Gender Differences in the Prevalence of Fibromyalgia and in Concomitant Medical and Psychiatric Disorders: A National Veterans Health Administration Study

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Abstract

Background: Fibromyalgia is a poorly understood, chronically disabling pain syndrome. While research has focused on its clinical presentation and treatment, less is known about fibromyalgia's clinical epidemiology in real-world healthcare systems. Gender differences have been difficult to study because relatively few males are diagnosed with fibromyalgia.

Methods: Veterans Health Administration (VHA) patients diagnosed with fibromyalgia nationwide in FY 2012 were compared to Veterans with other pain diagnoses on sociodemographic characteristics, medical and psychiatric diagnoses, health service use, and opioid and psychotropic prescription fills. Additional analyses compared characteristics of men and women diagnosed with fibromyalgia. Risk ratios and Cohen's *d* were used for bivariate comparisons, followed by logistic regression analyses to identify independent factors associated with a diagnosis of fibromyalgia in the VHA.

Results: Altogether, 77,087 of 2,216,621 Veterans with pain diagnoses (3.48%) were diagnosed with fibromyalgia. They were more likely to be female, younger than patients with other pain conditions, more likely to have multiple psychiatric comorbidities and other types of pain, and used more medical outpatient services. Women diagnosed with fibromyalgia were younger and more likely to have headaches, connective tissue diseases (CTD), and psychiatric comorbidities, while men had more comorbid medical conditions.

Conclusions: In this large, predominantly older male sample of Veterans with pain diagnoses, those with fibromyalgia were far more likely to be women. Gender comparisons showed women with fibromyalgia were more likely to be diagnosed with psychiatric disorders and CTD, while males were more likely to be diagnosed with medical conditions. Fibromyalgia shows a striking, gender-dependent picture of multimorbidity, which should be considered in treatment.

Keywords: Veterans Health Administration, fibromyalgia, gender differences

Introduction

Cₕᵣₒₙᵢc pain is a major source of disability and costly health service utilization, affecting approximately 100 million adults in the United States, or more than one-third of the adult population.[1] Fibromyalgia is a potentially disabling, but poorly understood rheumatic condition characterized by chronic widespread pain and tenderness, fatigue, cognitive difficulties, and overall functional impairment. Notably, fibromyalgia has a high incidence of psychiatric comorbidity, but no widely accepted etiology.[2–5]

In the United States, the prevalence of fibromyalgia has been estimated to range from 2% to 8%, affecting 5–10 million adults.[6,7] It is most prevalent among middle-aged

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women, encompassing 75%–90% of those diagnosed.[8–10] A diagnosis of fibromyalgia has classically been reliant on an evaluation of ''tender points,'' or areas of tenderness around joints, assessed by palpation or algometer.[11,12] Women tend to report more tender points than men,[13] and have been reported to feel pain more intensely at these sites.[14] The greater frequency of fibromyalgia among women has thus been largely attributed to this criterion. Recently revised diagnostic standards have eliminated the use of tender points as a determining factor, and as a result, gender differences in prevalence appear to be far smaller than previously estimated.[7,15] However, a recent study suggested that despite efforts to develop diagnostic tools for assessing symptoms related to fibromyalgia, these guidelines are not universally applied in clinical settings and lack physiological justification[16]; thus, there is no ''gold standard'' for a clinical diagnosis of fibromyalgia.

Fibromyalgia is commonly associated with psychiatric comorbidities.[7,17] International research has shown high rates of Axis I and II diagnoses, including depression, anxiety disorders, bipolar disorder, obsessive-compulsive disorder, personality disorders, and posttraumatic stress disorder (PTSD) in patients with fibromyalgia.[18–22] Furthermore, the underlying physical cause(s) of fibromyalgia remain unknown, although it is potentially associated with dysregulated dopamine in the brain reward circuitry.[23,24] Thus, diagnosis relies exclusively on self-report data.[25] As a result of this diagnostic ambiguity and substantial psychiatric comorbidity, fibromyalgia is frequently, and controversially, viewed as a somatoform psychiatric disorder.[15,26] Whether gender differences in prevalence of fibromyalgia are accompanied by other gender differences has not been systematically examined because of the small male samples in most studies.

Several studies from outside the United States have suggested that people diagnosed with fibromyalgia are significantly more impaired and utilize higher amounts of healthcare resources compared to the general population. Two Canadian studies of women with fibromyalgia found this cohort to be high consumers of conventional, as well as complementary and alternative medicine.[27,28] Furthermore, it has been reported that each comorbid condition accompanying fibromyalgia is associated with a 20% increase in healthcare costs,[28] with psychological vulnerability further increasing levels of service use and cost.[27] In United Kingdom, a diagnosis of fibromyalgia was related to higher rates of illness and healthcare resource use for at least 10 years before diagnosis.[29] Nearly 47% of a Scottish sample reported having lost their job due to impairment related to fibromyalgia, although further analyses revealed no difference in health service utilization between these patients and a clinic control group.[30]

Despite the host of international studies, few studies have evaluated the prevalence and correlates of fibromyalgia in large U.S. clinical populations. Sanchez et al. evaluated healthcare resource use based on claim data from Humana Inc. using ICD-9 codes representing fibromyalgia.[31] In the 6 months following a diagnosis of fibromyalgia, patients showed significantly increased rates of service utilization and use of pain-related medication compared to prediagnosis levels, although this rate returned to the baseline level within 3 years.[31] In a multisite study of rheumatology clinics, Wolfe et al.[32] reported increased healthcare utilization and cost associated with fibromyalgia severity and related functional

disability. Patients with fibromyalgia were also more likely to undergo various surgeries, and hospitalizations.[32]

A recent study examined gender differences in the demographics and clinical correlates of musculoskeletal disorders among Veterans. In that study, fibromyalgia was included among 14 groups of musculoskeletal disorders and was not examined separately.[33] Thus, no study, to our knowledge, has systematically compared sociodemographic characteristics, patterns of comorbidity, service use, and psychotropic medication prescription fills among patients with fibromyalgia in comparison to patients with other pain syndrome diagnoses, or between males and females diagnosed with fibromyalgia. In a previous study, however, we reported a high rate of fibromyalgia in a national sample of patients served by specialized pain clinics in the Veterans Health Administration (VHA) in FY 2012.[34] In this study, we sought to expand on this finding by comparing sociodemographic characteristics, medical and psychiatric comorbidities, and service use among Veterans diagnosed with fibromyalgia compared to Veterans with other pain diagnoses. Furthermore, taking advantage of the large proportion of men in the VHA, we further examined differences between men and women diagnosed with fibromyalgia on sociodemographic characteristics, concomitant diagnoses, and service use, including psychotropic and opiate prescription fills. We thus sought to replicate previous findings on gender differences in prevalence and to extend them with an examination of gender differences in multimorbidity and service use.

Materials and Methods

This study was approved by the Veterans Affairs (VA) Connecticut Healthcare System Human Subjects Subcommittee.

Sample, sources of data

The sample included all Veterans receiving a pain diagnosis in FY 2012 (October 1, 2011, to September 30, 2012) and patients who did not meet these parameters were not included. Data on sociodemographic characteristics, diagnoses (pain, medical, and psychiatric), and service use (mental health and medical-surgical service use) were obtained from the VA Northeast Program Evaluation Center using outpatient encounter files and the patient treatment files (reflecting inpatient discharges), while data on medications (opioids and psychotropic medications) were retrieved from the VA Drug Benefit Management database. Diagnoses were based on the International Classification of Diseases, 9th edition (ICD-9). A list of all ICD-9 codes included in analyses are available in Appendix Table A1.

Measures

Sociodemographics. Sociodemographic characteristics included age, race, gender, rural/urban residence classified as urban, small rural, large rural, and isolated rural,[35] Operation Enduring Freedom/Operation Iraqi Freedom military service, VA disability compensation (classified by disability ratings of ≥50% or <50%), receipt of a non-service connected VA pension, and homelessness (documented by use of a specialized homeless service program encounter codes or a V60 ICD-9 code).

Medical diagnoses. Based on ICD-9 codes, data on medical diagnoses were identified and selected from component diagnoses of the Charlson Comorbidity Index,[36] originally developed to predict mortality risk. It was used in this study to assess the severity of medical comorbidity and included the following: cancer (including metastatic), myocardial infarction, congestive heart failure, cerebrovascular accidents, peripheral vascular disease, paraplegia, liver disease, headaches, connective tissue disease (CTD), seizures, insomnia, HIV, peptic ulcer disease, chronic pulmonary disease, diabetes mellitus and related complications, renal disease, hepatic disease, and dementia.

Psychiatric diagnoses. Psychiatric diagnoses were selected based on ICD-9 codes, and were classified as follows: any substance abuse diagnosis, drug dependence, alcohol dependence, dual diagnosis, major depression, other depression (e.g., dysthymia), organic brain syndrome, bipolar disorder, anxiety disorder, adjustment disorder, personality disorder, PTSD, schizophrenia, other psychiatric diagnosis, and any mental health diagnosis.

Pain diagnoses. Patients with other pain diagnoses were compared to those with an ICD-9 code for fibromyalgia (729.1). Twenty-seven ICD-9 diagnostic codes for pain were clustered into six variables that were included for analysis as the other pain diagnoses. These six variables and their corresponding ICD-9 codes were as follows: (1) headache (784.00); (2) pain associated with diabetes and other peripheral neuropathies (250.6, 337.1); (3) joint pain, generalized pain, and central pain syndrome (338.00, 719.49, 780.96); (4) muscle spasm (728.85); (5) neuralgia, neuritis, and radiculitis (053.12, 729.2); and (6) other pain diagnoses (379.91, 478.1, 524.6, 526.9, 536.8, 625.9, 723.1, 724.1, 724.3, 724.2, 724.5, 307.89, 786.52, 729.5, 786.50, 786.52, 788.00, and 789.00).

Psychotropic medications. Psychotropic medications were analyzed as number of prescriptions filled, categorized according to eight classes: (1) antidepressants; (2) antipsychotics; (3) anticonvulsants/mood stabilizers; (4) anxiolytics/sedatives/hypnotics; (5) stimulants; (6) lithium; (7) opioids, and; (8) any psychotropics. The specific medications included in each class are available in Appendix Table A2.

Service use. Service use was represented by the number of outpatient mental health visits, and the number of medical-surgical and emergency department visits calculated from encounter file data classified by clinic stop codes. Use of any inpatient mental healthcare, based on discharge abstracts from the patient treatment file, was represented by a single dichotomous variable (yes/no).

Data analysis

Using Statistical Analysis Software (SAS), bivariate comparisons of Veterans with a diagnosis of fibromyalgia and those with other pain diagnoses addressed the following: (1) sociodemographic characteristics; (2) general medical diagnoses; (3) specific pain diagnoses; (4) psychiatric diagnoses; (5) psychotropic medication and opiate prescription fills; and (6) service use. Stepwise logistic regression was then used to identify factors that were independently associated with a diagnosis of fibromyalgia. Standardized regression coefficients (SRC) were included in the model output to allow comparison of effect sizes between dichotomous and continuous variables.

In bivariate analyses, we utilized risk ratios for comparison of groups on categorical variables (e.g., prevalence of medical and psychiatric diagnoses) and Cohen's d (difference in means divided by the pooled standard deviation)[37] for comparisons involving continuous variables (i.e., service use and number of psychotropic medication fills). These measures were chosen due to the fact that the large sample sizes involved in this study will inevitably yield highly significant p-values, regardless of the clinical meaningfulness of group differences. Given the large sample size, risk ratios >1.5 or <0.5 and Cohen's d values >0.2 or < −0.2 were considered to be inclusive and indicative of substantial differences, and were used to identify variables to be included in subsequent logistic regression analysis.

Because both continuous and dichotomous variables were included in the logistic regression analyses, SRC were used to compare the strength of association across independent variables.

Results

Sample

Participants included 2,216,621 Veterans who had a pain diagnosis in fiscal year 2012. Within this group, 77,087 (3.48%) were diagnosed with fibromyalgia, while 2,139,534 (96.52%) received other pain diagnoses. Of those diagnosed with fibromyalgia, 57,467 (74.5%) were male and 19,620 (25.5%) were female.

Veterans with fibromyalgia versus other pain diagnoses

The most notable sociodemographic difference between Veterans with fibromyalgia and those with other pain diagnoses was that those with fibromyalgia were over three times more likely to be female (25.5%) compared to 7.7% among those with other pain diagnoses (Table 1). Veterans diagnosed with fibromyalgia were substantially younger, at least one and a half times more likely to receive one of several psychiatric diagnoses, including bipolar disorder, depression, PTSD, or an anxiety disorder, and were more than twice as likely to be diagnosed with a personality disorder (Table 1). Furthermore, these patients were nearly three and a half times more likely to receive a diagnosis of CTD when compared to those with other pain conditions. Herpetic pain was nearly two and a half times more common in the cohort diagnosed with fibromyalgia, while muscle spasm pain and headache pain were over one and a half times more frequent (Table 1). There were no substantial differences in other medical diagnoses.

Prescription fills for anxiolytic-sedative hypnotics and anticonvulsants–mood stabilizers were more numerous among Veterans with fibromyalgia, with effect sizes of $d = 0.24$ and 0.32, respectively. Veterans diagnosed with fibromyalgia had more mental health outpatient visits than those with other pain diagnoses, and more medical-surgical outpatient visits as well ($d = 0.31$) (Table 1). A full list of all the variables analyzed as potential correlates of fibromyalgia

TABLE 1. PREVALENCE AND CORRELATES OF A FIBROMYALGIA DIAGNOSIS AMONG VETERANS IN FY 2012

	No Fibromyalgia	Fibromyalgia	
	N = 2,139,534 (96.52%)	N = 77,087 (3.48%)	
	Mean (SD)	Mean (SD)	Cohen's D
Demographics	58.83 (15.43)	55.12 (14.11)	0.25*
	N (%)	N (%)	Risk ratio
Age			
40–49	256,491 (12)	14,501 (18.8)	1.57*
>85	89,116 (4.2)	1,501 (1.9)	0.47*
Female	164,890 (7.7)	19,620 (25.5)	3.3*
Medical diagnosis: general			
Insomnia	125,116 (5.8)	7,045 (9.1)	1.6*
Connective tissue disease	27,735 (1.3)	3,413 (4.4)	3.42*
Pain diagnoses			
Headache	214,143 (10)	14,631 (19)	1.9*
Muscle spasm pain	79,689 (3.7)	4,289 (5.6)	1.5*
Herpetic pain	25,976 (1.2)	2,248 (2.9)	2.4*
Psychiatric diagnoses			
Bipolar disorder	63,435 (3)	3,827 (5)	1.7*
Major depression	186,601 (8.7)	12,889 (16.7)	1.92*
Other depression (e.g., dysthymia)	475,390 (22.2)	26,896 (34.9)	1.57*
PTSD	370,924 (17.3)	20,103 (26.1)	1.5*
Anxiety disorder	265,110 (12.4)	15,858 (20.6)	1.7*
Personality Disorder	31,294 (1.5)	2,665 (3.5)	2.32*
Service use			
Any mental health service use	739,466 (35)	38,922 (50.5)	1.5*
	Mean (SD)	Mean (SD)	Cohen's D
Medical surgical visits	10.4 (11.5)	14.32 (13.7)	0.31*
All outpatient visits	14.71 (21.78)	21.53 (27.4)	0.28*
Psychotropic medications			
Anxiolytic/sedative/hypnotic prescriptions	1.6 (4.6)	2.87 (6.05)	0.24*
Anticonvulsant/mood stabilizer prescriptions	0.2 (0.4)	0.34 (0.47)	0.32*

*Cohen's D > 0.2; Risk ratio < 0.5 or > 1.5.

is available in Supplementary Table S1 (Supplementary Data are available online at www.liebertpub.com/jwh).

Multivariate analysis of Veterans diagnosed with fibromyalgia versus other pain diagnoses

Among Veterans with a pain diagnosis in 2012, the strongest independent predictor of fibromyalgia was being female (SRC = 0.177 in Table 2). Furthermore, diagnoses of comorbid CTD (SRC = 0.074) and herpetic pain (SRC = 0.046), as well as medical-surgical outpatient visits (SRC = 0.089) were also notable (Table 2). In contrast to bivariate analyses, psychiatric comorbidities had only weak associations with fibromyalgia in multivariate analysis.

Bivariate analysis of those with fibromyalgia by gender

In a gender comparison of patients diagnosed with fibromyalgia, the most notable sociodemographic finding was that women diagnosed with fibromyalgia were nearly 9 years younger than their male counterparts (48.5 vs. 57.4 years, respectively), with 52.3% below the age of 49. (Table 1). Women were also one and a half times more likely to be black

than men (26.2% vs. 18%; Table 3), although this should be interpreted cautiously considering that in 19% of the sample, race was not identified.

Overall, women diagnosed with fibromyalgia had a greater likelihood of having a comorbid psychiatric diagnoses compared to men. Specifically, they were one and a half times more likely to be diagnosed with an anxiety disorder, and two and a half times as likely to be diagnosed with bipolar disorder and personality disorders. Men, on the other hand, were almost twice as likely to be diagnosed with alcohol dependence (Table 2).

Men were also substantially more likely to be diagnosed with accompanying medical diagnoses. These included cardiovascular diagnoses such as myocardial infarction, peripheral vascular disease, and cerebrovascular accidents. Men were also more likely to be diagnosed with dementia, diabetic complications, and paraplegia. Women were over two times more likely to be diagnosed with CTD and headache pain (Table 2).

Men and women diagnosed with fibromyalgia did not differ substantially on service use or psychotropic medication prescriptions. A full list of all the variables analyzed as potential correlates of fibromyalgia as a function of gender is available in Supplementary Table S2.

TABLE 2. PREDICTORS OF A FIBROMYALGIA DIAGNOSIS IN FY2012 (LOGISTIC REGRESSION)

	Fibromyalgia N = 77,087 (3.48%)				
	Coefficient	SE	SRC	OR	Lower, upper 95% CI
Demographics					
Female	1.162	0.009	0.177	3.2	3.1–3.2
Age	−0.007	<0.000	−0.058	0.993	0.993–0.994
Medical diagnoses: general					
Insomnia	0.229	0.013	0.03	1.26	1.22–1.29
Connective tissue disease	1.139	0.019	0.074	3.12	3.01–3.24
Pain categories					
Headache	0.328	0.01	0.055	1.39	1.36–1.42
Herpetic pain	0.738	0.023	0.046	2.09	2.00–2.19
Skeletal muscle spasm pain	0.323	0.017	0.034	1.38	1.34–1.43
Psychiatric diagnoses					
Bipolar disorder	0.077	0.018	0.007	1.08	1.04–1.12
Major depression	0.263	0.011	0.042	1.30	1.27–1.33
Other depression (dysthymia)	0.279	0.009	0.06	1.32	1.30–1.34
PTSD	0.175	0.009	0.037	1.19	1.17–1.21
Anxiety disorder	0.175	0.01	0.032	1.19	1.17–1.21
Any personality disorder	0.161	0.022	0.011	1.18	1.13–1.23
Service use					
Medical surgical visits	0.0141	<0.000	0.089	1.01	1.01–1.02
Psychiatric or substance abuse outpatient visits	−0.0007	<0.000	−0.007	0.99	0.99–1.00
Psychotropic medications					
Anxiolytic/sedative/hypnotic prescriptions	0.012	<0.000	0.031	1.01	1.011–1.013
Anticonvulsant/mood stabilizer prescriptions	0.001	<0.000	0.007	1.00	1.001–1.002

SE, standard error; SRC, standardized regression coefficient; OR, odds ratio; MH, mental health; SA, substance abuse; ER, emergency room; PTSD, posttraumatic stress disorder.

Multivariate analysis of female and male Veterans diagnosed with fibromyalgia

The variables most strongly associated with being female among Veterans diagnosed with fibromyalgia were age (SRC = −0.28), and diagnoses of CTD (SRC = 0.122) and headache pain (SRC = 0.172). Psychiatric diagnoses associated with female gender included bipolar disorder and major depressive disorder (SRC = 0.09 and 0.11, respectively) (Table 4).

Discussion

The findings of this study should be interpreted in the context of the large VHA sample that produced the analyzed dataset. While VHA datasets can be informative in terms of detailing the prevalence and correlates of a given diagnosis, it is important to note that this dataset reflects real-world practice by front-line clinicians in the VHA, and thus reflects how the VHA operates, including clinician biases in terms of diagnostic and treatment patterns.

This study compared Veterans receiving a diagnosis of fibromyalgia to those with other pain diagnoses nationally in the VHA in FY 2012. The 3.48% diagnosed with fibromyalgia were robustly more likely to be female, and younger than patients with other pain conditions. Taking advantage of the large proportion of men in VHA, we found that among those diagnosed with fibromyalgia, women were younger than their male counterparts. They also tended to have other pain-related conditions, including headaches and CTD. Finally, it is notable that these women also had higher rates of psychiatric comorbidity, while men had more comorbid medical conditions.

The major finding of the first set of analyses was the substantial gender disparity associated with a fibromyalgia diagnosis, with a female:male ratio of 4:1. This finding is consistent with an extensive literature reporting a substantially higher prevalence of fibromyalgia among women, with male:female ratios ranging from 1:2 to 1:9.[5,7,8] Generally, women are at greater risk for developing chronic pain, purportedly due to a number of factors ranging from gender expectations to hormonal influences.[38] The major theory that has historically explained the gender disparity specific to fibromyalgia has been the reliance on tender points for diagnosis. However, tender points are difficult to assess, and women have many such points when compared to men, biasing an already-disparate pain syndrome. More recent studies reflecting the 2010 removal of tender points as a diagnostic criterion for fibromyalgia have reported gender ratios approaching equality.[39] However, we do not have data on how and if the tender points criteria were applied by VA clinicians, although literature suggests that clinicians in general may have not been particularly vigilant in assessing this criterion, suggesting that it may not be of clinical importance in real-world practice.[16]

A second notable finding of this study is that Veterans with fibromyalgia were, on average, 4 years younger than their counterparts diagnosed with other pain conditions. The relationship between age and the likelihood of a fibromyalgia diagnosis has been a subject of debate. While it is commonly thought that fibromyalgia tends to appear in younger cohorts,[40] studies of the general population indicate that fibromyalgia can appear at any age, ranging from childhood to late adulthood, with risk increasing with age.[39,41,42] Overall, our findings regarding age are consistent with the

TABLE 3. COMPARISON OF THE PREVALENCE AND CORRELATES OF A FIBROMYALGIA DIAGNOSIS
IN FEMALE AND MALE VETERANS IN FY 2012

	Female	Male	
	N = 19,620 (25.45%)	N = 57,567 (74.55%)	
	Mean (SD)	Mean (SD)	Cohen's D
Demographics	48.5 (11.69)	57.37 (14.16)	−0.68*
	N (%)	N (%)	Risk ratio
Age			
<40	4,675 (24)	6,975 (12.1)	1.96*
40–49	5,552 (28.3)	8,949 (15.6)	1.82*
65–74	829 (4.2)	9,565 (16.6)	0.25*
75–85	220 (1.1)	4,152 (7.3)	0.16*
>85	109 (0.5)	1,392 (2.4)	0.23*
Black	4,668 (26.2)	9,053 (18)	1.5*
VA Pension	294 (1.5)	1,822 (3.2)	0.47*
Medical diagnosis: general			
Myocardial infarction	98 (0.5)	1,033 (1.8)	0.28*
Peripheral vascular disease	324 (1.7)	3,448 (6)	0.28*
Cerebrovascular accident	530 (2.7)	3,273 (5.7)	0.47*
Dementia	35 (0.2)	329 (0.6)	0.31*
Connective tissue disease	1,408 (7.2)	2,005 (3.5)	2.06*
Complications of diabetes	459 (2.3)	3,756 (6.5)	0.36*
Paraplegia	125 (0.6)	803 (1.4)	0.46*
Renal disease	326 (1.7)	3,239 (5.6)	0.3*
HIV	32 (0.2)	400 (0.7)	0.23*
Metastatic cancer	57 (0.3)	376 (0.7)	0.44*
	Mean (SD)	Mean (SD)	Cohen's D
Charlson medical severity diagnosis index	1.3 (1.4)	1.8 (1.9)	−0.3*
	N (%)	N (%)	Risk ratio
Pain diagnoses			
Headache	6,561 (33.4)	8,070 (14)	2.38*
Diabetic pain	402 (2)	3,185 (5.5)	0.37*
Psychiatric diagnoses			
Organic brain syndrome	38 (0.2)	372 (0.6)	0.3*
Alcohol dependence	907 (4.6)	5,323 (9.3)	0.5*
Bipolar disorder	1,739 (8.9)	2,088 (3.6)	2.44*
Major depression	5,048 (25.7)	7,841 (13.6)	1.89*
Other depression (e.g., dysthymia)	8,960 (45.7)	17,936 (31.2)	1.46*
Anxiety disorder	5,568 (28.4)	10,290 (17.9)	1.59*
Personality disorder	1,302 (6.6)	1,363 (2.4)	2.8*

*Cohen's D > 0.2; Risk ratio <0.5 or >1.5.

literature showing a prevalence of fibromyalgia in later middle age.[42–44]

The most distinctive feature of this study is the exploration of gender differences in patterns of multimorbidity. Mutimorbidity has been the focus of increasing attention in recent years because it has been noted that, while most randomized trials exclude co-morbid conditions, most patients, in fact, have multiple diagnoses.[45–47] Notably, women with fibromyalgia lacked major medical diagnoses that could elucidate complaints of diffuse pain, with the exception of CTD and headache pain. As fibromyalgia is difficult to diagnose itself, it is notable that women Veterans with fibromyalgia had a higher prevalence of both psychiatric diagnoses as well as CTD. Coinciding with the challenges associated with making a diagnosis fibromyalgia, CTD is also difficult to diagnose and is characterized by unspecified defects and in-

flammation of collagen and other connective tissue structures, as well as by pain, related to autoimmune disease processes.[48] Although fibromyalgia is likely not autoimmune in nature, some symptoms closely resemble autoimmune diseases such as rheumatoid arthritis. Rheumatoid conditions are often accompanied by fibromyalgia, which may be added as a diagnostic label for the resultant diffuse pain.[49]

In contrast to women, men with fibromyalgia were more likely to have several general medical conditions, including myocardial infarction, peripheral vascular disease, cerebrovascular accidents, and diabetic complications, including pain. It could be speculated that the greater age of men might explain this discrepancy, and while this was partially true, these differences persisted after adjustment for age in multiple logistic regression.

It is also notable that concomitant psychiatric disorders were more common among women compared to men. The higher

TABLE 4. PREDICTORS OF A FIBROMYALGIA DIAGNOSIS IN FEMALE VETERANS IN FY2012 (LOGISTIC REGRESSION)

	Female N = 19,620 (25.45%)				
	Coefficient	SE	SRC	OR	Lower, upper 95% CI
Demographics					
Age	−0.037	0.0008	−0.282	0.964	0.963–0.966
Black	0.46	0.022	0.099	1.576	1.509–1.646
VA pension	−0.49	0.069	−0.045	0.615	0.537–0.704
Medical diagnoses: general					
Myocardial infarction	−0.741	0.114	−0.049	0.476	0.381–0.596
Peripheral vascular disease	−0.649	0.063	−0.078	0.522	0.461–0.591
Cerebrovascular accident	−0.302	0.054	−0.037	0.739	0.665–0.821
Connective tissue disease	1.072	0.041	0.122	2.922	2.696–3.167
Complications from diabetes	−0.489	0.079	−0.062	0.613	0.525–0.716
Pain categories					
Headache	0.792	0.022	0.172	2.21	2.115–2.304
Diabetic pain	−0.294	0.085	−0.035	0.746	0.631–0.881
Psychiatric diagnoses					
Bipolar disorder	0.712	0.038	0.09	2.037	1.892–2.195
Major depressive disorder	0.533	0.023	0.111	1.704	1.628–1.784
Anxiety disorder	0.244	0.023	0.055	1.276	1.221–1.333
Any personality disorder	0.574	0.045	0.059	1.776	1.626–1.939

prevalence of bipolar disorder, anxiety disorders, personality disorders, and particularly major depression among women Veterans is consistent with the diagnostic pattern found among women with fibromyalgia in the general population,[50,51] and these findings largely persisted in multiple logistic regression analyses. These findings are consistent with previous studies that reported more frequent psychiatric conditions in female Veterans with chronic pain[52] or, more specifically, with musculoskeletal pain.[33]

Despite the higher prevalence of psychiatric comorbidity, women were no more likely than men to seek mental health treatment. However, Veterans with fibromyalgia do appear more likely to utilize medical-surgical services. Primary care providers may attempt to treat the comorbid pain and psychiatric conditions in women, rather than referring patients with fibromyalgia to mental health services, or these patients may be more likely to refuse mental health services. It is also possible that women are reluctant to accept that a psychiatric diagnosis may be complicating their pain, and are thus less likely to seek multidisciplinary pain treatment.

A final, particularly encouraging finding of this study is that, although opioids are often used to manage fibromyalgia pain in the general population, our data do not suggest extensive use of these potentially addictive drugs for Veterans with fibromyalgia. Longitudinal data from a multidisciplinary pain clinic indicated that patients receiving opioids for fibromyalgia have poorer outcomes, including more debilitating symptoms and reduced functionality.[53]

A particular strength of this study is the large sample, including high numbers of men, and one that reflects real-world clinician practice in a national healthcare system. It should be noted that a feature of large, administrative datasets such as this is that they reflect real-world practice by front-line clinicians. While this dataset may reflect clinician bias, it is important to understand provider behavior and how diagnoses are applied in the VHA. This study is the first to our knowledge, to examine gender differences in both the prevalence of fibromyalgia and

in patterns of multimorbidity in the VHA, and suggests that clinician practice in the VHA, as it relates to fibromyalgia, mimics that of physicians in the general population.

A limitation of this study is that, although this sample reflects data from FY 2012, it is likely that the sample included patients with a long-standing fibromyalgia diagnosis dating back to before the criteria for diagnosing fibromyalgia were changed to exclude "tender points." However, the new criteria do not indicate a lower incidence of fibromyalgia in women, but a higher incidence in men. As such, it is possible that our sample actually underestimates the incidence of fibromyalgia in male Veterans. A future study comparing the diagnostic rates and correlates of fibromyalgia in a more recent sample, taking tender points into consideration, would be informative. A second limitation is that data on the procedures VA clinicians used to diagnose fibromyalgia, as well as psychiatric diagnoses, in this sample were not available, and diagnosis is reliant exclusively on coding within each patient's medical record. Thus, it is unknown if evaluation of tender points was incorporated into their assessment of fibromyalgia, and what other factors resulted in this diagnosis. However, it seems likely that a diagnosis of fibromyalgia in real-world practice relies more heavily on factors other than tender points, including self-reported pain, functionality, and quality of life.[16] Furthermore, it is also important to note that psychiatric diagnoses are not necessarily systematic in the VA, and are thus reliant on individual patient-physician factors. Finally, as this analysis was performed using national VA data, which is representative of an older, male, more disabled population, the generalizability of these findings to the general population is unknown.

Conclusions

These results from a national VHA sample of Veterans comprised predominately of men, showed both that women were more likely to have fibromyalgia than men, and men and

women exhibit substantially different patterns of multi-morbidity. These patterns notably indicate concurrent psychiatric disorders in women, and alcohol use disorder and cardiovascular disorders in men. These findings are in line with previous studies that examined gender differences in musculoskeletal or chronic pain. Whether this difference in patterns of multimorbidity reflects biological differences, diagnostic gender bias, or inconsistent interpretation of symptoms, should be the subject of future research.

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APPENDIX TABLE A1. ICD-9 CODES FOR ANALYZED VARIABLES

	ICD-9 code
Medical diagnosis: general	
Seizures	780.39
Insomnia	780.52
Myocardial infarction	410.90
Congestive heart failure	428.0
Peripheral vascular disease	443.9
Cerebrovascular accident	434.91
Dementia	290.00–290.99; 294.10; 331.00
Chronic obstructive airway disease	491.22
Connective tissue disease	710.9
Peptic ulcer disease	533.9
Hepatic disease	571.9
Diabetes mellitus	250.00
Complications of diabetes	250.90
Paraplegia	344.1
Renal disease	585.9
HIV	042
Cancer	140–165; 170–172; 174–176; 179–195; 200–208; 238.6
Metastatic cancer	196–199
Pain diagnoses	
Headache	784.00
Fibromyalgia	729.1
Diabetic pain	250.6; 337.1
Musculoskeletal pain	338.00; 719.49; 780.96
Muscle spasm pain	728.85
Herpetic pain	053.12; 729.2
Other pain diagnoses	379.91; 478.1; 524.6; 526.9; 536.8; 625.9; 723.1; 724.1; 724.3; 724.2; 724.5; 307.89; 786.52; 729.5; 786.50; 786.52; 788.00; 789.00
Psychiatric diagnoses	
Organic brain syndrome	310.9
Alcohol dependence	303; 305.00
Drug dependence	292.01–292.99; 304; 305.20–305.99
Schizophrenia	295
Bipolar disorder	296.0×, 296.1×, 296.40–296.89
Major depression	296.2–296.39
Other depression	300.4; 296.9; 311; 301.10–301.19
PTSD	309.81
Anxiety disorder	300, excluding 300.4
Adjustment disorder	309, excluding 309.81
Personality disorder	301; 301.2; 301.99

APPENDIX TABLE A2. PSYCHOTROPIC MEDICATIONS IN EACH CLASS

Psychotropic medication class	Medications included
Antidepressant prescriptions	Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine, isocarboxazid, phenelzine, selegiline, tranylcypromine, bupropion, citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, fluvoxamine, maprotiline, mirtazapine, nefazodone, paroxetine, sertraline, trazodone, and venlafaxine
Anxiolytic/sedative/hypnotic prescriptions	Alprazolam, chlordiazepoxide, clorazepate, clonazepam, diazepam, estazolam, flurazepam, lorazepam, oxazepam, temazepam, triazolam, buspirone, chloral hydrate, eszopiclone, meprobamate, zaleplon, and zolpidem
Stimulants	Amphetamine, dextroamphetamine, lisdexamfetamine, methamphetamine, dexmethylphenidate, and methylphenidate
Anticonvulsant/mood stabilizer prescriptions	Carbamazepine, gabapentin, lamotrigine, oxcarbazepine, topiramate, valproate sodium, valproic acid, and divalproex sodium
All psychotropics	Any psychotropic medication
Opiates	Any opioid medication