Published in final edited form as:
Pain. 2010 December ; 151(3): 625–632. doi:10.1016/j.pain.2010.08.002.

Clinical Characteristics of Veterans Prescribed High Doses of Opioid Medications for Chronic Non-Cancer Pain

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Abstract

Little is known about patients prescribed high doses of opioids to treat chronic non-cancer pain, though these patients may be at higher risk for medication-related complications. We describe the prevalence of high-dose opioid use and associated demographic and clinical characteristics among veterans treated in a VA regional healthcare network. Veterans with chronic non-cancer pain prescribed high doses of opioids (>=180 mg/day morphine equivalent; n=478) for 90+ consecutive days were compared to two groups with chronic pain: Traditional-dose (5–179 mg/day; n=500) or no opioid (n=500). High-dose opioid use occurred in 2.4% of all chronic pain patients and in 3.4% of all chronic pain patients prescribed opioids long-term. The average dose in the high-dose group was 324.9 (SD=285.1) mg/day. The only significant demographic difference among groups was race (p=0.03) with black veterans less likely to receive high doses. High-dose patients were more likely to have four or more pain diagnoses and the highest rates of medical, psychiatric, and substance use disorders. After controlling for demographic factors and VA facility, neuropathy, low back pain, and nicotine dependence diagnoses were associated with increased likelihood of high-dose prescriptions. High-dose patients frequently did not receive care consistent with treatment guidelines: there was frequent use of short-acting opioids, urine drug screens were administered to only 40.8% of patients in the prior year, and 32.0% received concurrent benzodiazepine prescriptions, which may increase risk for overdose and death. Further study is needed to identify better predictors of high-dose usage, as well as the efficacy and safety of such dosing.

Keywords

Chronic pain; Opioids; Epidemiology; Quality of life; Pain/drug therapy

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No author reports having any potential conflict of interest with this study.

Introduction

The use of opioids for chronic non-cancer pain has increased in recent years [10,31] despite uncertainty regarding the efficacy of opioids in reducing pain or improving function [24,32]. A summary of the literature regarding opioid medications to treat chronic non-cancer pain indicates strong evidence of initial effectiveness in pain reduction, but less evidence to support long-term effectiveness [6,13].

Doses of opioid medications often remain stable [47] and the vast majority of pain patients are on opioid doses less than 100 mg morphine equivalents per day [40]. However, a small proportion of patients are prescribed high doses (defined here as greater than 180 mg morphine equivalent per day [5]). Limited empirical data are available regarding the prevalence of high-dose opioid use, clinical or demographic factors associated with high-dose opioid use, or outcomes associated with long-term high-dose opioid therapy [12]. Of the few randomized clinical trials that included high doses of opioids, time on active treatment was limited to one to eight weeks [5]. A planned three year registry study of patients taking controlled-release oxycodone for non-cancer pain found that, of 233 patients enrolled, 5% were taking 100 mg or more of oxycodone per day [40]. However, treatment discontinuation was high, as 133 (57%) participants voluntarily terminated the study, and the data on long-term benefit are not available. In a study of 1,226 patients with disabling musculoskeletal disorders, higher baseline opioid doses (greater than 61 mg morphine equivalent per day) were associated with poorer outcomes from an interdisciplinary functional restoration program [28].

There are numerous risks associated with opioids, including side effects, misuse, diversion, and other adverse health effects [27,34,35,44], in addition to concerns about effectiveness. These concerns are heightened for patients on high doses of opioids. There may also be additional side effects associated with high-dose opioid use that are not present at standard dose, such as arrhythmia, thyroid disease, hypogonadism with sexual dysfunction, or hyperalgesia [4,16,18,30]. Recent data from a retrospective cohort study examined patient factors and risks associated with opioid use. Analyzing data from 9,940 patients who were prescribed long-term opioid therapy, those patients who were prescribed doses greater than 100 mg morphine equivalent per day were at the greatest risk for overdose, relative to patients taking lower doses [21]. Additionally, risk of fractures for chronic pain patients older than 60 were highest among patients prescribed 50 mg per day morphine equivalent or more of opioids [45].

Few studies have examined the progression of opioids from traditional to high doses. Among patients with painful spine conditions, smoking status and nonsurgical treatment predicted long-term opioid use [29]. Other studies have examined factors associated with opioid prescribing and found that history of comorbid psychiatric disorders and substance use disorders were significantly linked to opioid prescriptions [8,49,50]. It is unclear whether these variables are also associated with high doses of opioids. The purpose of the present study was to describe the prevalence, demographic characteristics, and clinical features of chronic non-cancer pain patients who are prescribed high doses of opioid medications.

Methods

Data were collected from veterans receiving treatment at any VA facility in the Pacific Northwest (Washington, Oregon, Idaho, and Alaska) as part of routine care. Data were extracted from the Veterans Integrated Service Network (VISN)-20 Data Warehouse [51]. The Data Warehouse contains data from the main clinical software packages of regional VA healthcare facilities and two national VA databases. The Data Warehouse is updated monthly

and reliability checks are performed regularly. This study was approved by the Institutional Review Board at the Portland VA Medical Center.

Inclusion/Exclusion Criteria

Patients who received any medical care in VISN-20 at any time during calendar year 2008 were eligible for study inclusion. To identify patients with chronic pain, we reviewed electronic medical record pain Numeric Rating Scores (NRS; 26) during calendar year 2008. Patients with pain intensity scores ≥ 4 on the NRS, a scale of 0 – 10 (with 0 being low and 10 being high), recorded in at least three different months during 2008 were considered to have chronic pain. This is consistent with common definitions of chronic pain that require at least three to six month duration of moderate to severe pain [14,25]. Although consensus on the optimal NRS for moderate pain is lacking, most studies use either 4 or 5; we used 4 as the cutoff in this study due to its consistency with VA clinical practice and policy [15]. For those patients whose first pain scores occurred in November or December, the first two months of 2009 were also considered. Included subjects were classified into one of three groups: chronic non-cancer pain patients prescribed high doses of opioid medications (defined as ≥ 180 mg morphine equivalent per day) for at least 90 consecutive days, chronic non-cancer pain patients prescribed traditional doses of opioid medications (defined as 5 – 179 mg morphine equivalent per day) for at least 90 consecutive days, or chronic non-cancer pain patients not prescribed any opioid medications in the prior year. Previous studies have used 90 days of opioid use to indicate chronic use [22,53]. To calculate a morphine equivalent, each prescription was categorized into an opioid category and multiplied by a conversion factor to determine the same milligram amount per day of morphine (Table 1). The conversion factors were based on previously published recommendations [37,52,53].

Patients were excluded from the study if they had any visits to a VA opioid substitution (methadone maintenance) program in the region during 2008, had any cancer diagnosis in the six years prior to their index date, or any surgery within the past six months. In order to exclude patients who might have a terminal illness during the study period, we also excluded any patient who subsequently died in 2008 (Figure 1).

Defining Study Samples

Four hundred seventy-eight patients were identified as being in the high-dose opioid chronic pain group for at least 90 consecutive days. We also identified 5,339 patients who met chronic non-cancer pain criteria and who received traditional opioid use (opioid dose range from 5 – 179 mg morphine equivalent per day) for at least 90 consecutive days; 500 of these patients were selected as one comparison group. Among the patients meeting our chronic non-cancer pain inclusion criteria, there were 5,491 who had no opioid use in 2008. We randomly selected 500 of these patients to serve as an additional comparison group. In order to identify the two comparison groups, we used a random number generator to assign a random number to each subject in the group, and we then selected the first 500 subjects. In both the high-dose and traditional-dose groups we created an index date, to be used as a reference point for collecting medical diagnoses and pharmacy data. The index date was calculated as the earliest date in 2008 of a 90 consecutive day episode of opioid use. Clinical data for patients were retrieved for five prior years from the index date. The index date for the no opioid group was the date of their earliest pain score ≥ 4 in calendar year 2008.

Collection of Demographic Data, Medical Diagnoses, and Pharmacy Data

Demographic data including age, gender, race, marital status, and VA service-connected disability status were collected for all patients. Body mass index was derived from weight and height measurements at outpatient visits within six months of the index date, and was calculated by dividing weight in kilograms by the square of height in meters. Inpatient and outpatient

diagnoses were based on International Classification of Diseases, Clinical Modification – 9th Revision (ICD-9-CM). If a diagnostic code for a disorder was made any time in the five years prior to the index date, the individual was coded as having the disorder. Past-year inpatient hospitalization data and outpatient diagnoses were used to calculate a Charlson Comorbidity score [11], a measure which uses ICD-9-CM diagnostic codes for 17 health conditions to document the burden of medical comorbidity [42,43]; higher scores indicate more severe illness. Pharmacy data were reviewed to extract information on prescriptions of current opioids and non-opioid analgesics (data were available only from VA pharmacies).

Statistical Analyses

Demographic and diagnostic data were analyzed using chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables. Post-hoc tests were evaluated with Scheffe. A forward stepwise logistic regression model was used to evaluate characteristics associated with prescriptions of high doses of opioid medications. The dependent variable was prescription for high-dose (versus traditional-dose) of opioids. For this analysis, participants who were not prescribed any opioid medications were excluded, as the goal was to examine differences between patients prescribed traditional doses of opioids versus those prescribed high doses of opioids. Age, gender, and VA facility (one of eight medical centers in Washington, Oregon, Idaho, or Alaska) were entered into the model in Step 1. Age and gender were included because these variables have been associated with pain and opioid use in prior studies. The variable for VA facility was included to help control for practice variation, as regional deviations in opioid prescribing practices could impact the results. Other independent variables were eligible to be entered in Step 2 if they significantly differed ($p \leq 0.05$) between groups in bivariate testing. We also included variables that summed the total number of pain diagnoses, and total number of psychiatric diagnoses with which a participant was diagnosed; these variables were included to provide additional measures of comorbidity. In the regression analyses, only participants for whom all variables were available were included.

Results

Demographic Characteristics

High-dose opioids were prescribed for 2.4% of all participants with chronic non-cancer pain, 3.4% of all chronic non-cancer pain patients who received any prescription for opioid therapy, and 8.2% of chronic non-cancer pain patients who are prescribed opioids long-term (Figure 1). Demographic characteristics are reported in Table 2. The average participant was male (90.7%), 55.1 (SD=12.6) years old, married (49.3%) or divorced (32.5%), white (70.8%), overweight (mean BMI=31.1, SD=7.1), and had a VA service-connected disability (64.3%). The average pain numeric rating score did not differ between the two opioid groups, though both were higher than in the non-opioid group. Race significantly differed amongst groups (χ^2 (6) = 20.2, p = 0.03), as white veterans were over-represented in the high-dose group and black veterans were more likely to be included in the traditional-dose group or no opioid group (race data were missing for 14.8% of participants). No significant differences were detected among the three groups with respect to age, sex, marital status, BMI, or whether they had a VA service-connected disability.

Pain and other Medical Diagnoses

The high-dose group had a greater number of documented diagnoses for pain conditions compared with the traditional-dose group and the no opioid group (Table 3). The traditional-dose group also had higher rates than the no opioid group for most pain diagnoses. The proportion of patients in each group who were diagnosed with four or more pain diagnoses significantly differed; 35.6% of the high-dose group, 26.0% of the traditional-dose group, and 14.0% of the no opioid group had four or more pain diagnoses (χ^2 (2) = 60.9, $p < 0.001$).

Patients in the no opioid group were most likely to have only one pain diagnosis, χ^2 (2) = 15.7, $p < 0.001$ (19.0% of the no opioid group, 11.3% of the high-dose group, and 11.6% of the traditional-dose group).

Regarding other medical diagnoses (Table 4), there were statistically significant differences among the three groups in rates of hypertension, congestive heart failure, chronic pulmonary disease and paraplegia/hemiplegia, with the high-dose group having the highest rates of diagnoses for all conditions except hypertension, which was more common among patients in the traditional-dose group. There were also significant differences in rates of several psychiatric diagnoses, with patients in the high-dose group often having the highest frequencies. Patients in the high-dose group had significantly higher scores than the no opioid group on the Charlson Comorbidity Index (F (2, 1477) = 5.2, $p = 0.006$), indicating more severe illness; scores from the traditional-dose group and no opioid group did not significantly differ.

Medications

Patients in the high-dose group had an average daily opioid dose of 324.9 (SD=285.1) mg morphine equivalent per day (range = 180 – 5,496; median = 273.2). Patients in the traditional-dose group had an average daily dose of 32.4 (SD=20.1) mg morphine equivalent per day (range = 5 – 128; median = 27.5). Figure 2a displays comparisons between the high-dose group and traditional-dose group on types of opioid medications that were prescribed at the time of their index date. There were statistically significant differences between the two opioid groups with respect to the proportion of patients prescribed at least one of each opioid. The high-dose group had greater proportions of prescriptions for all of the long-acting medications (transdermal fentanyl, methadone, morphine sustained-release, and oxycodone controlled-release). There were also statistical differences in the proportions of the various short-acting medications prescribed and a statistically significant difference between groups in the proportion of patients prescribed two or more different types of opioids: 74.3% of the high-dose group versus 26.6% of the traditional-dose group (χ^2 (1) = 222.1, $p < 0.001$). However, there was no difference between the high-dose group and the traditional-dose group in the proportion of patients prescribed two or more *short*-acting opioids (9.0% versus 12.2%, χ^2 = 2.64, $p = 0.10$). Patients in the high-dose group were most likely to be prescribed the combination of only one long-acting opioid and no short-acting opioids (23.2% versus 7.6%; $\chi^2 = 46.2$, $p < 0.001$). There was a statistically significant difference among the three groups in current prescriptions for non-steroidal anti-inflammatory drugs (NSAID) and/or acetaminophen, capsaicin, antidepressants, and benzodiazepines (Figure 2b). The two opioid groups had higher rates of prescriptions for all medications than the no opioid group, with the high-dose group having the highest rate for all medications except NSAID/Acetaminophen.

Urine Drug Screen Results

We examined the frequency of past-year administrations of urine drug screen by group status; 39.9% (n=590) of all patients prescribed opioids were administered a urine drug screen in the past year. There was no significant difference among groups in the rate of administrations ($p = 0.85$) or the proportion of patients with a positive screen ($p = 0.44$). Twenty-two total patients had a positive urine drug screen for an illicit substance (1.7% high-dose group, 1.2% traditional-dose group, and 1.6% no opioid group). The most common illicit substance detected via urine drug screen was marijuana (n=19, 86.4% of positive tests).

Correlates of High-Dose Opioid Use

The results of the forward stepwise logistic regression analysis examining factors associated with prescriptions of high-dose of opioids are displayed in Table 5. After controlling for the effects of age, sex, and VA facility, diagnoses of neuropathy (OR = 1.95, 95% CI = 1.28 – 2.97), low back pain (OR = 1.88, 95% CI = 1.32 – 2.70), or nicotine disorder (OR = 1.36, 95%

CI = 1.00 – 1.86) were associated with increased likelihood of being prescribed high doses of opioids. Conversely, a diagnosis of hypertension (OR = 0.54, 95% CI = 0.39 – 0.75) was associated with a significantly decreased likelihood of being in the high-dose opioid group. No other variables were significantly associated with being prescribed high doses of opioids.

Discussion

High-dose opioid therapy was prescribed for 2–3% of veterans with chronic non-cancer pain who were prescribed opioids long-term. Patients in the high-dose opioid group were prescribed an average daily opioid dose of 325 mg per day morphine equivalent, a dose 10 times greater than that of patients in the traditional-dose opioid group. High-dose patients had pain intensity scores similar to patients in the traditional-dose group and significantly higher than patients in the no opioid group. Specific reasons why patients in the high-dose group had the highest pain intensity scores were not identified, but may be due to greater medical morbidity, increased tolerance to opioids, central sensitization, or to other factors not assessed (e.g., severity of illness).

In this study, certain demographic and clinical factors were associated with high-dose opioid use. Black patients were less likely to be in the high-dose group, a finding which is consistent with prior research indicating patients who are black receive fewer services for the treatment of chronic pain [36,38] and find pain treatment less effective [20]. Patients in the high-dose group were more likely to be diagnosed with four or more pain diagnoses, as well as a variety of medical, psychiatric, and substance use disorder diagnoses. These results are consistent with prior studies indicating that patients with chronic pain and comorbid psychiatric disorders are more likely to receive opioids than pain patients without comorbid psychopathology [7,48, 50], and extend prior literature by showing that these diagnoses are also associated with prescription of high opioid doses.

Results from the regression analysis identified several factors associated with being in the high-dose group relative to patients in the traditional-dose group. Significant results were found for certain pain diagnoses (neuropathy, low back pain) and nicotine dependence, which increased the likelihood of being prescribed high-doses of opioids. Contrary to our initial hypotheses, there were no statistically robust predictors of high-dose opioid use, as the significant odds ratios were all less than 2.0. The finding that a diagnosis of nicotine dependence was associated with an increased likelihood of receiving high doses of opioids is consistent with recent research which found that nicotine use predicted long-term opioid use among patients with painful spine conditions [29]. We also found that a diagnosis of hypertension was associated with a decreased likelihood of being in the high-dose group. While hypertension may be a marker for some other illness or treatment factor, previous literature has also documented a relationship between hypertension and pain sensitivity, showing a negative correlation between blood pressure and pain regulation [1,9,33].

Prior research indicates that opioid prescribing varies considerably by provider and that several factors inhibit prescription of opioid medications, including perceived regulatory scrutiny, knowledge gaps, concern about risk of dependence or addiction, and negative views about patients with chronic pain [39,41,54,55]. In a recent study of VA primary care providers, a large degree of variation in rates of prescribing opioids was associated with clinician panel size, job and resource satisfaction, and professional training [19]. Future research might also evaluate the relationship between opioid prescriber and opioid dose. In our study, we adjusted for practice variation using VA facility, though this variable was not significantly associated with prevalence of high-dose opioid prescriptions.

Guidelines have been published which provide recommendations for managing patients prescribed opioids for chronic non-cancer pain [2,3,13]. Although the primary purpose of the present study was not to evaluate the extent to which patients prescribed high doses of opioids received guideline-concordant care, some of our findings address these issues. Consistent with recommended guidelines was the small proportion of patients taking two or more short-acting opioids, which did not differ by group status (9.0% in the high-dose group versus 12.2% in traditional-dose group). Patients in the high-dose group were most likely to be prescribed a long-acting opioid; 96.9% in high-dose group versus 22.6% in the traditional-dose group. Patients in the high-dose group were more likely to be prescribed the combination of only one long-acting opioid and no short-acting opioids (23.2% versus 7.6%). Treatment recommendations generally support the use of long-acting opioids for chronic pain, though it has been suggested that this pattern of prescribing could also contribute to tolerance and possibly dose escalation [5].

Patients in the high-dose opioid group had the highest rates of alcohol or substance use disorders (36.6%). Although individuals with a substance use disorder should not necessarily be denied access to opioid therapy, this group is at greater risk for misuse of prescription medications and should receive more intensive structure and monitoring [13,35]. The overall rate of past-year administrations of urine drug screens was low, 39.9% in the entire sample, which did not differ by group status. Seventy-five percent of patients in the high-dose group were prescribed at least one short-acting opioid, and 9.4% were concurrently prescribed two or more short-acting opioids, rates which are higher than guideline-recommended care. Patients in the high-dose group had the highest rate of benzodiazepine prescriptions (32.0% versus 25.2% in traditional-dose group and 9.6% in no opioid group). The frequent use of short-acting opioids, high rates of sedative-hypnotic (benzodiazepine) prescribing, and relatively low rates of urine drug screen monitoring suggests that patients prescribed high doses of opioids may be at greater risk of not receiving guideline-level chronic pain care [13,46]. Other settings have identified a similar pattern of care among patients prescribed opioids for low back pain [17], suggesting these results are not unique to a specific geographical area or health system. More explicit opioid treatment guidelines regarding high-dose opioid use may be needed, as well as better system support to assist providers.

There are several limitations that are important to consider when reviewing the results from this study. Due to our research methodology, we were unable to identify reasons why these patients were prescribed high-dose opioid therapy or the effectiveness of treatment. Future studies using similar datasets may be able to assess the effectiveness of opioid therapy by tracking opioid dose and pain intensity (or pain-related function) scores over time. All data for this study were obtained from electronic medical records as part of standard clinical care. Medical and psychiatric diagnoses were not confirmed with laboratory data or via structured clinical interviews. Further, diagnoses were obtained over the past five years, and some disorders may have not been problematic at the time opioid use was assessed. This methodology provides a comprehensive assessment of medical comorbidity, but may not fully assess severity, which could be a better predictor of opioid dose. Participants included were veterans receiving medical care in the Pacific Northwest portion of the United States and results may not be generalizable to non-veterans or to veterans seeking care elsewhere. In addition, consistent with a general VA population, the majority of participants in our study were male, though chronic pain may be more common among women, and research suggests women may have different responses to opioid analgesia than men [23], further limiting the generalizability of our results. Our definition of chronic non-cancer pain was dependent upon having pain numeric rating scores ≥ 4 documented in the medical record in three separate months in 2008. This methodology is consistent with some prior research [25], but may skew our sample toward a cohort that utilizes medical services at a high rate and to patients with a moderate to high

degree of pain. Finally, we limited our examination to dose of opioid medication and did not assess other potentially relevant aspects of opioid exposure (e.g., duration).

Opioid medications are widely used in the management of chronic pain. Findings from this study indicate that two to three percent of patients with moderate to severe chronic non-cancer pain are prescribed high doses of opioids on a long-term basis and that certain clinical factors are associated with high-dose opioid use. Patients receiving high doses of opioids may not be receiving some aspects of guideline recommended care in that patients frequently receive short-acting opioids, there are high rates of sedative-hypnotic use, and relatively low rates of urine drug screen monitoring [13,46]. Additional empirical data are needed to replicate these findings, explore alternative factors that result in patients being prescribed high doses of opioids, and to assess the utility and safety of taking high doses of opioids.

Acknowledgments

This study was supported in part by award K23DA023467 from the National Institute on Drug Abuse to Dr. Morasco. Jonathan Duckart, MPS, was supported by a Research Enhancement Award Program grant from the VA Health Services Research and Development service. The authors appreciate assistance from Sharon Medley and for support provided from the Oregon Clinical and Translational Research Institute, grant number Ul1RR024140 from the National Center for Research Resources, a component of the National Institutes of Health and NIH Roadmap for Medical Research. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, National Institute on Drug Abuse, or the Department of Veterans Affairs.

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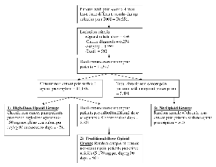

Figure 1.
Data Flow for Patients with Chronic Noncancer Pain on High Doses of Opioid Medications.

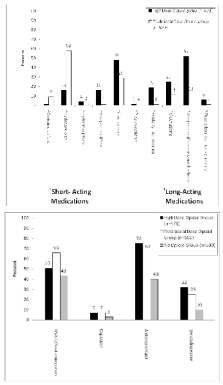

Figure 2. Proportions of Patients Prescribed Certain Medications

Panel A. Current Opioid Medications. Statistically significant differences occurred between the two groups in the proportion of patients prescribed each of these medications ($p < 0.05$). Panel B. Current Non-Opioid Medications. Statistically significant differences occurred among the three groups in the proportion of patients prescribed each of these medications ($p < 0.01$).

Table 1

Morphine Equivalent Conversion Factor.

Type of Opioid	Morphine equivalent conversion factor/mg of opioid
Codeine	0.17
Fentanyl Transdermal	3.6
Hydrocodone	1.0
Hydromorphone	4.0
Methadone	2.5
Morphine	1.0
Oxycodone	2.0
Propoxyphene	0.15

Note. The conversion factor for Transdermal Fentanyl assumes that one patch provides the dispensed micrograms per hour and remains affixed for three days.

Table 2

Comparison of Demographic Characteristics by Study Group.

	High-Dose Opioid Group (n=478)	**Traditional-Dose Opioid Group (n=500)**	**No opioid Group (n=500)**	**Test (df)**	***p*-value**
Average Daily Dose Morphine Equivalent (SD)	324.9 (285.1)	32.4 (20.1)	0	F (1, 977) = 523.4	< 0.001
Range, Median	180 – 5496, 273	5 – 128, 27.5	0		
Age	54.9 (10.7)	54.7 (12.5)	55.8 (14.2)	F (2, 1477) = .97	0.38
Body Mass Index	31.2 (7.7)	31.2 (6.9)	30.9 (6.8)	F (2, 1143) = .13	0.88
Male Gender	435 (91.0%)	461 (92.2%)	445 (89.0%)	χ^2 (2) = 3.1	0.21
Marital Status				χ^2 (8) = 13.9	0.09
Single/Never Married	39 (8.2%)	62 (12.4%)	59 (11.8%)		
Married	264 (55.2%)	236 (47.2%)	229 (45.8%)		
Separated/Divorced	142 (29.7%)	166 (33.2%)	173 (34.6%)		
Widow	17 (3.6%)	23 (4.6%)	26 (5.2%)		
Unknown	16 (3.3%)	13 (2.6%)	13 (2.6%)		
Race				χ^2 (6) = 20.2	0.03
Caucasian	365 (76.4%)	341 (68.2%)	346 (69.2%)		
Black	14 (2.9%)	43 (8.6%)	39 (7.8%)		
Other	13 (2.7%)	11 (2.2%)	19 (3.8%)		
Unknown or Declined to answer	86 (18.0%)	105 (21.0%)	96 (19.2%)		
VA Service-Connected	311 (65.1%)	327 (65.4%)	312 (62.4%)	χ^2 (2) = 1.2	0.56
Average Pain Score	6.7 (1.3)[a]	6.6 (1.3)[a]	6.2 (1.3)[b]	F (2, 1477) = 17.8	< 0.001

Note. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing.

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Table 3

Pain Diagnoses in the Past Five Years.

	High-Dose Opioid Group (n=478)	**Traditional-Dose Opioid Group (n=500)**	**No opioid Group (n=500)**	**Test (df)**	***p*-value**
Fibromyalgia	79 (16.5%)	55 (11.0%)	31 (6.2%)	χ^2 (2) = 26.3	< 0.001
Inflammatory	35 (7.3%)	22 (4.4%)	14 (2.8%)	χ^2 (2) = 11.2	0.004
Bowel Disease					
Low Back Pain	399 (83.5%)	371 (74.2%)	234 (46.8%)	χ^2 (2) = 164.5	< 0.001
Migraine Headache	102 (21.3%)	112 (22.4%)	72 (14.4%)	χ^2 (2) = 12.0	0.002
Neck or Joint Pain	392 (82.0%)	401 (80.2%)	315 (63.0%)	χ^2 (2) = 58.1	< 0.001
Neuropathy	86 (18.0%)	54 (10.8%)	56 (11.2%)	χ^2 (2) = 13.8	0.001
Rheumatism/ Arthritis	343 (71.8%)	321 (64.2%)	236 (47.2%)	χ^2 (2) = 65.4	< 0.001

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Table 4

Medical and Psychiatric Diagnoses in the Past Five Years.

	High-Dose Opioid Group (n=478)	Traditional-Dose Opioid Group (n=500)	No Opioid Group (n=500)	Test (df)	*p*-value
Medical Diagnoses					
Hypertension	298 (62.3%)	346 (69.2%)	292 (58.4%)	χ^2 (2) = 12.9	0.002
Congestive Heart Failure	59 (12.3%)	43 (8.6%)	32 (6.4%)	χ^2 (2) = 10.7	0.005
Myocardial Infarction	34 (7.1%)	32 (6.4%)	21 (4.2%)	χ^2 (2) = 4.1	0.13
Diabetes	151 (31.6%)	129 (25.8%)	133 (26.6%)	χ^2 (2) = 4.8	0.09
Sleep Apnea	97 (20.3%)	96 (19.2%)	82 (16.4%)	χ^2 (2) = 2.6	0.27
Cerebrovascular Disease	57 (11.9%)	51 (10.2%)	51 (10.2%)	χ^2 (2) = 1.0	0.61
Peripheral Vascular Disease	55 (11.5%)	45 (9.0%)	38 (7.6%)	χ^2 (2) = 4.5	0.11
Chronic Pulmonary Disease	176 (36.8%)	175 (35.0%)	146 (29.2%)	χ^2 (2) = 7.0	0.03
Paraplegia and/or Hemiplegia	26 (5.4%)	16 (3.2%)	11 (2.2%)	χ^2 (2) = 7.7	0.02
Psychiatric Diagnoses					
Major Depressive Disorder	320 (66.9%)	303 (60.6%)	200 (40.0%)	χ^2 (2) = 79.3	< 0.001
Dysthymic Disorder	87 (18.2%)	62 (12.4%)	50 (10.0%)	χ^2 (2) = 14.8	0.001
Bipolar Disorder	28 (5.9%)	45 (9.0%)	42 (8.4%)	χ^2 (2) = 3.8	0.15
Panic Disorder	33 (6.9%)	35 (7.0%)	15 (3.0%)	χ^2 (2) = 9.8	0.008
Posttraumatic Stress Disorder	179 (37.4%)	169 (33.8%)	134 (26.8%)	χ^2 (2) = 13.1	0.001
Other Anxiety Disorder	122 (25.5%)	122 (24.4%)	79 (15.8%)	χ^2 (2) = 16.4	< 0.001
Schizophrenia	13 (2.7%)	24 (4.8%)	18 (3.6%)	χ^2 (2) = 3.0	0.23

	High-Dose Opioid Group (n=478)	**Traditional-Dose Opioid Group (n=500)**	**No Opioid Group (n=500)**	**Test (df)**	***p*-value**
Any Sleep Disorder	103 (21.5%)	102 (20.4%)	64 (12.8%)	χ^2 (2) = 15.2	0.001
Any Alcohol or Substance Use Disorder	175 (36.6%)	165 (33.0%)	114 (22.8%)	χ^2 (2) = 23.8	< 0.001
Nicotine Disorder	172 (36.0%)	157 (31.4%)	99 (19.8%)	χ^2 (2) = 33.3	< 0.001
Past-Year Charlson Comorbidity Score, Mean (SD)	1.2 (1.6)[a]	1.0 (1.5)[a,b]	0.9 (1.4)[b]	*F* (2, 1477) = 5.2	0.006

Note. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing.

Table 5

Correlates of High-Dose Opioid Group (n=774).

	Beta (Standard Error)	Wald	*p*-value	Odds Ratio (95% Confidence Interval)
Age	−0.01 (.01)	1.30	0.25	0.99 (0.98 – 1.01)
Male Gender	−1.52 (.26)	0.33	0.56	0.86 (0.51 – 1.44)
VA Facility	0.01 (.01)	0.19	0.67	1.00 (0.99 – 1.00)
Neuropathy	0.67 (.21)	9.79	0.002	1.95 (1.28 – 2.97)
Low Back Pain	0.63 (.18)	11.98	0.001	1.88 (1.32 – 2.70)
Hypertension	−0.62 (.17)	13.35	<0.001	0.54 (0.39 – 0.75)
Nicotine Disorder	0.31 (.16)	4.00	0.048	1.36 (1.00 – 1.86)

Note. This analysis includes only those patients who had complete data and were currently prescribed at least one opioid medication. Variables that were potentially eligible to be included in the analysis, but ultimately were not included were: race, migraine headache, inflammatory bowel disease, neck or joint pain, fibromyalgia, congestive heart failure, chronic pulmonary disease, paraplegia and/or hemiplegia, major depressive disorder, dysthymic disorder, panic disorder, posttraumatic stress disorder, other anxiety disorder, any sleep disorder, any substance use disorder, Charlson Comorbidity Index score, number of pain diagnoses, and number of psychiatric diagnoses.