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Cohort Study

# Opioid use among patients with pain syndromes commonly seeking surgical consultation: A retrospective cohort

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ARTICLE INFO	A B S T R A C T				
Keywords: Chronic pain Opioids Psychiatric disorders Temporomandibular joint pain Anorectal pain Foot/ankle pain	<i>Background:</i> Surgeons often see patients with pain to exclude organic pathology and consider surgical treatment. We examined factors associated with long-term opioid therapy among patients with foot/ankle, anorectal, and temporomandibular joint pain to aid clinical decision making. <i>Methods:</i> Using the IBM MarketScan® Research Database, we conducted a retrospective cohort analysis of patients aged 18–64 with a clinical encounter for foot/ankle, anorectal, or temporomandibular joint pain (January 2007–September 2015). Multivariable logistic regression was used to estimate adjusted odds ratios for factors associated with long-term opioid therapy, including age, sex, geographic region, pain condition, psychiatric diagnoses, and surgical procedures in the previous year. <i>Results:</i> The majority of the cohort of 1,500,392 patients were women (61%). Within the year prior to the first clinical encounter for a pain diagnosis, 14% had an encounter for a psychiatric diagnosis, and 11% had undergone a surgical procedure. Long-term opioid therapy was received by 2.7%. After multivariable adjustment, older age (age 50–64 vs. 18–29: aOR 4.47, 95% CI 4.24–4.72, p < 0.001), region (South vs. Northeast, aOR 1.76, 95% CI 1.70–1.81, p < 0.001), encent surgical procedure (aOR 1.83, 95% CI 1.78–1.87, p < 0.001), male sex (aOR 1.14, 95% CI 1.12–1.16, p < 0.001) and recent psychiatric diagnosis (aOR 2.49, 95% CI 2.43–2.54, p < 0.001) were independently associated with long-term opioid therapy. <i>Conclusion:</i> Among patients with foot/ankle, anorectal, or temporomandibular joint pain, the risk of long-term opioid therapy significantly increased with older age, recent psychiatric diagnoses and surgical history. Surgeons should be aware of these risk factors in order to make high quality clinical decisions in consultations with these patients.				

#### 1. Introduction

The lack of standardized opioid prescribing practices and diversion of unused opioid medication have been identified as major contributing factors to the deadly opioid epidemic in the U.S [1–3]. The medical community has recognized the critical necessity of adopting opioid-sparing methods of pain management, prevention of opioid use disorder, and the development of more personalized strategies for effective management of acute and chronic pain [4–6]. Beyond the necessity of managing expected postoperative pain, surgeons also interact frequently with patients with acute or chronic pain in order to rule out organic and potentially operable etiologies. To effectively manage such pain diagnoses, surgeons must be aware of the risk factors for opioid dependence. One such risk factor is sex, as sex-related biologic differences in pain perception [7] and pharmacokinetic processes require different treatment strategies for women and men [8–10]. Women are more likely to experience chronic pain syndromes such as TMJ disease [11], interstitial cystitis/bladder pain syndrome [12], and fibromyalgia [13]. In addition to sex-specific biologic differences in the perception and treatment of pain, there are also sex-specific factors that mediate pain intensity and the subsequent psychological distress [14]. Overall, opioid use is also more common among women than men [15]. Psychiatric disorders also play a role in amplifying chronic pain and increasing the risk of long-term opioid use

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#### Table 1

Descriptive comparisons by pain condition and sex.

n 2 min47.56 (42.3)64.92 (77.7)17.995 (42.6)24.292 (7.4)6667 (72.3)25.899 (72.8)40.40108.800167.44536.202 (52.3)33.00 (47.7)12.3137.544 (75.3)50.64184.022310.60166.61		Foot/Ankle Pain			Anorectal pain			TMJ		
Median (OS)45.79 (1.4)67.27 (1.5)67.001067.27 (1.5)67.001047.60 (1.2)67.67 (1.5)<	Demographics	39%	61%	Р	50%	50%	Р	26%	74%	Р
Media (0R) Age caractor (0F)(0.00)(0.10) </td <td>Age</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	Age									
Age cargor, n (%)	Mean (SD)	45.79 (11.9)	46.72 (11.6)	$< 0.001^{a}$	43.79 (11.8)	41.95 (12.3)	$< 0.001^{a}$	42.60 (12.9)	42.67 (12.5)	0.27 <sup>a</sup>
n 2 minn 7,50 (42.3)64,527 (77)17,905 (42.6)24,222 (77.4)6667 (72.3)25,899 (72.8)40.40106,800167,44535,220 (52.3)33,00 (47.7)12,3137,544 (75.3)50.64164,022310,6036,501 (53.8)39,978 (46.2)12,3137,544 (75.3)Northesat77,450 (39.9)112,3706,501 (53.8)39,978 (46.2)17,75650,003 (73.8)Mikdwest164,50112,479 (51.5)23,597 (46.2)10,74430294 (73.8)0.001Northesat112,3706,251 (50.7)25,882 (49.3)10,74430294 (73.8)0.001Mikdwest160,62123,51050,291 (49.6)51,149 (50.4)17,496 (53.9)26,657 (73.9)10,74430294 (73.8)West163,62123,51022,936 (40.0)11,749 (50.4)17,491 (50.3)26,939 (73.8)10,74430294 (73.8)Umaxim160,62123,51023,939 (46.2)11,749 (50.4)17,491 (50.3)26,939 (73.8)10,74126,939 (73.8)Umaxim163,51210,12423,816 (73.1)10,24223,864 (73.8)10,74126,939 (73.8)10,77110,771Umaxim163,01211,27423,986 (51.0)12,996 (40.0)10,74113,67810,77113,678Umaxim114,79114,79514,47514,47514,47514,47514,47514,475Umaxim114,79112,79412,998 (15.1)11,67811,11113,67811,11113,678Umaxim11	Median (IQR)	48 (38, 56)	49 (39, 56)	$< 0.001^{b}$	45 (35, 53)	43 (32, 52)	$< 0.001^{b}$	44 (33, 54)	44 (33, 53)	0.84 <sup>b</sup>
39.3971.621 (42.2)91.53 (57.5)72.07 (48.7)26.11 (1.3)90.90 (24.0)90.375 (75.4)104.94108.980167.44552.0330.04710.21012.7512.75105.04104.02230.00565.01 (5.3)30.977 (4.5)20.7512.7510.7510.75105.04104.02230.00565.01 (5.3)30.978 (4.5)10.7510.7510.7510.75Repin-0.007-7.807 (4.5)25.897 (4.5)21.807 (4.5)20.957 (4.5)10.7430.947 (7.8)Northeat10.80110.92010.920 (5.5)25.897 (4.5)25.897 (4.5)10.7430.947 (7.8)10.75Northeat10.80110.31220.655 (5.0.7)25.897 (4.5)10.7450.303 (7.9)10.75Northeat10.80120.174 (4.5)23.868 (5.0)21.968 (4.0)17.4050.303 (7.9)10.97Northeat65.07510.312 (4.5)23.868 (5.0)21.968 (4.0)17.4050.303 (7.9)10.97Northeat65.07510.312 (4.5)23.868 (5.0)21.968 (4.0)10.9720.9720.97Northeat65.07510.312 (4.5)12.47710.412 (4.5)10.9720.9720.97Northeat60.9710.9710.463 (3.127)10.47510.463 (4.127)10.9710.9710.97Northeat60.9710.9710.463 (3.128)10.463 (4.127)10.9710.9710.9710.97Northeat60.9710.9710.46	Age category, n (%)			< 0.001 <sup>°</sup>			<0.001 <sup>c</sup>			<0.001 <sup>c</sup>
40-9410,80010,74466,6030,000 (7)12,3175,744 (7)75,744 (7)10,72010,72010,72010,72010,72010,72010,72010,72010,720Northeat75,500 (2)11,29010,72020,801 (2)20,801 (2)10,74020,801 (2)10,74020,901 (2)Malves10,92020,510 (2)10,71010,74020,901 (2)10,740		47,556 (42.3)	64,927 (57.7)		17,995 (42.6)	24,292 (57.4)		9687 (27.2)	25,899 (72.8)	
SoldS										
19-0419-089-070 (a)9-070 (a)9-0	40-49				36,220 (52.3)	33,000 (47.7)			37,544 (75.3)	
Region62.0360.01 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>										
Regionv. e.0.01v. e.0.01 <t< td=""><td>50-64</td><td>-</td><td>· · · ·</td><td></td><td>46,501 (53.8)</td><td>39,978 (46.2)</td><td></td><td></td><td>50,033 (73.8)</td><td></td></t<>	50-64	-	· · · ·		46,501 (53.8)	39,978 (46.2)			50,033 (73.8)	
NortheadPactorPa		(37.2)	(62.8)					(26.2)		
Mdwess Mathew	0			<0.001 <sup>c</sup>			<0.001 <sup>c</sup>			< 0.001 <sup>°</sup>
induction         (a)         induction         (a)         (a)<         (a)         (a)	Northeast	74,550 (39.9)			24,796 (51.5)	23,359 (48.5)		8812 (27.7)	22965 (72.3)	
Mest(2,7)(62,1)Math(2,4)(2,4)(2,4)West7,230 (42.)(3,1/4)23,868 (51.0)2,936 (49.0)(7,1/9)3,2619 (7,3.5)(7,1/9)	Midwest	96,818 (39.3)			26,625 (50.7)	25,882 (49.3)			30294 (73.8)	
Meric19,240(12)19,12429,868(5.0)29,296 (4.0)17,7929,219 (3.5)29,173	South	-	263,510		50,291 (49.6)	51,149 (50.4)		17,498	55003 (75.9)	
Index or intermediate interm										
Setting of index pain encounter, n             0.001 <sup>2</sup> 0.002 <sup>2</sup> 0.001 <sup>2</sup> 0.002 <sup>2</sup> 0.002 <sup>2</sup> 0.001 <sup>2</sup> 0	West	72,340 (41.2)			23,868 (51.0)	22,936 (49.0)			32619 (73.5)	
(%) <td>Unknown</td> <td>7650 (37.5)</td> <td>12,764 (62.5)</td> <td></td> <td>2343 (47.8)</td> <td>2555 (52.2)</td> <td></td> <td>889 (23.0)</td> <td>2970 (77.0)</td> <td></td>	Unknown	7650 (37.5)	12,764 (62.5)		2343 (47.8)	2555 (52.2)		889 (23.0)	2970 (77.0)	
interm         (39, 1)         (60, 9)         (50, 4)         (49, 6)         (25, 7)         (74, 3)           Psych diagnosis in prior year, n         (39, 1)         1366 (43, 9)         1114 (51, 3)         1104 (48, 7)         255 (21, 7)         920 (78, 3)           (40)         575, 642         542, 737         114, 559         104,483         43,103         113,678           (40, 9)         (59, 1)         (52, 3)         (47, 7)         (27, 5)         (72, 5)         (72, 5)           No         375,642         593,274         123,143         116,496         (27, 5)         130,360           Mod disorder          (40, 1)         (59, 9)         (51, 4)         (48, 6)         (26, 6)         13,491 (84, 7)           Yes         04,481         (23, 2)         4780 (33, 8)         9385 (66, 3)         2432 (15, 3)         13,491 (84, 7)           Traum and stressor-related				<0.001 <sup>c</sup>			0.38 <sup>c</sup>			0.002 <sup>c</sup>
Indefinit283 (5.0)186 (43.9)1164 (51.3)1104 (48.7)25 (21.7)92 (78.3)Pyretiagnosis </td <td>Outpatient</td> <td>409,798</td> <td>639,267</td> <td></td> <td>126,759</td> <td>124,777</td> <td></td> <td>49,427</td> <td>142,931</td> <td></td>	Outpatient	409,798	639,267		126,759	124,777		49,427	142,931	
Psych diagnosis in prior year, n (%)         (0.001 <sup>c</sup> Trauma and stressor-related         (30.44,81 (23.2)         (37.45,91 (7.6,8)         (37.46,10 (3.9,8)         (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431 (3.2,13,34) (38.431		(39.1)	(60.9)		(50.4)	(49.6)		(25.7)	(74.3)	
(%) $< 0.001^{\circ}$	Inpatient	2381 (56.1)	1866 (43.9)		1164 (51.3)	1104 (48.7)		255 (21.7)	920 (78.3)	
Any psychiatric diagnosis<<<<<< </td <td>Psych diagnosis in prior year, n</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	Psych diagnosis in prior year, n									
No         375,642         542,737         114,559         104,483         43,103         113,678           (40.9)         (59.1)         (52.3)         (47.7)         (27.5)         (72.5)         (72.5)           Mood disorder         <0.001°	(%)									
	Any psychiatric diagnosis			<0.001 <sup>c</sup>			<0.001 <sup>c</sup>			< 0.001 <sup>c</sup>
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	No	375,642	542,737		114,559	104,483		43,103	113,678	
Mood disorder $< 0.001^c$ $< 0.00$		(40.9)	(59.1)		(52.3)	(47.7)		(27.5)	(72.5)	
No397,698593,274123,143116,49647,250130,36014(40.1)(59,9)(51,4)(48,6)(26,0)(3,4)(7,3)(7,3)Trauma and stressor-related(40,1)(47,859 (76,8)9385 (66,3)9385 (66,3)2432 (15,3)13,491 (84,7)(3,0001)disorder(30,40)(22,6001)(22,6001)(21,51)84,571(3,64)(3,64)(42,2)(26,0)(7,4)No(39,4)(60,6)(50,8)(49,2)(26,0)(7,4)(3,60)(4,0)(4,0)(3,60)(4,0)Ankety/OC/psychogenic disorder(39,4)(60,0)(50,3)(48,7)(26,0)(25,52)(3,6)(4,0)No393,326589,128119,701113,457(26,0)(21,51)(3,6)(4,0)(3,6)(4,0)Personality disorder(40,0)(60,0)(51,3)(48,7)(20,6)(3,2)(4,0)(4	Yes	36,537 (27.1)	98,396 (72.9)		13,364 (38.4)	21,398 (61.6)		6579 (17.9)	30,173 (82.1)	
	Mood disorder			< 0.001 <sup>°</sup>			<0.001 <sup>c</sup>			< 0.001 <sup>c</sup>
Yes       14,481 (23.2)       47,859 (76.8)       4780 (33.8)       9385 (66.3)       2432 (15.3)       13,491 (84.7)         Trauma and stessor-related disorder   <	No	397,698	593,274		123,143	116,496		47,250	130,360	
Trauma and stressor-related       < 0.001°		(40.1)			(51.4)	(48.6)		(26.6)	(73.4)	
	Yes	14,481 (23.2)	47,859 (76.8)		4780 (33.8)	9385 (66.3)		2432 (15.3)	13,491 (84.7)	
(39.4)       (60.6)       (50.8)       (49.2)       (26.0)       (74.0)         Yes       7287 (28.3)       18,453 (71.7)       2454 (36.0)       4362 (64.0)       1111 (17.0)       5420 (83.0)         Anxiety/OCD/psychogenic disorder <t< td=""><td></td><td></td><td></td><td>&lt;0.001<sup>c</sup></td><td></td><td></td><td>&lt;0.001<sup>c</sup></td><td></td><td></td><td>&lt;0.001<sup>c</sup></td></t<>				<0.001 <sup>c</sup>			<0.001 <sup>c</sup>			<0.001 <sup>c</sup>
Yes7287 (28.3)18,453 (71.7)2454 (36.0)4362 (64.0)1111 (17.0)5420 (83.0)Anxiety/OCD/psychogenic disorder $< < < < < < < < < < < < < < < < < < < $	No	404,892	622,680		125,469	121,519		48,571	138,431	
Anxiety/OCD/psychogenic       <0.001°		(39.4)	(60.6)		(50.8)	(49.2)		(26.0)	(74.0)	
disorder       No       392,326       589,128       119,701       113,457       45,540       125,552         (40.0)       (60.0)       (51.3)       (48.7)       (26.6)       (73.4)         Yes       19,853 (27.6)       52,005 (72.4)       8222 (39.8)       12,424 (60.2)       4142 (18.5)       18,299 (81.5)         Personality disorder           0.007 <sup>e</sup> No       411,823       640,278       127,792       125,705       49,620       143,524            Yes       356 (29.4)       855 (70.6)       131 (42.7)       176 (57.3)       62 (15.9)       327 (84.1)          Substance use disorder <t< td=""><td>Yes</td><td>7287 (28.3)</td><td>18,453 (71.7)</td><td></td><td>2454 (36.0)</td><td>4362 (64.0)</td><td></td><td>1111 (17.0)</td><td>5420 (83.0)</td><td></td></t<>	Yes	7287 (28.3)	18,453 (71.7)		2454 (36.0)	4362 (64.0)		1111 (17.0)	5420 (83.0)	
No392,326589,128119,701113,45745,540125,552 $(40.0)$ $(60.0)$ $(51.3)$ $(48.7)$ $(26.6)$ $(73.4)$ Yes $19,853$ (27.6) $52,005$ (72.4) $8222$ (39.8) $12,424$ (60.2) $4142$ (18.5) $18,299$ (81.5)Personality disorder $--0.00^{76}---$				<0.001 <sup>c</sup>			< 0.001 <sup>c</sup>			< 0.001 <sup>c</sup>
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		202 226	E00 100		110 701	112 457		45 540	105 550	
Yes19,853 (27.6)52,005 (72.4)8222 (39.8)12,424 (60.2)4142 (18.5)18,299 (81.5)Personality disorder $< < < < < < < < < < < < < < < < < < < $	NO	-			-	,				
Personality disorder       <0.001 <sup>c</sup> 0.007 <sup>c</sup> <0.001 <sup>c</sup> No       411,823       640,278       127,792       125,705       49,620       143,524         (39.1)       (60.9)       (50.4)       (49.6)       (25.7)       (74.3)         Yes       356 (29.4)       855 (70.6)       131 (42.7)       176 (57.3)       62 (15.9)       327 (84.1)         Substance use disorder           <0.001 <sup>c</sup> <0.001 <sup>c</sup> <0.001 <sup>c</sup> No       410,400       639,996       127,460       125,653       49,477       143,532       <0.001 <sup>c</sup> No       410,400       639,996       (50.4)       (49.6)       (25.6)       (74.4)         Yes       (39.1)       (60.9)       (50.4)       (49.6)       (25.6)       (74.4)         Yes       179 (61.0)       1137 (39.0)       463 (67.0)       228 (33.0)       205 (39.1)       319 (60.9)         Surgical procedure in prior year         <0.001 <sup>c</sup> <0.001 <sup>c</sup> <0.001 <sup>c</sup> <0.001 <sup>c</sup> No       377,036       558,634       114,248       108,386       45,891       128,319         (40.3)       (59.7)       (51.3) <t< td=""><td>Vec</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>	Vec									
No411,823640,278127,792125,70549,620143,524 $(39.1)$ $(60.9)$ $(50.4)$ $(49.6)$ $(25.7)$ $(74.3)$ Yes $356$ (29.4) $855$ (70.6) $131$ (42.7) $176$ (57.3) $62$ (15.9) $327$ (84.1)Substance use disorder $< 0.001^{\circ}$ $< 0.001^{\circ}$ $< 0.001^{\circ}$ $< 0.001^{\circ}$ $< 0.001^{\circ}$ No410,400 $639,996$ $127,460$ $125,653$ $49,477$ $143,532$ $< 0.001^{\circ}$ Yes(39.1) $(60.9)$ $(50.4)$ $(49.6)$ $(25.6)$ $(74.4)$ Yes179 (61.0) $1137$ (39.0) $463$ (67.0) $228$ (33.0) $205$ (39.1) $319$ (60.9)Surgical procedure in prior year $< 0.001^{\circ}$ $< 0.001^{\circ}$ $< 0.001^{\circ}$ $< 0.001^{\circ}$ No $377,036$ $558,634$ $114,248$ $108,386$ $45,891$ $128,319$ $(40.3)$ $(59.7)$ $(51.3)$ $(48.7)$ $(26.3)$ $(73.7)$		19,853 (27.6)	52,005 (72.4)	<0.001 <sup>C</sup>	0222 (39.8)	12,424 (00.2)	0.0070	4142 (18.5)	18,299 (81.5)	<0.001 <sup>C</sup>
		411 000	640 279	<0.001	107 700	105 705	0.007	40.620	142 524	<0.001
Yes       356 (29.4)       855 (70.6)       131 (42.7)       176 (57.3)       62 (15.9)       327 (84.1)         Substance use disorder       <0.001°	100									
Substance use disorder         <0.001 <sup>c</sup> <td>Ves</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	Ves									
No         410,400         639,996         127,460         125,653         49,477         143,532           (39.1)         (60.9)         (50.4)         (49.6)         (25.6)         (74.4)           Yes         1779 (61.0)         1137 (39.0)         463 (67.0)         228 (33.0)         205 (39.1)         319 (60.9)           Surgical procedure in prior year                      319 (60.9) <t< td=""><td></td><td>550 (29.4)</td><td>000 (70.0)</td><td>&lt;0.001°</td><td>131 (42.7)</td><td>170 (37.3)</td><td>&lt;0.001°</td><td>02 (13.9)</td><td>32/ (04.1)</td><td>&lt;0.001°</td></t<>		550 (29.4)	000 (70.0)	<0.001°	131 (42.7)	170 (37.3)	<0.001°	02 (13.9)	32/ (04.1)	<0.001°
(39.1)         (60.9)         (50.4)         (49.6)         (25.6)         (74.4)           Yes         1779 (61.0)         1137 (39.0)         463 (67.0)         228 (33.0)         205 (39.1)         319 (60.9)           Surgical procedure in prior year <t< td=""><td></td><td>410 400</td><td>630 006</td><td>0.001</td><td>127 460</td><td>125 653</td><td>0.001</td><td>49 477</td><td>143 522</td><td>0.001</td></t<>		410 400	630 006	0.001	127 460	125 653	0.001	49 477	143 522	0.001
Yes         1779 (61.0)         1137 (39.0)         463 (67.0)         228 (33.0)         205 (39.1)         319 (60.9)           Surgical procedure in prior year <th< td=""><td>110</td><td>-</td><td></td><td></td><td>-</td><td></td><td></td><td></td><td>-</td><td></td></th<>	110	-			-				-	
Surgical procedure in prior year         <0.001 <sup>c</sup> <0	Vec									
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(40.3) (59.7) (51.3) (48.7) (26.3) (73.7)	• • • •	377 026	558 624	<0.001	114 249	108 384	<0.001	45 801	128 210	<0.001
	110									
Yes 35,143 (29.9) 82,499 (70.1) 13,675 (43.9) 17,495 (56.1) 3791 (19.6) 15,532 (80.4)	Ves									

<sup>a</sup> Two-sample *t*-test.

<sup>b</sup> Wilcoxon-Mann-Whitney test.

<sup>c</sup> Chi-square Test.

[16–20]. Patients with chronic pain syndromes are also more likely to have higher levels of depression and somatization [21-23].

Even when surgical consultation for acute or chronic pain reveals no discernible organic etiology of pain, patients often continue to seek care from surgeons for their symptoms, simply because there are no other physicians who feel qualified to manage the problem. The surgeon, who is the specialist of a particular anatomic site, thus bears the responsibility of offering non-operative treatment or referral to other appropriate specialists if available. Finding an effective treatment strategy may be hindered by the highly specialized nature of modern medicine, where a holistic approach to addressing pain in a discrete area may be necessary but overlooked.

To this end, we aimed to fill a critical gap in the understanding of patients with pain syndromes that overlap with surgical indications. We chose three discrete anatomic sites associated with pain syndromes for which patients often seek surgical consultation—foot/ankle, anorectal,

#### Table 2

Long-term opioid use by patient demographics and clinical characteristics.

	Foot/Ankle Pain		Anorectal pain		TMJ	
Characteristics	Long-term Opioids %	P <sup>a</sup>	Long-term Opioids %	P <sup>a</sup>	Long-term Opioids %	P <sup>a</sup>
Sex		0.010		0.026		< 0.001
Female	2.93		1.90		2.60	
Male	3.02		1.78		2.23	
Age category		< 0.001		< 0.001		< 0.001
18-29	0.77		0.58		0.86	
30-39	2.04		1.18		2.20	
40-49	3.01		1.97		2.82	
50-64	3.76		2.77		3.32	
Region		< 0.001		< 0.001		< 0.001
Northeast	1.98		1.21		1.56	
Midwest	3.06		1.86		2.33	
South	3.31		2.08		2.89	
West	3.13		1.99		2.73	
Unknown	2.31		1.49		2.41	
Setting of index pain encounter		< 0.001		< 0.001		< 0.001
Outpatient	2.94		1.77		2.47	
Inpatient	11.04		9.52		8.60	
Psych diagnosis in prior year						
Any psychiatric diagnosis		< 0.001		< 0.001		< 0.001
No	2.53		1.51		1.99	
Yes	5.98		3.95		4.71	
Mood disorder		< 0.001		< 0.001		< 0.001
No	2.72		1.66		2.22	
Yes	6.87		4.89		5.68	
Trauma and stressor-related disorder		< 0.001		< 0.001		< 0.001
No	2.94		1.80		2.46	
Yes	3.95		3.20		3.86	
Anxiety/OCD/psychogenic disorder		< 0.001		< 0.001		< 0.001
No	2.71		1.64		2.23	
Yes	6.48		4.06		4.66	
Personality disorder		< 0.001		0.002		< 0.001
No	2.96		1.84		2.50	
Yes	5.86		4.23		8.23	
Substance use disorder		< 0.001		< 0.001		< 0.001
No	2.96		1.83		2.49	
Yes	7.41		5.64		8.02	
Surgical procedure in prior year		< 0.001		< 0.001		< 0.001
No	2.68		1.53		2.24	
Yes	5.23		4.05		4.91	

<sup>a</sup> Chi-square test.

and temporomandibular joint. Assessing the three different pain syndromes in one analysis allowed us to elucidate commonalities and differences associated with the risk of long-term opioid treatment. For each pain condition, we sought to determine how opioid treatment differs by sex, age, geographic region, psychiatric diagnoses, and recent surgery. Our hypotheses were that patients across the three different anatomic sites of pain would have similar risk factors for long-term opioid therapy, and that women would have higher risk for long-term opioid therapy due to a higher risk for certain psychiatric illnesses such as depression, anxiety, and somatization disorders.

#### 2. Methods

#### 2.1. Study inclusion

This retrospective cohort study was determined to be exempt from review by the institutional review board due to the deidentified nature of the data. The IBM® MarketScan® Research Database was queried for adult patients aged 18–64 with an inpatient or outpatient encounter for at least one of three chronic pain conditions from January 2007 to September 2015: 1) temporomandibular joint (TMJ) pain (International Classification of Diseases, Ninth Revision, ICD-9: 524.60, 524.61, 524.62, 524.63, 524.64, 524.69), 2) anorectal pain (ICD-9: 569.42, 564.6, 565.0), or 3) foot/ankle pain (ICD-9: 719.47). We ended the study period before implementation of International Classification of Diseases, Tenth Revision to maintain diagnosis consistency using ICD-9 codes. The index pain encounter was defined as the first encounter for the pain condition. This study has been registered in ClinicalTrials.gov (NCT04928131, https://clinicaltrials.gov/ct2/show/NCT04928131?ter m=NCT04928131&draw=2&rank=1).

#### 2.2. Outcome measures

The primary outcome, long-term opioid therapy (LTOT), was defined as receipt of >90 days' opioid supply within 6 months after the index pain encounter, with no supply gaps over a month (>31 days) [6]. Patients were excluded from the study if they met any of the following criteria: 1) enrollment in the database for <1 year prior or <1 year after the IPE, 2) traumatic injury in the year prior to the IPE, 3) operation  $\leq$  30 days prior to the IPE. For the analysis of the secondary outcome of new LTOT, patients were excluded if they received LTOT in the year prior to the index pain encounter. Independent variables for both outcome models included sex, age, index pain encounter setting (outpatient vs. inpatient), US Census region (Midwest, Northeast, South, West, Unknown), a surgical procedure occurring in the previous year, and encounters for psychiatric diagnoses in the previous year. Psychiatric diagnoses were identified by ICD-9 diagnosis codes (Supplement Table 1) and included: bipolar I and II, major depression, dysthymia, adjustment disorder, post-traumatic stress disorder, anxiety, obsessive compulsive disorder, personality disorders, and alcohol and drug use

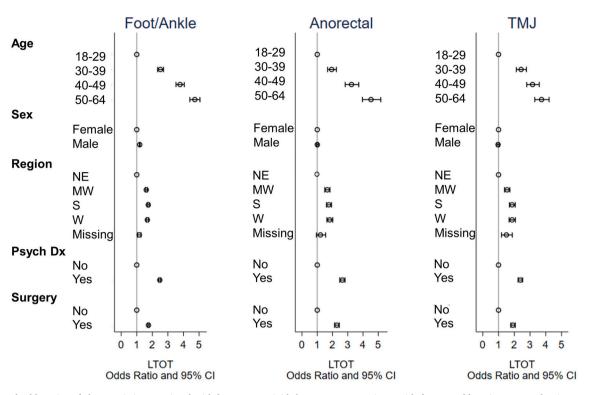


Fig. 1. Adjusted odds ratios of characteristics associated with long-term opioid therapy among patients with foot or ankle pain, anorectal pain, or temporomandibular joint pain.

#### disorders.

#### 2.3. Statistical analysis

Unadjusted analyses were performed to assess associations between patient characteristics and opioid use with chi-square tests for categorical variables, two independent sample t-tests for normally distributed continuous variables and Wilcoxon-Mann-Whitney test for nonparametric continuous variables. Frequency counts and percentages are reported for categorical variables, means (SD) and median (IQR) are presented for continuous variables. In multivariable analysis, we calculated logistic regression models to examine the independent effects of selected patient factors on LTOT and new LTOT. Multivariable models were calculated for the overall cohort (all pain conditions) as well as stratified models by pain condition. We report adjusted odds ratios (aOR), 95% confidence intervals (CI) and p-values. Statistical significance was assessed at the level of p < 0.05. All analyses were performed using SAS 9.4 (Cary, NC). This work has been reported in line with the STROCSS criteria [24].

#### 3. Results

The cohort included 1,500,392 patients who had at least one inpatient or outpatient visit for the indication of foot/ankle, anorectal, and TMJ pain. The majority of the cohort were women (61%). Almost all index pain encounters were outpatient visits (99.5%). A healthcare visit for the primary indication of a psychiatric diagnosis within the previous year was observed for 14% of this cohort; women were more likely to have had such a visit compared to men (16.5% vs. 9.6%, p < 0.001). Women were also more likely to have undergone a surgical procedure within the previous year (12.7% vs. 8.9%, p < 0.001).

Characteristics of each pain cohort were detailed in Table 1. Women comprised nearly three-quarters (74%) of the TMJ group and more than half (61%) of the foot/ankle pain group, while the anorectal pain group was evenly split between women and men. Across all three pain

conditions women were more likely to have encounters for psychiatric diagnoses and surgical procedures occurring in the year preceding the index pain encounter (all p < 0.001).

#### 3.1. Sex differences in long-term opioid therapy

A small proportion of the overall cohort received LTOT (2.7%). When stratified by pain condition, women with TMJ and anorectal pain were more likely to receive LTOT than men, with small but statistically significant sex differences (for TMJ, 2.60% women vs. 2.23% men, p < 0.001; for anorectal, 1.90% women vs. 1.78% men, p = 0.026). Men with foot/ankle pain were more likely to receive LTOT than women (2.93% women vs. 3.02% men, p = 0.010, Table 2).

In multivariable analysis of the overall cohort, after controlling for other factors in the model, men had 14% higher odds of receiving LTOT than women (aOR 1.14, 95%CI 1.12–1.16, p < 0.001). Stratified multivariable models revealed a significantly higher odds of LTOT for men with foot/ankle pain (aOR 1.19, 95% CI 1.16–1.22, p < 0.001), but no significant sex differences in LTOT for patients with anorectal pain (aOR 1.004, 95% CI 0.95–1.07, p = 0.88) or TMJ pain (aOR 0.97, 95% CI 0.90–1.04, p = 0.37) (Fig. 1).

## 3.2. Other factors associated with long-term opioid therapy across pain conditions

Stratified analyses by pain condition subgroups indicated similar associations between LTOT and age, geographic region, encounters for psychiatric disorder in the preceding year, and surgery in the preceding year (Table 2). Older patients and those residing in the South and West were more likely to receive LTOT in all three pain condition subgroups. Patients seen for a psychiatric disorder and those who underwent a surgical procedure in the preceding year had more than twice the odds of receiving LTOT. In multivariable analyses of the overall cohort, older age, Southern region, psychiatric diagnosis and surgical procedure in the preceding year were associated with higher odds of LTOT (Table 3).

#### Table 3

Multivariable logistic regression model results for long-term opioid therapy (LTOT) and new long-term opioid therapy.

Covariates	LTOT (N $=$ 1,	500,392)	New LTOT (N = 1,475,466)		
	aOR (95% CI)	P-value	aOR (95% CI)	P-value	
Age		< 0.001		< 0.001	
18–29	Ref	< 0.001	ref	< 0.001	
30–39	2.39 (2.25,	< 0.001	1.69 (1.50,	< 0.001	
40-49	2.54) 3.56 (3.37, 3.76)	<0.001	1.90) 2.22 (1.99, 2.48)	< 0.001	
50–64	4.47 (4.24, 4.72)	<0.001	2.40 (2.16, 2.67)	< 0.001	
Sex	-				
Female	Ref		ref		
Male	1.14 (1.12, 1.16)	< 0.001	1.30 (1.23, 1.36)	< 0.001	
Region	1.10)	< 0.001	1.00)	< 0.001	
Northeast	Ref	<0.001	ref	0.001	
Midwest	1.61 (1.55,	< 0.001	1.63 (1.50	< 0.001	
South	1.66) 1.76 (1.70, 1.81)	< 0.001	1.78) 1.83 (1.69, 1.99)	< 0.001	
West	1.72 (1.66, 1.78)	< 0.001	1.64 (1.50, 1.80)	< 0.001	
Unknown	1.21 (1.11, 1.31)	< 0.001	1.74 (1.45, 2.09)	< 0.001	
Pain conditions		< 0.001		< 0.001	
Anorectal pain	ref		ref		
TMJ	1.35 (1.30, 1.41)	< 0.001	1.24 (1.12, 1.37)	< 0.001	
Foot/Ankle Pain	1.53 (1.48, 1.58)	< 0.001	1.43 (1.32, 1.54)	< 0.001	
Multiple pain conditions	1.27 (0.56, 2.87)	0.56	1.23 (0.17, 8.82)	0.83	
Any psychiatric diagnosis <sup>a</sup>	,		,		
No	ref		ref		
Yes	2.49 (2.43, 2.54)	<0.001	2.23 (2.10, 2.36)	< 0.001	
Surgical procedure in previous year	ŕ		÷		
No	ref		ref		
Yes	1.83 (1.78, 1.87)	< 0.001	1.75 (1.64, 1.87)	< 0.001	

aOR: Adjusted Odds Ratio.

<sup>a</sup> Psychiatric diagnoses were based on encounter diagnosis codes within 1 year prior to index pain visit.

Stratified multivariable models indicated similar results as the overall model: older age, region of residence, and recent history of a surgical procedure and recent psychiatric diagnosis were associated with higher odds of receiving LTOT (Fig. 1).

#### 3.3. New long-term opioid therapy

After excluding 24,926 patients who had received LTOT during the year prior to the index pain encounter, the analysis of new LTOT was performed on a cohort of 1,475,466 opioid-naïve patients. Only 6406 patients (0.43%) received new LTOT, which was similar between women (0.41%) and men (0.47%).

The multivariable regression analysis demonstrated similar patterns of association as the univariate analysis, where men were slightly more likely to be prescribed new LTOT than women after controlling for other covariates. Patients who had encounters with a psychiatric diagnosis or a surgical procedure in the preceding year had significantly higher odds of receiving new LTOT regimen after adjustment for covariates (psychiatric diagnosis: aOR, 2.23, 95% CI 2.10–2.36, p < 0.001; surgical procedure: aOR, 1.75, 95% CI 1.64–1.87, p < 0.001, Table 3). In stratified multivariable analysis, there was a small but significantly higher likelihood for men with foot/ankle pain to receive new LTOT (aOR 1.37,

95% CI 1.29–1.45, p < 0.001). Older age, geographic region, an encounter with psychiatric diagnosis and a surgical procedure in the preceding year were all associated with higher rates of new LTOT (all p < 0.001, Supplemental Table II).

#### 4. Discussion

This study examined the risk factors for long-term opioid use in patients presenting with new diagnoses of foot/ankle, anorectal, and TMJ pain. These diagnoses may have potential surgical treatments, but may also be caused by conditions that cannot be corrected surgically. We found that recent psychiatric diagnoses, recent surgery, residence outside the Northeast region and older age were independently associated with long-term opioid use in all three pain conditions. Contrary to our hypothesis that women would be at greater risk for long-term opioid therapy, our analyses found no sex differences in LTOT for patients with TMJ or anorectal pain, and 16% lower odds of LTOT for women with foot/ankle pain. These risk factors and patterns were reflected in the analysis of new LTOT as well.

Notably, patients seen for psychiatric diagnoses in the preceding year had nearly 2.5 times the odds of requiring LTOT as those without those diagnoses. Mood disorders accountd for over 40% of these psychiatric diagnoses, with anxiety, OCD, and psychogenic disorders accounting for the majority of the remainder. Our findings are supported by studies that have found associations between psychiatric disorders and initiation and use of prescribed opioids [17–19]. TMJ pain has long been associated with depression and somatization disorders, and there is evidence of a high prevalence of anxiety, depression and neuroticism in patients with foot and ankle pain; however this association has not been noted for patients with anorectal pain [21,25,26]. Our analysis on TMJ and foot/ankle pain was consistent with these prior findings, but we also found that 14% of patients with anorectal pain had recent encounters for psychiatric disorders, which has not been previously described.

Consistent with prior epidemiological reports of chronic pain conditions, there was a high proportion of women in our study population [27]. While the majority of patients with TMJ pain (74%) and anorectal pain (61%) were women, the distribution in anorectal pain was even. Across all three pain condition subgroups, the proportion who had a recent psychiatric diagnosis was higher in women, as was the proportion who had a recent operation.

This study has several limitations – mostly due to the inherent characteristics of retrospective analysis and claims data, which preclude the ability to make causal interpretations. Additionally, we were unable to include patients 65 and older since this database was a private insurance claims and thus would not have included full claims information on the older beneficiaries of Medicare.

#### 5. Conclusions

In a health care system that is increasingly specialized and siloed, our findings demonstrate the importance of patient-centered and multidisciplinary approaches to treat highly-specialized pain syndromes. It is important for surgeons to recognize the risks associated with initiation of chronic opioid use in this patient population, as comorbid psychiatric disorders are likely to complicate the management of pain. Further investigation to elucidate connections between psychiatric diagnoses and pain is critical to understand the pathophysiology of these disorders and to develop effective treatment strategies. Understanding the risk factors for LTOT in patients presenting for evaluation of pain symptoms that may or may not be surgically treated will inform treatment decision-making for surgeons and other providers who see these patients.

#### Declaration of competing interest

No conflicts of interest to declare.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102704.

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Women's Health and Sex Differences in Medicine Center at Stanford University School of Medicine. Data for this project were accessed using the Stanford Center for Population Health Sciences Data Core. The PHS Data Core is supported by a National Institutes of Health National Center for Advancing Translational Science Clinical and Translational Science Award (UL1 TR001085) and from Internal Stanford funding

#### Consent

The data source was an insurance claims database, therefore no patient consents were needed nor possible.

#### Ethical approval

Stanford University Institutional Review Board deemed it exempt due to deidentified nature of the data.

#### Author contributions

Cindy Kin: conception and design of the study, acquisition, analysis, and interpretation of data, drafting and revising.

Loretta Chou: interpretation of data and critical revisions.

Debra Safer: interpretation of data and critical revisions.

Arden Morris: interpretation of data and critical revisions.

Qian Ding: analysis and interpretation of data and critical revisions. Amber Trickey: design of study, acquisition, analysis and interpretation of data and critical revisions.

Sabine Girod: conception and design of the study, acquisition and interpretation of data, and critical revision.

#### Trial registry number

- 1. Name of the registry: clinicaltrials.gov
- 2. Unique Identifying number or registration ID: NCT04928131
- Hyperlink to your specific registration (must be publicly accessible and will be checked): https://clinicaltrials.gov/ct2/show/NC T04928131?term=NCT04928131&draw=2&rank=1

#### Guarantor

Cindy Kin, Loretta Chou, Debra Safer, Arden Morris, Amber Trickey, Qian Ding, and Sabine Girod all accept full responsibility fo the work and the conduct of the study, had access to the data, and controlled the decision to publish.

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