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Chronic Pain Among Patients With an Opioid Use Disorder

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Background and Objectives: Chronic pain is not well understood in opioid-dependent populations. We report the prevalence of chronic pain and pain characteristics in an opioid-dependent population by treatment type and gender.
Methods: This cross-sectional study opportunistically recruited 569 patients (32% women) receiving treatment for opioid use disorder (DSM-5) in Norway during 2016-2018 (83% received opioid maintenance treatment, 17% received treatment without medication). We asked about chronic pain (≥3 months; ICD-11), pain severity (NRS-11), and other pain characteristics.
Results: Overall, 55% reported chronic pain (≥3 months), with a higher prevalence among women (61% vs 52%, $P = .041$) and patients receiving methadone (66%) compared with buprenorphine or no medication (46% and 45%, $P < .001$). Chronic pain was associated with higher age ($P < .001$) and higher doses of methadone ($P = .048$). The average duration of pain was 11 years. The most frequently reported pain locations were the lower extremities (59%) and the back (54%), and 69% reported more than one pain location. Constant pain and migrating pain were significantly associated with both moderate (adjusted odds ratio [aOR]: 2.04, confidence interval [CI]: 1.12-3.74 and aOR: 2.44, CI: 1.09-5.43) and severe pain intensity (aOR: 2.08, CI: 1.14-3.80 and aOR: 2.46, CI: 1.10-5.47). Reporting no effect of analgesics was associated with severe pain intensity (aOR: 0.54, CI: 0.29-0.99).
Conclusions and Scientific Significance: Over half reported chronic pain, and rates were highest among women and patients receiving methadone. New contributions to the field are descriptions of pain characteristics by gender and pain severity, and interactions between medication type and age. (© 2021 The Authors. *The American Journal on Addictions* published by Wiley Periodicals LLC on behalf of The American Academy of Addiction Psychiatry). (Am J Addict 2021;00:00–00)

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INTRODUCTION

A high prevalence of chronic pain, ranging from 36% to 57%, has been seen in opioid-dependent populations. This includes populations not in treatment,[1] seeking treatment,[2] and in opioid maintenance treatment (OMT) with methadone[3-6] or buprenorphine.[5,7] Although there are variations in the reported prevalence rates across these studies, almost all are higher than the overall 19% prevalence of chronic pain found in the general populations of 15 European countries,[8] and the 11% to 31% prevalence in the general population of the United States.[9,10]

Opioid use can result in increased sensitivity toward pain (hyperalgesia)[11] and may contribute to aggregating and increasing pain over time,[12] which again could maintain and escalate opioid use. Discontinuing opioid use may not necessarily lead to increased levels of pain; for instance, chronic pain patients treated with high doses of opioids have experienced a reduction in pain levels after detoxification from opioids.[13] Similarly, opioid-dependent patients reported no increase in pain levels when treated with the opioid receptor antagonist naltrexone that blocks the effects of opioids.[14] The many interactions between chronic pain, opioid dependence, and opioid therapy for pain can make chronic pain conditions particularly difficult to treat among opioid-dependent patients.

Adding to the complexity, opioid-dependent patients often present with a range of comorbidities that could cause or influence their perception of pain. Such comorbidities can be related to both physical[4,15] and mental health; the latter includes insomnia,[6] posttraumatic stress,[16] personality disorders,[17] depression,[15,17] and anxiety.[17] Further, the OMT

patient populations are growing older, which may increase the overall prevalence of pain conditions in this patient group.

However, chronic pain etiology and characteristics among opioid-dependent patients have not been well described. Previous research has mainly focused on patients who have received opioid therapy as pain management and subsequently developed a secondary opioid dependence. These studies may not be representative of the demography and etiology of the overall patient group with opioid dependence. In studies that do focus on primarily opioid-dependent populations, the sample sizes have been relatively small. The seven studies where the pain was defined as chronic ranged from $n = 44$ to $n = 390$ (mean $n = 209$),[1-7] and most provided limited information about the pain characteristics beyond the presence of chronic pain. Studies beyond these had no criteria for chronicity; for instance, the one European study we identified reported "any pain."[18] Few of the studies reported chronic pain prevalence by gender and none have reported pain characteristics by gender. As women have a higher risk for chronic pain conditions and there is evidence that women have a higher sensitivity towards pain,[19] gender perspective is important when investigating pain in any population.

Continued research on chronic pain in primarily opioid-dependent patients is warranted as chronic pain has been associated with poorer treatment outcomes, including substance use outcomes[20] and higher levels of craving.[4] Treatment of pain is also important in a social context, as chronic pain can be a barrier for work and social activities,[8] and can lead to further isolation of an already marginalized group.[21] In fact, the level of loneliness has been found to correlate with pain intensity among opioid-dependent patients.[22] Focus on comorbid pain in treatment of opioid dependence can contribute to a better understanding of the etiology and maintenance of the dependence on an individual level and improve treatment quality and outcomes.

The current paper contributes to the field by describing chronic pain among a representative Norwegian sample ($n = 569$) of patients with opioid use disorder. We aimed to (a) estimate the prevalence of chronic pain, both by gender and treatment medication, (b) to describe the characteristics of the reported pain, and (c) to investigate the characteristics of pain for patients experiencing mild, moderate, and severe intensity of chronic pain.

METHODS

Design and Setting

This explorative study had a cross-sectional, multicenter design and included data from all outpatient addiction clinics and detoxification units connected to the two largest hospitals in Norway, Akershus University Hospital and Oslo University Hospital. The hospitals are situated near and in Oslo, respectively, with catchment areas including urban, suburban, and rural areas. The hospitals serve about 1/3 of the substance use patients in Norway, including 2700 patients receiving OMT (2018).[23] All substance use treatment in Norway, including detoxification and outpatient treatment, is provided by specialist health services connected to regional hospitals and at no cost for the patient. Patients apply for treatment through social services or general practitioners, and the threshold for receiving treatment is relatively low.

Participants

The inclusion criterion for participation was opioid use disorder, according to DSM-5. Patients received ongoing OMT (83%) or treatment without OMT medication (17%) in outpatient addiction services or short-term in-patient detoxification. Patients undergoing detoxification could not have clinical symptoms of abstinence at the time of participation.

Procedure

Patients were opportunistically recruited by staff at the treatment centers in the period May 2016 to December 2018 and asked to complete a one-page questionnaire. In the case of no pain, only six questions were filled out. Clinicians assisted patients in filling in the questionnaire to avoid misinterpretations of the questions.

Measures

Chronic pain was defined as pain lasting for a minimum of 3 months,[2,5] in line with the ICD-11 diagnostic criteria for chronic pain. For comparison to previous studies that have defined pain and chronic pain differently, we also reported the wider definition "any pain" in the last 4 weeks,[24] and the more stringent definition of "moderate to severe chronic pain" defined as lasting a minimum of 3 months and severity of at least 5 on the Pain NRS-11.[3,4,16,21]

The research group developed the questionnaire specifically for this study to include clinically relevant questions regarding pain. All participants provided background information on their gender, age, whether they were currently in OMT, type and dose of medication, and years in OMT.

Patients who had experienced pain in the last 4 weeks (yes; no) answered further questions about the characteristics of their pain. This included the first onset of pain (when the pain first manifested, month and year), whether the onset was acute or gradual, cause of the pain (injury/accident; surgery; illness/disease; unknown), the temporality of the pain (constant; intermittent),[8] pain radiation (yes; no), pain migration (yes; no), pain triggers (food intake; movement; stress; exercise; other), and whether pain medications, prescribed or over the counter, had any effect (yes; no).

Up to five different pain locations could be listed. The reported pain locations were categorized into the anatomical areas of the body most frequently used in clinical practice (head; shoulder/neck; upper extremities; chest/abdomen; back upper/lower; lower extremities; entire body).

Current pain intensity was measured using Pain NRS-11,[25] a validated numeric rating scale from 0 to 10, where 0 is anchored with "no pain" and 10 with "worst pain

imaginable." For patients reporting chronic pain, the current pain intensity was categorized as mild (0-4), moderate (5-6), or severe (7-10) according to commonly used cut-offs in similar study populations.[1,4,18]

Statistical Analyses

Independent samples t tests or Pearson's χ^2 tests were used for all comparisons between pain groups, gender and OMT medication groups. As patients receiving methadone on average were 10 years older compared with the other patients, age and OMT medication type were further explored by dividing the sample into tertiles according to age. We estimated odds ratios (ORs) for pain characteristics of the moderate and severe chronic pain groups compared with the mild chronic pain group using univariate multinomial logistic regression analyses. Age, gender, and pain characteristics that were statistically associated with moderate or severe pain in univariate analyses ($P < .05$) were included in an adjusted multinomial regression model, estimating adjusted ORs (aORs). IBM SPSS Statistics 25 was used for all analyses with the threshold for statistical significance set to 5%. The analyses were not preregistered and we did not apply a correction for multiple significance testing as all analyses were explorative.[26]

RESULTS

Participant Characteristics

In total, 572 patients completed the questionnaire. Three patients were excluded from the data set as they stated no opioid dependence, leaving a final sample of 569 participants.

Mean age was 42 years (SD: 10.6, range: 19-65) and 32% were women. The age distribution was similar for both genders (women: mean 41 years, SD: 11.0; men: mean 42 years, SD: 10.4).

OMT was received by 468 (83%) while 98 (17%) did not receive any prescribed medication for their opioid use disorder at the time of the study.

Of those in OMT, 53% ($n = 247$) received methadone (women: 57%, men: 51%) and 47% ($n = 216$) received buprenorphine-based medications (women: 43%, men: 49%). The average time in OMT was 7.4 years (7.9 years for women and 7.2 years for men).

The mean age within the treatment groups was 37 years for the no medication group (median: 36, SD: 11.2), 47 years for the methadone group (median: 48, SD: 8.9), and 38 years for the buprenorphine-based medication group (median: 37, SD: 9.4).

Prevalence of Pain

Chronic pain was reported by 55% of the participants ($n = 306$). When adding a criterion for pain severity, 34% ($n = 193$) reported moderate to severe chronic pain. Any pain, chronic or not, in the last 4 weeks was endorsed by 60% ($n = 340$).

Figure 1a shows that the prevalence of any pain and chronic pain was higher among women compared with men ($\chi^2(1) = 7.6$, $P = .006$ and $\chi^2(1) = 4.2$, $P = .041$, respectively), and the same pattern was seen in all treatment groups for women vs men (no medication: 53% vs 42%, methadone: 68% vs 64%, buprenorphine: 54% vs 43%). Patients with chronic pain were overall older compared with the no chronic pain group (Table 1).

There was a higher prevalence of chronic pain among methadone patients compared with those receiving buprenorphine-based medications or those not receiving any

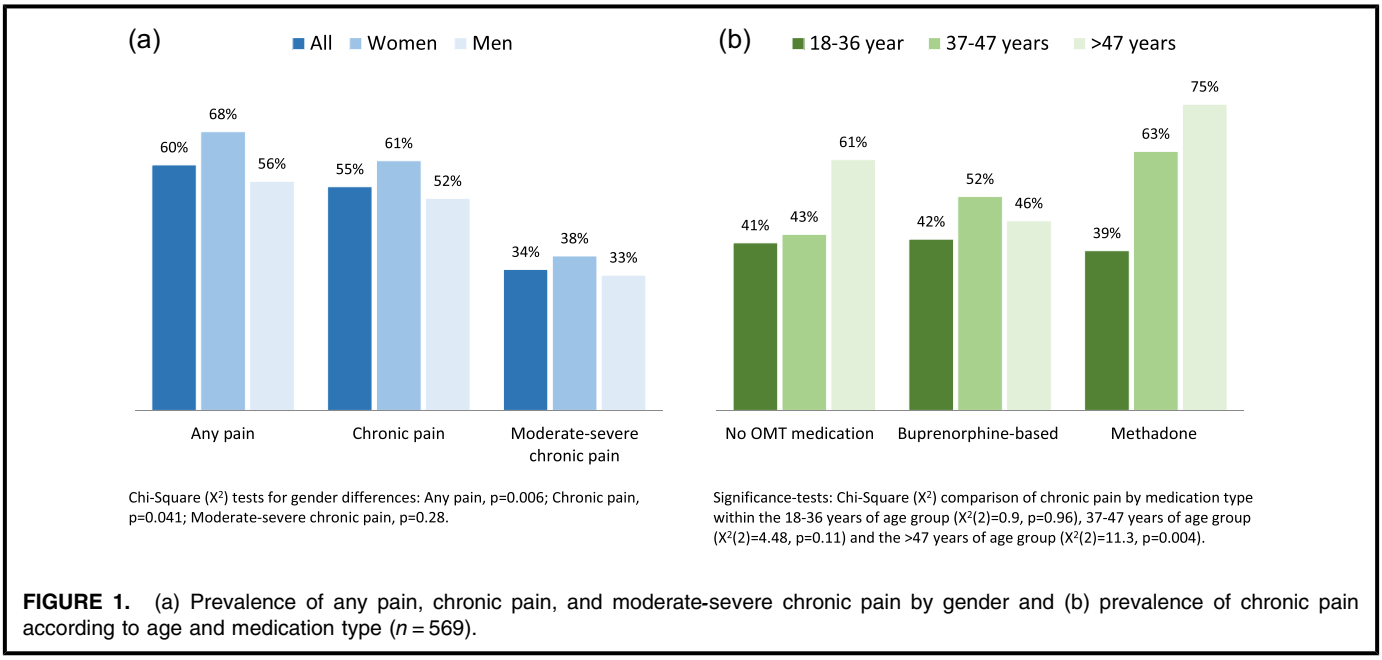

FIGURE 1. (a) Prevalence of any pain, chronic pain, and moderate-severe chronic pain by gender and (b) prevalence of chronic pain according to age and medication type ($n = 569$).

TABLE 1. Age, gender, and OMT status for chronic pain and no chronic pain groups ($n = 569$)

All participants, $n = 569$	No chronic pain, $n = 255$	Chronic pain, $n = 306$	Test-statistic (df)[a]	P values
Age, mean (median, SD)	39.2 (38, 10.6)	44.2 (45, 10.1)	$t(559) = -5.62$	**<.001**
Gender, n (%)				
• Women	71 (39)	110 (61)	$\chi^2(1) = 4.18$	**.041**
• Men	184 (48)	196 (52)		
OMT medication, n (%)				
• None	52 (55)	43 (45)	$\chi^2(2) = 21.89$	**<.001**
• Methadone	84 (34)	161 (66)		
• Buprenorphine-based	115 (54)	98 (46)		
Participants not receiving OMT medication, $n = 95$	No chronic pain, $n = 52$	Chronic pain, $n = 43$		
Age, mean (median, SD)	35.7 (33, 10.5)	39.5 (37, 12.0)	$t(93) = 2.05$	.11
Gender, n (%)				
• Women	14 (47)	16 (53)	$\chi^2(1) = 1.15$	.28
• Men	38 (58)	27 (42)		
Participants receiving methadone, $n = 247$	No chronic pain, $n = 84$	Chronic pain, $n = 161$		
Age, mean (median, SD)	44.5 (44, 10.1)	48.7 (50, 8.0)	$t(139) = -3.31$[b]	**<.001**
Gender, n (%)				
• Women	27 (32)	58 (68)	$\chi^2(1) = 0.37$	.54
• Men	57 (36)	103 (64)		
Years in OMT, mean (median, SD)	9.7 (9, 5.6)	9.9 (10, 5.8)	$t(221) = -0.023$	.82
Dose (mg), mean (median, SD)	89.6 (90, 26.9)	98.5 (90, 35.8)	$t(238) = -1.99$	**.048**
Participants receiving buprenorphine-based medication, $n = 216$	No pain, $n = 115$	Chronic pain, $n = 98$		
Age, mean (median, SD)	37.2 (36, 9.7)	39.1 (38, 8.9)	$t(211) = -1.48$	.14
Gender, n (%)				
• Women	29 (46)	34 (54)	$\chi^2(1) = 2.28$	.13
• Men	86 (57)	64 (43)		
Years in OMT, mean (median, SD)	3.7 (2, 3.7)	5.1 (4, 4.5)	$t(163) = -2.19$[a]	**.030**
Dose (mg), mean (median, SD)	13.3 (14, 6.1)	13.8 (14, 6.3)	$t(201) = -0.56$	.58

Missing data: chronic pain: $n = 8$, medication type: $n = 8$, years in OMT: $n = 57$, medication dose: $n = 15$. Significant P values ($P < .05$) are in bold.
OMT = opioid maintenance treatment.
[a]Independent samples t tests or χ^2 tests.
[b]Equal variances not assumed.

OMT medications (Table 1). Within the patient group that received methadone, those with chronic pain received higher doses of methadone and were significantly older compared with methadone patients without chronic pain (Table 1). When dividing the total sample into tertiles according to age (ages 18-36, 37-47, and >47), the prevalence of chronic pain for those older than 47 years was significantly higher among methadone patients compared with patients receiving buprenorphine-based medications or no medications ($\chi^2(2) = 11.3$, $P = .004$, Fig. 1b).

Characteristics of Chronic Pain

Within the chronic pain group ($n = 306$; Table 2), mild, moderate, and severe pain intensity was reported by about one-third each. The average intensity score within each category was mild: 2.4, moderate: 5.5, and severe: 7.8.

Patients reported that the chronic pain on average had lasted over 10 years and the onset was gradual for 64%. The cause of the pain was injury/accident (37%), disease (29%), surgery (9%), and unknown (38%). Sixty-nine percent reported more than one location for their pain; the most common locations were the lower extremities and the back. The chronic pain was constant for 46% and intermittent for 54%. The pain radiated to other areas of the body for 66%, and migrating pain was reported by 22%. The most-reported triggers for pain were stress (56%) and movement (50%). Sixty-three percent reported that pain medication, prescribed or over the counter, had an effect on their pain.

TABLE 2. Pain characteristics for the chronic pain group by gender ($n = 306$)

	Women ($n = 110$)	Men ($n = 196$)	All ($n = 306$)	Test-statistic (df)	P values
Age, mean (median, SD)	43.8 (45, 10.7)	44.4 (45, 9.8)	44.2 (45, 10.1)	$t(304) = 0.51$	.61
In OMT, n (%)	93 (85)	168 (86)	44.2 (45)	$\chi^2(1) = 0.04$	.84
Pain characteristics					
• Intensity of current pain (NRS-11), n (%)					
∘ Mild (0-4)	41 (38)	69 (36)	110 (36)	$\chi^2(2) = 0.13$	.94
∘ Moderate (5-6)	34 (31)	63 (32)	97 (32)		
∘ Severe (7-10)	34 (31)	62 (32)	96 (32)		
• Years of pain, mean (median, SD)	12.1 (9, 11.3)	10.5 (7, 10.2)	11.1 (8, 10.6)	$t(285) = -1.21$	.23
• Type of onset, n (%)					
∘ Acute	43 (39)	68 (35)	111 (36)	$\chi^2(1) = 0.68$	.41
∘ Gradual	66 (61)	128 (65)	194 (64)		
• Cause of pain, n (%)					
∘ Injury/accident	38 (35)	74 (38)	112 (37)	$\chi^2(1) = 0.31$	.58
∘ Surgery	11 (10)	15 (8)	26 (8.5)	$\chi^2(1) = 0.50$	.48
∘ Disease	32 (29)	57 (29)	89 (29)	$\chi^2(1) = 0.00$	1.00
∘ Unknown	45 (41)	70 (36)	115 (38)	$\chi^2(1) = 0.81$	.37
• Pain location, n (%)					
∘ Head	23 (21)	27 (14)	50 (16)	$\chi^2(1) = 2.74$	.10
∘ Neck/shoulders	36 (33)	40 (20)	76 (25)	$\chi^2(1) = 5.96$	**.015**
∘ Upper extremities	17 (16)	41 (21)	58 (19)	$\chi^2(1) = 1.29$	.26
∘ Chest/Abdomen	22 (20)	39 (20)	61 (20)	$\chi^2(1) = 0.00$	.95
∘ Back (upper/lower)	64 (59)	101 (52)	165 (54)	$\chi^2(1) = 1.46$	.23
∘ Lower extremities	55 (50)	126 (64)	181 (59)	$\chi^2(1) = 5.55$	**.018**
∘ Entire body	18 (17)	32 (16)	50 (16)	$\chi^2(1) = 0.00$	.97
• No. of pain locations, mean (median, SD)	2.2 (2, 1.0)	2.1 (2, 1.0)	2.1 (2, 1.0)	$t(303) = -0.71$	.48
• Pain persistence, n (%)					
∘ Intermittent	66 (60)	100 (51)	166 (54)	$\chi^2(1) = 2.15$	.14
∘ Constant	44 (40)	95 (49)	139 (46)		
• Pain radiates, n (%)	79 (72)	121 (62)	200 (66)	$\chi^2(1) = 2.97$	.09
• Pain migrates, n (%)	24 (22)	43 (22)	67 (22)	$\chi^2(1) = 0.00$	.93
• Pain triggers, n (%)					
∘ Food intake	14 (13)	19 (10)	33 (11)	$\chi^2(1) = 0.67$	.41
∘ Movement	54 (49)	100 (51)	154 (50)	$\chi^2(1) = 0.10$	.75
∘ Stress	67 (61)	104 (53)	171 (56)	$\chi^2(1) = 1.76$	.18
∘ Exercise	15 (14)	35 (18)	50 (16)	$\chi^2(1) = 0.92$	.34
∘ Other triggers	40 (37)	73 (37)	113 (37)	$\chi^2(1) = 0.02$	.88
• Pain medication has effect, n (%)	73 (67)	112 (60)	185 (63)	$\chi^2(1) = 1.34$	.25

χ^2 tests or independent samples t tests. Missing data: in OMT: $n = 2$; intensity of current pain: $n = 3$, years of pain: $n = 19$; onset of pain: $n = 1$; pain location: $n = 1$; pain medication effect: $n = 11$. Significant P values ($P < .05$) are in bold.

OMT = opioid maintenance treatment.

There were some differences in pain characteristics between women and men (Table 2). The most frequently reported location of pain for men was the lower extremities (64%), while back pain was most prevalent for women (59%). Pain in the neck/shoulder area was significantly more frequent among women (30% vs 20% for men). There were significant differences in the characteristics of pain for those with mild, moderate, and severe chronic pain (Table 3). In univariate multinomial comparisons, the moderate and severe pain groups had a higher prevalence of constant pain and migrating pain compared with the mild pain group. The severe pain group had a higher number of pain locations and was less likely to report that pain medication had an effect on their pain, compared with the mild pain group. The moderate pain group was more likely to experience stress and exercise as triggers for their pain, compared with the mild pain group.

When the significant variables from the univariate comparisons were included in an adjusted multinomial model (Table 3), constant and migrating pain were significantly associated with moderate and severe pain.

TABLE 3. Characteristics of pain among opioid-dependent patients with mild, moderate, and severe chronic pain intensity

				Moderate vs mild		Severe vs mild	
	Mild ($n = 110$)	Moderate ($n = 97$)	Severe ($n = 96$)	OR (CI)	aOR (CI)[a]	OR (CI)	aOR (CI)[a]
Age, mean (median, SD)	43.2 (42, 9.5)	44.0 (46, 9.8)	45.1 (47, 11.0)	1.01 (0.98-1.04)	1.01 (0.98-1.04)	1.02 (0.99-1.05)	1.02 (0.99-1.05)
Women	41 (37)	34 (35)	34 (35)	0.91 (0.51-1.60)	0.98 (0.53-1.80)	0.92 (0.52-1.63)	0.99 (0.54-1.82)
In OMT	91 (83.5)	88 (91)	80 (84)	1.93 (0.82-4.53)		1.05 (0.50-2.23)	
Pain characteristics							
• Years of pain, mean (median, SD)	10.5 (6.5, 10.6)	10.6 (7.8, 10.3)	12.0 (9.0, 10.9)	1.00 (0.97-1.03)		1.01 (0.99-1.04)	
• Type of onset, *n* (%)							
◦ Acute	43 (39)	35 (36)	33 (34)	1.12 (0.64-1.97)		1.23 (0.69-2.16)	
◦ Gradual	67 (61)	61 (64)	63 (66)				
• Cause of pain, *n* (%)							
◦ Injury/accident	41 (37)	34 (35)	37 (39)	0.91 (0.51-1.60)		1.06 (0.60-1.86)	
◦ Surgery	6 (5)	11 (11)	9 (9)	2.22 (0.79-6.24)		1.79 (0.61-5.24)	
◦ Disease	29 (26)	23 (24)	35 (36)	0.87 (0.46-1.63)		1.60 (0.88-2.90)	
◦ Unknown	42 (38)	41 (42)	31 (32)	1.19 (0.68-2.07)		0.77 (0.43-1.37)	
• Pain location, *n* (%)							
◦ Head	19 (17)	16 (17)	14 (15)	0.96 (0.46-1.99)		0.82 (0.39-1.73)	
◦ Neck/shoulders	23 (21)	24 (25)	28 (29)	1.26 (0.66-2.42)		1.56 (0.82-2.94)	
◦ Upper extremeties	16 (15)	24 (25)	16 (17)	1.96 (0.97-3.96)		1.18 (0.55-2.50)	
◦ Chest/Abdomen	22 (20)	17 (18)	21 (22)	0.86 (0.43-1.74)		1.12 (0.57-2.19)	
◦ Back (upper/lower)	56 (51)	54 (56)	55 (57)	1.24 (0.72-2.15)		1.29 (0.75-2.24)	
◦ Lower extremeties	61 (55)	61 (64)	57 (59)	1.40 (0.80-2.45)		1.17 (0.67-2.04)	
◦ Entire body	15 (14)	12 (13)	20 (21)	0.90 (0.40-2.04)		1.67 (0.80-3.47)	
• No. of locations, mean (median, SD)	1.9 (2, 0.9)	2.2 (2, 1.0)	2.2 (2, 1.1)	1.29 (0.97-1.71)	1.09 (0.79-1.49)	**1.33 (1.00-1.77)**	1.23 (0.89-1.68)
• Pain persistence, *n* (%)							
◦ Intermittent	68 (64)	45 (47)	42 (44)	**2.25 (1.28-3.95)**	**2.04 (1.12-3.74)**	**2.30 (1.31-4.05)**	**2.08 (1.14-3.80)**
◦ Constant	39 (36)	51 (53)	53 (56)				
• Pain radiates, *n* (%)	65 (59)	66 (68)	67 (71)	1.47 (0.83-2.61)		1.66 (0.93-2.97)	
• Pain migrates, *n* (%)	14 (13)	25 (27)	26 (27)	**2.48 (1.20-5.12)**	**2.44 (1.09-5.43)**	**2.55 (1.24-5.23)**	2.46 (1.10-5.47)

(*Continued*)

TABLE 3. Continued

	Mild ($n = 110$)	Moderate ($n = 97$)	Severe ($n = 96$)	Moderate vs mild		Severe vs mild	
				OR (CI)	aOR (CI)[a]	OR (CI)	aOR (CI)[a]
• Pain triggers, *n* (%)							
∘ Food intake	8 (7)	10 (10)	15 (16)	1.47 (0.55-3.88)		2.36 (0.95-5.84)	
∘ Movement	57 (52)	48 (49)	48 (50)	0.91 (0.53-1.57)		0.93 (0.54-1.61)	
∘ Stress	52 (47)	62 (64)	55 (57)	**1.98 (1.13-3.45)**	1.68 (0.91-3.12)	1.50 (0.86-2.60)	1.33 (0.72-2.45)
∘ Exercise	12 (11)	22 (23)	16 (17)	**2.40 (1.11-5.15)**	2.05 (0.91-4.62)	1.63 (0.73-3.65)	1.67 (0.72-3.87)
∘ Other triggers	39 (35)	37 (38)	34 (35)	1.12 (0.64-1.98)		1.00 (0.56-1.77)	
• Pain medication has effect, *n* (%)	73 (68)	61 (66)	49 (53)	0.91 (0.51-1.64)	0.93 (0.49-1.74)	**0.55 (0.31-0.97)**	**0.54 (0.29-0.99)**

Unadjusted ORs and adjusted ORs with CI for moderate and severe pain vs mild pain ($n = 303$) are given. Missing data: In OMT: $n = 2$; intensity of current pain: $n = 3$, years of pain: $n = 19$; onset of pain: $n = 1$; pain location: $n = 1$; pain medication effect: $n = 11$. Significant odds ratios ($P < .05$) are in bold.

aOR = adjusted odds ratio; CI = confidence interval; OMT = opioid maintenance treatment; OR = odds ratio.

[a]Adjusted model ($n = 288$ with valid responses on all variables in the model) includes age, gender, and variables significant at the 5% level in univariate analyses (pain persistence, pain migration, number of pain locations, effect of pain medication, stress and exercise).

Reporting no effect of pain medication was also significantly associated with severe pain.

DISCUSSION

In this opioid-dependent population, more than half the patients reported chronic pain with a duration of at least 3 months. The prevalence of chronic pain was higher among women and among methadone patients compared with patients receiving buprenorphine-based medication or no medication. Chronic pain was further associated with higher age, and with higher doses of methadone. Higher pain intensity was associated with describing the pain as constant and migrating, and no effect of pain medications. The distribution of age, gender, and type of medication falls in line with national reports of substance use populations in Norway.[23]

Overall Prevalence of Pain

Chronic pain was present in 55% of our population, which is more than twice the reported prevalence (24%) in the general population of Norway.[27] The prevalence was also higher compared with most studies on opioid-dependent populations, where rates have ranged from 36% to 55%.[1-7] The variations in the reported prevalence rates could be explained by differences in the selected populations, relatively small sample sizes for many of the studies, as well as social and healthcare-related differences in the settings in which the data were collected. Still, an overall conclusion appears to be that studies have shown a high prevalence of chronic pain among opioid-dependent patients.

Our finding of more chronic pain among women compared with men is in line with previous studies of pain in general populations[19,28] and in a large registry-based study of patients with opioid use disorder.[29]

Chronic pain has been defined and reported in different ways. To facilitate a comparison with other studies, we have also presented prevalence rates for *any recent pain* and *moderate-severe chronic pain.* Of the full sa60% reported *any recent pain*, which was comparable with the 66% reported in a previous study.[24] *Moderate-severe chronic pain* was experienced by 34% in our sample, which is somewhat lower but comparable to other studies with prevalences ranging from 31% to 48%.[3,4,7]

Age and Chronic Pain

The chronic pain group was significantly older than the no pain group, which has previously been seen in general populations[8,27] and in opioid-dependent populations.[7] This could be a result of increased morbidity with higher age. A previous study found no independent association between age and pain after controlling for somatic comorbidities and depression.[15] However, it is also possible that endogenous pain-reducing mechanisms become less efficient with increased age, resulting in higher sensitivity towards pain.[30] Although the chronic pain group in this study was older; age did not contribute toward explaining higher pain intensity within the chronic pain group.

OMT Medication and Chronic Pain

Methadone patients had a higher prevalence of chronic pain. This finding could have several explanations. First, age could be a confounder. Methadone patients in Norway are older compared with patients receiving buprenorphine-based medications. This could in part be a result of treatment guidelines from 2010, where buprenorphine-based medications became the preferred choice in OMT. As a result, methadone patients to a larger degree entered OMT before 2010 and are naturally older.[23] However, age does not fully explain the difference. Methadone patients older than 47 years reported significantly higher rates of chronic pain compared with buprenorphine patients older than 47 years. A second potential explanation is that there is a selection of chronic pain patients toward methadone treatment by the patients themselves or the treatment staff. It is also possible that buprenorphine patients that develop chronic pain switch to methadone to alleviate the pain or are more likely to drop out of treatment. A third explanation could be that methadone increases sensitivity towards pain. For instance, an increase in inflammatory markers among methadone patients with concurrent chronic pain could increase pain sensitivity.[31] There are case reports stating that chronic pain developed after starting methadone treatment, or that pain was reduced when first starting methadone treatment but then increased again.[21] The association between methadone and chronic pain needs further investigation before any conclusions about the relationship can be drawn.

As in previous studies,[3,15] patients with chronic pain received higher methadone doses (on average 98 mg) compared with those without chronic pain (on average 90 mg). The overall average methadone doses for the OMT population in Norway has been 92 to 95 mg in the last years.[23] It is possible that methadone patients with pain were prescribed higher doses for the purpose of managing pain. However, it is difficult to tell if the 8 mg mean difference in dose between the groups is of clinical relevance.

Characteristics of Chronic Pain

On average, patients with chronic pain reported a pain duration of over 11 years, which is comparable with the average duration of 13 years seen in the general population.[27] Over one-third reported that the cause of their pain was unknown, which is lower compared with a general population study where over half reported an unknown cause for their pain.[27] In the current study, disease was reported as the primary cause of pain by nearly one-third, which is notably higher compared with 12% in the general population.[27] This could be explained by the elevated rates of hepatitis, HIV/AIDS, and other infections or aftereffects of previous infections seen in substance-dependent populations.[32]

Over half of the participants reported the lower extremities and the back as pain locations. These two pain locations have

been reported as the most prevalent in previous studies of substance-using populations.[5,21] Pain in the lower extremities was significantly more prevalent among men, while women reported more pain in the neck and shoulders. The latter gender difference has also been seen in the general population.[19] Nearly half described their pain as constant, which is in line with a European general population study.[8]

Stress was a trigger for pain in more than half of the patients. This may reflect that stress can affect pathways involved in pain sensation, which, in turn, can increase vulnerability to opioid abuse and the reinforcing value of opioids.[33] In about half of the patients, movement was a trigger for the pain, which is also common in the general population. More than one-third reported "other triggers," which means that the types of pain triggers experienced by this patient group have yet to be described in full. Triggers related to mental health should be explored, due to associations between pain and for example, depression/anxiety.

Characteristics of Mild, Moderate, and Severe Chronic Pain

When adjusting for other variables, describing the pain as constant or migrating was associated with moderate and severe pain compared with mild pain intensity. Constant pain has previously been associated with higher pain intensity in multiple sclerosis.[34] Migrating pain could be an indicator for centrally maintained pain with pain sensitization (hyperalgesia), which is a pain state that can be worsened by opioid use through additional opioid-induced hyperalgesia.[12]

Reporting that pain medication had no effect on the pain was associated with more severe pain intensity. This could indicate that the pain intensity was too high for efficient pharmacological treatment, or that this subgroup experiences pain rooted in neuroinflammation or neuroimmune activation not directly modulated by the opioid receptors.[35]

Limitations and Strengths

The exploratory survey was designed for the purpose of being easy to fill out and to give an estimate of chronic pain prevalence and pain characteristics through questions relevant to clinical practice. For this reason, many important measures known to be relevant to chronic pain were not included. Also, the here and now wording of the pain intensity scale could miss the intensity of intermittent pain or be affected by withdrawal symptoms. On the other hand, this is one of the larger self-report studies of an opioid-dependent population designed explicitly for investigation of pain and pain characteristics. The study was well-received by patients and few declined to participate. The study contributes to a foundation for further exploration of the etiology and mechanisms of chronic pain among opioid-dependent patients. The sample size allowed comparisons of women and men, and of mild, moderate, and severe pain intensity groups, which has not been done previously. It is also one of few studies that include patients receiving methadone, buprenorphine, or no medication from the same treatment centers in the same catchment areas.

CONCLUSION

The high prevalence of chronic pain underscores the need for a better understanding of the etiology and mechanisms of chronic pain among opioid-dependent patients. This includes potential relationships between pain and OMT medication type, gender differences, social factors, and physical and mental health. Treatment outcomes for opioid dependence may be improved by sufficient management of pain conditions, and an improved understanding of how chronic pain and opioid dependence interact in clinical practice.

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper. The content and results have not been submitted or published elsewhere.

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