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CORRELATES OF HIGHER DOSE OPIOID MEDICATION USE FOR LOW BACK PAIN IN PRIMARY CARE

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Abstract

Factors associated with high-dose opioid therapy for non-cancer pain are poorly understood. We document the prevalence of high-dose opioid use, as well as associated demographic, clinical, and health service utilization correlates among low back pain patients. Patients prescribed higher-dose opioids (≥100 mg/day morphine equivalent at last dispensing; n=453) and receiving opioids for 90+ consecutive days were compared to two groups: lower-dose (1–99 mg/day; n=4,815) or no opioid use (n=10,184). Higher-dose opioid use occurred in 2.9% of patients who received any opioids and in 8.6% of patients who received opioids long-term. The median dose in the higher-

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dose group was 180.0 mg/day. Compared to the no opioid group, higher-dose users reported poorer health. Compared to either comparison group, patients in the higher-dose group had higher rates of mental health and substance use disorders, concurrent sedative-hypnotic use (60.5%; n=274), and health service utilization. After adjusting for select covariates, male gender (Odds ratio (OR) 1.68, 95%CI 1.37,2.06), higher comorbidity, Medicare coverage (OR 1.65, 95% CI 1.22,2.23), any mental health or substance use diagnosis (OR 1.58, 95% CI 1.28,1.95), co-prescriptions of sedative-hypnotics (OR 1.75, 95% CI 1.42,2.16), and more Emergency Department and specialty pain clinic visits were associated with higher likelihood of high-dose prescriptions.

Keywords

Chronic pain; Back pain; Opioids; Epidemiology; Pain/drug therapy

Introduction

Opioid prescribing for the treatment of chronic non-cancer pain (CNCP) in primary care has increased dramatically since the mid 1990s despite ongoing concerns surrounding effectiveness and safety.[3,6,19] This increase is mirrored by a parallel increase in the misuse, abuse and overdose of prescription opioids.[3] Thus, opioid prescribing requires a balancing act between potential benefits and risks.

Most patients receiving opioid therapy take low to moderate doses.[6] However, a substantial number are on higher-dose opioid therapy for CNCP.[19,23] Conventional wisdom suggests there is no absolute limit to opioid dose because development of tolerance varies among individuals, and there is no consensus on definitions of lower-dose versus higher-dose therapy. Rather, higher-dose opioid therapy is increasingly defined empirically based on elevated risks associated with certain doses. For example, daily doses of 100 mg or more morphine equivalents may be considered high-dose use because of the substantial risks for side effects, overdose and mortality associated with this dosage or higher.[3,6,11,17,26]

Evidence for the efficacy of high-dose opioid therapy for CNCP is sparse and mixed.[2,7] A three-year registry study found that only 5% of the 233 patients who were on more than 100 mg of oxycodone per day were able to achieve sustained analgesic benefit from opioid therapy.[25] In a study of patients with disabling musculoskeletal disorders, Kidner and colleagues[19] found that higher doses of opioids (greater than 61mg/day of morphine equivalents) predicted worse outcomes, including program non-completion, lower rates of return to work, and higher healthcare utilization.

Beyond uncertain efficacy, important safety concerns are associated with long-term opioid therapy, including side effects, addiction, misuse, and possible diversion. These harms may be more prominent for patients on high-dose opioid therapy. Prior research suggests that patients on higher-doses of opioids may experience unique side effects, such as endocrinologic abnormalities, arrhythmia (with methadone), and fracture risk.[8,9,21,26] Most troubling is the association of higher-doses with increased risk of overdose and death.[11,17] Morasco and colleagues[23] found that high-dose opioid therapy (180 mg of morphine-equivalent per day or greater) was associated with multiple pain diagnoses and high levels of other medical, mental health and substance use comorbidity in a sample of veterans in the Pacific Northwest.

Identifying the personal, clinical, and health service utilization characteristics of higher-dose opioid users may help to identify patients most likely to progress to higher-dose use and

suggest strategies for improving their care. We therefore sought to examine correlates of higher-dose opioid use among patients in a routine primary care setting, taking advantage of the large population and electronic records of an integrated health plan with mainly pre-paid insurance coverage. We focused on patients with back pain because it is common, a leading reason for opioid prescribing, often occurs in the absence of major systemic diseases, and provides a more homogenous sample than considering all pain conditions. Our goals were to: 1) determine the prevalence of higher-dose opioid prescribing, 2) identify the demographic and clinical characteristics of patients receiving higher-dose opioids, and 3) examine health service utilization patterns among higher-dose opioid users. We compared patients receiving more or less than 100 mg of morphine equivalents per day because this dose is associated with substantially increased risk of overdose and death.[11] We also compared opioid users with patients who had back pain but were not receiving opioids.

Methods

Our methods and patient population have been described elsewhere.[10] This study was conducted in the Kaiser Permanente Northwest (KPNW) region, a large, not-for-profit, integrated health care system. KPNW serves the Portland, Oregon and Vancouver, Washington metropolitan area. KPNW currently has an annual membership of about 470,000 people with demographic characteristics similar to the community it serves, and covers 17% of the metropolitan area.

Dispensed prescriptions are recorded through an automated outpatient pharmacy system. Based on patient surveys, an estimated 90 percent of prescriptions are filled at a program pharmacy.[28] While physicians may prescribe any marketed medication, KPNW has a formulary of recommended medications. Data from this system are linked to administrative and research databases with detailed information on the patient, clinician, and medication for each dispensed prescription. KPNW's data systems are accessible for research purposes. This study was approved by the Institutional Review Boards at the Kaiser Permanente Center for Health Research (KPCHR) and at Oregon Health & Science University (OHSU).

Patient Selection

Participants were adult ambulatory patients aged 18 and older. We made use of electronic medical and pharmacy data in a "virtual data warehouse" at KPCHR. To select patients with back pain, we chose as an index visit the first visit in 2004 with any one of 32 ICD-9 diagnoses associated with low back pain.[10] We used electronic pharmacy and medical record data for 6 months before and after the index visit. Because our focus was on patients with musculoskeletal back pain, we excluded patients with cancer, spinal infections, open fractures, or pregnancy.

Defining Opioid Dose Groups

We analyzed electronic pharmacy and medical record data for 6 months before and after the 2004 index visit, including data from 2003 and 2005. Participants were classified into one of three study groups based on their last prescription dispensed: pain patients not prescribed any opioids, those prescribed lower-doses of opioids (defined as 1 – 99 mg morphine equivalent per day), and those prescribed higher-doses of opioids (defined as ≥ 100 mg morphine equivalent per day). Because we were interested in long-term use of opioid medications, for both the lower and higher-dose groups, we selected patients who used opioids for greater than 90 consecutive days. These were patients who met the definition set by Von Korff et al[20] as "episodic" or "chronic" opioid use. Patients with short-term use (<90 days) were excluded for several reasons: (1) short-term use is less likely to be higher-dose use, (2) our focus was on long-term use rather than short duration or acute use because these

patients are less likely to suffer serious long-term consequences, (3) our goal was to generate data comparable to previous studies that have restricted samples to long-term, higher-dose users, and (4) we strove for straight forward interpretation of our analysis by dosage as we previously described opioid use by duration in a separate report. [10]

We considered use of any of the opioids listed by Von Korff et al.[20] and classified opioids as long or short acting based on their definitions. To calculate morphine-equivalents, each prescription was given a conversion factor to estimate the same milligram amount per day of morphine, and doses of multiple opioids were summed. Conversion factors were those of Von Korff and colleagues.[20]

Measures of Psychiatric Diagnoses, Comorbidity and Health Services Utilization

We assessed several patient characteristics, including demographics, medical and psychiatric comorbidity, and health behaviors (e.g., smoking, body mass index). We also measured several aspects of health services utilization, including co-prescription of sedative-hypnotics, emergency department (ED) visits, clinic visits, pain clinic visits, number of opioid providers, and hospital care.

Psychiatric diagnoses were based on medical record search for one year before the index visit for any coded ICD-9 diagnoses for depression (codes 296.2, 296.3, 300.4, 309.0, 309.1, 311); anxiety (codes 300.0 – 300.09); posttraumatic stress disorder (code 309.81); or substance use disorder (codes 303.xx, 304.xx, 305.xx). These diagnoses were based on clinician judgments as detailed in the electronic medical record.

Sedative-hypnotic drugs were those identified in the Medi-Span Generic Product Identifier[32] or the American Hospital Formulary Service drug information compendium with Benzodiazepines represented the largest group percentage.[1,14]

Comorbidity was measured using the RxRisk score. The RxRisk is a pharmacy-based risk assessment model designed to predict future health care costs based on patient age, sex, Medicare or Medicaid coverage, and use of drugs closely linked to specific chronic conditions (e.g., biguanides, insulins, sulfonylureas for diabetes).[15,16] It was developed in a managed care system with electronic records very similar to KPNW. A score is calculated from a regression model that weights each diagnosis according to its ability to predict future costs. The RxRisk calculation for adults excludes analgesics, because they are prescribed with too much discretion to be appropriate for a payment adjustment model.[16]

Statistical Analysis

We used the Wald Chi-square test for trend to compare proportions across ordered categories of opioid dose. For continuous data, which generally had skewed distributions, we used the Kruskall-Wallis nonparametric rank-sum test followed by post-hoc testing using the Wilcoxon. Significance levels for pairwise post-hoc tests were adjusted using a Bonferroni correction. Multivariate analysis used a backward elimination logistic regression to evaluate characteristics associated with prescriptions of higher-dose opioid medications adjusting for age and sex. The dependent variable was prescription for higher-dose (versus lower-dose) of opioids. Because our goal was to examine differences between patients prescribed lower- doses of opioids versus those prescribed higher-dose opioids, this analysis excluded patients who were not prescribed any opioid medications. Independent variables were eligible to be entered into Step 1 if they significantly differed between groups in the bivariate analysis ($p < 0.10$). Only participants for whom all variables were available were included in the multivariate analysis. All statistical analyses were performed in STATA Version 12 (Stata Corp, College Station, Texas).

Results

Patient Demographics

We identified 26,014 patients with a diagnosis of low back pain who met our eligibility criteria (Figure 1). Most patients with back pain (78%) received non-specific diagnoses such as “low back pain,” or “sprains and strains.” Another 12% had herniated discs, sciatica, degenerative discs, or spinal stenosis. The remainder received a variety of diagnoses (e.g. spondylolisthesis, closed vertebral fractures, post-surgical pain).

Among patients with a back pain diagnosis, 15,830 (61%) received at least one opioid prescription in the year surrounding the index visit, 2.9% of these patients received a higher-dose opioid prescription as their final prescription. Among patients receiving long-term opioids, 8.6% received a higher-dose opioid prescription as their final prescription. Patient demographic characteristics are reported in Table 1. The typical back pain patient was 50.3 years old (SD = 16.6), female (56.5%), and non-Hispanic white (89.3%). Average age did not differ between the lower versus higher-dose opioid users. Non-Hispanic white patients were overrepresented in the higher-dose opioid group compared to Black or Hispanic patients (data missing for race 31.3% and for ethnicity 48.4% of participants). A significantly higher proportion of women were represented in the lower-dose group than in the no-opioid group or higher-dose group. A significantly higher proportion of Medicare patients were in the higher-dose opioid group.

Health Behaviors, Psychiatric Characteristics, and Comorbidity

Patients in the higher-dose group had several indications of poorer health than patients in the lower-dose or no opioid groups (Table 2). Health behaviors, including obesity and smoking, were significantly associated with increasing opioid dose in a graded fashion. Among the higher-dose group, 52% had a Body Mass Index (BMI) ≥30 and 57% were recent or current smokers compared to 50% with a BMI ≥30 and 51% smokers in the lower-dose group. Psychiatric diagnoses also increased consistently with opioid dose, with patients in the higher-dose group having higher frequencies than other groups for depression (42%), anxiety (20%), post-traumatic stress disorder (PTSD; 4%), and substance use disorder (SUD; 31%) relative to the lower-dose group which had frequencies for depression (30%), anxiety (11%), PTSD (2%), and SUD (24%). Patients in the higher-dose group and lower-dose group also had significantly higher medical comorbidity scores compared to patients in the no-opioid group.

Medications and Health Services Utilization

Patients in the higher-dose group had a median daily opioid dose at last dispensing of 180.0 mg morphine equivalent per day (Interquartile range or IQR = 120 – 257.1; range = 100 – 2160) as noted in Table 3. Patients in the lower-dose group showed a median daily dose of 25.7 (IQR = 13.5 – 41.7) mg morphine equivalent per day (range = 1 - 98.6). Most patients in the higher-dose group were prescribed long-acting opioid medications (88%). Greater sedative-hypnotic use was associated with greater opioid dose in a graded fashion with patients in the higher-dose group showing the highest use (61%).

Visits to the ER increased steadily with opioid dose, with half the patients in the higher-dose opioid group having an ER visit during the study period; about a third of these were associated with a back pain diagnosis. Patients in the higher-dose group had a higher proportion of filling an opioid prescription within five days following an ER visit (63%) compared to patients in the lower-dose group (56%), though this difference was not statistically significant.

Patients in the higher-dose group also had the greatest number of clinic visits within the study year, with a median number of 22 compared to 8 for those in the no-opioid group, and intermediate for the lower-dose group. Most patients were not concurrently seen in a specialty pain clinic, but relative to those in the lower-dose group (11%), patients in the higher-dose group were twice as likely to attend the pain clinic (23%; $p = <.001$). Across the dose groups, few hospitalizations occurred; however, patients in the higher-dose group had the highest mean frequency. The number of different prescribers increased with dose, with higher-dose patients having the highest number (Table 3).

Independent Correlates of High Dose Opioid Use

In logistic regressions, after adjusting for age and sex, several characteristics remained independently associated with higher-dose opioid use (Table 4). These included male gender (OR = 1.68, 95% CI = 1.37 – 2.06), higher comorbidity scores (OR = 1.20; 95% CI = 1.06 – 1.37), having Medicare insurance (OR = 1.65, 95% CI = 1.22 – 2.23), any 1 of the 4 mental health diagnoses (OR = 1.58, 95% CI = 1.28 – 1.95), co-prescriptions of sedative-hypnotics (OR = 1.75, 95% CI = 1.42 – 2.16), having an ED visit (OR = 1.29, 95% CI = 1.05 – 1.58), and pain clinic visits (OR = 2.30, 95% CI = 1.80 – 2.94). The discrimination index (C, measured as area under the receiver operating characteristic curve) was 0.67 (95% CI: 0.65 – 0.70) with the final model showing no evidence of a lack of fit (χ^2 (8df) = 6.72, $p = 0.57$; Hosmer – Lemeshow lack of fit test).

Discussion

High-dose opioid therapy was prescribed to over eight percent of patients with low back pain who received long-term opioids. Patients receiving higher-dose opioid therapy were prescribed a median daily opioid dose of 180 mg per day morphine equivalent at their last dispensing, a dose seven times greater than the average of patients receiving lower-dose opioids. The prevalence of higher-dose use in our study is similar to the prevalence found in a sample of veterans (8.2%),[23] suggesting that this pattern of prescribing is not unusual.

High-dose opioid therapy was characterized by certain demographic, clinical, and utilization features. However, the strength of these independent predictors to discriminate individual higher-dose users from lower-dose users was modest, suggesting that predicting individual risk for higher-dose use will require studies with greater individual detail. Being male, white, and having Medicare were significantly associated with higher-dose use. Our finding that Black patients were less likely to be in the higher-dose group is consistent with previous research indicating that Black patients are less likely to receive opioids for pain treatment compared to white patients.[23,24] However, whether receiving less opioids for chronic pain treatment reflects better or worse care is unclear.

Our results are consistent with studies suggesting that chronic pain patients with comorbid psychiatric diagnoses are more likely to be prescribed opioids compared to patients without psychiatric diagnoses.[4,12,27,31] Moreover, our findings are consistent with reports that chronic pain patients with co-morbid psychiatric diagnoses tend to receive higher-dose opioid prescriptions.[4,23,,27] Thus, not only is long-term opioid therapy more common among patients with psychiatric disorders, but they also tend to receive higher doses. Patients with mental health and substance use disorders are routinely excluded from clinical trials of opioid medication efficacy,[13,18] yet, these patients clearly suffer from pain indications. Our findings suggest an acute need for inclusion of these patients in clinical trials of pain therapy to help guide prescribing and use of opioids in this population.

Though we cannot identify the reasons for greater use of long-term higher-dose opioids among patients with comorbid psychopathology, there are plausible explanations. We have

found that the prevalence of mental health diagnoses increases with increasing duration of opioid use (from acute to chronic), and not just beyond some threshold of duration.[10] In sequential surveys, depression and anxiety at the first survey were associated with greater likelihood of opioid initiation and continuation at the second survey 3 years later.[31] Kroenke recently demonstrated a bi-directional relationship between depression and persistent pain, suggesting that depression and pain have a potentially causative influence on one another.[22] Thus, depression may lead to more opioid use (prevalence and dose), opioid use may cause or exacerbate depression, or both may be true. Our results support the need for providers to carefully screen opioid therapy candidates for mental health and substance use disorders and either treat or refer them for specialty mental health care. The hope is to avoid Sullivan's concept of "adverse selection:" pairing higher-dose therapy with high-risk patients.[29]

Most patients prescribed higher-dose opioids received long-acting opioids (88%) rather than short-acting opioids alone, consistent with some expert recommendations. In contrast, the higher rate of concurrent sedative-hypnotic prescriptions associated with higher-dose opioid use (61% vs. 42% in the lower-dose and 10% in the no opioid group) we observed is contrary to most recommendations and presents potential safety risks.[11] We previously reported a 44% rate of sedative hypnotic use (mostly benzodiazepines) in long-term opioid users.[10] The 61% rate among long-term higher-dose patients may represent an opportunity for improving prescribing, as this is a particularly high-risk group for overdose.

Since these data were collected, Kaiser Permanente Northwest has implemented risk mitigation strategies with the goal of improving the safety of opioid prescribing for pain. For example, clinicians now stratify patients receiving opioids according to their level of risk for misuse and safety depending on their clinical profiles (i.e., current or past history of substance use disorder, opioid dosage, poly-prescriptions, etc.) and tailor follow-up frequency accordingly. Providers could consider other strategies, such as setting and enforcing a maximum recommended daily dosage, requiring urine drug screens, and use of electronic records to identify patients who are receiving opioid medications and risky co-prescriptions.[33] Efforts could also be made to reduce dosages for patients already receiving higher-doses; for example, optimizing use of non-opioid medications, and making referrals to specialty mental health, chiropractic and acupuncture treatment.

Patients in the higher-dose group were high utilizers of medical services overall. If patients are on long-term higher-dose opioid therapy, it is reasonable to expect higher utilization attributable to medication refills, in addition to possible mental health visits and management of comorbid conditions. However, the greater emergency department use among higher-dose opioid users suggests that greater utilization is not strictly explained by scheduled visits.

Higher-dose patients had the highest number of different opioid prescribers. This may be an inevitable consequence of long-term higher-dose opioid therapy, requiring providers to be available for medication refills, and increasing the primary care burden. However, it may also suggest continuity of care problems, potential "doctor-shopping," or more uncontrolled pain.

Strengths of our study include a large study population, use of electronic records, and nearly complete capture of health care utilization. However, there are some important limitations. Though our study population was representative of the racial and ethnic composition of the Portland, Oregon, metropolitan area, our results may not be generalizable to regions with higher concentrations of minority populations. Most of our study population had commercial health insurance. Thus, our findings may not necessarily be generalizable to more socio-economically disadvantaged populations.

While we focused on patients with a known back pain diagnosis, we do not know whether this was the reason for being prescribed higher dose opioid therapy, particularly given high levels of co-morbidity. We also do not know the relative effectiveness of higher-dose treatment, as we did not have measures of pain severity or functional outcomes. We were reliant on clinician diagnoses of mental health disorders rather than standardized measures, limiting comparisons with other studies. Although we found several factors associated with higher-dose opioid prescribing, given our design, we cannot infer causation or the direction of causality.

In conclusion, we found that over eight percent of patients with low back pain were prescribed higher-dose opioid therapy on a long-term basis. Patients on higher-dose opioid therapy were characterized by higher rates of psychiatric comorbidity, co-prescriptions of sedative hypnotics, and higher health service utilization. Further research is needed to ascertain the balance of benefits and harms of long-term higher-dose opioid therapy for chronic non-cancer pain, as well as factors that lead to the progression of higher-dose use.

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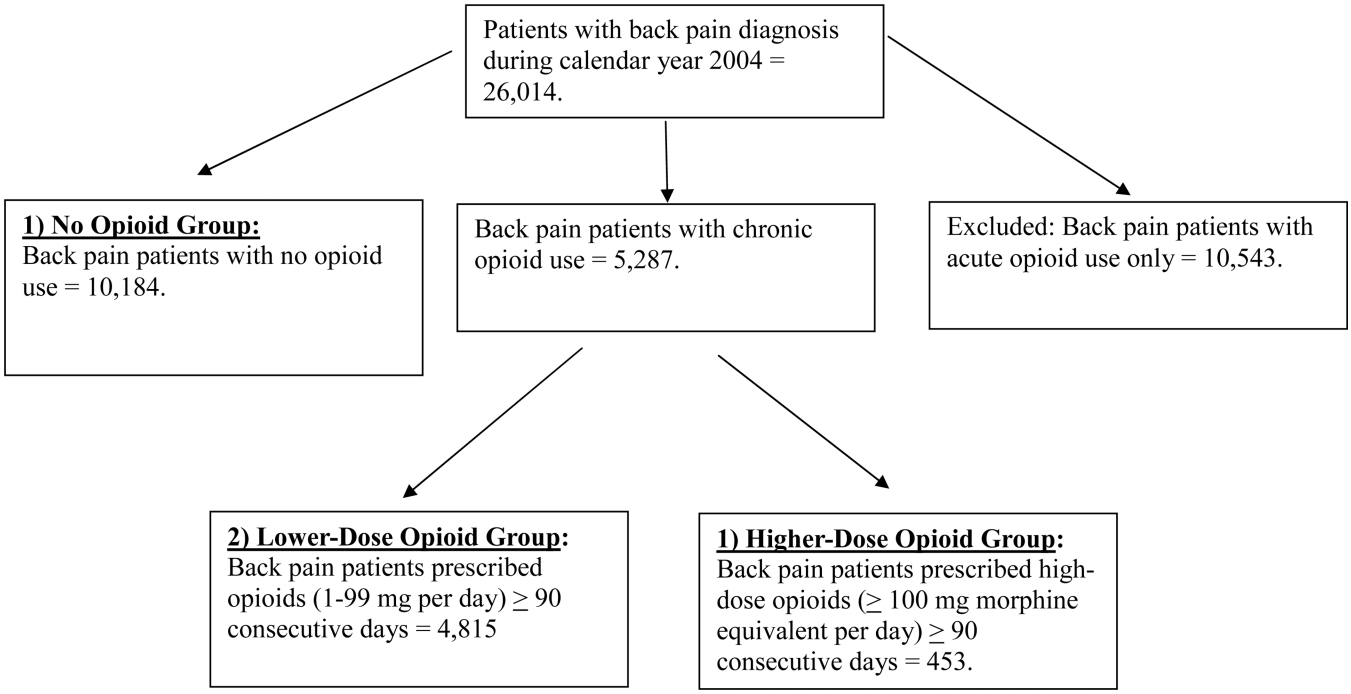

Figure 1.

Data Flow for Back Pain Patients on Higher Doses of Opioid Medications.

Note. 5,287 patients were initially identified as having a long-term episode of opioid use based on pharmacy record; however, for 19 of these patients dose level was not recorded in the pharmacy record, resulting in a total sample of 5,268 (4,815 + 453) for patients on lower and higher-dose opioids.

Table 1

Comparison of Demographic Characteristics by Opioid Dose Group

	No Opioid Group (n=10,184)	Lower-Dose Opioid Group (n=4,815)	Higher-Dose Opioid Group (n=453)	Test (df)	*p*-value
Age, mean (SD) *	49.1 (16.7)[a]	54.7 (15.5)[b]	54.7 (15.0)[b]	χ^2 (2, 15452) = 352.8	< 0.001
Female Gender †, %	54.3[a]	63.3[b]	55.6[ac]	χ^2 (1) = 72.9	< 0.001
Race ‡ (%)					
Caucasian	5,673 (55.7)	3,614 (75.1)	362 (79.9)		
Black	143 (1.4)	134 (2.8)	7 (1.6)		
Native American/Alaskan Native	71 (0.7)	49 (1.0)	9 (2.0)		
Asian Pacific Islander	256 (2.5)	40 (0.8)	4 (0.9)		
Other	270 (2.7)	99 (2.1)	7 (1.6)		
Unknown/Declined to answer	3,771 (37.0)	879 (18.3)	64 (14.1)		
Hispanic Ethnicity †,§	259 (5.2)[a]	93 (3.2)[b]	5 (1.8)[ab]	χ^2 (1) = 22.9	< 0.001
Medicaid †, %	3 (0.03)[a]	3 (0.06)[b]	1 (0.22)[c]	χ^2 (0) = 2.7	0.14
Medicare †, %	1,816 (17.8)[a]	1,352 (28.l)[ab]	154 (34.0)[ab]	χ^2 (1) = 237.4	<0.001

*Kruskal-Wallis non-parametric test was used for continuous variables followed by Wilcoxan post-hoc testing. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing and adjusted with a Bonferroni correction.

†Wald Chi-Square test for trend was used for categorical variables. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing and adjusted with a Bonferroni correction.

‡Race data were missing for 8,145 or 31.3% of participants.

§Ethnicity data were missing for 12,579 or 48.4% of participants.

Table 2

Health Behaviors, Psychiatric Characteristics, and Comorbidity by Opioid Dose Group

	No- Opioid Group (n=10,184)	Lower-Dose Opioid Group (n=4,815)	Higher-Dose Opioid Group (n=453)	Test (df)	*p*-value
Health Behaviors					
BMI ≥ 30*, %	36.8[a]	49.6[b]	51.9[b]	χ^2 (1) = 216.8	<0.001
Smoker*, %	37.4[a]	51.7[b]	56.6[b]	χ^2 (1) = 280.6	<0.001
Psychiatric Diagnoses					
Depression Diagnosis*, %	12.2[a]	29.6[b]	41.9[c]	χ^2 (1) = 750.0	< 0.001
Anxiety Diagnosis*, %	4.41[a]	10.6[b]	19.7[c]	χ^2 (1) = 293.2	< 0.001
PTSD Diagnosis*, %	0.53[a]	2.0[b]	4.4[b]	χ^2 (1) = 98.3	< 0.001
Substance Use Disorder diagnosis*, %	9.29[a]	23.9[b]	31.1[c]	χ^2 (1) = 601.4	< 0.001
Any of the 4 mental health diagnoses*, %	21.5[a]	47.0[b]	61.8[c]	χ^2 (1) = 1101.4	< 0.001
Median Comorbidity score – RxRisk, (IQR)†	658.1[a] (520 – 1205)	895.9[b] (653– 1432)	895.9[b] (653 – 2115)	χ^2 (2) = 190.4	< 0.001

*Wald Chi-Square test for trend was used for categorical variables. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing and adjusted with a Bonferroni correction.

†Kruskal-Wallis non-parametric test was used for continuous variables followed by Wilcoxon post-hoc testing. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing and adjusted with a Bonferroni correction.

Table 3

Medications and Health Services Utilization by Opioid Dose Group

	No- Opioid Group (n=10,184)	Lower-Dose Opioid Group (n=4,815)	Higher-Dose Opioid Group (n=453)	Test (df)	*p*-value
Medications or Type of Health Service Used					
Median daily dose at last dispensing, morphine equivalent (IQR) †	NA*	25.7 (13.5 – 41.7)	180 (120 – 257.1)	χ^2 (1, 5268) = 1241.9	< 0.001
Range	NA*	1 – 98.6	100 – 2160	χ^2 (1, 5268) = 237.4	<0.001
Long-acting Opioids‡, %	NA*	34	88.4	χ^2 (1, 5268) = 510.6	<0.001
Median opioid prescribers†	NA*	3	4	χ^2 (1, 5268) = 30.3	<0.001
Sedative-hypnotic Rx 6- mos. before/after index visit‡, %	10.0[a]	42.0[b]	60.5[c]	χ^2 (1, 15452) = 1917.0	<0.001
ER visit 6 mos. before/after index date‡, %	16.9[a]	38.8[b]	49.7[c]	χ^2 (1, 15452) = 895.6	<0.001
ER visit with back pain diagnosis‡, % of patients with any ER visit	23.5[a]	27.8[b]	28.9[ab]	χ^2 (1, 3816) = 9.08	<0.005
Filled opioid rx after ER visit‡, % of patients with any ER visit	0.1[a]	55.5[b]	62.7[b]	χ^2 (1, 15452) = 681.7	<0.001
Median clinic visits of any type 6-mos before/after index date†	8[a]	17[b]	22[c]	χ^2 (2, 15397) = 2715.4	<0.001
Any pain clinic visit 6 mos. before/after index date‡, %	0.97[a]	10.5[b]	22.7[c]	χ^2 (1, 15452) = 787.4	<0.001
Mean hospitalizations 6 mos. before/after index date†, (SD)	1.3 (0.73)[a]	1.5 (1.1)[b]	1.9 (1.3)[c]	χ^2 (2, 1460) = 21.515	<0.001

*Not applicable. This category not included in tests of statistical significance.

†Kruskal-Wallis non-parametric test was used for continuous variables followed by Wilcoxan post-hoc testing. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing and adjusted with a Bonferroni correction.

‡Wald Chi-Square test for trend was used for categorical variables. Scores with different superscripts differed significantly ($p < 0.05$) in post-hoc testing and adjusted with a Bonferroni correction.

Table 4

Associations with Higher-Dose Opioid Prescribing Compared to Lower-Dose Opioid Prescribing in Logistic Regression Analysis (n = 5,268)

	Adjusted Odds Ratio	*P* Value	95% Confidence Interval
Male gender	1.68	< 0.001	1.37 – 2.06
Age	0.95	0.03	0.90 – 1.00
Comorbidity score (RxRisk)	1.20	0.005	1.06 – 1.37
Medicare	1.65	0.001	1.22 – 2.23
Any 1 of 4 mental health diagnoses	1.58	< 0.001	1.28 – 1.95
Co-prescription of sedative-hypnotics	1.75	< 0.001	1.42 – 2.16
ED visit	1.29	0.013	1.05 – 1.58
Pain clinic	2.30	< 0.001	1.80 – 2.94

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: BMI ≥ 30, smoker, depression diagnosis, anxiety/PTSD diagnosis, substance use disorder diagnosis, receipt of opioid rx at ED visit, clinic visits, hospitalization, and number of opioid prescribers. Comorbidity score measured in quartiles.