

# Chronic Overlapping Pain Conditions and Long-term Opioid Treatment

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**M**ore than 29 million people in the United States receive health services at community health centers (CHCs).<sup>1</sup> CHCs care for a disproportionately high number of patients with low income (91% have incomes  $\leq$  200% of the federal poverty level) and with Medicaid insurance (46% of CHC patients), patients who are uninsured (22%), and patients in racial and ethnic minority groups (63%). Socioeconomically vulnerable patients with higher rates of chronic conditions are commonly seen at CHCs.<sup>1</sup> However, less is known about chronic pain conditions among this population.<sup>2</sup>

Overall, between 20% and 62% of individuals with chronic pain, defined as pain that persists or recurs for longer than 3 months,<sup>3</sup> experience multiple pain conditions simultaneously.<sup>3,4</sup> The National Institutes of Health has recognized the concept of frequently co-occurring pain conditions that are likely to share central sensitization as a common mechanism<sup>5</sup> and has designated these to be chronic overlapping pain conditions (COPCs) (Table 1).<sup>4,6,7</sup> Historically, those conditions often were studied in isolation. Little is known about the epidemiology of COPC combinations in primary care and how various combinations of COPCs affect treatment patterns, including the prescription of opioids.<sup>8,9</sup>

The presence of multiple pain conditions is associated with greater pain severity, emotional distress, and utilization of health care services.<sup>8,10</sup> Primary care physicians report that they struggle with management of chronic pain among patients because of limited time to conduct opioid risk assessment or lack of training in pain management.<sup>11</sup> Findings of recent studies show that opioids are commonly used for treatment of pain in ambulatory settings, especially in the presence of multiple pain conditions,<sup>12</sup> even though this practice is not considered the standard of care because of unclear benefits and harms for patients with COPCs.<sup>13,14</sup> A better understanding of opioid use among individuals with COPCs is needed.

Pain medication clinical trials often exclude individuals with more than 1 pain condition.<sup>15</sup> Additionally, COPCs co-occur frequently with other chronic physical and mental health conditions, which further increases the likelihood of being prescribed an opioid.<sup>16-18</sup> Evidence suggests that individuals with pain and mental health comorbidities might benefit more from multimodal treatment

## ABSTRACT

**OBJECTIVES:** One in 5 people in the United States lives with chronic pain. Many patients with chronic pain experience a subset of specific co-occurring pain conditions that may share a common pain mechanism and that have been designated as chronic overlapping pain conditions (COPCs). Little is known about chronic opioid prescribing patterns among patients with COPCs in primary care settings, especially among socioeconomically vulnerable patients. This study aims to evaluate opioid prescribing among patients with COPCs in US community health centers and to identify individual COPCs and their combinations that are associated with long-term opioid treatment (LOT).

**STUDY DESIGN:** Retrospective cohort study.

**METHODS:** We conducted analyses of more than 1 million patients 18 years and older based on electronic health record data from 449 US community health centers across 17 states between January 1, 2009, and December 31, 2018. Logistic regression models were used to assess the relationship between COPCs and LOT.

**RESULTS:** Individuals with COPCs were prescribed LOT 4 times more often than individuals without a COPC (16.9% vs 4.0%). The presence of chronic low back pain, migraine headache, fibromyalgia, or irritable bowel syndrome combined with any of the other COPCs increased the odds of LOT prescribing compared with the presence of a single COPC.

**CONCLUSIONS:** Although LOT prescribing has declined over time, it remains relatively high among patients with certain COPCs and for those with multiple COPCs. These study findings suggest target populations for future interventions to manage chronic pain among socioeconomically vulnerable patients.

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## TAKEAWAY POINTS

Findings of this study suggest that although long-term opioid treatment prescribing has declined over time, it remains relatively high among patients with chronic overlapping pain conditions (COPCs) in US community health centers.

- ▶ Individuals with COPCs were prescribed long-term opioid treatment 4 times more often than individuals without a COPC.
- ▶ The highest rates of long-term opioid prescribing can be seen in those with multiple COPCs.
- ▶ The presence of chronic low back pain, migraine headache, fibromyalgia, or irritable bowel syndrome combined with any of the other COPCs increased the odds of long-term opioid treatment prescribing compared with the presence of a single COPC.

**TABLE 1.** List of Chronic Overlapping Pain Conditions

Chronic pain condition	Abbreviation
Chronic low back pain	CLBP
Chronic tension-type headache	CTTH
Endometriosis	ENDO
Fibromyalgia	FM
Irritable bowel syndrome	IBS
Migraine headache	MHA
Myalgic encephalomyelitis/chronic fatigue syndrome	MECFS
Temporomandibular disorder	TMD
Urologic chronic pelvic pain syndrome	UCPPS
Vulvodynia	VVD

programs that include mental health than from opioids to manage their COPCs.<sup>17</sup> Although opioid prescribing,<sup>12</sup> frequency of COPCs, and burden of mental health disorders are more common in patients with low income and/or underinsured patients,<sup>19</sup> no studies have specifically explored COPCs in CHCs. Additionally, these health centers face multitudes of barriers such as underfunding, short staff, high turnover, and complex patient populations with high rates of social needs.<sup>20-23</sup> It is critical to understand the extent of opioid treatment among patients with COPCs receiving care in CHCs to identify patient populations who might benefit from targeted multimodal care management programs intended to improve chronic pain management and further reduce opioid prescribing. Thus, the aim of this study is to identify individual COPCs and their combinations that are associated with long-term opioid treatment (LOT) in a network of CHCs.

## METHODS

### Study Design, Data Source, and Study Population

This study is a secondary analysis of electronic health record (EHR) data. The data were obtained from OCHIN and the Accelerating Data Value Across a National Community Health Center Network (ADVANCE) Clinical Research Network of CHCs.<sup>24</sup> In 2018, the OCHIN network included 449 clinics in 17 states; these were primarily CHCs (federally qualified health centers, county health

department clinics, and not-for-profit clinics) that provided health care access regardless of patients' insurance status.<sup>25</sup> Our population included more than 1 million patients 18 years or older who received primary care at one of these clinics between January 1, 2009, and December 31, 2018. We further limited our study sample to patients with 2 or more ambulatory visits during the study period to ensure some continuity of care received within the CHC setting. We excluded patients who received care in hospice to exclude those with terminal cancer-related opioid prescribing.

### Measures

**Outcome variable: LOT.** Using prescription order data, we identified opioid orders by searching the generic names for all opioid medications that can be ordered with a prescription in outpatient settings in the United States. We included medications with a pharmaceutical class of analgesic and excluded those with a class of expectorant, antitussive, or antidiarrheal and all that were not oral or transdermal in form. We excluded rectal formulations because they are rarely used and, when used, are often given to individuals with cancer-related pain. To exclude patients receiving medications for opioid use disorders, we excluded liquid methadone and limited buprenorphine to the 2 forms approved for treatment of pain by the FDA. Detailed information on opioid order identification has been published elsewhere.<sup>26</sup> We defined patients receiving LOT as those who were prescribed, within any calendar quarter, 160 or more opioid pills (short-acting or long-acting), 90 or more long-acting opioid pills, or any methadone pills or fentanyl patches.<sup>26</sup> We categorized patients into 3 groups to describe their opioid use during our 10-year study period: (1) those who were never prescribed an opioid, (2) those with at least 1 opioid prescription but never LOT, and (3) those meeting our LOT definition during at least 1 calendar quarter.

**Independent variables.** We included the conditions in Table 1 because they have been previously used to define the COPC construct.<sup>6,7</sup> We identified all diagnoses of these conditions in the patients' EHR problem lists (Table 1) using *International Classification of Diseases, Tenth Revision (ICD-10)* codes<sup>6,7</sup> and converted to *International Classification of Diseases, Ninth Revision* codes using general equivalence mapping tables.<sup>27</sup> We assessed 10-year, period prevalence of each condition, as well as a count variable describing all COPCs prevalent during the 10-year study period. When modeling the effect of a second COPC, we limited analysis to cohorts having the nominal COPC and no more than 1 additional COPC, constructing a categorical variable within each cohort, having levels of 1 COPC and each dyad combination. For example, in the fibromyalgia cohort, patients with irritable bowel syndrome (IBS) are in the fibromyalgia-IBS category and are compared with the fibromyalgia-only reference group.

**Covariates.** The following covariates were included: patients' sex, age as of the study end, race/ethnicity, preferred spoken language, health insurance type at the start of study period, rural location, smoking status, and having 1 or more physical or mental health chronic condition other than a COPC (Table 2). Chronic conditions were identified in the same manner as COPCs. We were not able to adjust for education and income in the regression analysis because of missing data.

### Statistical Analysis

Frequencies and percentages for categorical variables and means and SDs for continuous variables for the COPC and non-COPC groups were calculated to compare patient characteristics. We assessed the percentage of patients in each of 3 categories of opioid prescribing status (no prescription, some opioid analgesic but not LOT, or LOT) for individual COPCs and by count-based COPC groups (none, 1, 2, or  $\geq 3$  conditions). Modeling of LOT prevalence was stratified by cohorts limited to patients having each COPC, comparing LOT in patients with a single COPC with that in those having dyads (1 additional COPC). For clarity in describing pairwise effects, patients with COPC counts greater than 2 were not modeled ( $< 3\%$  of study sample). Logistic regression models in each COPC cohort assessed the odds of LOT status for dyads compared with individual COPC (reference category). In all models, we used a cluster robust variance estimator to account for the clustering of observations within states. We included 405 patients with vulvodynia in descriptive analysis but did not model this cohort, as small cell counts caused convergence issues. Statistical significance was set at an  $\alpha$  less than .05. Statistical analysis was conducted using SAS version 9.4 (SAS Institute). This study was approved by the Oregon Health & Science University Institutional Review Board.

## RESULTS

Overall, the study sample included 1,197,477 patients, with a mean age of 40 years, 58.3% women, 44.3% with Medicaid insurance coverage, and 25.8% uninsured (Table 2). Nearly 20% of individuals had at least 1 COPC. Table 2 shows characteristics of the COPC and non-COPC groups.

**TABLE 2.** Characteristics of Study Population<sup>a</sup>

Characteristics	All OCHIN primary care patients, 2009-2018	$\geq 1$ COPC <sup>b</sup> diagnosis	Non-COPC group
Study population, n (row %)	1,197,477 (100)	238,750 (19.9)	958,727 (80.1)
Age in years, mean (SD)	40 (17)	49 (15)	46 (17)
Female, n (column %)	698,102 (58.3)	156,751 (65.7)	541,351 (56.5)
Race/ethnicity, n (column %)			
Hispanic	342,939 (28.6)	58,598 (24.5)	284,341 (29.7)
NH Asian	49,401 (4.1)	7,617 (3.2)	41,784 (4.4)
NH Black	183,528 (15.3)	37,628 (15.8)	145,900 (15.2)
NH other/missing	87,242 (7.3)	16,765 (7.0)	70,477 (7.4)
NH White	534,367 (44.6)	118,142 (49.5)	416,225 (43.4)
FPL, n (column %)			
$\leq 138\%$	763,600 (63.8)	160,887 (67.4)	602,723 (62.9)
$> 138\%$	159,528 (13.3)	29,125 (12.2)	130,403 (13.6)
Unknown	274,349 (22.9)	48,748 (20.4)	225,601 (23.5)
Insurance status, n (column %)			
Medicaid	530,807 (44.3)	114,250 (47.9)	416,557 (43.5)
Medicare	120,966 (10.1)	30,426 (12.7)	90,540 (9.4)
Other public	53,750 (4.5)	9,205 (3.9)	44,545 (4.7)
Private	182,256 (15.2)	32,392 (13.6)	149,864 (15.6)
Uninsured	309,218 (25.8)	52,378 (21.9)	256,840 (26.8)
Missing	480 (<1)	99 (<1)	381 (<1)
English-language preference, n (column %)	888,864 (74.2)	184,734 (77.4)	704,130 (73.4)
Rural location, n (column %)	39,377 (3.3)	7,026 (2.9)	32,351 (3.4)
Current smoker, n (column %)	250,624 (20.9)	54,498 (22.8)	196,126 (20.5)
BMI, mean (SD)	29.0 (7.0)	29.9 (7.4)	28.8 (6.9)
Chronic conditions			
No. of chronic conditions overall, mean (SD)	1.8 (1.9)	2.6 (2.2)	1.6 (1.8)
No. of mental health conditions, <sup>c</sup> mean (SD)	0.6 (1.0)	1.1 (1.2)	0.5 (0.9)
No. of physical conditions, <sup>d</sup> mean (SD)	1.1 (1.5)	1.6 (1.7)	1.0 (1.4)
$\geq 1$ mental health condition, n (column %)	442,902 (37.0)	134,238 (56.2)	308,664 (32.2)
$\geq 1$ physical condition, n (column %)	615,269 (51.4)	155,651 (65.2)	459,618 (47.9)
No. of office visits during first year, mean (SD)	5.5 (7.0)	7.4 (9.3)	5.0 (6.1)
No. of unique providers seen during first year, mean (SD)	2.4 (1.8)	2.8 (2.2)	2.3 (1.6)
Long-term opioid treatment, n (column %)	78,542 (6.6)	40,407 (16.9)	38,135 (4.0)

BMI, body mass index; COPC, chronic overlapping pain condition; FPL, federal poverty level; NH, non-Hispanic.

<sup>a</sup>Patient age was calculated at the end of 2018, whereas other patient characteristics were estimated at the beginning of study enrollment. For descriptive analysis, missing/unknown data were included as an "unknown" category.

<sup>b</sup>COPCs were fibromyalgia, irritable bowel syndrome, temporomandibular disorder, urologic chronic pelvic pain syndrome, endometriosis, vulvodynia, chronic low back pain, chronic tension type headache, migraine headache, and myalgic encephalomyelitis/chronic fatigue syndrome.

<sup>c</sup>Mental health conditions included the following categories: anxiety/dissociative/somatoform disorders, bipolar disorder/affective psychosis, dementia (including Alzheimer and other senile dementias), depression, posttraumatic stress disorder, schizophrenia, sleep disorders, and substance abuse disorders (non-opioid drug and alcohol).

<sup>d</sup>Physical conditions included the following categories: arthritis, asthma, autism spectrum disorder, cancer, cardiac arrhythmias, chronic kidney disease, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease, diabetes, hepatitis, hyperlipidemia, hypertension, human immunodeficiency virus, osteoporosis, and stroke.

**TABLE 3.** Prevalence of COPCs and Opioid Prescribing Status: 10-Year Observation Period

Health conditions	All OCHIN primary care patients (N = 1,197,477)	Opioid prescribing status		
		No prescriptions	≥ 1 prescription	Long-term therapy
All patients, n (%)		969,224 (80.1)	149,711 (12.5)	78,542 (6.6)
Number of COPCs, n (%)				
0	958,727 (80.1)	819,511 (85.5)	101,081 (10.5)	38,135 (4.0)
1	200,340 (16.7)	130,075 (64.9)	39,457 (19.7)	30,808 (15.4)
2	32,182 (2.7)	17,114 (53.2)	7526 (23.4)	7542 (23.4)
≥3	6228 (0.5)	2524 (40.5)	1647 (26.4)	2057 (33.0)
Pain-related conditions, n (%)				
Chronic low back pain	155,949 (13.0)	92,260 (59.2)	32,717 (21.0)	30,972 (19.9)
Migraine headache	53,779 (4.5)	34,772 (64.7)	11,619 (21.6)	7388 (13.7)
Fibromyalgia	30,523 (2.5)	15,953 (52.3)	6572 (21.5)	7998 (26.2)
Irritable bowel syndrome	15,358 (1.3)	9118 (59.4)	3414 (22.2)	2826 (18.4)
Chronic tension-type headache	14,186 (1.2)	10,667 (75.2)	2401 (16.9)	1118 (7.9)
Temporomandibular disorder	5682 (0.5)	3628 (63.9)	1254 (22.1)	800 (14.1)
Myalgic encephalomyelitis/chronic fatigue syndrome	4944 (0.4)	3405 (68.9)	798 (16.1)	741 (15.0)
Urologic chronic pelvic pain syndrome	2618 (0.2)	1592 (60.8)	581 (22.2)	445 (17.0)
Endometriosis	1168 (0.1)	619 (53.0)	358 (30.7)	191 (16.4)
Vulvodynia	405 (0.0)	282 (69.6)	92 (22.7)	31 (7.7)

COPC, chronic overlapping pain condition.

Individuals with a COPC tended to be older and White and to have Medicaid or Medicare insurance coverage, and they were more likely to have 1 or more mental or physical health comorbidities than those without a COPC. Individuals without a COPC were more likely to be Hispanic, have private insurance coverage or to be uninsured, and live in rural areas compared with those in the COPC group.

Of those who had COPCs, 83.9% had 1 COPC, 13.5% had 2 COPCs, and 2.6% had 3 or more COPCs. Overall, the most frequent COPCs in the study population were chronic low back pain (13.0%), migraine headache (4.5%), and fibromyalgia (2.5%) (Table 3). See eAppendix Table 1 (eAppendix available at [ajmc.com](http://ajmc.com)) for percentages of co-occurring COPC diagnosis.

Individuals with COPCs were prescribed LOT 4 times more often than individuals without a COPC (16.9% and 4.0%, respectively) (Table 2). The prevalence of LOT increased with number of COPCs, from 15.4% with 1 COPC to 33.0% among those with 3 or more COPCs (Table 3). Overall, the prevalence of LOT varied from 7.7% in the vulvodynia cohort to 26.2% in the fibromyalgia cohort (Table 3).

The Figure shows LOT prevalence within 4 COPC cohorts: comparing baseline (single COPC) with each dyad. Dyads increased the prevalence of LOT within each cohort, with the exception of those dyads that included chronic tension headache and vulvodynia. Prevalence of LOT was 19.9% in the back pain–only group and varied between 15.9% in the back pain–tension headache dyad to 33.3% in back pain–fibromyalgia dyad. Similarly, LOT prevalence

was 26.2% in the fibromyalgia-only group and ranged from a low of 22.3% in the fibromyalgia–tension headache dyad up to 35.4% in the fibromyalgia-IBS dyad. LOT prevalence was 12.9% in the migraine-only group and varied between 15.9% in migraine-IBS dyad to 26.5% in the migraine-fibromyalgia dyad, whereas in the IBS-only group it was 17.5% and increased to 29.5% in the IBS-fibromyalgia dyad. See eAppendix Figure [A-F] for other COPC cohorts.

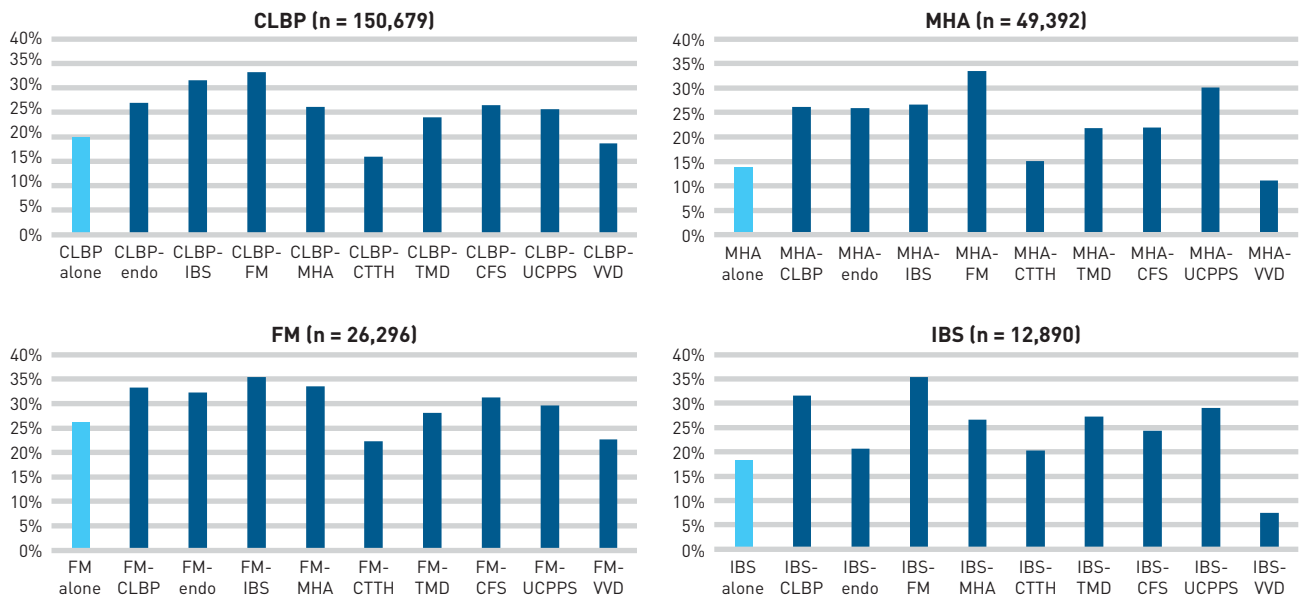
Adjusted model results for odds of LOT in our 4 largest COPC cohorts are shown in Table 4. In each cohort, individuals with COPC dyads that included any combination of back pain, migraine, fibromyalgia, or IBS had higher odds of LOT compared with single COPCs. For example, among those with back pain who also had either migraine, fibromyalgia, endometriosis, or IBS, the odds of LOT were increased by 32% (odds ratio [OR], 1.32; 95% CI, 1.27-1.37), 60% (OR, 1.60; 95% CI, 1.44-1.76), 75% (OR, 1.75; 95% CI, 1.58 to 1.95), and 16% (OR, 1.16; 95% CI, 1.08-1.23), respectively, compared with the back pain–only group. In the migraine headache cohort, the odds for LOT were significantly higher among those with all other COPCs except myalgic encephalomyelitis/chronic fatigue syndrome.

See eAppendix Table 2 for other COPC cohorts.

## DISCUSSION

Overall, 1 in 5 patients receiving care in CHCs had at least 1 COPC. The most frequent condition was chronic low back pain, as has been noted in previous literature on non-CHC populations.<sup>4,7</sup> We found that individuals with 1 or more COPC were 4 times more likely to receive LOT compared with individuals without a COPC. Previous studies based on survey and administrative data reported similar increased risk of LOT with a higher number of chronic pain conditions.<sup>9</sup> Previous LOT studies have predominantly focused on association with individual pain conditions or larger musculoskeletal pain patterns; fewer studies have evaluated overlapping pain conditions.<sup>9</sup> Romanelli et al evaluated different groups, including a group with unclassified pain that included fibromyalgia, pelvic pain, abdominal pain, and general pain, and reported that the unclassified group had the highest prevalence of prescriptions for opioids (14.2%).<sup>12</sup> Hassan et al evaluated the association between overlapping pain conditions and opioid use utilizing tertiary pain clinic charts data, but the study sample was small.<sup>28</sup> This study adds to the literature by further evaluating common combinations of COPC, as those combinations are understudied,<sup>29</sup> to better understand how overlapping pain conditions might affect opioid prescribing in socioeconomically vulnerable patients receiving care in CHCs across the United States.

**FIGURE.** Prevalence of Long-term Opioid Treatment in Pain Dyads Compared With Single Pain Condition in Common Chronic Overlapping Pain Condition Cohorts<sup>a</sup>



CFS, myalgic encephalomyelitis/chronic fatigue syndrome; CLBP, chronic low back pain; CTTH, chronic tension-type headache; ENDO, endometriosis; FM, fibromyalgia; IBS, irritable bowel syndrome; MHA, migraine headache; TMD, temporomandibular disorder; UCPPS, urologic chronic pelvic pain syndrome; VVD, vulvodynia.  
<sup>a</sup>See eAppendix Figure [A-F] for TMD, UCPPS, ENDO, VVD, CTTH, and CFS cohorts.

The prevalence of LOT prescribing varied significantly among the chronic pain conditions in our study, from 7.7% in the vulvodynia cohort to 26.2% in the fibromyalgia cohort. Although opioid prescribing has been decreasing over the past decade,<sup>26,30</sup> patients with fibromyalgia, chronic low back pain, and chronic pelvic pain still received LOT more often than those with other COPCs. There is conflicting evidence as to whether opioids are an effective treatment for many chronic pain conditions. Previous studies generally do not support use of LOT for chronic pain, reporting risk of opioid misuse and other adverse sequelae.<sup>31,32</sup> Although many patients report pain relief with use of opioids,<sup>33,34</sup> they might benefit more from using medications that target the central nervous system, such as antidepressants,<sup>35</sup> or from nonpharmacological pain management approaches. Providers serving patients in CHCs should be aware of COPC combinations more commonly associated with LOT, as these patients may benefit from non-opioid treatment modalities.

Our findings showed an additive effect of some pain conditions; dyads that included chronic low back pain, fibromyalgia, IBS, or

**TABLE 4.** Association Between Pain Dyads and LOT Compared With Single Pain Condition Across Common COPC Cohorts: Adjusted OR (95% CI)<sup>a</sup>

COPC	Chronic low back pain cohort (n = 150,637)	Migraine headache cohort (n = 49,365)	Fibromyalgia cohort (n = 26,276)	IBS cohort (n = 12,883)
Chronic low back pain	Ref	<b>2.59 (2.38-2.83)</b>	<b>1.70 (1.42-2.03)</b>	<b>2.60 (2.29-2.94)</b>
Migraine headache	<b>1.32 (1.27-1.37)</b>	Ref	<b>1.34 (1.23-1.45)</b>	<b>1.76 (1.60-1.94)</b>
Fibromyalgia	<b>1.60 (1.44-1.76)</b>	<b>2.63 (2.46-2.81)</b>	Ref	<b>2.75 (2.48-3.04)</b>
IBS	<b>1.16 (1.08-1.23)</b>	<b>1.51 (1.41-1.62)</b>	<b>1.17 (1.04-1.31)</b>	Ref
Chronic tension-type headache	0.99 (0.94-1.04)	<b>1.32 (1.21-1.44)</b>	0.93 (0.75-1.17)	<b>1.35 (1.00-1.83)</b>
Temporomandibular disorder	<b>1.11 (1.03-1.20)</b>	<b>1.38 (1.19-1.59)</b>	<b>1.18 (1.07-1.30)</b>	1.16 (0.95-1.42)
Urologic chronic pelvic pain syndrome	1.09 (0.98-1.23)	<b>2.22 (1.96-2.52)</b>	1.11 (0.69-1.78)	<b>2.31 (1.62-3.27)</b>
Endometriosis	<b>1.75 (1.58-1.95)</b>	<b>2.18 (1.80-2.64)</b>	<b>2.06 (1.38-3.10)</b>	1.53 (0.79-2.97)
Myalgic encephalomyelitis/chronic fatigue syndrome	1.03 (0.96-1.10)	<b>0.64 (0.46-0.91)</b>	0.92 (0.82-1.02)	0.62 (0.27-1.43)

COPC, chronic overlapping pain condition; IBS, irritable bowel syndrome; LOT, long-term opioid treatment; OR, odds ratio; ref, reference.

<sup>a</sup>Separate logistic regression models were conducted using generalized estimating equations with robust sandwich estimators to account for clustering within states to assess the association between LOT and COPC dyads for each COPC cohort (see column). Row represents second condition in dyads in each cohort (or column). Reference category: patients with single pain condition in each COPC cohort. The regression models were adjusted for age, gender, race/ethnicity, primary language, insurance type, urban/rural location, smoking status, and presence of mental health and physical health comorbidity. Results are presented as OR and 95% CI. Values in bold are statistically significant at P = .05. In several models, dyads with the vulvodynia group were not included due to low count of patients.

See eAppendix Table 2 for temporomandibular disorder, urologic chronic pelvic pain syndrome, endometriosis, chronic tension-type headache, and myalgic encephalomyelitis/chronic fatigue syndrome cohorts.



migraine headache were associated with a higher likelihood of LOT compared with any single chronic pain condition or dyads without these 4 conditions. Previous studies have shown that the presence of a chronic pain condition is a predictor for having other chronic pain conditions,<sup>36</sup> and individuals with COPCs often experience pain amplification and greater pain sensitivity,<sup>37,38</sup> greater emotional burden, and dysfunctional pain attitudes.<sup>10</sup> It is also known that patients with more widespread pain experience poorer treatment response,<sup>39</sup> so it is possible that providers justify use of opioids as a treatment of last resort for patients who have run out of other options. Further studies are needed to investigate patients' and providers' motivations and barriers for opioid prescribing to better understand prescription patterns in groups with multiple COPCs.

Although our findings showed an additive effect for certain COPCs, previous studies have reported that not all patients with COPCs experience pain amplification.<sup>40</sup> Differences in the association between LOT and COPC combinations within each cohort suggest that there may be more complicated pairwise interactions that warrant targeted study. Further, we found that the prevalence of chronic comorbidities, especially mental health conditions, was higher in those with at least 1 COPC compared with those with none (Table 2). Current treatment modalities for pain management tend to focus on sensory aspects of pain despite the fact that mental health conditions, including depression, anxiety,<sup>41,42</sup> and sleep disorders,<sup>43</sup> are also important risk factors for both COPCs and opioid misuse.<sup>44</sup> Maixner et al<sup>4</sup> concluded that combinations of medications and nonpharmacological interventions produce better pain relief, especially in fibromyalgia, IBS, chronic lower back pain, and headache. CHC patients with COPCs may benefit from further integration of mental health support services in safety-net clinical practices to improve care for socioeconomically disadvantaged population.

### Strengths and Limitations

This study used EHR data and a large sample of CHC patients, including a large percentage of uninsured patients and patients with a significant chronic condition burden, particularly mental health problems, who often are less well represented in the other studies. CHC patients are more likely to remain in CHCs compared with patients from other settings, allowing for capture of multiple years of observations for each individual.<sup>45</sup> Although use of EHR data has many advantages (eg, avoiding recall bias in reporting chronic conditions, medication use, and health services utilization), it also has limitations. Our use of EHR problem lists to identify pain conditions might underestimate or overestimate their prevalence. It has been reported in the literature that problem list completeness ranges between 60.2% and 99.4%.<sup>46</sup> We identified both COPCs and opioid status over a 10-year study period but did not account for temporality of these factors. Patients with COPCs often experience delay in diagnosing pain conditions. For example, it takes on average more than 2 years from experiencing first symptoms to record fibromyalgia diagnoses.<sup>47</sup> We did not account for other pain conditions

(eg, osteoarthritis) that may or may not be chronic. Patients with less frequent visits may have undiagnosed pain conditions, which may underestimate the proportion of patients with COPC, but using a 10-year period prevalence decreases the risk of underreporting COPCs. We were unable to reliably measure the duration of pain conditions, instead using *ICD-10* codes to identify the presence of pain conditions that are generally chronic. We used prescription order data and cannot confirm that patients took the medications, possibly overestimating the actual use of opioids. We were not able to determine reasons for any health services delivered outside our system of CHCs. We included long-term use of tramadol in the LOT definition. Although tramadol may be prescribed for more resistant pain conditions as a second line of treatment (eg, to manage some cases of fibromyalgia<sup>48</sup>), a systematic review did not show sufficient evidence to support or refuse tramadol to manage pain conditions.<sup>49</sup> Our results may not be generalizable to non-CHC populations, nor to all CHC populations, as the OCHIN network is disproportionately represented by West Coast states. However, CHCs provide care to more than 29 million people in the United States, and their socioeconomically vulnerable patients are at higher risk for both chronic conditions and opioid prescribing.<sup>9,12</sup> In regression analyses, we were not able to control for severity of chronic pain conditions, patient preferences for chronic opioid prescribing, patient education level, provider characteristics (eg, type of provider who prescribed opioids), patient-provider relationships, or site-level characteristics, which may affect opioid prescribing patterns.

Our findings reinforce the value of integrated care programs including mental health providers to manage complex patients in primary care settings. There are many known barriers to increasing the use of nonpharmacological alternatives to long-term opioid prescribing, including access and cost of care, lack of clinician knowledge of these treatments, and shortage of providers of these treatments (eg, shortages of cognitive behavioral therapists with experience dealing with chronic pain problems and patients' lack of motivation).<sup>50</sup> Future studies are needed to evaluate the various effects of pharmacological and nonpharmacological pain modalities in patients who have both COPCs and mental health disorders.

## CONCLUSIONS

This study provides critical insight into opioid prescribing among patients with COPCs who are socioeconomically disadvantaged. The highest rates of long-term opioid prescribing can be seen in those with multiple COPCs. Among people with more than 1 COPC, the presence of chronic low back pain, migraine headache, fibromyalgia, or IBS increased the odds of LOT prescribing compared with having a single COPC. This study identifies target populations for future interventions to improve medication and nonpharmacological treatment for COPCs and further reduce use of opioid analgesics. ■

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**eAppendix Table 1.** Percent of co-occurring COPC Diagnosis (10-year observation)

<b>Dyad occurrence.</b>	<b>CLBP</b>	<b>Endo</b>	<b>IBS</b>	<b>FM</b>	<b>MHA</b>	<b>CTTH</b>	<b>TMD</b>	<b>CFS</b>	<b>UCPPS</b>	<b>VVD</b>
<b>n</b>	155949	1168	15358	30523	53779	14186	5682	4944	2618	405
<b>% of top condition having dyad with row condition.</b>										
<b>CLBP</b>		32%	26%	34%	24%	25%	28%	26%	26%	22%
<b>Endo</b>	0%		1%	1%	0%	0%	0%	0%	2%	1%
<b>IBS</b>	3%	8%		8%	5%	3%	6%	7%	10%	7%
<b>FM</b>	7%	14%	16%		9%	7%	13%	18%	13%	13%
<b>MHA</b>	8%	22%	16%	16%		13%	16%	13%	14%	18%
<b>CTTH</b>	2%	5%	3%	3%	4%		5%	3%	3%	6%
<b>TMD</b>	1%	2%	2%	2%	2%	2%		2%	2%	4%
<b>CFS</b>	1%	2%	2%	3%	1%	1%	2%		2%	2%
<b>UCPPS</b>	0%	4%	2%	1%	1%	1%	1%	1%		7%
<b>VVD</b>	0%	1%	0%	0%	0%	0%	0%	0%	1%	

Note: fibromyalgia (FM), irritable bowel syndrome (IBS), temporomandibular disorder (TMD), urologic chronic pelvic pain syndrome (UCPPS), endometriosis (ENDO), vulvodynia (VVD), chronic low back pain (CLBP), chronic tension type headache (CTTH), migraine headache (MHA), and myalgic encephalomyelitis/chronic fatigue syndrome (MECFS).



**eAppendix Table 2.** Association between COPC dyads and long-term opioid treatment compared with single pain condition across COPC cohorts. Unadjusted and Adjusted Odd Ratio, 95% confidence interval.

COPC	Chronic tension type headache cohort (n=12,770)		Temporomandibular disorder cohort (n=4729)		Urologic chronic pelvic pain syndrome cohort (n=2162)		Endometriosis cohort (n=898): (adjusted model did not converge)		Myalgic encephalomyelitis/ chronic fatigue syndrome cohort (n=4148)	
	Unadj.OR (95% CI)	Adj.OR (95% CI)	Unadj.OR (95% CI)	Adj.OR (95% CI)	Unadj.OR (95% CI)	Adj.OR (95% CI)	Unadj.OR (95% CI)	Adj.OR (95% CI)	Unadj.OR (95% CI)	Adj.OR (95% CI)
Chronic low back pain	<b>3.73</b> (2.47-5.63)	<b>2.65</b> (2.28-3.09)	<b>3.67</b> (2.42-5.57)	<b>2.67</b> (1.90-3.77)	<b>2.89</b> (2.40-3.48)	<b>2.35</b> (1.97-2.79)	<b>5.01</b> (3.60-6.97)	Did not converge	<b>3.70</b> (2.63-5.21)	<b>2.86</b> (2.22-3.68)
Migraine headache	<b>2.19</b> (1.74-2.74)	<b>1.90</b> (1.72-2.11)	<b>1.72</b> (1.16-2.55)	<b>1.67</b> (1.24-2.24)	<b>2.41</b> (2.03-2.86)	<b>2.03</b> (1.68-2.45)	<b>2.38</b> (1.26-4.48)	Did not converge	0.86 (0.46-1.62)	0.84 (0.51-1.36)
Fibromyalgia	<b>4.09</b> (2.87-5.82)	<b>2.66</b> (2.23-3.17)	<b>4.08</b> (2.96-5.62)	<b>3.06</b> (2.55-3.68)	<b>3.23</b> (1.99-5.25)	<b>2.42</b> (1.04-5.63)	<b>4.30</b> (2.85-6.50)	Did not converge	<b>3.95</b> (2.97-5.25)	<b>2.49</b> (1.97-3.16)
Irritable bowel syndrome	<b>2.55</b> (1.57-4.15)	<b>1.62</b> (1.20-2.19)	<b>1.74</b> (1.08-2.81)	<b>1.13</b> (0.83-1.54)	<b>2.30</b> (1.88-2.82)	<b>1.90</b> (1.26-2.84)	2.23 (0.68-7.31)	Did not converge	0.90 (0.43-1.91)	0.72 (0.29-1.75)
Chronic tension type headache	<b>Ref.</b>	<b>Ref.</b>	0.42 (0.05-3.29)	0.68 (0.13-3.58)	1.33 (0.38-4.67)	1.11 (0.18-6.82)	<b>2.93</b> (1.31-6.56)	Did not converge	1.00 (0.28-3.55)	1.78 (0.65-4.87)
Temporomandibular disorder	0.89 (0.22-3.65)	0.90 (0.28-2.92)	<b>Ref.</b>	<b>Ref.</b>	0.81 (0.09-7.11)	0.81 (0.04-18.52)	<b>2.37</b> (1.04-5.38)	Did not converge	1.28 (0.93-1.76)	<b>1.74</b> (1.49-2.03)
Urologic chronic pelvic pain syndrome	2.87 (0.83-9.94)	1.58 (0.34-7.36)	1.06 (0.14-7.83)	1.10 (0.13-9.06)	<b>Ref.</b>	<b>Ref.</b>	<b>3.14</b> (1.44-6.87)	Did not converge	<b>4.34</b> (2.59-7.27)	<b>5.53</b> (2.08-14.66)
Endometriosis	<b>4.85</b>	<b>7.04</b>	2.28	<b>4.57</b>	2.07	3.62	<b>Ref.</b>	<b>Ref.</b>	2.78	5.11

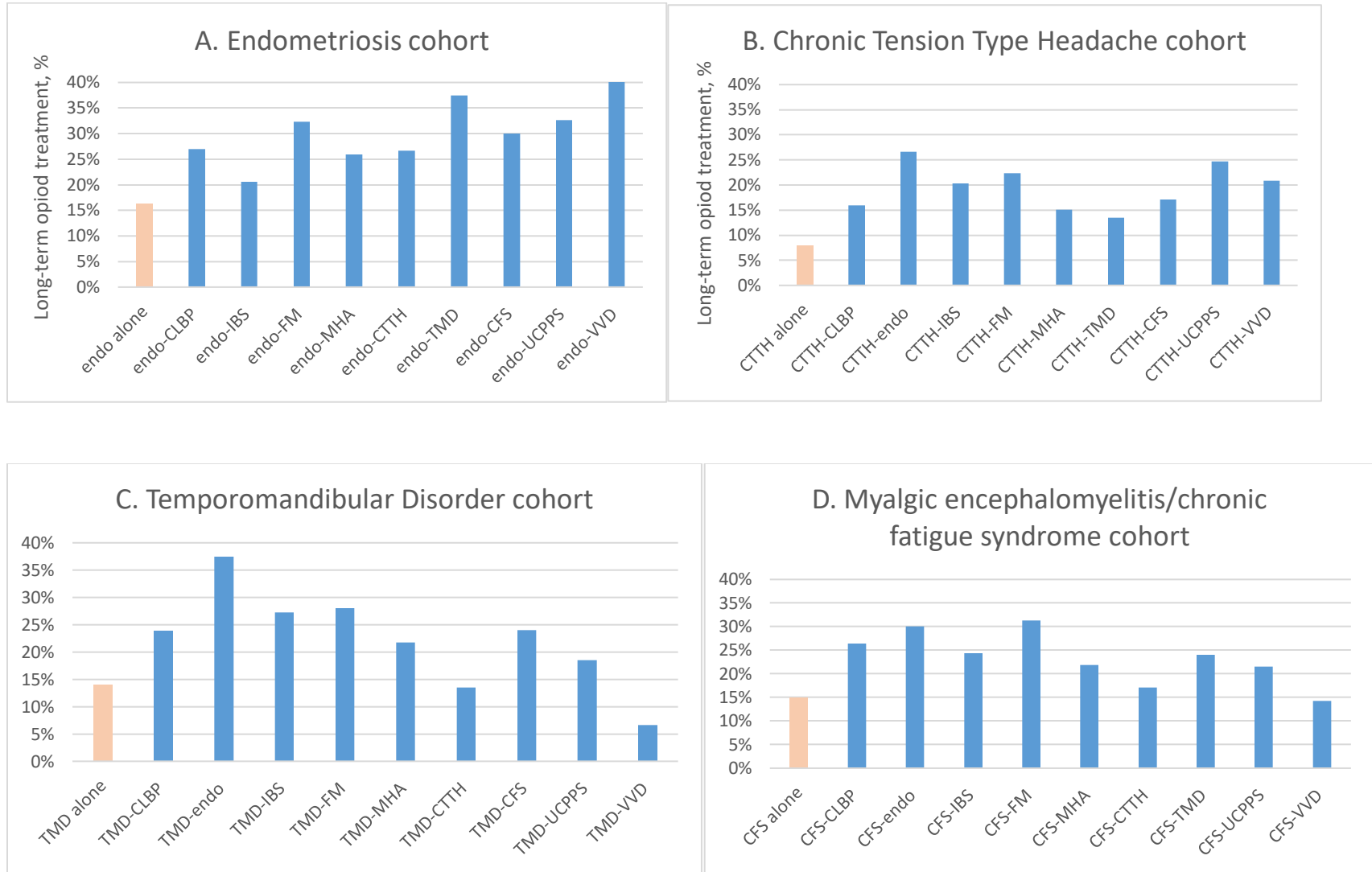
	<b>(2.19-10.74)</b>	<b>(3.61-13.75)</b>	(0.84-6.23)	<b>(1.52-13.76)</b>	(0.54-7.89)	(0.82-15.93)			(0.15-51.13)	(0.43-60.36)
Myalgic encephalomyelitis/chronic fatigue syndrome	1.89 (0.76-4.72)	1.75 (0.64-4.81)	1.29 (0.83-2.00)	<b>1.39</b> <b>(1.18-1.65)</b>	<b>3.31</b> <b>(2.28-4.80)</b>	<b>4.14</b> <b>(1.32-12.99)</b>	3.64 (0.37-35.96)	Did not converge	<b>Ref.</b>	<b>Ref.</b>

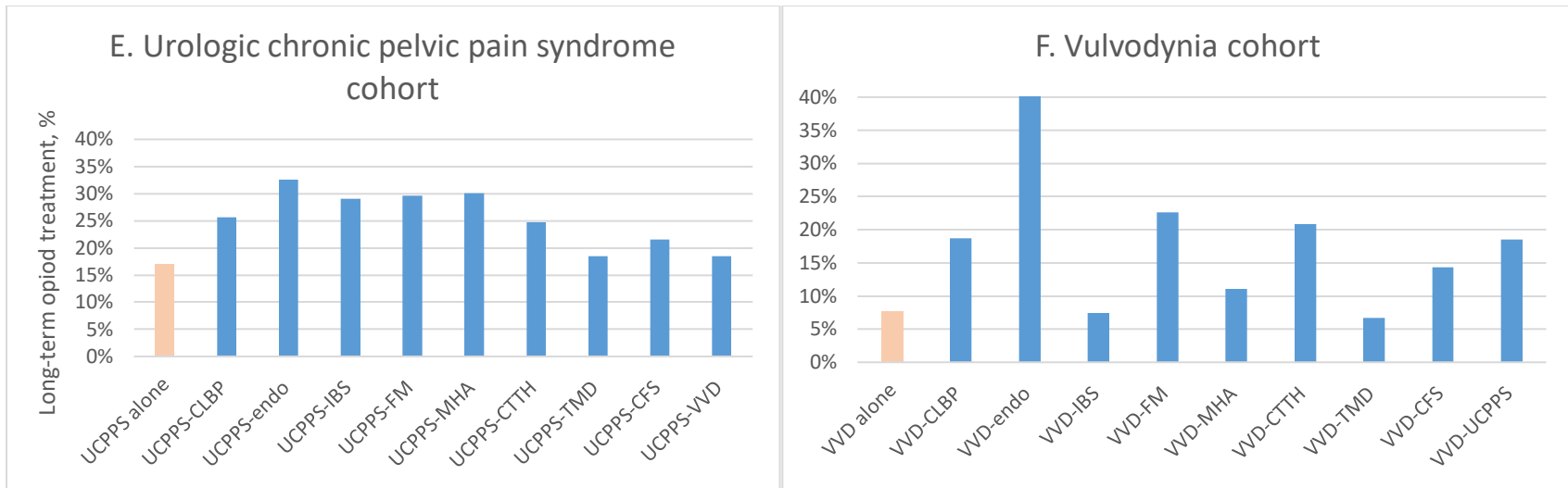
Note: Vulvodynia cohort (n=324) - neither model converged

Values in bold are statistically significant at p = 0.05.

Note: Separate logistic regression models were conducted using generalized estimating equations with robust sandwich estimators to account for clustering within states to assess the association between LOT and COPC dyads for each COPC cohort (see column). Row represents second condition in dyads in each cohort (or column). Reference category: patients with single pain condition in each COPC cohort. The regression models were adjusted for: age, gender, race/ethnicity, primary language, insurance type, urban/rural location, smoking status, presence of mental health and physical health comorbidity. Results are presented as odds ratios (OR) and 95% CI. Values in bold are statistically significant at p = 0.05.

**eAppendix Figure (A-F).** Prevalence of long-term opioid treatment in COPC dyads compared with single pain condition in COPC cohorts.





Note: fibromyalgia (FM), irritable bowel syndrome (IBS), temporomandibular disorder (TMD), urologic chronic pelvic pain syndrome (UCPPS), endometriosis (ENDO), vulvodynia (VVD), chronic low back pain (CLBP), chronic tension type headache (CTTH), migraine headache (MHA), and myalgic encephalomyelitis/chronic fatigue syndrome (MECFS).