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Original Article

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Longitudinal outcomes among patients with fibromyalgia, chronic widespread pain, or localized chronic low back pain

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Abstract

Objectives: The objective of this study was to compare longitudinal outcomes of patients with FM, CWP, or localized chronic low back pain (LBP) to determine whether FM is an extreme manifestation of the CWP continuum.

Methods: A retrospective cohort study was conducted within a national pain research registry from August 2019 to July 2023. A total of 310 participants with FM (and CWP), CWP (without FM), or LBP were followed for 12 months to measure pain intensity, back-related disability, and health-related quality of life (HRQOL). Multivariable analyses were performed with generalized estimating equations (GEEs), including baseline and longitudinal covariates to adjust for potential confounding.

Results: The mean age of the participants was 52.3 (standard deviation [SD], 13.6) years, and 238 (76.8 %) were female. There were 64 (20.6 %) participants with FM, 56 (18.1 %) with CWP, and 190 (61.3 %) with LBP. There were no differences in pain intensity among the groups. Compared with back-related disability in the LBP group (mean, 12,7; 95 % confidence interval [CI], 11.4–14.1), the FM group (mean, 15.3; 95 % CI, 13.7–17.0; p=0.006) and CWP group (mean, 16.2; 95 % CI, 14.8–17.7; p<0.001) had greater disability. There were no clinically relevant differences in pain and disability between the FM and CWP groups. Compared with the LBP group, the FM group had worse outcomes on five HRQOL scales, and the CWP group had worse outcomes on all seven scales. Clinically relevant HRQOL differences between the FM and CWP groups involved anxiety and depression, with results favoring the FM group.

Conclusions: These findings do not support the view that FM is an extreme manifestation of the CWP continuum, involving greater pain, disability, or HRQOL deficits.

The criteria for fibromyalgia (FM) and chronic widespread pain (CWP) and their interrelationship have evolved. The American College of Rheumatology (ACR) proposed widespread pain and tenderness at 11 or more of the 18 designated points as FM criteria in 1990 [1]. It developed an FM case definition in 2010 to facilitate the evaluation of patients without the need of physical or tender-point examination [2]. This was based on an assessment of the widespread pain index and symptom severity scale score for fatigue, sleep disturbance, and cognitive symptoms. These FM criteria were unofficially modified in 2011 to enable epidemiological studies based only on participant self-report [3]. This modification required sustained symptoms for at least 3 months that were not explicable by other clinical disorders.

Dual-purpose criteria for clinical diagnosis or research were established in 2016 [4]. In 2018, the Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks partnership with the US Food and Drug Administration and the American Pain Society developed the ACTTION-APS Pain Taxonomy (AAPT) as a diagnostic system to be clinically useful and consistent across chronic pain disorders [5]. Therein, in addition to pain in at least six of the nine sites, moderate to severe symptoms involving either chronic sleep problems or fatigue were included in the FM diagnostic criteria.

The International Classification of Diseases, 11th Revision (ICD-11) defines CWP as diffuse pain in at least four of the five body regions that is associated with significant emotional distress (anxiety, anger/frustration, or depressed mood) or functional disability (interference in daily life activities and reduced participation in social roles) [6]. It notes that biological, psychological, and social factors

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contribute to CWP and that FM is included within the CWP spectrum. The National Institutes of Health Task Force on Research Standards for Chronic Low Back Pain (National Institutes of Health [NIH] TF) identified CWP as a key comorbid condition that may extend beyond localized chronic low back pain (LBP) [7].

The Centers for Disease Control and Prevention estimated the prevalence of FM at approximately four million adults (2 %) in the United States [8]. CWP prevalence was estimated at 4.7 % adults in the National Health and Nutrition Examination Survey (NHANES) [9]. However, CWP prevalence is greater in other global regions [10]. Moreover, approximately 25 % of patients with chronic LBP in primary care settings may exhibit CWP [11]. Considering that CWP is a precursor of FM [12] provides a rationale for screening patients at risk, and simple tests for FM among patients with chronic pain have been proposed [13], including examiner-based testing for tenderness to digital pressure, blood pressure cuff-evoked pain, and patient self-reporting of persistent deep aching over most of the body. The single item on the NIH TF Minimum Dataset for bothersomeness of widespread pain [7] may also be a candidate screening test for FM.

This purpose of this study was to measure longitudinal outcomes involving pain, function, and health-related quality of life (HRQOL) among patients with FM, CWP, or localized chronic LBP to determine whether they support the view that FM is an extreme manifestation of the CWP continuum. A secondary aim was to assess the bothersomeness of the widespread pain item of the NIH TF Minimum Dataset as an FM screening test.

Methods

Study design and participants

This retrospective cohort study included participants from the Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation (PRECISION) from August 2019 through July 2023 [14]. The registry recruited participants from the 48 contiguous states primarily utilizing social media advertising. Eligible registry participants were 21–79 years of age and had chronic LBP (≥3 months) and sufficient language proficiency to complete case report forms in English. Persons who reported being pregnant or residing at institutional facilities were not eligible. Study participants completed case report forms at enrollment and subsequent quarterly encounters for up to 12 months. This research was approved by the North Texas Regional Institutional Review Board (IRB protocol 2015-169), and the participants gave written informed consent prior to providing data.

Classification of the FM, CWP, and LBP groups

Registry participants were asked at enrollment and the 12-month follow-up encounter if they were currently diagnosed with FM. Participants with a current FM diagnosis at both encounters comprised the FM group. Similarly, CWP was measured at both encounters utilizing the bothersomeness of widespread pain item on the NIH TF Minimum Dataset [7]. It queried participants about how much they were bothered by widespread pain (or pain in most of the body) during the past 4 weeks, with response options including “not at all,” “a little bit,” or “a lot.” Participants who were not classified as having FM, but who were bothered a lot by widespread pain at both encounters, comprised the CWP group. Participants who did not have a current FM diagnosis at both encounters, and were also not at all bothered by widespread pain at both encounters, comprised the LBP group. The remaining participants without a group classification were excluded from the study.

Outcome measures

The primary outcomes included pain and function. A numerical rating scale ranging from 0 to 10 measured typical LBP intensity in the 7 days prior to an encounter. The Roland-Morris Disability Questionnaire measured function [15]. It consists of 24 items that measured back-related disability on the encounter date, with scores ranging from 0 to 24. The HRQOL outcomes were assessed with scales from the Patient-Reported Outcomes Measurement Information System with 29 items (PROMIS-29) that measured physical function, anxiety, depression, fatigue, sleep disturbance, participation in social roles, and pain interference [16]. Scale scores were normed according to the US general population to have a mean (standard deviation [SD]) of 50 (10) [16]. As an exception, the sleep disturbance scale was normed with a calibration sample enriched for chronic illness. All pain, function, and HRQOL outcomes were measured at enrollment and at quarterly encounters for up to 12 months. Higher scores represent worse outcomes on all measures, except on the HRQOL scales for physical function and participation in social roles.

Baseline and longitudinal covariates

Comprehensive data pertaining to chronic LBP were collected at enrollment [14], and a series of baseline variables were selected to characterize participants and control for potential confounding. Sociodemographic characteristics included age, gender, race, ethnicity, and educational level. Health history included cigarette smoking status, musculoskeletal comorbidities (herniated disc, sciatica, osteoarthritis, and osteoporosis), and general medical comorbidities (hypertension, heart disease, diabetes mellitus, asthma, and depression). Psychological factors included pain catastrophizing and pain self-efficacy, measured with the Pain Catastrophizing Scale [17] and Pain Self-Efficacy Questionnaire [18], respectively. The chronic LBP history was characterized by ongoing duration (<1 year, 1–5 years, and >5 years). Data on treatments included nonpharmacological treatments ever utilized (exercise therapy, yoga, massage therapy, spinal manipulation, acupuncture, and cognitive behavioral therapy [CBT]), opioid therapy, and lumbar spine surgery. Current opioid use and prior lumbar spine surgery were measured at each encounter.

Statistical analysis

The utility of the bothersomeness of widespread pain item on the NIH TF Minimum Dataset [7] as an FM screening test was measured utilizing sensitivity, specificity, and positive and negative predictive values, and depicted with a receiver operating characteristic curve. Baseline participant characteristics were described according to chronic pain group (CPG), utilizing number (%) or mean (SD). Group differences were assessed utilizing the chi-square test for categorical variables and analysis of variance for continuous variables. Post-hoc comparisons were performed if omnibus p values were ≤0.05 to identify significant differences between the FM and CWP groups utilizing 2x2 subtables for chi-square analyses or the least significant difference for analysis of variance.

Generalized estimating equation (GEE) models were utilized to measure longitudinal outcomes over 12 months, initially utilizing a partially adjusted model that included a time variable. These GEE models utilized an autoregressive AR(1) correlation structure, fixed effects, and a CPG x time interaction term. The GEE analyses were repeated utilizing a comprehensive multivariable model that included baseline and longitudinal covariates to adjust for potential confounding in addition to measuring time trends. The clinical relevance of differences in outcomes among CPGs were assessed utilizing thresholds for the magnitude of Cohen's *d* statistic (small effect, *d*=0.2; medium effect, *d*=0.5; large effect, *d*=0.8) [19]. Differences involving magnitudes of *d*<0.2 were not considered clinically relevant. All Cohen's *d* statistics were transformed so that larger values represented worse outcomes compared with referents (i.e., for FM or CWP groups compared with the LBP group, or for the FM group compared with the CWP group).

Statistical power was estimated with the General Linear Mixed Model Power and Sample Size program for repeated-measures designs [20], and involved hypothesized mean between-group differences in outcomes over 12 months=0 (i.e., no differences in outcomes between groups). The sample size was sufficiently large to exceed 80 % statistical power in a variety of scenarios involving the base correlation between pain and function and the decay rate of the base correlation. The study was not designed to detect time interaction effects owing to uncertainties about the potential interactions (reversed, fully attenuated, or partially attenuated) and thresholds for clinical relevance [21]. Data were managed and analyzed utilizing the IBM SPSS Statistics Software (Version 29). Hypotheses were assessed at an alpha level of 0.05 utilizing two-sided tests.

Results

Participant characteristics

The 1,531 participants with chronic LBP ranged in age from 21 to 79 years at baseline, with a mean of 53.0 (SD, 13.2) years, and 1,132 (73.9 %) were female. Among 1,358 (88.7 %) participants who completed 12 months of follow-up, 312 (23.0 %) were initially classified as having FM (n=66), CWP (n=56), or LBP (n=190). A total of 64 participants with FM tested positive on the bothersomeness of widespread pain item (sensitivity, 0.97). Conversely, 190 of 246 participants without FM tested negative on this item (specificity, 0.77). The positive and negative predictive values were 0.53 and 0.99, respectively (Supplemental Figure 1). The area under the receiver operating characteristic curve was 0.87 (95 % confidence interval [CI], 0.83–0.91) (Supplemental Figure 2). Two participants with FM but without CWP were excluded from further analysis on the theoretical grounds that patients with FM should have CWP.

Baseline participant characteristics according to chronic pain group

The mean age of the 310 remaining participants was 52.3 (SD, 13.6) years, and 238 (76.8 %) were female. These included 64 (20.6 %) participants with FM, 56 (18.1 %) with CWP, and 190

(61.3 %) with LBP. Characteristics that differed across CPGs included gender, educational level, cigarette smoking status, all medical comorbidities except osteoporosis and heart disease, pain catastrophizing, pain self-efficacy, and use of spinal manipulation, CBT, and opioid therapy (Table 1). However, the differences between the FM and CWP groups were limited to gender and the use of four treatments (spinal manipulation, acupuncture, CBT, and opioid therapy). The FM group was more likely to include females and to have utilized the nonpharmacological treatments, whereas the CWP group currently utilized opioid therapy more frequently.

Table 1: Baseline participant characteristics according to the chronic pain group.[a]

		Chronic pain group							
		FM (n=64)		CWP (n=56)		Localized pain (n=190)			
Characteristic		**No.**	**%**	**No.**	**%**	**No.**	**%**	**Omnibus *P***	**FM vs. CWP *P***
Age (years) (mean, SD)		51.2	11.8	52.5	13.2	52.6	14.2	0.76	0.59
Gender								0.007	0.002
Female		58	90.6	38	67.9	142	74.7		
Male		6	9.4	18	32.1	48	25.3		
Race								0.65	0.43
American Indian/Alaskan Native		1	1.6	1	1.8	1	0.5		
Asian		0	0.0	2	3.6	3	1.6		
Black/African American		8	12.5	5	8.9	16	8.4		
Native Hawaiian/Pacific Islander		0	0.0	1	1.8	1	0.5		
White		55	85.9	47	83.9	169	88.9		
Ethnicity								0.11	0.26
Hispanic		5	7.8	8	14.3	11	5.8		
Non-hispanic		59	92.2	48	85.7	179	94.2		
Educational level (mean, SD)		4.1	1.7	4.1	1.8	5.4	1.8	<0.001	0.98
Cigarette smoking status								0.02	0.13
Never or former smoker		55	85.9	42	75.0	171	90.0		
Current smoker		9	14.1	14	25.0	19	10.0		
History of medical comorbidities									
Herniated disc								0.02	0.43
	No	32	50.0	32	57.1	130	68.4		
	Yes	32	50.0	24	42.9	60	31.6		
Sciatica								0.001	0.20
	No	17	26.6	21	37.5	98	51.6		
	Yes	47	73.4	35	62.5	92	48.4		
Osteoarthritis								<0.001	0.14
	No	18	28.1	23	41.1	116	61.1		
	Yes	46	71.9	33	58.9	74	38.9		
Osteoporosis								0.05	0.70
	No	52	81.3	47	83.9	174	91.6		
	Yes	12	18.8	9	16.1	16	8.4		

Table 1: (continued)

Hypertension								0.02	0.33
	No	32	50.0	23	41.1	117	61.6		
	Yes	32	50.0	33	58.9	73	38.4		
Heart disease								0.09	0.15
	No	54	84.4	52	92.9	177	93.2		
	Yes	10	15.6	4	7.1	13	6.8		
Diabetes mellitus								0.01	0.70
	No	46	71.9	42	75.0	165	86.8		
	Yes	18	28.1	14	25.0	25	13.2		
Asthma								0.001	0.27
	No	36	56.3	37	66.1	150	78.9		
	Yes	28	43.8	19	33.9	40	21.1		
Depression								<0.001	0.45
	No	15	23.4	10	17.9	94	49.5		
	Yes	49	76.6	46	82.1	96	50.5		
Pain catastrophizing		29.2	13.4	26.6	13.6	13.7	10.8	<0.001	0.23
Pain self-efficacy		22.7	12.2	25.4	14.4	39.7	13.6	<0.001	0.27
Duration of low back pain (years)								0.05	0.51
<1		3	4.7	1	1.8	18	9.5		
1–5		9	14.1	11	19.6	48	25.3		
>5		52	81.3	44	78.6	124	65.3		
Nonpharmacological treatments ever used for chronic low back pain									
Exercise therapy								0.32	0.71
	No	12	18.8	12	21.4	52	27.4		
	Yes	52	81.3	44	78.6	138	72.6		
Yoga								0.08	0.04
	No	39	60.9	44	78.6	121	63.7		
	Yes	25	39.1	12	21.4	69	36.3		
Massage therapy								0.15	0.06
	No	21	32.8	28	50.0	82	43.2		
	Yes	43	67.2	28	50.0	108	56.8		
Spinal manipulation								0.05	0.01
	No	20	31.3	30	53.6	78	41.1		
	Yes	44	68.8	26	46.4	112	58.9		
Acupuncture								0.09	0.05
	No	41	64.1	45	80.4	144	75.8		
	Yes	23	35.9	11	19.6	46	24.2		
Cognitive behavioral therapy (CBT)								<0.001	0.008
	No	37	57.8	45	80.4	163	85.8		
	Yes	27	42.2	11	19.6	27	14.2		
Current opioid use for chronic low back pain								<0.001	0.04
No		43	67.2	27	48.2	149	78.4		
Yes		21	32.8	29	51.8	41	21.6		
Ever had lumbar spine surgery								0.22	0.25
No		47	73.4	46	82.1	158	83.2		
Yes		17	26.6	10	17.9	32	16.8		

[a]Table entries are No. and % unless otherwise indicated. Educational level was classified as “no high school diploma” (1); “high school graduate or high school equivalency diploma” (2); “some college, no degree” (3); “occupational/technical/vocational program” (4); “associate’s degree” (5); “bachelor’s degree” (6); “master’s degree” (7); or “professional school degree or doctoral degree” (8). CWP, chronic widespread pain; FM, fibromyalgia; SD, standard deviation.

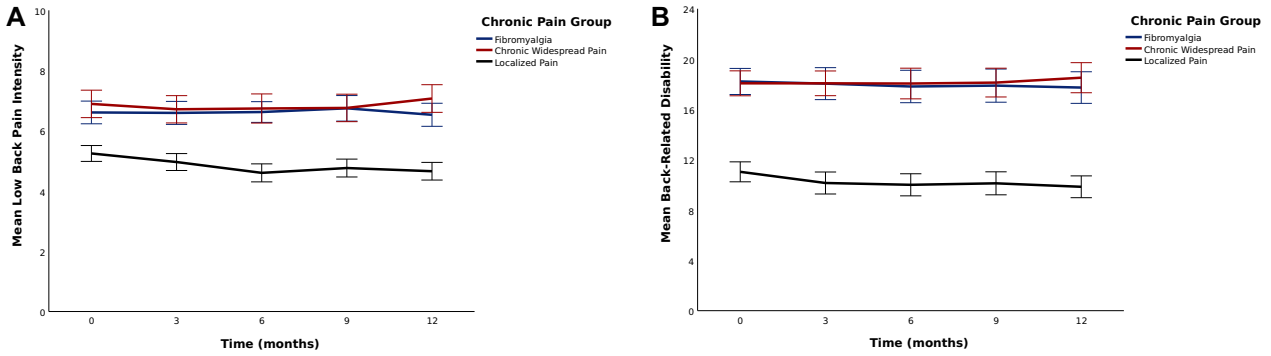

Figure 1: Pain and function outcomes over time. Low Back Pain intensity was measured with a numerical rating scale ranging from 0 to 10 for the typical pain intensity in the 7 days prior to an encounter. Back-related disability was measured with the Roland-Morris questionnaire on the encounter date, with scores ranging from 0 to 24. Error bars represent 95 % confidence intervals. p values were derived from generalized estimating equations for the overall outcomes over 12 months of follow-up. p values were <0.001 for both outcomes.

Partially adjusted outcomes

A total of 1,535 encounters were completed over 12 months, including 316 (20.6 %), 276 (18.0 %), and 943 (61.4 %) in the FM, CWP, and LBP groups, respectively. The FM and CWP groups both had greater LBP intensity than the LBP group (Figure 1A). Mean (95 % CI) pain intensity scores were 6.6 (6.3–6.9), 6.9 (6.5–7.3), and 4.9 (4.7–5.1) in the FM, CWP, and LBP groups, respectively, adjusted for time and CPG x time interaction effects (Supplemental Table 1). Compared with the LBP group, there were large differences in pain intensity in the FM group (d=0.83) and CWP group (d=0.98). However, the difference in pain intensity between the FM and CWP groups was not clinically relevant (d=−0.15). Pain intensity decreased over time (β, −0.145; 95 % CI, −0.213 to −0.078; p<0.001). There were FM x time (β, 0.130; 95 % CI, 0.015 to 0.245; p=0.03) and CWP x time (β, 0.191; 95 % CI, 0.081 to 0.301; p<0.001) interaction effects, each indicating that the differences in pain intensity between the respective CPGs and the LBP group increased over time.

The FM and CWP groups both had greater back-related disability than the LBP group (Figure 1B). Mean (95 % CI) disability scores were 18.0 (16.9–19.0), 18.3 (17.3–19.2), and 10.4 (9.6–11.2), in the FM, CWP, and LBP groups, respectively, adjusted for time and time interaction effects (Supplemental Table 1). Disability decreased over time (β, −0.295; 95 % CI, −0.442 to −0.148; p<0.001). There was a CWP x time interaction effect (β, 0.406; 95 % CI, 0.159 to 0.654; p=0.001), indicating that the difference in disability between the CWP and LBP groups increased over time.

The FM and CWP groups both reported worse HRQOL than the LBP group on all scales (Figure 2). The differences between the FM and LBP groups ranged from d=0.75 for depression to d=1.24 for fatigue, whereas the differences between the CWP and LBP groups ranged from d=0.87 for sleep disturbance to d=1.05 for pain interference (Supplemental Table 2). The FM group had worse HRQOL than the CWP group on five scales; however, only the difference in fatigue was clinically relevant (d=0.21). Conversely, The FM group had better HRQOL pertaining to depression (d=−0.23). Physical function (β=0.228; 95 % CI, 0.048 to 0.408; p=0.01) and participation in social roles (β=0.362; 95 % CI, 0.102 to 0.622; p=0.006) both increased over time, and pain interference decreased over time (β=−0.528; 95 % CI, −0.742 to −0.315; p<0.001). There was an FM x time interaction effect for depression (β=−0.583; 95 % CI, −1.141 to −0.025; p=0.04), indicating that the difference in depression between the FM and LBP groups decreased over time. There was also a CWP x time interaction effect for pain interference (β=0.487; 95 % CI, 0.061 to 0.914; p=0.03), indicating that the difference in pain interference between the CWP and LBP groups increased over time.

Fully adjusted outcomes

There were no differences in LBP intensity among the CPGs in the fully adjusted model that included a wide array of potential confounders (Table 2). Pain intensity decreased over time (β=−0.143; 95 % CI, −0.210 to −0.076; p<0.001). There were FM x time (β=0.129; 95 % CI, 0.016 to 0.243; p=0.03) and CWP x time (β=0.190; 95 % CI, 0.081 to 0.299; p<0.001) interaction effects, each indicating that the respective differences in pain intensity between these groups and the LBP group

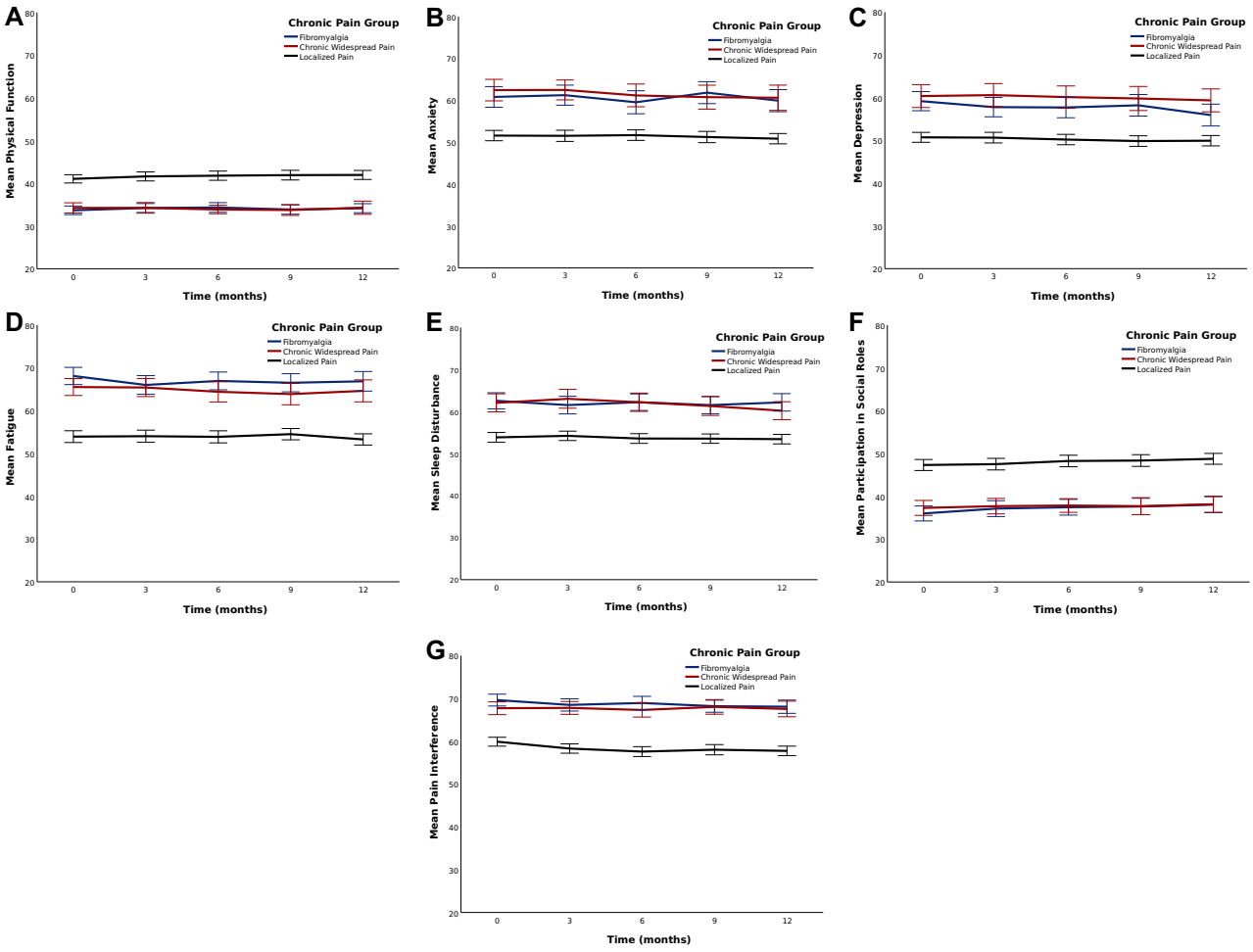

Figure 2: Health-related quality-of-life (HRQOL) outcomes over time. Each aspect of HRQOL was measured with the Patient-Reported Outcomes Measurement Information System with 29 items. Error bars represent 95 % confidence intervals. p values were derived from generalized estimating equations for the overall outcomes over 12 months of follow-up. p values were <0.001 for all outcomes.

increased over time. Characteristics associated with greater pain intensity were: age; being non-White, Hispanic, or a current smoker; longer duration of LBP; and pain catastrophizing; whereas greater educational level and pain self-efficacy were inversely associated with pain intensity (Supplemental Table 3).

Mean (95 % CI) back-related disability scores were 15.3 (13.7–17.0), 16.2 (14.8–17.7), and 12.7 (11.4–14.1), in the FM, CWP, and LBP groups, respectively (Table 2). Disability decreased over time (β=−0.291; 95 % CI, −0.433 to −0.149; p<0.001). There was a CWP x time interaction effect (β=0.424; 95 % CI, 0.175 to 0.673; p<0.001), indicating that the difference in disability between the CWP and LBP groups increased over time. Characteristics associated with disability were the number of medical comorbidities, pain catastrophizing, and current use of opioid therapy, whereas educational level and pain self-efficacy were inversely associated with disability (Supplemental Table 3). There were no clinically relevant differences in pain or disability between the FM and CWP groups (Table 2).

The FM group had worse HRQOL than the LBP group on all scales except anxiety and depression, whereas the CWP group had worse HRQOL on all scales (Table 3). Physical function (β=0.234; 95 % CI, 0.060 to 0.408; p=0.008) and participation in social roles (β=0.374; 95 % CI, 0.121 to 0.628; p=0.004) increased over time, whereas pain interference (β=−0.523; 95 % CI, −0.730 to −0.317; p<0.001) decreased over time. There was an FM x time interaction effect for depression (β=−0.563; 95 % CI, −1.109 to −0.018; p=0.04), indicating that the difference in depression between the FM and LBP groups decreased over time. There was also a CWP x time interaction effect for pain interference (β=0.484; 95 % CI,

Table 2: Pain and function outcomes adjusted for time, time interaction effects, and the full array of covariates.[a]

Outcome	Mean	95 % CI			*P*			Effect size matrix (*d*)	
					CPG	Time	CPG x Time		
Low back pain intensity									
Chronic pain group									
Localized pain	5.9	5.5	–	6.3	…		…	…	…
Chronic widespread pain	6.7	6.2	–	7.1	0.35		<0.001	0.39	…
Fibromyalgia	6.5	6.0	–	6.9	0.48		0.03	0.28	−0.11
Time						<0.001			
Back-related disability									
Chronic pain group									
Localized pain	12.7	11.4	–	14.1	…		…	…	…
Chronic widespread pain	16.2	14.8	–	17.7	<0.001		<0.001	0.52	…
Fibromyalgia	15.3	13.7	–	17.0	0.006		0.25	0.39	−0.13
Time						<0.001			

[a]Results are based on 310 participants and 1,534 encounters. Outcomes were measured at quarterly encounters over 12 months. Low back pain intensity was measured with a numerical rating scale, ranging from 0 to 10. Back-related disability was measured with the Roland-Morris Disability Questionnaire, ranging from 0 to 24. Means were derived from generalized estimating equations. Results for time interactions are for participants with chronic widespread pain, or fibromyalgia relative to those with localized pain. Effect sizes were computed utilizing Cohen's *d* statistic for participants with chronic widespread pain, or fibromyalgia compared with referents having localized pain and for participants with fibromyalgia compared with referents having chronic widespread pain. Positive effect sizes represent worse outcomes compared with the reference group. The *d* statistics having a magnitude≥0.20 are considered clinically relevant. CPG, chronic pain group.

0.063 to 0.904; p=0.02), indicating that the difference in pain interference between the CWP and LBP groups increased over time. In comparison with the LBP group, there were small to medium differences in HRQOL in the FM group (ranging from *d*=0.32 for physical function to *d*=0.59 for fatigue) and in the CWP group (ranging from *d*=0.33 for depression to *d*=0.58 for fatigue). The only clinically relevant differences between the FM and CWP groups involved anxiety (*d*=−0.32) and depression (*d*=−45), wherein the FM group had better outcomes (Table 3). Females reported worse physical function and greater pain interference than males (Supplemental Table 4). Pain self-efficacy was consistently associated with better outcomes on all HRQOL scales, whereas pain catastrophizing increased anxiety, depression, fatigue, and pain interference.

Discussion

Our study initially found large differences (expressed as large effect sizes) in virtually all pain, function, and HRQOL outcomes between the FM or CWP groups and the LBP group in the partially adjusted models (Supplemental Tables 1 and 2). However, these differences were attenuated after multivariable analyses adjusted for the full array of covariates (ranging from clinically irrelevant to medium effect sizes in Tables 2 and 3). The only clinically relevant differences between the FM and CWP groups that remained following multivariable adjustment involved anxiety and depression, each favoring the FM group. A possible explanation for this finding is that the FM group had utilized CBT more often than the CWP group at baseline. However, another explanation may involve diagnostic labeling. In comparison with having vague CWP symptoms, giving patients a FM diagnosis provides validation of their symptoms, rules out serious underlying pathology, and potentially affords them greater insurance coverage for treatment [22].

The FM group did not have greater depression than the LBP group in the multivariable analysis and there was an FM x time interaction effect indicating that the difference in observed depression between the FM and LBP groups decreased over time (as suggested by Figure 2C). This finding is not consistent with the ACR 2010 criteria that were unofficially modified in 2011 to include depression as an important aspect of FM [3]. Also, in the multivariable analyses, there were virtually no differences in fatigue or sleep disturbance between the FM and CWP groups. These findings do not align with the AAPT diagnostic system, which considers fatigue and sleep disturbance as important aspects

Table 3: Health-related quality-of-life outcomes adjusted for time, time interaction effects, and the full array of covariates.[a]

Outcome	Mean	95 % CI			*P*			Effect size matrix (d)	
					CPG	Time	CPG x Time		
Physical function									
Chronic pain group									
Localized pain	39.3	38.0	–	40.7	…		…	…	…
Chronic widespread pain	36.2	34.6	–	37.8	<0.001		0.10	0.42	…
Fibromyalgia	37.0	35.3	–	38.7	0.007		0.43	0.32	−0.10
Time						0.008			
Anxiety									
Chronic pain group									
Localized pain	52.2	50.2	–	54.2	…		…	…	…
Chronic widespread pain	57.3	54.9	–	59.8	<0.001		0.31	0.49	…
Fibromyalgia	53.9	51.2	–	56.7	0.19		0.96	0.17	−0.32
Time						0.17			
Depression									
Chronic pain group									
Localized pain	51.9	49.9	–	53.9	…		…	…	…
Chronic widespread pain	55.2	52.9	–	57.5	0.005		0.94	0.33	…
Fibromyalgia	50.8	48.3	–	53.3	0.64		0.04	−0.11	−0.45
Time						0.10			
Fatigue									
Chronic pain group									
Localized pain	53.0	50.8	–	55.2	…		…	…	…
Chronic widespread pain	59.3	56.8	–	61.7	<0.001		0.81	0.58	…
Fibromyalgia	59.4	56.9	–	62.0	<0.001		0.58	0.59	0.01
Time						0.35			
Sleep disturbance									
Chronic pain group									
Localized pain	54.9	52.9	–	56.9	…		…	…	…
Chronic widespread pain	58.9	56.3	–	61.4	<0.001		0.14	0.45	…
Fibromyalgia	58.8	56.3	–	61.3	0.004		0.92	0.44	−0.01
Time						0.35			
Participation in social roles									
Chronic pain group									
Localized pain	46.6	44.9	–	48.4	…		…	…	…
Chronic widespread pain	41.9	39.8	–	44.0	<0.001		0.48	0.48	…
Fibromyalgia	43.1	40.8	–	45.5	<0.001		0.53	0.35	−0.13
Time						0.004			
Pain interference									
Chronic pain group									
Localized pain	60.4	59.0	–	61.9	…		…	…	…
Chronic widespread pain	64.3	62.6	–	66.1	0.004		0.02	0.45	…
Fibromyalgia	63.9	62.1	–	65.7	<0.001		0.48	0.40	−0.05
Time						<0.001			

[a]Results are based on 310 participants and 1,534 encounters. Outcomes were measured at quarterly encounters over 12 months using the Patient-Reported Outcomes Measurement Information System with 29 items, including its scales for physical function, anxiety, depression, fatigue, sleep disturbance, participation in social roles, and pain interference. All scales except sleep disturbance are normed according to the US, general population with mean, 50 and SD, 10 (see text for additional details). Means were derived from generalized estimating equations. Results for time interactions are for participants with chronic widespread pain, or fibromyalgia relative to those with localized pain. Effect sizes were computed utilizing Cohen's d statistic for participants with chronic widespread pain, or fibromyalgia compared with referents having localized pain and for participants with fibromyalgia compared with referents having chronic widespread pain. Positive effect sizes represent worse outcomes compared with the reference group. The d statistics having a magnitude≥0.20 are considered clinically relevant. CI, confidence interval; CPG; chronic pain group; SD, standard deviation.

of FM [5]. Rather, our multivariable findings are in accord with ICD-11, which states that CWP is associated with anxiety, depression, and functional disability, and notes that FM is included within the CWP spectrum [6].

Our overall findings do not clearly implicate FM as an extreme form of CWP, but they support the view that both share common pain pathways that may respond to similar therapies. Nevertheless, given the practical importance of making an FM diagnosis, the bothersomeness of the widespread pain item of the NIH TF Minimum Dataset [7] may warrant consideration as a simple screening test for FM among patients with chronic LBP. Simply asking such patients if they were bothered a lot by widespread pain during the past 4 weeks yielded high sensitivity, high negative predictive value, and a favorable receiver operating characteristic curve. However, this screening test was performed in an unconventional manner in our study because participants were classified as having FM or CWP only if they consistently reported these at both the baseline and 12-month follow-up encounters. The parameters of this test may differ if utilized in a more typical screening scenario involving only a single cross-sectional assessment.

A strength of our study was selecting participants from PRECISION, which is a national pain research registry that includes participants comparable to adults with chronic LBP in the United States on such characteristics as age, gender, education, cigarette smoking, and medical comorbidities, as reported in the NHANES [23]. Thus, our study has important implications for osteopathic physicians who often provide primary care for patients with chronic LBP and other musculoskeletal conditions. The results also reinforce the osteopathic tenet that the person is a unit of body, mind, and spirit, because participants having CWP or FM reported substantial departures from health involving not only physical function, but also anxiety, depression, fatigue, and sleep disturbance. Other strengths included a longitudinal cohort design with 12 months of follow-up and multivariable analyses to adjust for a large array of covariates as potential confounders. However, there were also study limitations. First, PRECISION is not a population-based registry and we excluded participants who were unable to complete case report forms in English. Second, all data were self-reported by participants and were not otherwise corroborated, including FM diagnoses as well as other comorbidities, nonpharmacological and pharmacological treatments, and prior lumbar spine surgery. Finally, the study planning focused on statistical power for pain and function outcomes, not for HRQOL outcomes or interaction effects. Nevertheless, the criteria utilized to assess the clinical relevance of our findings (i.e., Cohen's *d*) are independent of sample size [24].

Conclusions

In conclusion, our multivariable results indicate that patients with FM or CWP have clinically relevant differences involving back-related disability and several HRQOL deficits compared with patients having LBP. However, FM was not associated with worse outcomes in pain, function, or HRQOL compared with CWP. These findings do not support the view that FM is an extreme manifestation of the CWP continuum, involving greater pain intensity, disability, or such HRQOL deficits as anxiety, depression, fatigue, or sleep disturbance.

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