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Chronic overlapping pain conditions and long-term opioid treatment

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Abstract

Objectives: One in five people in the United States lives with chronic pain. Many chronic pain patients 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 in COPC patients in primary care settings, especially among socioeconomically vulnerable patients. This study aims to evaluate opioid prescribing among patients with COPCs in the 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 >1 million patients aged ≥18 years based on electronic health record (EHR) data from 449 US community health centers across 17 states between 01/01/2009 and 12/31/2018. Logistic regression models were used to assess the relationship between COPCs and LOT.

Results: Individuals with COPCs were prescribed LOT four 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 to a single COPC.

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Conclusions: While LOT prescribing has declined over time, it remains relatively high among COPC patients with certain conditions and for those with multiple COPCs. Study findings suggest target populations for future interventions to manage chronic pain among socioeconomically vulnerable patients.

Précis

Little is known about opioid prescribing patterns in patients with chronic overlapping pain conditions. Study suggests target populations for interventions to manage chronic pain.

Keywords

chronic overlapping pain conditions; multiple pain conditions; long-term opioid treatment; chronic opioid treatment; opioid prescribing

INTRODUCTION

Over 29 million people in the US receive health services at community health centers (CHCs).[1] CHCs care for a disproportionally high number of patients with low income (91% ≤200% of the federal poverty level), with Medicaid insurance (1 in 5 Medicaid beneficiaries), patients who are uninsured (20%), and patients of racial and ethnic minorities (1 in 7 patients). Socioeconomically vulnerable patients with higher rates of chronic conditions are commonly seen at CHCs.[1] However, less is known about chronic pain conditions among this population.[2]

Overall, between 20-62% of people with chronic pain, defined as pain that persists or recurs for longer than three months,[3] experience multiple pain conditions simultaneously.[3, 4] The National Institutes of Health have recognized the concept of frequently co-occurring pain conditions that are likely to share central sensitization as a common mechanism[5] and have designated these to be chronic overlapping pain conditions (COPCs, see Table 1).[4,6,7] 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 impact treatment patterns, including opioid prescribing.[8,9]

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

Pain medication clinical trials often exclude people with more than one pain condition.[15] Additionally, COPCs co-occur frequently with other chronic physical and mental health conditions which further increases the likelihood of being prescribed an opioid.[16-18] Evidence suggests that individuals with pain and mental health comorbidities might benefit

more from multimodal treatment programs that include mental health than from opioids to manage their COPCs.[17] Although opioid prescribing,[12] frequency of COPCs, and burden of mental health disorders are more common in patients with low-income and/or underinsured patients,[19] no studies have specifically explored COPCs in CHCs. Additionally, these health centers face multitudes of barriers such as underfunded, short staff, turnover, and serve complex patient populations with high rate of social needs.[20-23] It is critical to understand the extent of opioid treatment among patients with COPCs receiving care in CHCs to identify patient populations that 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 and Data Source and Study Population

This study is a secondary analysis of electronic health record (EHR) data. The data were obtained from OCHIN (not an abbreviation), and the Accelerating Data Value Across a National Community Health Center Network (ADVANCE) Clinical Research Network of CHCs.[24] 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), providing health care access regardless of patients' insurance status.[25] Our population included >1 million patients ≥18 years of age who received primary care at one of these clinics between 01/01/2009 and 12/31/2018. We further limited our study sample to patients with ≥2 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 people with terminal cancer-related opioid prescribing.

Measures

Outcome variable: Long-term opioid treatment—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 class of expectorant, antitussive, antidiarrheal, and all that were not oral or transdermal in form. We excluded rectal formulations because they are only rarely used and often for individuals with cancer-related pain. In order to exclude patients receiving medications for opioid use disorders, we excluded liquid methadone and limited buprenorphine to the two forms approved for treatment of pain by the U.S. Food and Drug Administration (FDA). Detailed information on opioid order identification has been published elsewhere.[26] We defined patients receiving long-term opioid treatment (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 pills, or any methadone pills or fentanyl patches.[26] We categorized patients into three 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 one opioid prescription but never LOT and 3) those meeting our LOT definition during at least one calendar quarter.

Independent Variables—We included conditions in Table 1 as they have been previously used to define the chronic overlapping pain condition (COPC) construct.[6,7] We identified all diagnoses of these conditions in the patients' EHR problem lists (see Table 1) using ICD-10 codes[6,7] and converted to ICD-9 codes using general equivalence mapping tables.[27] We assessed 10-year, period prevalence of each condition, as well as a count variable describing all COPCs prevalent during 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 one additional COPC, constructing a categorical variable within each cohort, having levels of one COPC and each dyad combination. For example, in the fibromyalgia cohort, patients with IBS are in the fibromyalgia-IBS category and are compared to 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, having one or more physical or mental health chronic condition other than a COPC (see 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 due to missing data.

Statistical Analysis

Frequencies and percentages for categorical variables and means and standard deviations for continuous variables for COPC and non-COPC group were calculated to compare patient characteristics. We assessed the percentage of patients in each of three categories of opioid prescribing status (no prescription, some opioid analgesic but not LOT, LOT) for individual COPCs and by count-based COPC groups (none, one, two, ≥3 conditions). Modeling of LOT prevalence was stratified by cohorts limited to patients having each COPC, comparing LOT in patients with a single COPC to those having dyads (one additional COPC). For clarity in describing pairwise effects, patients with COPC counts greater than two were not modeled (<3% of study). Logistic regression models in each COPC cohort assessed the odds of LOT status for dyads compared to 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 vulvodynia patients in descriptive analysis but did not model this cohort, as small cell counts caused convergence issues. Statistical significance was set at alpha<0.05. Statistical analysis was conducted using SAS, version 9.4 (SAS Institute, Cary NC, USA). This study was approved by the Institutional Review Board.

RESULTS

Overall, the study sample included 1,197,477 patients, with 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 one COPC. Table 2 shows characteristics of the COPC and non-COPC groups. Individuals with COPC tended to be older, white, have Medicaid or Medicare insurance coverage, and were more likely to have one 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 to those in the COPC group.

Of those who had COPCs, 83.9% had one COPC, 13.5% had two 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).

Individuals with COPCs were prescribed LOT four 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 one 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).

Figure 1 shows LOT prevalence within four COPC cohorts: comparing baseline (single COPC) to each dyad. Dyads increased the prevalence of LOT within each cohort with the exception of those 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 group with migraine only group and varied between 15.9% in migraine-IBS dyad to 26.5% in migraine-fibromyalgia dyad, while in the IBS only group it was 17.5%, and increased to 29.5% in the IBS-fibromyalgia dyad.

Adjusted model results for odds of LOT in our four largest COPC cohorts are shown in Table 4. In each cohort, individuals with COPC dyads which included any combination of back pain, migraine, fibromyalgia, or irritable bowel had higher odds of LOT compared to single COPCs. For example, among those with back pain who also had either migraine, fibromyalgia, endometriosis, or irritable bowel syndrome, the odds of LOT were increased by 32% (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 to 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.

DISCUSSION

Overall, one in five patients receiving care in CHCs had at least one COPC. The most frequent condition was chronic low back pain, as has been noted in previous literature on non-CHC populations.[4,7] We found that individuals with one or more COPC were four times more likely to receive LOT compared to individuals without COPCs. Previous studies based on survey and administrative data reported similar increased risk of LOT with a higher number of chronic pain conditions.[9] Previous LOT studies predominantly focuses on association with individual pain conditions, or larger musculoskeletal pain patterns, fewer studies evaluated overlapping pain conditions.[9] Romanelli et al. evaluated different groups, including unclassified pain group which included fibromyalgia, pelvic pain, abdominal

pain, and general pain, and reported that unclassified group had the highest prevalence of prescriptions for opioids (14.2%).[12] Hassan et al. evaluated association between overlapping pain conditions and opioid use utilizing tertiary pain clinic charts data, however the study sample was small.[28] This study adds to the literature by further evaluating common combinations of COPC, as those combinations are understudied,[29] to better understand how overlapping pain conditions might affect opioid prescribing in socioeconomically vulnerable patients receiving care in CHCs across US.

The prevalence of LOT prescribing varied significantly between different chronic pain conditions in our study, from 7.7% in the vulvodynia cohort to 26.2% in the fibromyalgia cohort. While opioid prescribing has been decreasing over the last decade, [26,30] 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.[31, 32] While many patients report pain relief with use of opioids,[33,34] they might benefit more from using medications that target the central nervous system, such as anti-depressants,[35] or from non-pharmacological pain management approaches. Providers serving CHC patients should be aware of CHC 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 migraine headache were associated with a higher likelihood of LOT compared to any single chronic pain condition or dyads without these four conditions. Previous studies have shown that the presence of a chronic pain condition is a predictor for having other chronic pain conditions,[36] and individuals with COPCs often experience pain amplification and greater pain sensitivity,[37,38] greater emotional burden, and dysfunctional pain attitudes.[10] It is also known that patients with more widespread pain experience poorer treatment response,[39] 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.

While our findings showed an additive effect for certain COPCs, previous studies reported that not all patients with COPCs experience pain amplification.[40] Differences in the association between LOT and COPC combinations within each cohort suggest 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 one COPC compared to 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,[41,42] and sleep disorders,[43] are also important risk factors for both COPCs and opioid misuse.[44] Maixner et al.[4] 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. CHCs patients are more likely to remain in CHCs compared to patients from other settings, allowing for capture of multiple years of observations for each individual.[45] While use of EHR data has many advantages (*e.g.* 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 under- or-overestimate their prevalence. It has been reported in the literature that problem list completeness ranges between 60.2%-99.4%.[46] 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 over two years between experiencing first symptoms to record fibromyalgia diagnoses.[47] We did not account for other pain conditions (e.g., 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. While tramadol may be prescribed for more resistant pain conditions as a second line of treatment, for example to manage some cases of fibromyalgia,[48] a systematic review did not show sufficient evidence to support or refuse tramadol to manage pain conditions.[49] 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 over 29 million people in the US, and their socioeconomically vulnerable patients are at higher risk for both chronic conditions and opioid prescribing.[9,12] 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 (*e.g.* type of provider 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 non-pharmacological alternatives to long-term opioid prescribing, including access and cost of care, lack of clinician knowledge of these treatments, shortage of providers of these treatments, *e.g.* shortages of cognitive behavioral therapists with experience dealing with chronic pain problems, patient's lack of motivation, etc.[50] 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 one COPC, the presence of chronic low back pain, migraine headache, fibromyalgia, or IBS increased the odds of LOT prescribing compared to having a single COPC. This study identifies target populations for future interventions to improve medication and non-pharmacological treatment for COPCs and further reduce use of opioid analgesics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Takeaway Points

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

- Individuals with COPC were prescribed long-term opioid treatment four 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 to a single COPC.

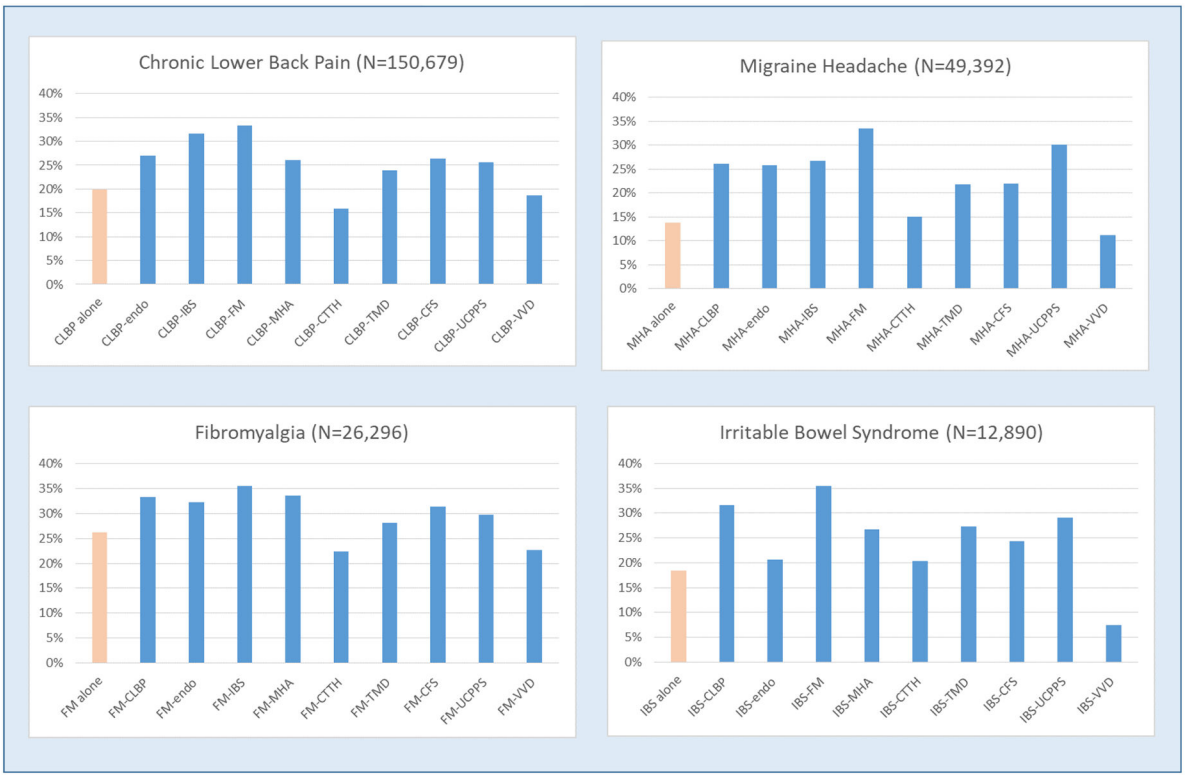

Figure 1. Prevalence of long-term opioid treatment in pain dyads compared to single pain condition in common chronic overlapping pain condition cohorts.

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).

See supplement Figure 2 for temporomandibular disorder, urologic chronic pelvic pain syndrome, endometriosis, vulvodynia, chronic tension type headache, and myalgic encephalomyelitis/chronic fatigue syndrome cohorts.

Table 1.

List of chronic overlapping pain conditions.

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

Table 2.

Characteristics of Study Population.

Characteristics	All OCHIN primary care patients, 2009-2018		≥1 COPC[a] diagnosis		Non-COPC group	
Study population, n (row %)	1197477	(100)	238750	(19.9)	958727	(80.1)
Age (years), mean (SD)	40	(17)	49	(15)	46	(17)
Female, n (col %)	698102	(58.3)	156751	(65.7)	541351	(56.5)
Race/Ethnicity, n (col%)						
Hispanic	342939	(28.6)	58598	(24.5)	284341	(29.7)
NH[b]-Asian	49401	(4.1)	7617	(3.2)	41784	(4.4)
NH-Black	183528	(15.3)	37628	(15.8)	145900	(15.2)
NH-Other/Missing	87242	(7.3)	16765	(7.0)	70477	(7.4)
NH-White	534367	(44.6)	118142	(49.5)	416225	(43.4)
FPL[c], n (col%)						
≤138%	763600	(63.8)	160887	(67.4)	602723	(62.9)
>138%	159528	(13.3)	29125	(12.2)	130403	(13.6)
Unknown	274349	(22.9)	48748	(20.4)	225601	(23.5)
Insurance status, n (col%)						
Medicaid	530807	(44.3)	114250	(47.9)	416557	(43.5)
Medicare	120966	(10.1)	30426	(12.7)	90540	(9.4)
Other Public	53750	(4.5)	9205	(3.9)	44545	(4.7)
Private	182256	(15.2)	32392	(13.6)	149864	(15.6)
Uninsured	309218	(25.8)	52378	(21.9)	256840	(26.8)
Missing	480	<1	99	<1	381	<1
English-language preference, n (col%)	888864	(74.2)	184734	(77.4)	704130	(73.4)
Rural location, n (col%)	39377	(3.3)	7026	(2.9)	32351	(3.4)
Current smoker, n (col%)	250624	(20.9)	54498	(22.8)	196126	(20.5)
BMI[d], mean (SD)	29.0	(7.0)	29.9	(7.4)	28.8	(6.9)
Chronic Conditions						
# Chronic conditions overall, mean (SD)	1.8	(1.9)	2.6	(2.2)	1.6	(1.8)
# Mental health conditions[e], mean (SD)	0.6	(1.0)	1.1	(1.2)	0.5	(0.9)
# Physical conditions[f], mean (SD)	1.1	(1.5)	1.6	(1.7)	1	(1.4)
≥1 Mental health conditions, n (col%)	442902	(37.0)	134238	(56.2)	308664	(32.2)
≥1 Physical conditions, n (col%)	615269	(51.4)	155651	(65.2)	459618	(47.9)
# Office visits during first year, mean (SD)	5.5	(7.0)	7.4	(9.3)	5.0	(6.1)
# 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 (col%)	78542	(6.6)	40407	(16.9)	38135	(4.0)

Note: [a]COPC – chronic overlapping pain conditions (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). Patient age was calculated at end of 2018, while other patient characteristics were estimate at the beginning of study enrollment.

[b]NH-Non-Hispanic

[c] FPL- federal poverty level

[d] BMI-Body mass index

[e] Mental health conditions included following categories: anxiety/dissociative/somatoform disorders, bipolar disorder/affective psychosis, dementia (including Alzheimer's and other senile dementias), depression, post-traumatic stress disorder, schizophrenia, sleep disorders, stroke, substance abuse disorders (non-opioid drug and alcohol).

[f] Physical conditions included 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. For descriptive analysis, missing/unknown data were included as an "unknown" category.

Table 3.

Prevalence of chronic overlapping pain conditions 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 (%)			969224 (80.1)	149711 (12.5)	78542 (6.6)
Number of COPC, n (%)					
0	958727	(80.1)	819511 (85.5)	101081 (10.5)	38135 (4.0)
1	200340	(16.7)	130075 (64.9)	39457 (19.7)	30808 (15.4)
2	32182	(2.7)	17114 (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	155949	(13.0)	92260 (59.2)	32717 (21)	30972 (19.9)
Migraine headache	53779	(4.5)	34772 (64.7)	11619 (21.6)	7388 (13.7)
Fibromyalgia	30523	(2.5)	15953 (52.3)	6572 (21.5)	7998 (26.2)
Irritable bowel syndrome	15358	(1.3)	9118 (59.4)	3414 (22.2)	2826 (18.4)
Chronic tension type headache	14186	(1.2)	10667 (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)
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)

Table 4.

Association between pain dyads and long-term opioid treatment compared to single pain condition across common chronic overlapping pain conditions cohorts. Adjusted Odds Ratio, 95% confidence interval.

COPC	Chronic low back pain cohort (n=150637)	Migraine headache cohort (n=49365)	Fibromyalgia cohort (n=26276)	IBS cohort (n=12883)
Chronic low back pain	Ref.	**2.59 (2.38-2.83)**	**1.70 (1.42-2.03)**	**2.60 (2.29-2.94)**
Migraine headache	**1.32 (1.27-1.37)**	Ref.	**1.34 (1.23-1.45)**	**1.76 (1.60-1.94)**
Fibromyalgia	**1.60 (1.44-1.76)**	**2.63 (2.46-2.81)**	Ref.	**2.75 (2.48-3.04)**
Irritable bowel syndrome	**1.16 (1.08-1.23)**	**1.51 (1.41-1.62)**	**1.17 (1.04-1.31)**	Ref.
Chronic tension type headache	0.99 (0.94-1.04)	**1.32 (1.21-1.44)**	0.93 (0.75-1.17)	**1.35 (1.00-1.83)**
Temporomandibular disorder	**1.11 (1.03-1.20)**	**1.38 (1.19-1.59)**	**1.18 (1.07-1.30)**	1.16 (0.95-1.42)
Urologic chronic pelvic pain syndrome	1.09 (0.98-1.23)	**2.22 (1.96-2.52)**	1.11 (0.69-1.78)	**2.31 (1.62-3.27)**
Endometriosis	**1.75 (1.58-1.95)**	**2.18 (1.80-2.64)**	**2.06 (1.38-3.10)**	1.53 (0.79-2.97)
Myalgic encephalomyelitis/chronic fatigue syndrome	1.03 (0.96-1.10)	**0.64 (0.46-0.91)**	0.92 (0.82-1.02)	0.62 (0.27-1.43)

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 an exponentiated β-coefficients or odds ratios (OR) and 95% CI. Values in bold are statistically significant at p = 0.05.

In several models, dyads with vulvodynia group were not included due to low count of patients.

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