Published in final edited form as:
Am J Addict. 2013 May ; 22(3): 212–217. doi:10.1111/j.1521-0391.2012.00327.x.

Pain and Associated Substance Use among Opioid Dependent Individuals Seeking Office-Based Treatment with Buprenorphine-Naloxone: A Needs Assessment Study

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Abstract

Background and Objectives—A paucity of studies has examined the pain experiences of opioid dependent individuals seeking office-based buprenorphine-naloxone treatment (BNT). We set out to examine, among those seeking BNT: (a) the prevalence of pain types (i.e., recent pain, chronic pain), (b) the characteristics of pain (intensity, frequency, duration, interference, location, and genesis), and (c) substance use to alleviate pain.

Methods—We surveyed 244 consecutive individuals seeking office-based buprenorphine-naloxone treatment (BNT) for opioid dependence about physical pain and associated substance use.

Results—Thirty-six percent of respondents reported chronic pain (CP) (i.e., pain lasting at least 3 months) and 36% reported “some pain” (SP) (i.e., past week pain not meeting the threshold for CP). In comparison to SP respondents, those with CP were, on average, older; reported greater current pain intensity, pain frequency, typical pain duration, typical pain intensity, and typical pain interference; were more likely to report shoulder or pelvis and less likely to report stomach or arms as their most bothersome pain location; and were more likely to report accident or nerve damage and less likely to report opioid withdrawal as the genesis of their pain. Both pain subgroups reported similarly high rates of past-week substance use to alleviate pain.

Conclusions and Scientific Significance—The high rates of pain and self-reported substance use to manage pain suggest the importance of assessing and addressing pain in BNT patients.

INTRODUCTION

Pain is generally—but not always[1]—a negative prognostic indicator of opioid use disorder treatment outcome. Among opioid dependent patients (In this manuscript, the terms “opioid dependence” and “opioid dependent” are used in accordance with the *DSM-IV-TR* (APA, 2000)), unrelieved pain has been associated with lower rates of drug abstinence and higher

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Declaration of Interest:
Dr. Fiellin has received honoraria for serving on an external advisory board monitoring diversion and abuse of buprenorphine from Pinney Associates. The other authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

rates of prescription and nonprescription medication use, sleep disturbance, psychiatric distress, and relapse to illicit opioids following detoxification.[2–8] Providers report difficulty and frustration treating patients with co-occurring opioid dependence and chronic pain, defined here as non-cancer physical pain lasting at least three months.[9–11]

Research to date on chronic pain and its associated morbidity and treatment implications among opioid dependent patients has focused on patients: a) in detoxification programs,[4, 7, 12, 13] b) seeking methadone maintenance treatment (MMT),[14, 15] or c) already enrolled in MMT.[1–3, 6, 8, 16] Office-based buprenorphine-naloxone treatment (BNT) is a relatively new treatment modality for opioid dependence in the U.S. and internationally, which in comparison to MMT has attracted a new and different population of opioid dependent patients into opioid agonist treatment.[17] Consequently, it is important to assess the pain experiences of opioid dependent patients seeking BNT independent of the pain experiences of those seeking MMT. However, there is little published research that has examined physical pain among patients seeking BNT for opioid dependence: One notable exception is a recent study of opioid dependent youth, aged 15–21, which found that higher levels of pain reported in the week prior to treatment were associated with higher buprenorphine-naloxone dose levels during treatment.[18]

Research findings point to the importance of assessing recent pain (i.e., pain experienced in the past week) as well as chronic pain among opioid dependent patients entering treatment.[2, 19, 20] Therefore, the aim of this needs assessment study was to examine the pain experiences of opioid dependent individuals seeking BNT. Specifically, we set out to examine, among those seeking BNT: (a) the prevalence of pain types (i.e., recent pain, chronic pain), (b) the characteristics of pain (intensity, frequency, duration, interference, location, and genesis), and (c) substance use to alleviate pain. Data on pain types and characteristics form important components of a comprehensive pain assessment, while taking substances to alleviate pain is likely to establish and reinforce behaviors that can complicate the course of opioid dependence treatment. Consequently, such information is likely to be useful for BNT resource and treatment planning.

METHODS

Participants were 244 adults who were consecutively evaluated for enrollment to office-based BNT between January 2008 and October 2010 as part of a buprenorphine-naloxone research program at the Yale University School of Medicine. All those who presented for enrollment, 100% compliance, completed the study survey as part of the screening process for determining BNT study eligibility; typically, the survey was filled out at least two days prior to BNT induction. Respondents were informed that their answers to the survey did not affect their enrollment into the BNT study. This study received appropriate institutional review board approval.

Data collection

As described elsewhere,[15] the study questionnaire was designed to be brief (< 10 minutes), self-administered, and easy to understand in order to increase compliance and to minimize respondent burden. Survey questions assessed multiple domains, including: (a) the prevalence of pain types (i.e., recent pain, chronic pain), (b) the characteristics of pain (intensity, frequency, duration, interference, location, and genesis), (c) substances used to alleviate pain, and (d) demographics (gender, race, and age).

Recent pain and current chronic pain were assessed by asking participants whether they had experienced ongoing physical pain in the last week (yes/no) and whether they were experiencing an episode of physical pain that had lasted at least three months (yes/no). Pain

intensity (current and typical level in the last 7 days) items asked participants to rate how much physical pain they were currently experiencing and the typical level of physical pain experienced in the last 7 days (on similar ordinal scales between 1 [none/minimal] to 5 [unbearable]).

Pain frequency assessed how often physical pain was experienced in the last 7 days (on an ordinal scale between 1 [never] to 5 [all the time]). Pain duration assessed the length of the typical pain episode experienced in the last 7 days (on an ordinal scale between 1 [less than one hour] and 5 [all day]). Pain interference assessed the degree to which pain interfered with participants' everyday life in the last 7 days (on an ordinal scale between 1 [did not interfere] to 5 [interfered completely]). Pain location assessed where on the participant's body he/she experienced the most bothersome pain in the last 7 days, and pain genesis assessed how the pain experienced in the last 7 days began (participants were provided with a list of answer choices for each). The pain location response list included: back, shoulder, pelvis, hands, feet, stomach, head, face, legs, arms, and "other," and the pain genesis response list included: accident, surgery, nerve damage, arthritis, HIV, cancer, opioid withdrawal, "don't know," and "other."

To identify substances that were used to alleviate pain, participants were provided with a list of substances that opioid dependent patients in our opioid agonist treatment programs have indicated using for analgesic purposes and were asked, "Which of the following have you used in the last 7 days to help you relieve ongoing physical pain?" The list included: (a) "More than prescribed opiate medication (e.g., Demerol, Fentanyl, Morphine, Oxycontin, Percocet, Percodan, Tylenol with Codeine, etc.)," (b) "Somebody else's opiate pain medication," (c) "Heroin," (d) "Street methadone," (e) "More than prescribed non-opiate medication (e.g., Celebrex, Celexa, Clonidine, Depakote, Elavil, Fiorinal, Ketalar, Ketaset, Neurontin, Prozac, Soma, Tegretol, Topamax, etc.)," (f) "Somebody else's non-opiate pain medication," (g) "More than prescribed benzodiazepine (e.g., Ativan, Halcion, Klonopin, Valium, Xanax, etc.)," (h) "Somebody else's benzodiazepine medication," (i) "Other street drugs (e.g., cocaine, marijuana, etc.)," and (j) "Alcohol." Thus, substance use, as defined in this study, included medication misuse (i.e., taking for analgesic purposes more medication than prescribed or someone else's medication) and use of alcohol or illicit drugs for pain relief.

Pain Groups

Respondents' answers to pain-related items were used to classify them into one of two pain groups: "chronic pain" (i.e., pain lasting at least three months) and "some pain" (i.e., pain reported in the past week but not meeting the duration threshold for chronic pain).

Data Analysis

Data analyses focused on respondents who reported pain in the past week (i.e., recent pain). Pain group (i.e., chronic pain [CP], some pain [SP]) and recent pain (yes/no) differences on demographic variables were examined using t-tests for continuous data and Pearson chi-square tests for categorical data. Since the CP and SP groups differed significantly on age, we performed a multivariate analysis of covariance (MANCOVA) to control for age on comparisons involving pain-related continuous data (i.e., current pain intensity, pain frequency, typical pain duration, typical pain intensity, and typical pain interference).

We examined differences between the CP and SP groups on pain-related categorical variables by conducting two series of binary regression models (adjusting and not adjusting for age) with pain location, pain genesis, and pain-related substance use as the predictor variables of interest and the 2-level pain variable (i.e., CP, SP) as the dependent variable.

Since a similar pattern of findings emerged in both series, in this paper we report only on regression model findings adjusting for age. Our analyses began by examining pain-related binary variables (i.e., "yes"/"no") grouped into pain location, pain genesis, and pain-related substance use categories. When significant associations were found between these categories and pain groups, we pursued further analysis of the individual variables. The SP category was used as a reference level for calculating adjusted odds ratios: CP versus SP. We removed the "opioid withdrawal" variable from the binary logistic model involving pain genesis because of concerns about multicollinearity, and, instead, we conducted a separate χ^2 with a Bonferroni adjustment to control for multiple comparisons within the pain genesis category (i.e., [.05 ÷ 9 = 0.0056]). For all other analyses, statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS Version 17.0 for Windows (SPSS, Inc., Chicago, IL).

RESULTS

Demographic characteristics

Of the 244 respondents, 84% (n = 204) were white, 68% (n = 167) were male, 72% (n = 175) reported recent pain, and 36% (n = 88) reported chronic pain. Twenty eight percent (n = 69) did not report recent pain (i.e., pain in the past week). Whereas respondents with and without recent pain did not differ on gender ($\chi^2 = 0.46$, df = 1, p = 0.54) or race ($\chi^2 = 0.25$, df = 1, p = 0.70), those with recent pain were older (mean = 34.8 years) than those with no recent pain (mean = 31.4 years) (t = 2.31, df = 242, p = 0.02). Among the 175 respondents with recent pain, 30% (n = 53) characterized their typical pain intensity in the past week as minimal or mild, 44% (n = 76) as moderate, and 26% (n = 46) as severe or unbearable.

As summarized in Table 1, among respondents reporting recent pain, those with (50%; n = 88) and those without chronic pain (50%; n = 87) did not differ on gender or race but did differ on age: on average, the chronic pain group was older than the some pain group (36.3 years vs. 33.2 years).

Pain characteristics

Overall, after controlling for age, the CP and SP groups differed on pain characteristics, $F(5, 166) = 17.49$, $p < 0.001$. As summarized in Table 1, after controlling for age, in comparison to respondents with some pain, those with chronic pain reported higher (all p's < 0.001) current pain intensity and past-week pain frequency, typical pain duration, typical pain intensity, and typical pain interference.

Adjusted odds ratios from multivariate models investigating the strength of associations between pain location, pain genesis, pain-related substance use, and pain groups are presented for CP and SP respondents in Table 2, using the SP group for reference. Among participants reporting pain in the past week, the most frequently endorsed pain locations were as follows: back (78%), legs (47%), shoulder (26%), and stomach (23%). In comparison to those with some pain, those with chronic pain were more likely, in multivariable analyses, to identify shoulder (AOR = 2.9, p = 0.01) or pelvis (AOR = 6.7, p = 0.04) and less likely to identify stomach (AOR = 0.4, p = 0.03) or arms (AOR = 0.1, p = 0.005) as the location of their most bothersome pain in the past week.

Among respondents reporting recent pain, the most frequently endorsed causes of recent pain were accident, nerve damage, and "don't know" for those with chronic pain, and "other," opioid withdrawal, and accident for those with some pain, respectively. In comparison to those with some pain, those with chronic pain were more likely, in multivariable analyses, to report accident (AOR = 6.2, p = 0.001) and nerve damage (AOR = 15.7, p = 0.001) (see Table 2) and were less likely, in univariate analyses, after controlling

for multiple comparisons, to report opioid withdrawal (0% vs. 32%, $\chi^2 = 33.72$, $p < 0.001$) as the genesis of their recent pain.

Pain-related substance use characteristics

As summarized in Table 2, the CP and SP groups did not differ on reported substance use to alleviate pain; for example, comparably high rates of both groups reported in the past week taking more than prescribed opioid medication, taking someone else's prescription opioid medication, using heroin, using other street drugs, and using alcohol to alleviate pain.

DISCUSSION

This study is among the first to examine the pain experiences of individuals seeking BNT for office-based treatment of opioid dependence. Similar to studies on patients entering or already enrolled in MMT, we found high rates of chronic pain (36%) and some pain (36%) among respondents seeking BNT.[1–3, 6, 8, 15, 16] In comparison to respondents with some pain, those with chronic pain exhibited higher pain intensity (current and typical), pain frequency, pain duration, and pain interference. On average, the chronic pain group rated their past-week pain interference—a key measure of pain-related functioning—as being between "moderate" and "a lot." These data suggest that similar to their opioid dependent counterparts seeking MMT, patients seeking BNT have elevated rates of chronic pain that interfere with their functioning.[15]

Whereas the CP and SP groups did not differ on gender or race, they differed on age: the CP group was, on average, significantly older than the SP group (36.3 vs. 33.2). Age has been found to be a predictor of chronic pain in MMT patients.[2, 8] Back and face were the most, and least, frequently endorsed locations of the most bothersome pain experienced in the past week by the CP and SP groups, respectively. These findings parallel those reported in a study of patients seeking MMT for opioid dependence.[15] Back pain is frequently endorsed as a location of chronic pain among patients with substance use disorders.[20] In multivariable analyses, the CP group was more likely than the SP group to report shoulder or pelvis and less likely to report stomach or arms as the location of their pain. In comparison to the SP group, the CP group was more likely to report that their pain emanated from an accident and nerve damage and was less likely to report that it emanated from opioid withdrawal. Opioid withdrawal can produce pain through several mechanisms, including bone aches, muscle cramps, and gastrointestinal distress. It is noteworthy that while opioid withdrawal was endorsed as a genesis of recent pain by approximately one-third of the SP group, it was not endorsed by any of the CP group. Thus, the recent pain reported by the CP group does not appear to be a function of opioid withdrawal. The higher rates of endorsement of stomach pain among the SP as compared to the CP group may be a function of opioid withdrawal.

In multivariable analyses, we did not find any significant differences on self-reported substance use to alleviate pain in the past week among the CP and SP groups; e.g., a similarly substantial proportion of each recent pain group reported heroin use, taking somebody else's prescription opioid medication, street methadone use, and other street drug use (e.g., cocaine, cannabis) for analgesic purposes. The finding that many participants reported using more than prescribed opioid medication suggests that these medications had been recently prescribed for them, but the proportions did not differ as a function of chronic pain status. The relatively high rates of opioids, alcohol, and, to a lesser extent, benzodiazepines to alleviate pain also indicate that these patients may have a proclivity to "self-medicate" for pain relief. These elevated rates also suggest that BNT clinicians might benefit from screening for pain at intake, including pain in their differential diagnosis regarding ongoing substance use, and adding it to their list of triggers to assess and address for potential lapses/relapses to substance use (i.e., "people, places, pain, and things").

Non-medical use of benzodiazepines among those reporting recent pain may be an important target for BNT resource and program planning given the associated risk of overdose and sedation.[21] Additionally, approximately one-quarter of respondents with recent pain reported past-week alcohol use to relieve pain. These findings extend those previously reported regarding the elevated rate of prescription opioid use and misuse for pain relief among out-of-treatment substance users in New York City by documenting a wide range of opioid and non-opioid substances used by BNT seekers to mange pain.[22] Our findings suggest that patients with recent pain entering BNT might benefit from psychoeducation regarding the risks (e.g., medical, psychiatric) of using substances to alleviate pain, including the potential adverse health effects of combining substances used for pain relief (e.g., non-medical use of benzodiazepines, alcohol) and buprenorphine/naloxone. Patient attributions regarding substance use to relieve pain may be particularly important to assess and address in future research on individuals with pain seeking BNT for opioid dependence. Furthermore, given office-based provider concerns that patients may be inappropriately using prescription opioid analgesics to manage psychiatric symptomatology, further research assessing the medical and psychiatric co-morbidity of opioid dependent patients with pain entering BNT may be warranted.[10]

Several potential limitations are worth considering. Participants were seeking BNT as part of a research study; thus, our findings may or may not generalize to non-research-based BNT programs. Data regarding medical and psychiatric status and drug treatment history (including MMT) were not assessed in the study survey. The survey was cross-sectional and thus limits statements regarding causation between study variables. No independent assessments of participants' self-reported substance use (e.g., urinalysis) or pain status (e.g., abnormal physical or laboratory findings, diagnosis of painful diseases) were conducted. Information regarding "other" pain genesis responses was not qualified further. Given the absence of published pain-related needs assessment measures for BNT, we used an instrument that had been developed for patients seeking entry into MMT; although face-valid, it has not yet been formally validated.[15]

Future research investigations might also benefit from a more detailed chronology of pain and substance use to alleviate pain. For example, the potential prognostic significance of the timing of substance use disorder and chronic pain onsets is unclear. The analgesic properties and favorable safety profile of buprenorphine coupled with the interest of those with chronic pain and opioid dependence in accessing pain management via their BNT provider suggest that research on the potential efficacy of BNT in managing both pain and addiction among patients with these co-occurring chronic medical conditions is warranted. Such research should be conducted in accordance with current Food and Drug Administration approvals in the U.S. which are for treatment of opioid dependence and not pain or potentially under an Investigational New Drug authorization. The high prevalence of recent pain and chronic pain as well as self-reported substance use to manage pain suggest that such pain may affect clinical outcomes if not addressed. Therefore, BNT programs might improve patient outcomes by systematically assessing and addressing both the presence of different pain types (e.g., some pain, chronic pain) and self-reported substance use (e.g., alcohol, heroin) to manage pain. Finally, given findings regarding brain morphological changes associated with chronic back pain (the most frequently endorsed pain location in the current study) in non-addicted patients (e.g., reduced gray and white matter density),[23] future research on chronic pain in patients seeking BNT for opioid dependence might profit from examining brain scan data.

Acknowledgments

This study was supported in part by grants K23 DA024050 (Dr. Barry), K01 DA022398 (Dr. Moore), K24 DA000445, R01DA024695 (Dr. Schottenfeld), and R01 DA019511, RO1 DA020576 (Dr. Fiellin) from the National Institute on Drug Abuse, Bethesda, MD.

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Table 1

Comparison of CP and SP groups on demographics and pain intensity, frequency, duration, and interference

	CP (n = 88)	SP (n = 87)	Statistical test	P
Demographics				
Gender (% male)	68	71	$\chi^2 = 0.19$	0.74
Race (% white)	85	81	$\chi^2 = 0.70$	0.43
Age (mean age, ± SD)	36	33	$t = -1.98$	0.049
Pain characteristics[a]				
Current pain intensity (mean intensity, ± SD)	3.2 ± 0.9	2.2 ± 1.0	$F = 51.85$	<0.001
Pain frequency[b] (mean frequency, ± SD)	4.0 ± 1.0	2.7 ± 1.0	$F = 74.62$	<0.001
Typical pain duration[b] (mean duration, ± SD)	3.9 ± 1.0	3.0 ± 1.2	$F = 25.73$	<0.001
Typical pain intensity[b] (mean intensity, ± SD)	3.4 ± 0.7	2.4 ± 1.0	$F = 57.18$	<0.001
Typical pain interference[b] (mean interference, ± SD)	3.3 ± 1.1	2.2 ± 1.1	$F = 48.92$	<0.001

CP = Chronic pain, SP = Some pain.

[a] Controlling for age.

[b] Past week.

Table 2

Comparison of CP and SP groups on pain location, pain genesis, and pain-related substance use[a]

	CP (n = 88) %	**SP (n = 87) %**	**χ^2**	**P**	**AOR (95% CI)**	**P**
Pain location			35.6	<0.001		
Back	84	72			2.3 (0.9–5.3)	0.06
Shoulder	33	20			2.9 (1.3–6.6)	0.01
Pelvis	10	2			6.7 (1.1–39.9)	0.04
Hands	9	3			4.3 (0.8–22.8)	0.08
Feet	13	12			1.3 (0.4–4.2)	0.71
Stomach	16	31			0.4 (0.1–0.9)	0.03
Head	19	23			1.0 (0.4–2.6)	0.95
Face	2	3			0.9 (0.1–9.5)	0.93
Legs	48	47			1.4 (0.7–2.8)	0.42
Arms	6	15			0.1 (0.03–0.5)	0.005
Other	25	18			1.7 (0.7–3.9)	0.21
	CP (n = 88) %	SP (n = 87) %	χ^2	P	AOR (95% CI)	P
Pain genesis			48.2	<0.001		
Accident	57	25			6.2 (2.1–18.1)	0.001
Surgery	11	6			1.8 (0.4–8.4)	0.45
Nerve damage	21	2			15.7 (2.9–84.5)	0.001
Arthritis	11	1			5.9 (0.5–67.3)	0.15
HIV	0	0			--	--
Cancer	0	0			--	--
Don’t know	21	23			2.8 (0.8–9.5)	0.10
Other	19	46			0.7 (0.2–2.2)	0.58
Pain-related Substance Use in Past Week			17.1	0.10		
More than prescribed opiate medication	33	18			1.5 (0.6–3.4)	0.35
Somebody else’s opiate pain medication	61	45			1.6 (0.8–3.3)	0.19

	CP (n = 88) %	**SP (n = 87) %**	**χ^2**	**P**	**AOR (95% CI)**	**P**
Heroin	39	33	1.1 (0.5–2.2)	0.88		
	CP (n = 88) %	SP (n = 87) %	χ^2	P	AOR (95% CI)	P
Street methadone	15	9			1.1 (0.4–3.2)	0.89
More than prescribed non-opiate medication	11	3			2.0 (0.4–9.7)	0.38
Somebody else's non-opiate medication	13	7			0.9 (0.3–3.6)	0.95
More than prescribed benzodiazepine medication	11	5			1.5 (0.3–7.0)	0.59
Somebody else's benzodiazepine medication	14	5			1.6 (0.3–7.3)	0.55
Other street drugs	36	24			1.5 (0.6–3.5)	0.34
Alcohol	24	25			0.5 (0.2–1.2)	0.13

CP = Chronic pain, SP = Some pain, AOR = Adjusted odds ratio.

[a]Controlling for age.