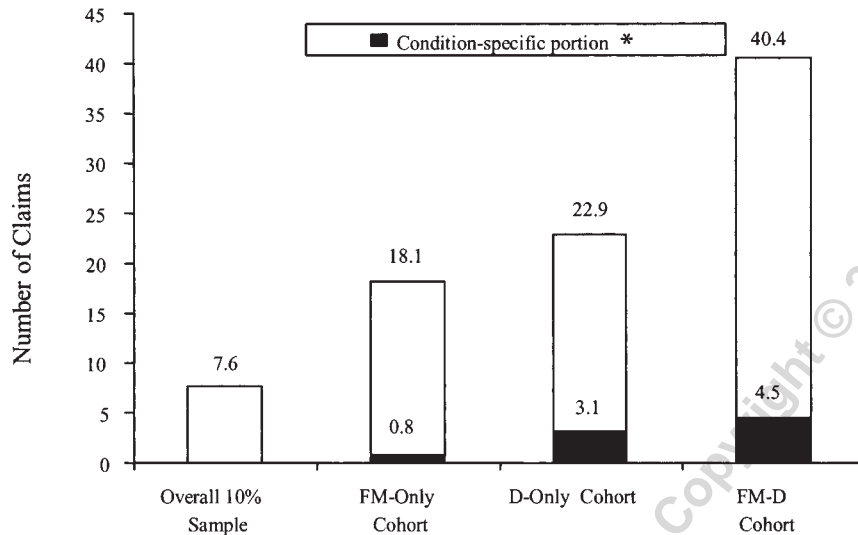


Figure 1. Average number of medical claims per patient in 1998: overall 10% sample, fibromyalgia-only (FM-only), depression-only (D-only), and fibromyalgia-depression (FM-D) cohorts. The difference in the average number of medical claims for each patient group was significant ($p < 0.01$, Bonferroni adjustment) compared to the overall 10% sample. The difference in the average number of medical claims for the FM-D cohort was significant ($p < 0.01$, Bonferroni adjustment) compared to the FM-only cohort. *For the FM-only cohort, the condition-specific portion refers to FM claims with an ICD-9 of 729.1. For the depression-only cohort, the condition-specific portion refers to depression claims with an ICD-9 of 296.2, 296.3, 300.4, 309.0, 309.1, or 311. For the FM-D cohort, the condition-specific portion refers to FM or depression claims with an ICD-9 of 729.1, 296.2, 296.3, 300.4, 309.0, 309.1, or 311.

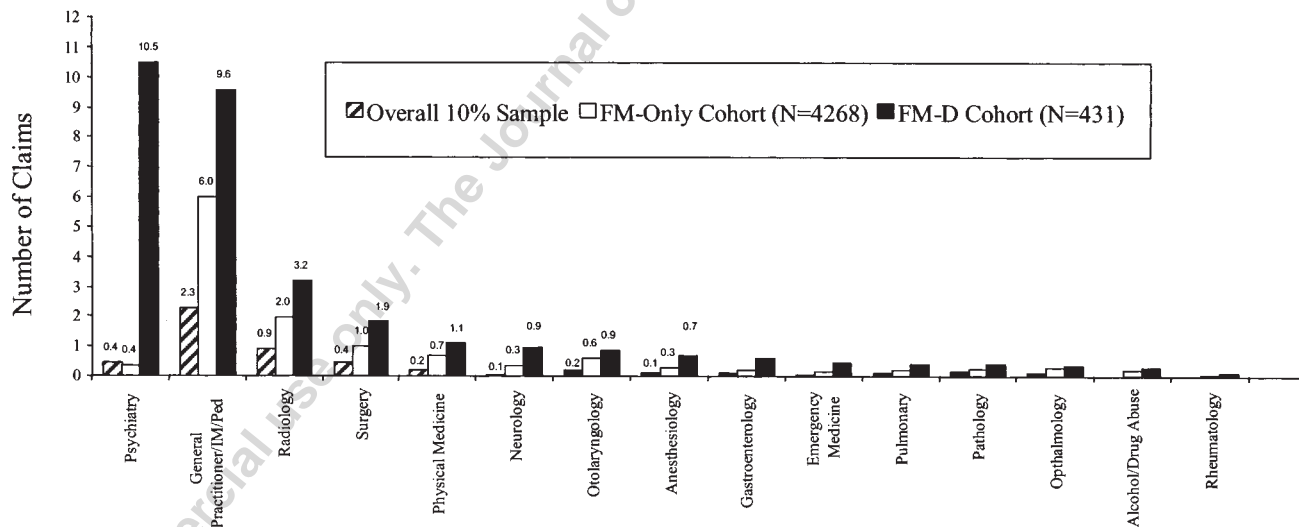


Figure 2. Average number of medical claims per patient in 1998 by selected provider specialty: fibromyalgia-only (FM-only), fibromyalgia-depression (FM-D), and employer overall sample cohorts. Specialties shown are those for which disease-specific samples had more than twice the number of claims per patient as for patients in the overall 10% sample. Physician specialties are sorted by number of claims by each specialty for patients in the FM-D cohort ($n = 431$). Patients in the FM-D cohort used significantly more medical services provided by physicians practicing psychiatry, general medicine, radiology, surgery, neurology, anesthesiology, gastroenterology, and emergency medicine than patients in either the overall 10% sample or the FM-only cohort (all $p < 0.017$, Bonferroni adjustment).

and allergic rhinitis ($p < 0.017$, Bonferroni adjustment). The average number of claims per patient in the FM-depression cohort was greater than in the overall 10% sample for each comorbidity except allergic rhinitis and rheumatoid arthritis

(RA) ($p < 0.017$, Bonferroni adjustment). The average number of claims per patient in the FM-only cohort was greater than in the overall 10% sample for each comorbidity except other mental disorders ($p < 0.017$, Bonferroni adjust-

Table 3. Selected prescription therapies taken by patients with fibromyalgia (FM) alone and those with both fibromyalgia and depression (D) compared with the employer overall sample for 1998^{a,b}.

Drug Class	% FM + D Cohort, n = 431	% FM Only Cohort, n = 4268	% Overall 10 % Sample
Narcotic analgesics	62.4	42.1	20.5
NSAID salicylates	61.3	49.7	21.9
SSRI antidepressants	58.5	13.5	6.3
Antianxiety agents	55.7	18.1	8.0
Other antidepressants	42.5	12.5	5.7
Antiallergy agents	40.6	29.9	15.3
Proton pump inhibitors/H ₂ antagonists	39.4	25.4	11.6
Skeletal muscle relaxants	38.5	27.0	6.5
Anxiolytics, sedatives, and hypnotics	27.6	9.7	3.9
Adrenal corticosteroids	26.7	18.0	8.7
Non-narcotic analgesics	24.4	12.4	3.2
Other mental illness agents	22.5	3.4	2.1
Asthma drugs	21.6	11.9	7.4
TCA antidepressants	21.5	11.2	3.1
Anticonvulsants	19.3	4.1	1.6
Antimigraine agents	4.8	4.8	1.5
Antirheumatics	2.3	1.2	0.5
Total	596.6	294.9	127.8
Unique individuals using selected drugs	97.9	82.2	52.3
Unique individuals not using any drugs	2.1	17.8	26.0

^a $p < 0.017$ (Bonferroni adjustment) for each drug class for each sample compared to overall 10% sample. ^b $p < 0.017$ (Bonferroni adjustment) for FM/D sample compared to FM-only sample except antirheumatics.

Table 4. 1998 mean number of medical claims per patient for selected comorbidities (see Results for significant differences).

Selected Comorbidities	FM + D Cohort, n = 431		FM Only Cohort, n = 4268		Overall 10 % Sample	
	Mean No. Claims	% Pts with 1 Claim	Mean No. Claims	% Pts with 1 Claim	Mean No. Claims	% Pts with 1 Claim
Musculoskeletal/connective tissue*	4.74	83.8	2.61	73.3	0.63	16.3
Respiratory/chest	1.68	68.0	0.99	22.6	0.38	12.8
Back	2.14	66.4	1.46	54.1	0.27	7.9
Abdominal pain	1.13	50.8	0.50	32.7	0.17	6.2
Mental disorders**	3.11	45.7	0.27	17.9	0.29	5.1
Head/neck	0.44	42.0	0.21	22.6	0.05	2.8
Chronic sinusitis	0.28	33.6	0.19	21.2	0.06	3.3
Hypertension	0.49	30.9	0.48	27.6	0.26	9.9
Ulcer or stomach	0.30	29.7	0.14	18.1	0.05	2.4
Chronic fatigue syndrome	0.25	27.1	0.13	14.3	0.05	2.4
Osteoarthritis	0.66	21.1	0.23	15.7	0.06	2.3
Allergic rhinitis	0.15	15.8	0.26	14.6	0.14	3.4
Migraine headache	0.20	15.5	0.14	8.4	0.02	0.9
Anxiety	0.30	14.4	0.09	3.7	0.03	0.8
Sleep disturbances	0.16	12.5	0.05	4.4	0.02	0.8
Irritable bowel syndrome	0.07	11.8	0.04	5.0	0.01	0.6
Rheumatoid arthritis	0.12	6.7	0.004	3.3	0.02	0.4

FM: fibromyalgia; D: depression. * Does not include fibromyalgia, other unspecified disorders of the back, osteoarthritis, or rheumatoid arthritis. ** Does not include depression, anxiety, or multisomatoform disorder.

ment). The average number of claims per patient with FM-depression was significantly greater than in the FM-only cohort except for allergic rhinitis and RA ($p < 0.017$, Bonferroni adjustment).

Compared with both the overall 10% sample and the FM-only claimants, a higher percentage of FM-depression

claimants had claims for other diseases of the musculoskeletal and connective tissue, symptoms involving the respiratory system, back disorders, abdominal pain, other mental disorders, symptoms involving head and neck, chronic sinusitis, ulcer or stomach problems, chronic fatigue syndrome, migraine, anxiety, sleep disturbances, irritable

bowel syndrome, or RA (all $p < 0.017$), not including hypertension, allergic rhinitis, and osteoarthritis (Table 4).

Costs. Mean payments by the employer in 1998 were \$5,163 (SD \$9,483) per FM-only claimant, \$8,073 (SD \$14,052) per depression-only claimant, \$11,899 (SD \$14,450) per FM-depression claimant, and \$2,486 (SD \$6,749) per patient in the overall 10% sample (Figure 3). Mean costs were higher for FM-depression claimants than for claimants in each of the other 3 cohorts ($p < 0.0001$).

The mean total incremental cost per FM-depression claimant was \$9,413, more than the sum (\$8,264) of the incremental per-claimant costs of FM-only and depression-only claimants. Thus, the incremental costs of claimants treated for both FM and depression were more than the added incremental costs of claimants treated for FM only and depression only.

For every dollar spent on FM-specific healthcare treatment for FM-depression claimants, the employer spent another \$80 on additional direct (healthcare) and indirect (workplace) costs. Direct costs include medical and pharmacy costs, while indirect costs include estimates of the cost of absenteeism and disability. Similarly, for every dollar spent on FM- or depression-specific healthcare treatment for FM-depression claimants, the employer spent another 10 dollars on additional direct and indirect costs. For every dollar spent on FM healthcare costs (medical care plus prescriptions), the employer spent \$57 to \$143 on additional direct and indirect costs.

For the FM-depression cohort, direct costs of medical

services and prescription drugs as a percentage of total claimant costs were 63% and 10%, respectively. The remaining 27% included indirect workplace costs for disability and absenteeism.

DISCUSSION

Despite the known limitations of detecting diagnoses in claims databases, the rates of depression and FM separately were consistent with epidemiologic research. Additionally, our demographic findings were consistent with previous reports that the incidence of FM and depression alone are higher in women. However, the incidence of current comorbid depression among FM claimants was much lower than that identified in epidemiologic studies⁵⁻⁸. Most epidemiologic studies use screening instruments or structured psychiatric diagnostic interviews to assess current illness rather than the claims rates employed in this study. Nonetheless, these findings suggest that FM and depression tend to be diagnosed and treated as separate conditions, and are less frequently diagnosed and treated as comorbid conditions than previously reported⁵⁻⁸.

Claimants treated for FM-depression had considerably more comorbid conditions than the average beneficiary in the overall sample, and comorbidity was elevated to a lesser extent in claimants with FM only. The high average number of claims for comorbidities underscores the complexity of treating claimants with these conditions, either separately or in combination. In addition to diseases of the musculoskeletal system and connective tissue (including

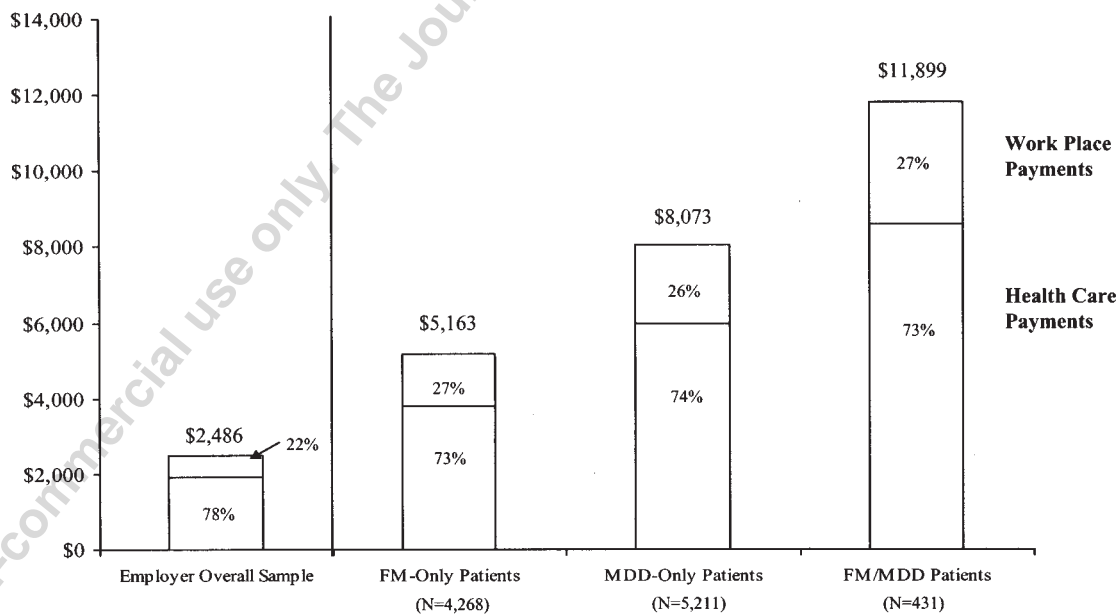


Figure 3. 1998 employer payments per treated patient: healthcare and workplace. Data illustrated include absenteeism and disability; absenteeism costs are imputed based on days when medical care was provided. If an employee was not on disability when medical care occurred during normal workdays, these days were counted as sickness work-loss days in the case of hospital care or as a half-day in the case of office visits. The difference between the average cost per patient in the FM-D sample and each of the 3 other research samples is statistically significant at $p < 0.01$ (Bonferroni adjustment). MDD: major depressive disorder.

osteoarthritis and RA), these claimants were most frequently treated for other mental disorders, back disorders, respiratory and other chest symptoms, and abdominal pain. There was also a higher rate of claims for emergency codes within the FM-depression cohort. Future studies may be useful to determine whether this may be extrapolated to a greater tendency toward risky behaviors or suicide attempts.

Our findings suggest that claimants with both FM and depression draw heavily on all medical services, an observation that reinforces the need to treat physical and emotional complaints. A more than additive relationship was found between the incremental costs (in excess of the treatment costs of the overall 10% sample) for FM-depression claimants (i.e., \$11,899 – \$2,486 = \$9,413) and the incremental costs for FM alone (i.e., \$5,163 – \$2,486 = \$2,677) and depression alone (i.e., \$8,073 – \$2,486 = \$5,587). Given the extensive healthcare use by claimants with both FM and depression, it is not surprising that the total cost per FM-depression claimant was 4.8 times the total cost per beneficiary in the overall 10% sample and 2.3 times the total cost of a FM-only claimant.

In our study, the total cost of \$5,163 for the FM-only cohort was in agreement with that of other chronic conditions when depression was not addressed. For example, total costs to the employer were \$7,193 for RA in 1997³⁶ and \$7,778 for diabetes in 1998³⁷. However, as Evans and colleagues³⁸ point out, comorbid depression has been reported to increase morbidity and economic cost in several conditions, including coronary artery disease, cancer, human immunodeficiency virus, Parkinson's disease, pain, and the sex hormone changes of aging. Sheehan³⁹ compared the per capita annual medical costs of treating patients with and without depression who also had one of several common chronic conditions (i.e., heart failure, allergic rhinitis, asthma, migraine, back pain, diabetes, hypertension, or ischemic heart disease), and found that comorbid depression increased the per-patient cost of treating these conditions by a factor of 2 to 4 times. For example, Sheehan found that patients with back pain and depression had medical costs 2.8 times higher than patients with back pain alone. As depression is often overlooked in medically ill patients, much of the higher healthcare cost in such patients was due to a generalized increase in healthcare utilization unattributable to a specific cost segment, rather than to mental health treatment³⁸.

Our findings with respect to toll of comorbid depression were consistent with those of studies of depression in other chronic conditions. Patients with diabetes were more than twice as likely to be clinically depressed as the general population, and depressed diabetic patients required quantitatively and on a cost-basis more ambulatory care and more prescriptions⁴⁰. Among patients with diabetes, increased depressive symptom severity was associated with increased unadjusted 6-month total health care costs (low depressive

symptoms, \$2,094; medium, \$2,653; and high, \$3,654). When costs were adjusted for age, sex, medical comorbidity, diabetes severity, and diabetes knowledge, patients with higher depressive symptoms had greater costs⁴¹.

Arthritis also is often accompanied by depression and other psychological responses that heighten pain and increase disability⁴². In a 4-year longitudinal study of RA, Katz and Yelin found that depressed patients had significantly poorer clinical characteristics and function, and had significantly more physician visits and hospitalizations related to RA⁴³. As research continues, the role of depression in accelerating healthcare use and cost in still more chronic diseases will likely become evident.

Most of the costs incurred by FM claimants were for treatment of non-FM diagnoses. Only 1% of this employer's total costs for FM-depression claimants were related to treatment of FM; 10% went for treatment of depression and another 45% for selected comorbid conditions commonly found to be related to FM or depression from the literature. The remaining 44% of costs were associated with other conditions. The share of costs accounted for by drugs was 21% for the overall 10% sample versus 10% in the FM-depression cohort, with similar patterns for the other disease cohorts. The reduced cost of drugs in these cohorts was offset by equivalent increases in the share of medical and work-loss costs.

While the total costs of FM and depression were high, they are most likely understated because they reflect total employer payments for treatments received, yet FM and depression are both undertreated. Regardless of the ongoing debate in the medical community about the etiology of FM, it is clear that the costs of this syndrome and of related conditions are considerable, and worthy of attention by third-party payers.

The cost to the employer of any chronic condition can be significant, but because FM-depression is highly comorbid with other conditions, it is even more costly. Our findings underscore the need to comprehensively treat both the depression and the pain that characterize the co-occurrence of FM and depression. The influence of alternative treatments on the course and cost of FM and depression occurring separately and together may warrant further study.

Limitations. Because this study relied on insurance claims data, our findings are subject to the usual limitations of administrative data sets, including possibly inaccurate diagnoses and incomplete assembly of claims (e.g., missing bills, multiple plan coverage)⁴⁴.

FM and depression are difficult to diagnose, and there is no information on the accuracy of the diagnostic indications and the severity of the underlying illnesses. The complexity of FM and controversy about its definition may influence the breadth of comorbid conditions associated with the disease. Comorbid illnesses may reflect misdiagnosis or delay in the diagnosis of FM because many of its symptoms

mimic or overlap those of other diseases. Given the chronic nature and complexity of FM, this cohort was identified in this study on the basis of at least one FM claim over a 3-year period.

A sensitivity analysis, in which the Bonferroni adjustment was applied to a sample limited to employees with FM claims in 1998 only, yielded results consistent with those of the main analysis. In this cohort, per capita total costs of FM rose modestly (by 9%, to \$8,477), but still only amounted to 6% of total per-employee costs. Thus, even granting that the diagnosis of FM is controversial and that the accuracy of medical records used to identify the syndrome is questionable, when patients have at least one claim for FM in a one-year period, they are likely to make up a distinct and more costly cohort worthy of further study.

The costs presented here underestimate the true burden of depression and FM on society. Sick time at home and productivity at work were not fully measured. Only that part of work loss due to illness associated with disability or medical treatment was recorded. The actual payments for disability reported here reflect only a fraction of the employer's total-opportunity cost for work-force disruptions due to disability. Other likely workplace costs include reduced on-the-job productivity, administrative and training expenses for replacement workers, and days missed for sick time.

Our findings reveal that for every dollar for FM health-care costs (medical care plus prescriptions) of employees, the employer spent an additional \$57 to \$143 on other direct and indirect costs. However, treatment for conditions diagnosed as FM is virtually indiscernible from treatments for other conditions. Failure to account fully for the broader consequences of depression and FM, at least to the level observed in this study, would result in a significant under-assessment of the cost of these conditions to this employer.

REFERENCES

1. Greenberg PE, Kessler RC, Birnbaum HG, et al. The economic burden of depression in the United States: how did it change between 1990 and 2000. *J Clin Psychiatry* 2003;64:1465-75.
2. Birnbaum HG, Greenberg PE, Barton M, Kessler RC, Rowland CR, Williamson TE. Workplace burden of depression: a case study in social functioning using employer claims data. *Drug Benefit Trends* 1999;11:6-12.
3. Claxton AJ, Chawla AJ, Kennedy S. Absenteeism among employees treated for depression. *J Occup Environ Med* 1999;41:605-11.
4. Croghan TW, Obenchain RL, Crown WE. What does treatment of depression really cost? *Health Affairs* 1998;17:198-208.
5. Celiker R, Borman P, Oktem F, Gokce-Kutsal Y, Basgoze O. Psychological disturbance in fibromyalgia: relation to pain severity. *Clin Rheumatol* 1997;16:179-84.
6. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995;38:19-28.
7. Anderberg UM, Forsgren T, Ekselius L, Marteninsdottir I, Hallman J. Personality traits on the basis of the temperament and character inventory in female fibromyalgia syndrome patients. *Nordic J Psychiatry* 1999;53:353-9.
8. Epstein SA, Kay G, Clauw D, et al. Psychiatric disorders in patients with fibromyalgia. *Psychosomatics* 1999;40:57-63.
9. Bogetto F, Bonatto Revello R, Bertoli C, et al. Fibromyalgia. Psychopathologic aspects. *Minerva Psichiatrica* 1999;40:129-38.
10. Cathebras P, Lauwers A, Rousset H. Fibromyalgia. A critical review. *Ann Med Interne* 1998;149:406-14.
11. Hudson JI, Goldenberg DL, Pope HG Jr, Keck PE Jr, Schlesinger L. Comorbidity of fibromyalgia with medical and psychiatric disorders. *Am J Med* 1992;92:363-7.
12. Hudson JI, Pope HG. The concept of affective spectrum disorder: Relationship to fibromyalgia and other syndromes of chronic fatigue and chronic muscle pain. *Baillieres Clin Rheumatol* 1994;8:839-56.
13. Korszun A. Sleep and circadian rhythm disorders in fibromyalgia. *Curr Rheumatol Rep* 2000;2:124-30.
14. Wacker HR. Epidemiology and comorbidity of depressive disorders. *Ther Umsch* 2000;57:53-8.
15. Juhl JH. Fibromyalgia and the serotonin pathway. *Altern Med Rev* 1998;3:367-75.
16. Ackenheil M. Genetics and pathophysiology of affective disorders: relationship to fibromyalgia. *Z Rheumatol* 1998;57 Suppl 2:5-7.
17. Arnold LM, Keck PE Jr, Welge JA. Antidepressant treatment of fibromyalgia. *Psychosomatics* 2000;41:104-13.
18. Waylonis GW, Heck W. Fibromyalgia syndrome. New associations. *Am J Phys Med Rehabil* 1992;71:343-8.
19. Spath M. Current experience with 5-HT₃ receptor antagonists in fibromyalgia. *Rheum Dis Clin North Am* 2002;28:319-28.
20. Robinson RL, Birnbaum HG, Morley MA, Sisitsky T, Greenberg PE, Claxton AJ. Economic costs and epidemiological characteristics of patients with fibromyalgia claims. *J Rheumatol* 2004; in press.
21. de Girolamo G. Epidemiology and social costs of low back pain and fibromyalgia. *Clin J Pain* 1991;7 Suppl 1:S1-S7.
22. Wolfe F, Anderson J, Harkness D, et al. A prospective, longitudinal, multicenter study of service utilization and costs in fibromyalgia. *Arthritis Rheum* 1997;40:1560-70.
23. Burton WN, Conti DJ, Chen C-Y, Schultz AB, Edington DW. The role of health risk factors and disease on worker productivity. *J Occup Environ Med* 1999;41:863-7.
24. Burton WN, Conti DJ. Use of an integrated health data warehouse to measure the employer costs of five chronic disease states. *Dis Manage Health* 1998;2:17-26.
25. Barnett A, Birnbaum H, Cremieux P-Y, Fendrick AM, Slavin M. The costs of cancer to a major employer in the United States: a case control analysis. *Am J Managed Care* 2000;6:1243-51.
26. Drummond MF, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford: Oxford Medical Publications; 1987.
27. Kessler RC, Zhao S, Katz SJ, et al. Past-year use of outpatient services for psychiatric problems in the National Comorbidity Survey. *Am J Psychiatry* 1999;156:115-23.
28. Rossy LA, Buckelew SP, Dorr N, et al. A meta-analysis of fibromyalgia treatment interventions. *Ann Behav Med* 1999;21:180-91.
29. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. *Arch Gen Psychiatry* 1994;51:8-19.
30. White MT, Lemkau JP, Clasen ME. Fibromyalgia: a feminist biopsychosocial perspective. *Women & Therapy* 2001;23:45-58.
31. Reiffenberger DH, Amundson LH. Fibromyalgia syndrome: a review. *Am Fam Physician* 1996;53:1698-712.
32. McCain GA. A cost-effective approach to the diagnosis and treatment of fibromyalgia. *Rheum Dis Clin North Am* 1996;22:323-49.
33. Quijada-Carrera J, Valenzuela-Castaño A, Povedano-Gómez J, et al. Comparison of tenoxicam and bromazepam in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled trial.

- Pain 1996;65:221-5.
34. Wilke WS. Treatment of "resistant" fibromyalgia. *Rheum Dis Clin North Am* 1995;21:247-60.
 35. Norregaard J, Volkmann H, Danneskiold-Samsøe B. A randomized controlled trial of citalopram in the treatment of fibromyalgia. *Pain* 1995;61:445-9.
 36. Birnbaum HG, Barton M, Greenberg PE, et al. Direct and indirect costs of rheumatoid arthritis to an employer. *J Occup Environ Med* 2000;42:588-96.
 37. Ramsey S, Summers KH, Leong SA, Birnbaum HG, Kemner JE, Greenberg P. Productivity and medical costs of diabetes in a large employer population. *Diabetes Care* 2002;25:23-9.
 38. Evans DL, Staab JP, Petitto JM, et al. Depression in the medical setting: biopsychological interactions and treatment considerations. *J Clin Psychiatry* 1999;60 Suppl 4:40-55.
 39. Sheehan DV. Establishing the real cost of depression. *Managed Care* 2002;11:7-10.
 40. Egede LE, Zheng D, Simpson K. Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. *Diabetes Care* 2002;25:464-70.
 41. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med* 2000;160:3278-85.
 42. Keefe FJ, Smith SJ, Buffington ALH, Gibson J, Studts JL, Caldwell DS. Recent advances and future directions in the biopsychosocial assessment and treatment of arthritis. *J Consult Clin Psychol* 2002;70:640-55.
 43. Katz PP, Yelin EH. Prevalence and correlates of depressive symptoms among persons with rheumatoid arthritis. *J Rheumatol* 1993;20:790-6.
 44. Birnbaum HG, Cremieux P-Y, Greenberg PE, LeLorier J, Ostrander J, Venditti L. Using healthcare claims data for outcomes research and pharmaco-economic analyses. *Pharmacoeconomics* 1999;16:1-8.