Type of Pain and Its Effect on Sustained Use of Opioid Prescriptions Among Adolescent Patients

By
Maura Olcese

THESIS

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ABSTRACT

Introduction: The rate of prescription opioids for adolescent patients is increasing. Initial exposure to opioids is most commonly from prescriptions and the increasing rate of opioid misuse is linked to prescription exposure. There are limited recommendations on indications for opioid use among adolescents.

Methods: This is a retrospective cohort study using electronic health records at Oregon Health and Science University. Among patients 14-19 years old who received an opioid prescription from the emergency department or ambulatory settings in 2014, we compared those receiving opioids for musculoskeletal (n=379) versus non-musculoskeletal pain (n=478) types. We used a multivariate logistic regression model to examine the change in estimates of risk of sustained opioid use, defined as a new prescription within 1 month to 12 months after study visit, after adjusting for other covariates of interest.

Results: There was no association between pain type and sustained opioid use. When adjusting for medical history, there is an association that is then attenuated after adjusting for quantity of take-home prescription. There is an increased odds of sustained opioid use with increasing quantities of take-home prescription, regardless of pain type or self-reported pain intensity score.

Conclusion: Pain type is not associated with an increased odds sustained opioid use, but quantity of take-home prescription is. Given opioid misuse is linked to prescription exposure, limiting the amount of opioids available at home may help. There is a role for better physician patient communication surrounding opioid prescriptions and tailoring discussion and follow-up appointments around known risk factors.

INTRODUCTION

Current opioid recommendations.

Opioid medications are widely accepted for the relief of acute, self-limited pain in adults.[1] Opioids play a crucial role in the management of visceral and neuropathic pain in oncology patients. With intensive assessment and close follow-up, opioid prescriptions are also used for chronic, non-cancer pain and facilitated through a management plan between the adult patient and physician. However, opioid use has many side effects, not limited to misuse and abuse, and there is limited support for detailed indications as to when to initiate their use, appropriate duration for use, and patient age. Specifically, evidence regarding benefits and harms of long-term opioid use in pediatric patients is sparse.

Opioid prescriptions in the United States.

Chronic opioid use and opioid dependence have become major public health issues for the United States as seen by the increasing prevalence of opioid abuse over the past decades. In fact, unintentional opioid overdoses now surpass motor vehicle accidents as the leading cause of injury-related death in US.[2] The majority of opioid use comes from prescription medication and physician prescription practices have been found to be one of the contributors.[3] The increasing rates of opioid abuse in adults is well researched, with Emergency Department visits for opioid abuse doubling in recent years and a 400% increase in substance abuse treatment programs.[3] Additionally, of those patients presenting to their doctor with non-cancer pain (NCP), an estimated 20% leave with an opioid prescription.[4] Prediction tools for adult opioid abuse are emerging, but less is known about risk factors for opioid abuse in the adolescent population.[5] Opioid analgesics are important prescriptions in the treatment of acute pain from injury or illness. While their effectiveness for short-term pain control has been demonstrated, there is limited data on the effectiveness of long-term opioid use for controlling chronic pain.

Adolescent opioid prescription rate is increasing.

Controlled medications are prescribed at an increasing rate in the adolescent population as well, with opioids now becoming the most commonly prescribed controlled substance for adolescents.[6] [7] In fact, the rate at which opioids are prescribed to adolescents has doubled between 1994 and 2007.[7] According to the CDC, 2 million Americans over the age of 12 either abused or were dependent on opioids in 2013 and studies estimate that 1 in 4 high school seniors in the US have had some exposure to prescription opioids either medically or non-medically.[7] Despite indications, a large proportion of adolescents are given opioid prescriptions for conditions such as headache and sports-related injuries.[8] In fact, it has been reported that 50% of adolescents seen for a headache receive an opioid.[9] Further, a cross-sectional study among adolescents in the United States found that among adolescents who had received an opioid prescription for medical reasons, 22% of them reported misuse of that prescription.[10] Adolescents who misuse opioid medications often misuse medications from their own previous prescriptions and in fact, 80% of high school students reporting misuse stated the prescription initially prescribed by a physician.[11] [12] [13]Of more concern, 2.6 of 100,000 persons between 15 and 24 years old die of overdoses related to prescription opioids.[1] Specifically among teens, a study investigating illicit drug use found that opioids account for 97% of the significant morbidity and 100% of the deaths.[14] Opioid prescriptions constitute a significant amount of prescriptions made for adolescents for both injury and non-injury-related visits.[3] There is some evidence to show that early misuse of opioids is associated with later addition. For example, the

use of prescribed opioid pain medications before graduating high school is associated with a 33% increase in the risk of future opioid use and that the misuse of opioid medications in these years predicts future heroin use.[15] [16] It has been found that those who abuse prescriptions are more likely to abuse other substances, but research focusing on predictive characteristics is limited.[17] Adolescents and young adults are more likely to sustain use of opioids compared to older adults.[18]

Mental health disorders are associated with increased risk of opioid abuse.

The risk of opioid abuse among individuals with mental health disorders has been demonstrated thoroughly in research studying both adult and adolescent populations. Individuals with a mental health disorder are not only at a higher risk of experiencing sustained opioid use but also with receiving an opioid prescription in the first place compared to individuals without a mental health disorder.[19] [20] [21] Additionally, adults reporting opioid abuse were more likely to report poor health, anxiety, depression, and other substance abuse.[22] In a cohort study of adults who underwent minor surgical procedures, pre-surgical depressive symptoms were predictive of having sustained 6-month opioid use.[23] Preoperative pain level and anxiety also predict higher post-operative pain.[24]

Prescription of opioids among adolescents with non-cancer pain (NCP) is common, and the prescription rate is higher among adolescents with multiple pain conditions and comorbid mental health disorders.[8] Specifically, a diagnosis of major depressive disorder (MDD) is associated with opioid use, abuse, and dependence among adolescents.[25] In a prospective cohort study investigating predictors of sustained opioid use up to 1 year after an acute injury and trauma admission, it was found that among 120 adolescents, the 12.5% who reported sustained use at 1 year also had an increased likelihood of pre-injury marijuana use and higher baseline pain scores.[26] In the outpatient setting as well, adolescents with mental health diagnoses have increased risk of sustained opioid use, defined as continued use at 1 year, compared with those without a mental health diagnosis.[8] Similar results have been shown among patients with a chronic pain diagnosis, panic attacks, trait anxiety, and the presence of a personality disorder.[27] [28]

Opioid use differs across sociodemographic variables.

In the adult population, the literature demonstrates racial and ethnic differences in sustained opioid use and abuse. In a retrospective cohort study, African Americans were half as likely to initiate extramedical opioid use compared to white individuals; and Hispanics who initiated opioids extramedically were more likely to sustain use compared to whites.[17] Further, while mental illness has been shown to be a risk factor for opioid misuse, the same association has not been shown among African American individuals specifically.[29] Whether these differences are due to differences in prescribing practices remains unclear. Recently, it has been found that physicians prescribe opioid analgesics to African American patients less frequently than age- and injury-matched white patients.[28] Other research shows that adolescents from rural/small urban environments are more likely to misuse opioid prescriptions than those from large urban environments.[30] In adolescents (12-17 years old, female gender, lower socioeconomic status, and unstable social support have also been found to be predictive of nonmedical abuse of opioid prescriptions.[31] Whether differences can be wholly attributed to prescribing practices, sociodemographic differences appear to exist among opioid users and non-users.

Opioids are frequently received from the Emergency Department.

Injury is the leading cause for Emergency Department (ED) visits among adolescents.[2] However, adolescents increasingly rely on the ED for non-injury-related pain and non-acute issues, probably due to decreased reliance on primary care among adolescents.[32] In a retrospective cohort analysis comparing patients with acute pain who received opioids with those who did not, those with a prescription had higher healthcare utilization and were more likely to receive the first prescription from the ED.[33] However, for adolescents specifically, the risk of recurrent opioid use after ED prescription remains unknown.[2]

Type of pain and risk of opioid misuse.

Some professional associations, like the American Academy of Family Physicians, recommend that opioids not be used for central or visceral pains such as fibromyalgia, headaches, or abdominal pain.[34] Given these prescription recommendations, physicians may be less comfortable prescribing opioid medications for non-injury pain, possibly delaying pain management in these patients. However, studies point to the effectiveness of opioids in the relief of visceral pain.[35] In the adolescent population, while opioids are prescribed for both injury and non-injury pain presentations, it is unclear whether the type of pain carries a different risk for sustained use or misuse. Visceral and non-injury pain, by nature, can be poorly defined and difficult to diagnose. Moreover, visceral pain, notably abdominal pain, migraines, and fibromyalgia, are often associated with a mental health diagnosis.[36] [37] Therefore, while the risk of misuse may be confounded by other factors associated with non-injury pain, the risk associated with different pain presentations requires further study.

Sustained opioid use is associated with opioid misuse, abuse, and addiction.

Sustained opioid use and its association with misuse and dependence have been reported repeatedly in the literature.[11] [16] [17] [38] Even having a history of a prescription opioid medication increases the risk of opioid use disorder and overdose.[37] [39] Further, opioid misuse is associated with overdose, death, development of chronic pain syndrome, recurrent prescriptions, and sustained use.[2] [7] Less is known about individual characteristics predictive of sustained opioid use. It has been found that the average time from opioid prescription to abuse is less than one year.[32] In a recent study of patients 15-64 years old prescribed opioids for non-cancer pain, it was found that one in 550 patients died from an opioid-related overdose at a median of 2.6 years from their first opioid prescription and one in 32 patients whose prescription was increased to a dose >200 morphine milligram equivalents (MME) died from an opioid-related overdose.[40] Therefore, many investigators have used this as a crucial window in studying subsequent use.[25] [41] In a retrospective cohort study among "opioid naïve" adults who underwent a minor (short-stay) surgery, adults who received a subsequent opioid prescription within a week of hospital discharge were 44% more likely to be using opioids one year later compared to those who did not receive a subsequent opioid prescription after same surgery.[40]

The EHR can be used to assess risk.

With the advent of the electronic health record (EHR), patients and physicians have access to massive amounts of information. This information, in turn, can help clinicians make more informed clinical decisions about their patients and unique follow-up needs. Many studies assessing opioid prescribing practices come from EHR databases. However, modeling risk is dependent on whether information is available and accessible in the electronic record. In

assessing documentation, it has been found that the EHR identifies aberrant drug use behaviors with sensitivity, but not prescription drug misuse behaviors, among primary care patients.[42] Additionally, while the accuracy of self-reported pain severity scores are heavily debated, they are documented in only 23% of EHR's in the United States.[43] Given the association between pain and risk for opioid misuse, this is a significant limitation in EHR documentation.

This project seeks to close gaps in knowledge surrounding adolescent opioid use in the context of an increasing trend in prescriptions and its relationship to misuse. Specifically, this study aims to explore the role of presenting pain type and the risk associated with sustained opioid use among adolescents. Recognizing and understanding pre-injury risk factors for sustained prescription opioid use with different presenting pain types could help physicians identify and intervene for those patients at higher risk and cater to specific conversations and needs.

STUDY SUBJECTS AND METHODS

Study design

This is a retrospective cohort study comparing frequencies of sustained opioid use between adolescents presenting with musculoskeletal and those with non-musculoskeletal pain types. Musculoskeletal pain is defined as muscle and bone pain such as, for example, sprains, strains, fractures, back pain and arthritis.

Study population and Data Source

We used a database compiled from electronic medical records of all adolescent patients who received an opioid prescription from Oregon Health and Science University (OHSU) Emergency Department and ambulatory clinic settings. In compiling this database, we used OHSU's Oregon Clinical and Translational Research Institute's (OCTRI) Research Data Warehouse (RDW) tool - a repository of electronic health record (EPIC) data providing patient medical record numbers and clinical data. Using RDW, we identified all patients 14 to 19 years old who received an opioid prescription (any narcotic analgesic) in the outpatient setting at OHSU (includes Emergency Department and any Ambulatory general or specialty clinic). See Figure 1. Patients with an active diagnosis of cancer or blood disorder were excluded from the search given that opioids are a part of routine management in these patients. Subjects for whom an opioid prescription was made in the inpatient setting were also excluded, including patients admitted directly from the emergency room or ambulatory clinic, under the assumption that these patients have a higher clinical severity, and consequently require more intensive pain management plans, than patients seen in the outpatient or discharged home from the ED.

Chart Review

RDW identified patients' MRNs and provided demographic data. The remainder of the database was confirmed for eligibility and compiled using chart review with OHSU's EHR EPIC. Variables pertaining to pain presentation itself were collected from the body of the EHR physician note on date of presentation. Variables relating to patient medical history and medications were also collected from the body of the physician note (usually manually entered or auto populated from patient's medical history). Details confirming opioid received, prescription method, and quantity on date of presentation were collected in the physician note and confirmed in "Medication History" tab on EHR. To collect our outcome variable, sustained opioid use,

"Medication History" tab was reviewed for subsequent opioid prescriptions and we accessed outside local records using "Care Everywhere" physician notes available in the Epic system.

Measurements

Primary Exposure

The primary exposure was type of presenting pain/reason for visit. This was defined as a dichotomous variable for musculoskeletal pain or non-musculoskeletal pain. Previous literature describing adolescent opioid prescriptions differentiates pain type along these definitions.[44 45] Presenting pain type was identified using RDW and confirmed with chart review.

Primary Outcome

The primary outcome was sustained opioid use, a dichotomous variable defined as a new opioid prescription received between 1 month and 12 months from the date of initial clinical encounter for pain type.[25] Delaying the outcome variable at 1 month accounts for subsequent prescriptions made immediately after visit encounter. Given that all patients were treated in the ED and outpatient setting, a new prescription at any point during this time window would qualify as sustained use. This outcome variable was confirmed through EPIC medication history and through Care Everywhere current medications and historical provider notes.

Patient demographics and Medical History as covariates

Patient demographics included age, gender, race, ethnicity, whether the patient has a primary care provider, and insurance type.[17] Patient medical history at the time of pain type encounter included number of ED visits in the year prior, presence of a mental health disorder or prescription for a mental health disorder, presence of ADHD, and history of a chronic pain diagnosis.[18 19 20]

Characteristics of Pain Presentation

Covariates related to patient pain presentation/reason for visit included prescribing department, acute or chronic (> 3 months according to the CDC) timeframe of pain presentation, whether the opioid prescription was a result of a surgery, and self-reported pain severity score.[1] Pain intensity score was that recorded in the patient's EHR at the time of initial clinical encounter on a scale of 0-10.[25]

Characteristics of Opioid Prescription Received

Characteristics of the opioid prescription patients receive at the time of presentation included whether the opioid was received in the ED, if the patient was given as take-home prescription, and the quantity of any take-home prescription.

Statistical Analysis

Statistical analysis

Categorical variables were reported using both absolute and relative frequencies. Differences between categorical variables were reported using chi-square testing and continuous variables were reported using means and standard deviations with two-sample t-testing. A continuous variable that was not normally distributed - quantity of take-home prescription - was categorized into precise levels according to frequency to minimize potential confounding.

Univariate and multivariate logistic regression were used to determine if a possible association exists between reason for visit and sustained opioid use at 1 year. Variables of interest were added to the model by purposeful selection, assessing the change in estimate of odds ratios of our primary exposure with each adjustment. Variables of interest initially included from the univariate analysis into the multivariable model were added in a step-wise approach beginning with characteristics of the presentation (timeframe and surgery), then medical history (history of mental health diagnosis, history of pain diagnosis, history of ADHD, and history of ED visits in the year prior), then sociodemographic variables (age, gender, race), and finally characteristics about the prescription itself (in-house or take-home, and take-home quantity). This same approach was used to include pain intensity score pain score as part of characteristics of the presentation, using this as the final model.

Model diagnostics were performed using goodness-of-fit and ROC curves.

As an additional analysis, and given its importance in our model, two-sample testing was used to explore a possible association between self-reported pain severity score and covariates of interest. Given that self-reported pain score was reported at different frequencies in different settings, we performed a post-hoc sub analysis comparing variables by department type using chi square testing and one-way ANOVA. Given that self-reported pain scores were more likely reported in the ED, compared patient variables by pain type using only those patients who presented to the ED to control for differences that may exist in patients that present to different settings and subsequently, report a pain severity score.

All analyses were performed using Stata version 13.

Power Analysis

Previous literature finds that 12% of all adolescents who receive an opioid prescription are taking an opioid 1 year later.[12] Therefore, using a baseline estimate of 12% of patients with sustained opioid use 1 year later, our study has power of 80% to detect a difference in proportions of sustained use of approximately 20 percentage points using a two-sided level of significance of 0.05.

Ethical Considerations

The Oregon Health and Science University Institutional Review Board approved this study.

RESULTS

Table 1 displays the pain type for clinical encounter for all study patients. The majority of visits in which an opioid was received were for musculoskeletal pain (44%). Table 2 and 3 display study patient demographics, medical history, characteristics of visit, and nature of opioid prescription received according to type of pain at the clinical encounter. Patient characteristics were similar between those presenting with musculoskeletal pain and those with non-musculoskeletal pain, except for insurance type ($p=0.003$), presence of a history of a pain diagnosis (7% versus 12%, $p=0.02$), prescribing department ($p=0.009$), and if sent home with a prescription, quantity of opioid ($p<0.001$). There was a significant difference in timeframe of

pain type between those presenting with MSK type pain compared to those with non-MSK type pain (acute timeframe 68% versus 60%, respectively; p value =0.009).

Sustained Use

Univariate Analysis

Results are presented in Table 4a. The odds of sustained opioid use were lower for non-musculoskeletal pain types, but the association was not significantly significant (unadjusted OR .79, p=0.11). Significant associations were found for age (OR 1.09, p=0.048), female gender (OR 1.42, p=0.02), having a primary care provider (OR 1.6, p=0.007), an acute presentation (OR 1.53, p=0.004) and receiving an opioid for post-op surgery (OR .58, p<0.001). Additionally, an increased pain score, history of mental health diagnosis and prescription, history of a pain diagnosis, increased ED visits in the year prior, taking a prescription home, and prior opioid prescription use were all significantly associated with an increased odds of sustained opioid use a year later.

Multivariate Analysis and Final model

Results are presented in Table 4b-c. In the final model, which included self-reported pain intensity score, there was no significant association between visit pain type and sustained opioid use 1 year later. After adjusting for characteristics of visit and then for medical history, the odds of sustained opioid use among adolescents presenting with non-MSK type pain decreased (OR .79 to OR .76 to OR .66) compared to those presenting with MSK pain type. The relationship between those presenting with MSK pain type and sustained opioid use was significant after considering medical history and demographics (p=0.03 and p=0.04, respectively). However, this relationship was no longer significant when adjusting for the nature of opioid prescriptions received (quantity of take-home prescriptions) (p=0.42). Timeframe of chronic presentation and prior ED visits were both significantly associated with increasing odds of sustained opioid use 1 year later. Age, gender, race, and receiving an opioid in the ED setting were not associated with sustained opioid use 1 year later. Increasing quantity of take home opioids was associated with increasing odds of sustained opioid use. No clinically significant effect modifiers were identified.

Model fit/predictive ability

We used goodness-of-fit model diagnostics to assess models with and without pain score before adjusting for nature of opioid prescription variables and found similar calibration (p=0.95 and p=0.97, respectively). Comparing final models with and without pain score data, the calibration of the model that includes pain data was better (p=0.57 and p=0.87, respectively). Therefore, we chose the model with all variables with interest and pain score data as our final model. Generating an ROC curve with this model results in an AUC=0.75, or fair predictive ability (Figure 2). Our distributional boxplot shows some beginning separation, but with shows substantial overlap. In other words, the model may show some discrimination in predicting values between groups, but not to the level required for making confident predictions.

Self-Reported Pain Severity Score

In assessing the effect of pain type on risk of sustained opioid use, we felt that self-reported pain severity score was a valuable covariate to include in the model. Therefore, despite the reduction in sample size, we decided to keep self-reported pain severity score in the model. Exploring patient reported pain score, there was more variation in reported scores in those presenting with

MSK pain type (Figure 3). However, the association between pain severity score and presenting pain type was not significant. Table 5 displays the relationship between patient reported pain severity score and covariates of interest There is a significant association between increasing pain severity score and acute timeframe of presentation ($p < 0.001$), presence of a mental health diagnosis ($p=0.01$), receiving an opioid in the ED ($p<0.001$), sustained opioid use 1 year later ($p=0.001$), and with quantity of opioids taken home. We did not find a significant interaction between pain severity score and timeframe, nor did it change the fit of the final model.

While patient demographics were similar between those presenting to different departments, there were significant differences between adolescent patients presenting to different departments (Table 3c). Adolescents receiving an opioid for a MSK pain type were more common in the ED and from a surgical department compared to primary care and specialty clinics ($p=0.009$). Those receiving an opioid from the ED presented with a higher self-reported pain score compared to those receiving an opioid from other departments (<0.001). Adolescent patients were more likely to go home with higher quantities of opioid prescription from surgical departments (<0.001).

Among adolescents presenting to the ED only, those presenting with MSK type pain compared to non-MSK type pain were very similar (Table 3b). Adolescents presenting to the ED with a non-MSK type pain were more likely to have a history of a pain diagnosis, have had ED visits in the year prior, and presented with a chronic timeframe for their pain type compared to those presenting with MSK type pain (p value $=0.001$, $p = 0.02$, and $p = 0.002$, respectively). Interestingly, there were no significant differences between self-reported pain severity score and whether the patient received an opioid in-house in the ED between those presenting with MSK versus non-MSK type pain. However, there were significant differences take-home opioid prescriptions between those presenting with MSK versus non-MSK pain types with a higher proportion of adolescents with non-MSK taking home smaller quantities of opioid and those presenting with MSK pain type taking home larger quantities of opioid (p value $=0.006$).

DISCUSSION

Among adolescent patients presenting with musculoskeletal pain, there is an increased odds of sustained opioid use compared to those presenting with non-musculoskeletal pain. While the unadjusted odds ratios were not significant, adjusting for characteristics surrounding the pain presentation, and further for medical history, enhanced the significance of this finding. However, when adjusting for characteristics about the opioid prescription received, the significance is attenuated. Specifically, the risk of sustained opioid use increases with increasing increments of take-home prescription opioids, regardless of the presenting pain type, pain presentation, and medical history.

Our results are consistent with previous studies that suggest that mental health diagnoses and chronic pain are associated with increased odds of sustained opioid use. When pain presentation is adjusted for medical history, the association with MSK pain and sustained use becomes significant. This study population captures those who have already received an opioid prescription and given that those with a mental health diagnosis are more likely to receive an opioid prescription, these findings may be artificially strengthened.[36] Given the link between

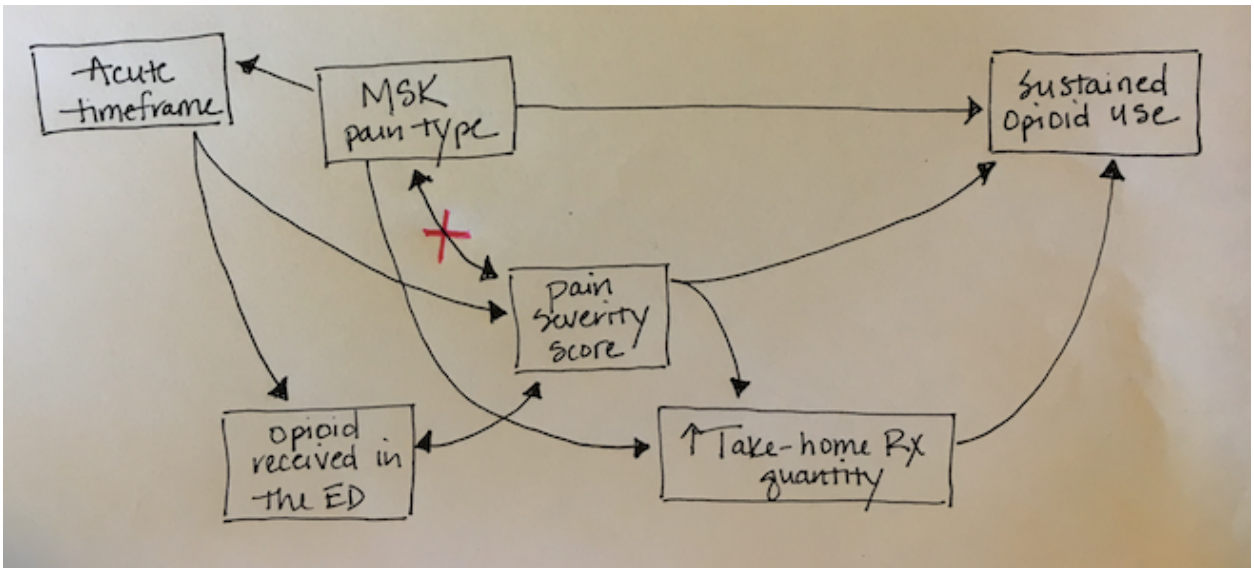
mental health and poor health outcomes, it is unclear whether increased odds of sustained use are related to higher medical needs or a different process in experiencing pain. Substance use and abuse has been shown in the literature to be associated with sustained opioid use but was not shown in our study. This is possibly due to the sparse information on substance use in the electronic medical record (especially for youth) the indiscriminate questions asked during patient visits, and the sensitive nature of these questions, especially in an adolescent population.

Those with MSK pain types take home larger quantities of opioids, which is associated with sustained opioid use. Interestingly though, those presenting with MSK type pain take home larger quantities regardless of the self-reported pain severity score. It is difficult to draw conclusions from a self-reported pain severity score. Given that the context in which patients report this score, and therefore the nature of the presenting pain type, we explored how this self-reported score may influence our findings (Figure 4). Possibly due to the workflow of the Emergency Department, self-reported pain severity scores were more commonly reported in the ED. However, adolescents presenting to the ED with MSK and non-MSK pain types were similar except for a history of pain diagnosis, ED utilization in the year prior and chronic timeframes were more common among non-MSK pain types (Table 3b). Adolescents with an acute pain type more commonly presenting to the ED setting and MSK pain types were more likely to be acute than non-MSK pain types. Interestingly, reported pain score and whether a patient received an opioid in the ED did not differ between pain types. The distribution of take-home prescription quantity was the same as our larger sample with those presenting with non-MSK type pain taking home smaller quantities and those with MSK type pain taking home larger quantities.

Despite no difference in reported pain intensity scores, patients with MSK type pain took home larger quantities. In other words, an increasing self-reported pain intensity score doesn't help explain the dose effect in take home prescription quantity. What dictates take-home quantity, however, is not evident. This is possibly due to physician prescribing practices given that opioid recommendations support prescriptions for acute presentations and self-limiting diagnoses or may be due to prescription conventions. While, differences in pain type and pain characteristics may be recorded at patient presentation, this may not necessarily translate to a personalized pain control for home.

Given that the quantity of take-home prescription is associated with sustained use, our results support a need investigate appropriate quantities of take-home prescription to help limit excess prescription available. Additionally, these results support a need for thorough discussion between patients and clinicians about risks of sustained use.

FIGURE 4 – Directed Acyclic Graph



LIMITATIONS

There are three limitations worth mentioning in this study. First, there is limited external validity given that the study population of OHSU adolescents is an urban, higher socioeconomic status, mostly white population, which may limit the generalizability of these findings. Additionally, OHSU is an academic center, which may have different adolescent prescribing practices than community or rural settings. However, it is reassuring that the two exposure groups were similar and sustained use rates were similar to those reported in the literature.

Second, information bias might exist in this type of chart review, relying only on information that has been recorded and available in the electronic medical record. Additionally, some data was missing and there may be something about these patients that have missing recordings that may influence results. For example, pain severity scores were more likely to be recorded in an ED setting and therefore, there may be something about those patients presenting with pain types to the ED that may influence the outcome. Further, while Care Everywhere helps capture variables outside OHSU, this is still limited to local providers using this electronic feature.

Additionally, this chart review relies on already reported diagnoses. Therefore, mental health not yet diagnosed, family history not yet asked, substance use not yet recorded would all be missed (Ref). Further, given this adolescent population, more sensitive topics such as substance use and mental health may not be reported accurately to a provider, especially if parents are present. Given that a past or current drug or alcohol substance use disorder is associated with opioid misuse in the general population, this information may be valuable to include. (Ref) Because we could not confirm prescription usage, only whether an opioid is written, it is possible that the opioid prescription was not used. On the other hand, patients may have received other opioid prescriptions at an outside network. Therefore, it is unclear how our results would be influenced.

Significant measurement bias exists in this study. Given little previous literature to guide pain definitions and the nature of pain itself, it is possible that effects may be deluded in the binary definition. While we attempted to capture the timeframe of presenting pain, actual timeframe is

unclear without patient contact. Additionally, we defined sustained opioid use as 1 year given previous literature definitions and studies investigating timeframe for misuse, but it is possible that a longer timeframe may capture a higher prevalence of sustained use.

And finally, this was an unblinded chart review. Therefore, it is possible that results were enhanced when other known risk factors were more evident in the medical record.

CONCLUSIONS/IMPACT

While pain type is not associated with a different risk in sustained opioid use, this study suggests risk of sustained opioid use may be associated with increasing quantities of opioid prescription, regardless of presenting pain type or severity. This helps illuminate the risks of large quantities of take-home opioid prescriptions and extra opioid "just in case". This also points to re-evaluating patients who may be experiencing pain that continues longer than expected and help direct communication, resources, and alternative pain control to better supporting these patients. The findings of this study may inform future research on adolescent screening at the time of prescriptions and ultimately, better pain control and care.

Future Directions

Future studies may build on these findings by employing a prospective cohort design and utilizing validated surveys on mental health and substance use habits prior to receiving opioid prescriptions, by collecting more information on self-reported pain scores, and by more clearly confirming opioid prescription use. Future research may be directed toward developing a screening tool to predict individual risk factors in adolescents who may be at increased risk of sustained opioid abuse and misuse and indications for quantity of take home prescription. Further, understanding what contributes to clinicians' decisions with when and how much to prescribe may help shed light on our knowledge gaps about prescribing. Clearer indications for opioid management among adolescents will ultimately provide safer care for this population. This may help emphasize the value of assistance on safer prescribing practices for clinicians, patients, and families.

FIGURES + TABLES

FIGURE 1: Patients identified and enrolled using Oregon Health and Science University EPIC EHR with RDW.

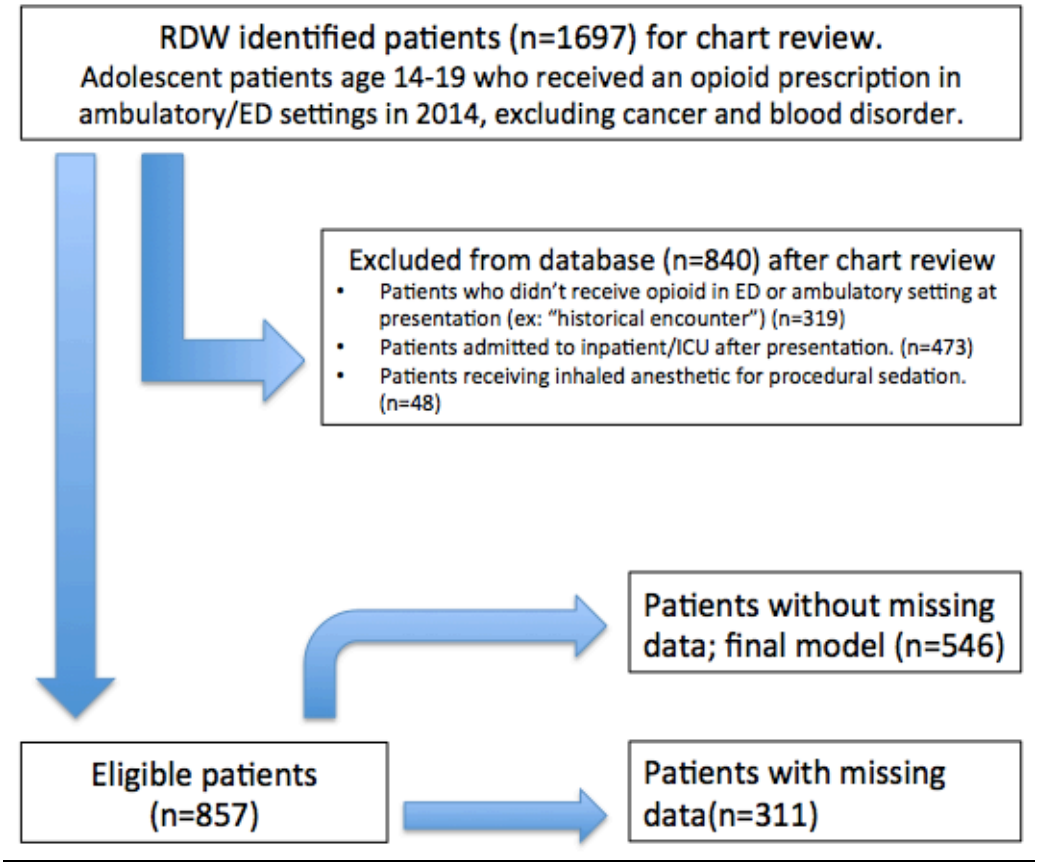


TABLE 1
Presentations for Patients Receiving Opioid in the ED or Take-Home Rx (n=857)

Pain Presentation	#	Frequency
Musculoskeletal Pain	379	44.22%
Visceral Pain	193	22.52%
Infection	165	19.25%
Dental Pain	64	7.47%
Laceration	33	3.85%
Other	23	2.68%

TABLE 2
Patient Characteristics

Variable	#	Mean or Frequency
Gender Male	445	51.93%

Female	412	48.07%
Age	857	16.5 (14-19)
Ethnicity		
Not-Hispanic	714	85%
Hispanic	126	15%
Race**		
White	702	85.61%
Non-White	118	14.39%
PCP		
No	235	27.42%
Yes	622	72.58%
Presentation**		
MSK	379	44.22%
Non-MSK	478	55.78%
Prescribing Department		
ED	370	43.17%
Primary Care	34	3.97%
Subspecialty	26	3.03%
Surgical	427	49.82%
Timeframe of Presentation		
Acute	543	63.43%
Chronic	313	36.57%
Pain Score	546	4.8 (0-10)
Opioid for Surgery		
No	445	51.93%
Yes	412	48.07%
History of Mental Health Dx		
No	691	80.63%
Yes	166	19.37%
History of Chronic Pain Dx		
No	770	89.85%
Yes	87	10.15%
Dx of Obesity		
No	792	92.42%
Yes	65	7.58%
Dx of ADHD		
No	773	90.20%
Yes	84	9.80%
Prior ED visit		
No	613	71.53%
Yes	244	28.47%
Substance Use		
None	749	89.59%
Any	87	10.41%
Received Prior Opioid		
No	709	82.73%
Yes	141	17.27%
Rx Received in the ED		

No Yes	620 237	72.35% 27.65%
If sent home with Rx, Quantity	857	27.46 (0 – 330)
Subsequent Opioid Rx No Yes	 583 274	 68.03% 31.97%
** = re-coded		

TABLE 3a. Variables by pain type.

	Type of Pain		
	MSK	Non-MSK	p-Value
Patient Demographics	n=379	n=478	
Age in years, (±SD)	16.47 (±1.75)	16.52 (±1.73)	0.66
Male, No. (%)	207 (54)	238 (49)	0.16
White, No. (%)	324 (87)	384 (84)	0.18
Non-Hispanic, No. (%)	331 (88)	383 (83)	0.03
PCP, No. (%)	284 (75)	338 (71)	0.17
Insurance Type, No. (%)			0.003*
None	16 (4)	24 (5)	-
Medicaid	115 (30)	196 (41)	-
Private	248 (66)	258 (54)	-
Medical History			
Rx Mental Health, No. (%)	56 (15)	74 (15)	0.78
Hx of Mental Health Dx, No. (%)	70 (18)	96 (20)	0.55
Hx of Pain Dx, No. (%)	28 (7)	59 (12)	0.02*
Hx of ADHD, No. (%)	38 (10)	46 (10)	0.84
Hx of Prior Opioid, No. (%)	75 (20)	73 (15)	0.08
Prior ED visit, (±SD)	.41 (±. 79)	.47 (± .87)	.30
Characteristics of Visit			
Pain Score (±SD)	4.77 (±3.2)	4.80 (±3.5)	0.83
Acute Timeframe, No. (%)	258 (68)	285 (60)	0.009*
Surgery performed, No. (%)	181 (48)	231 (48)	0.87
Department, No. (%)			0.009*
ED	167 (44)	203 (42)	-
Primary Care	8 (2)	26 (5)	-
Specialty	6 (2)	20 (4)	-
Surgical	198 (52)	229 (48)	-
Nature of Opioid Prescription			
Rx in ED, No. (%)	103 (27)	134 (28)	0.78
Rx sent home, No. (%)			<.001*
< 7 tabs	74 (20)	132 (28)	
8 - 15 tabs	146 (39)	284 (59)	
16 - 30 tabs	94 (25)	52 (11)	
> 30 tabs	65 (17)	10 (2)	

TABLE 4 – Regression Analysis for Sustained Opioid Use

Table 4a - Univariate Analysis

Variable	Variable type	Coeff	SE	P value	OR (95% CI)
Presentation, non-MSK	Dichotomous	-.2346977	.1471149	.111	.79 (.59-1.06)
Age	Continuous	.0836918	.0422382	.048	1.09 (1.00-1.18)
Gender, female	Dichotomous	0.3501724	0.1470236	0.017	1.42 (1.06-1.89)
Ethnicity, Hispanic	Dichotomous	-.330313	.2176811	0.129	.72 (.47 – 1.10)
Race, non-white	Dichotomous	-.0431969	.0467723	.356	.96 (.87-1.05)
PCP	Dichotomous	.4570954	.1689507	0.007	1.60 (1.13-2.20)
Insurance	Categorical			0.544	
1		.3098297	.3737698	0.407	1.36 (.66-2.84)
2		.1705744	.366915	0.642	1.19 (.58-2.43)
Timeframe, chronic	Dichotomous	.4288456	.1502895	.004	1.53 (1.14-2.06)
Surgery	Dichotomous	-.5378556	.149029	0.000	0.58 (.43-.78)
Department	Categorical			0.041	
1		.2445913	.3650291	0.503	1.28 (.62-2.61)
2		.2911113	.4115744	0.479	1.33 (.60-2.99)
3		-.3613904	.1533901	0.018	.69 (.52-.94)
Pain score	Continuous	.0920439	.0269862	0.001	1.09 (1.04-1.16)
Rx MH	Dichotomous	.7201492	.1938417	0.000	2.05 (1.41-3.00)
Rx Pain	Dichotomous	1.025127	1.025127	0.001	2.79 (1.56-4.99)
Hx MH	Dichotomous	.9623347	.1770084	0.000	2.62 (1.85-3.70)
Hx substance	Dichotomous	-.8643537	.7780883	0.267	0.42 (.09-1.94)
Hx Pain dx	Dichotomous	1.192078	.2309173	0.000	3.29 (2.09-5.18)
Hx obesity	Dichotomous	.2382868	.2681454	0.374	1.27 (.75-2.15)
Hx ADHD	Dichotomous	.4674601	.2345983	0.046	1.60 (1.01-2.53)
Prior ED visit	Continuous	.6414506	.0922213	0.000	1.90 (1.59-2.28)
Substance use	Dichotomous	.5533234	.2301814	0.016	1.74 (1.11-2.73)
Rx in ED	Dichotomous	.21714	.1613364	0.178	1.24 (.91-1.70)
Rx for Home	Continuous	.0061645	.0025156	0.014	1.01 (1.00-1.01)
Prior Rx	Dichotomous	2.489439	.2170396	0.000	12.05 (7.88-18.45)

TABLE 4b - Multivariable Analysis; without pain score (n=857).

Characteristic	Unadjusted OR (95% CI)	Adjusted for Presenting Variables	Adjusted for Medical History	Adjusted for Demographics	Final MM
Presentation	**.79 (.59-1.06)**	**.72 (.54-.98)**	**.65 (.47-.88)**	**.63 (.46-.87)**	**.85 (.60-1.21)**
Acute		2.39 (1.69-3.38)	2.19 (1.52-3.14)	2.17 (1.49-3.15)	2.02 (1.38-2.96)
Surgery		.40 (.29-.56)	.53 (.37-.76)	.57 (.39-.82)	.39 (.24-.62)
Hx of MH			1.75 (1.18-2.59)	1.69 (1.13-2.53)	1.74 (1.15-2.62)
Hx of Pain			2.19 (1.33-3.62)	2.14 (1.27-3.61)	2.03 (1.21-3.43)
Hx ADHD			1.30 (.79–2.15)	1.23 (.73-2.07)	1.19 (.69-2.02)
Hx Prior ED			1.75 (1.44-2.13)	1.82 (1.49-2.23)	1.82 (1.49-2.23)
Age				1.06 (.97-1.16)	1.03 (.94-1.13)
Gender				1.09 (.79-1.50)	1.13 (.81-1.56)
Race				1.00 (.91-1.10)	.99 (.89-1.10)
Rx ED					1.17 (.71-1.93)

Rx Home 1 2 3					 1.17 (.71-1.92) 2.56 (1.33-4.92) 3.96 (1.84-8.52)

Table 4c – Multivariable Analysis; with pain score (n=546)

Characteristic	Unadjusted OR (95% CI)	Adjusted for Presenting Variables	Adjusted for Medical History	Adjusted for Demographics	Final MM** OR (95% CI), p
Presentation	**.79 (.59-1.06), p=.11**	**.76 (.534-1.10), p=.14**	**.66 (.45-.97), p=.03**	**.67 (.45-.99), p=.04**	**.84 (.55-1.29), p=.42**
Acute		3.01 (1.91-4.44)	2.67-1.65-4.32)	2.70 (1.64-4.44)	2.38 (1.42-3.97), p=.001
Surgery		.64 (.37-1.10)	.75 (.43-1.32)	.82 (.46-1.45)	.50 (.26-.97), p=.04
Pain score		1.13 (1.06-1.21)	1.10 (1.01-1.18)	1.10 (1.02-1.19)	1.10 (1.02-1.19), p=.01
Hx of MH			1.84 (1.15-2.92)	1.83 (1.13-2.95)	1.89 (1.16-3.07), p=.01
Hx of Pain			2.05 (1.16-3.63)	2.01 (1.11-3.63)	1.86 (1.03-3.37), p=.04
Hx ADHD			1.54 (.84-2.84)	1.42 (.76-2.70)	1.33 (.70-2.54), p=.36
Hx Prior ED			1.71 (1.36-2.16)	1.72 (1.35-2.18)	1.73 (1.36-2.19), p<.001
Age				1.07 (.96-1.19)	1.04 (.92-1.16), p=.55
Gender				1.10 (.74-1.63)	1.16 (.77-1.73), p=.49
Race				.98 (.87-1.11)	1.01 (.58-1.77), p=.97
Rx ED					.96 (.54-1.72), p=.90
Rx Home 8- 2 3					 1.23 (.69-2.19), p=.48 2.53 (1.08-5.90), p=.03 4.70 (1.77-12.49), p=.002

Figure 2a -
To assess predictive accuracy of our model, we generated a Receiver Operating Characteristics (ROC) curve –

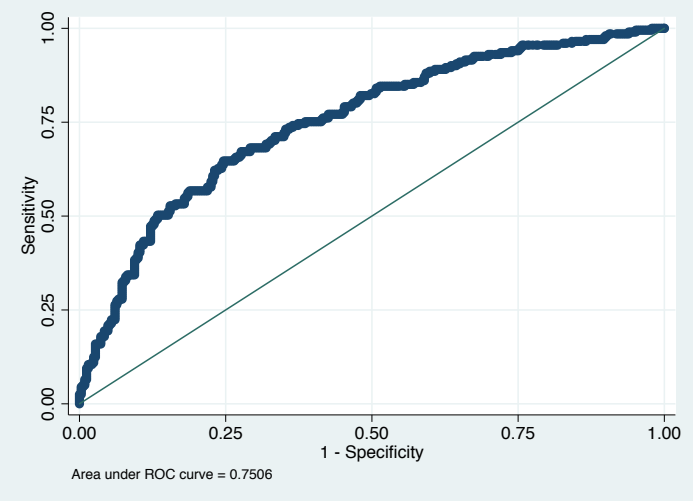


Figure 2b – Distributional box plot to show "predictive" ability of our model.

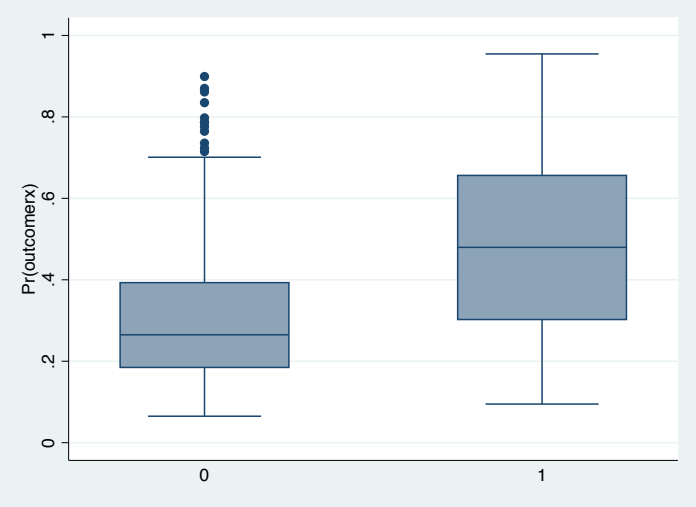


Figure 3 – Variation in reported pain score between those presenting with MSK and non-MSK reason for visits.

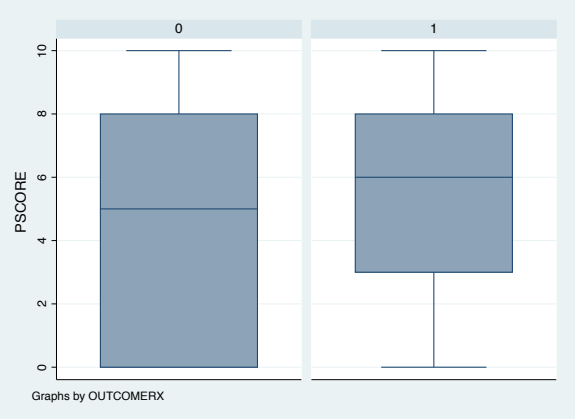


Table 5 –Patient reported pain score (0-10) and covariates of interest.

	Variable		P value
Pain score Mean (±SD)	MSK 4.77 (±3.21)	Non-MSK 4.83 (±3.52)	0.83
	Acute 5.81 (±2.93)	Chronic 3.07 (±3.39)	<0.001
	Male 4.51 (±3.47)	Female 5.09 (±3.27)	0.04
	No Hx of MH dx 4.61 (±3.40)	Hx of MH dx 5.47 (±3.20)	0.01
	No Hx of Pain dx 4.71 (±3.36)	Hx of pain dx 5.45 (±3.45)	0.08
	No Prior opioid rx	Prior opioid rx	0.66

	4.77 (±3.40)	4.93 (±3.28)	
	No opioid in ED 3.74 (±3.44)	Opioid received in ED 6.62 (±2.33)	<0.001
	No Sustained use 4.42 (±3.47)	Sustained opioid use 5.45 (±3.12)	0.001

Prior ED visits presented as correlation coefficient 0.229.

Logistic regression for Take-Home prescription

Rx sent home			<0.001
< 7 tabs	Reference	-	-
8 -15 tabs	-1.46	0.34	<0.001
16 - 30 tabs	-2.38	0.40	<0.001
> 60 tabs	-2.42	0.45	<0.001

Table 6. Timeframe of pain type (n=857)

	MSK pain type	Non-MSK pain type
Acute timeframe	258	285
Chronic timeframe (> 3 mo)	120	193

Pearson chi2(1)=6.7784 p value=0.009

TABLE 3b. Variables by pain type; only ED patients. (n=370)

	Type of Pain		
Patient Demographics	MSK n=167	Non-MSK n=203	p-Value
Age in years, (±SD)	16.76 (±1.76)	16.79 (±1.81)	0.86
Male, No. (%)	91 (55)	102 (50)	0.42
White, No. (%)	141 (84)	157 (77)	0.09
Non-Hispanic, No. (%)	149 (90)	165 (82)	0.03
PCP, No. (%)	98 (59)	115 (57)	0.69
Insurance Type, No. (%)			0.238
None	13 (8)	14 (7)	-
Medicaid	47 (28)	74 (36)	-
Private	107 (64)	115 (57)	-
Medical History			
Rx Mental Health, No. (%)	24 (14)	40 (20)	0.18
Hx of Mental Health Dx, No. (%)	37 (22)	49 (24)	0.65
Hx of Pain Dx, No. (%)	10 (6)	34 (17)	0.001*
Hx of ADHD, No. (%)	21 (13)	22 (11)	0.60
Hx of Prior Opioid, No. (%)	23 (14)	42 (21)	0.09
Prior ED visit, (±SD)	.44 (±. 92)	.69 (± 1.03)	.02*
Characteristics of Visit			
Pain Score (±SD)	6.24 (±2.41)	6.54 (±2.58)	0.30
Acute Timeframe, No. (%)	153 (92)	163 (80)	0.002*

Nature of Opioid Prescription			
Rx in ED, No. (%)	102 (61)	130 (64)	0.56
Rx sent home, No. (%)			0.006*
< 7 tabs	70 (42)	113 (56)	
8 - 15 tabs	85 (51)	87 (43)	
16 - 30 tabs	11 (7)	3 (1)	
> 30 tabs	1 (1)	0 (0)	

TABLE 3c. Variables by department (n=857)

	Department				
	ED	Primary Care	Specialty	Surgical	p-Value
Patient Demographics	n=370	n=34	n=26	n=427	
Age in years, (±SD)	16.8 (±1.79)	16.8 (±1.63)	16.4 (±1.86)	16.2 (±1.66)	0.48
Male, No. (%)	193 (52)	18 (53)	8 (31)	226 (53)	0.18
White, No. (%)	298 (83)	31 (97)	25 (100)	354 (86)	0.02*
Non-Hispanic, No. (%)	314 (85)	28 (88)	22 (88)	350 (84)	0.92
PCP, No. (%)	213 (58)	32 (94)	20 (77)	357 (84)	<0.001*
Insurance Type, No. (%)					0.007*
None	27 (7)	1 (3)	2 (7)	10 (2)	-
Medicaid	121 (33)	8 (24)	9 (35)	173 (40)	-
Private	222 (60)	25 (73)	15 (58)	244 (57)	-
Medical History					
Hx of Mental Health Dx, No. (%)	86 (23)	10 (30)	10 (38)	60 (14)	<0.001*
Hx of Pain Dx, No. (%)	44 (12)	7 (20)	8 (31)	28 (7)	<0.001*
Hx of ADHD, No. (%)	43 (11)	3 (9)	4 (15)	34 (8)	0.26
Hx of Prior Opioid, No. (%)	65 (17)	4 (12)	7 (27)	72 (17)	0.48
Characteristics of Visit					
MSK pain type, No (%)	167 (45)	8 (23)	6 (23)	198 (46)	0.009*
Pain Score (±SD)	6.41 (±2.50)	4.33 (±3.04)	4.06 (±3.31)	2.30 (±3.11)	<0.001*
Acute Timeframe, No. (%)	316 (85)	28 (82)	11 (42)	188 (44)	<0.001*
Nature of Opioid Prescription					
Rx in ED, No. (%)	232 (63)	0 (0)	1 (4)	4 (1)	<0.001*
Rx sent home, No. (%)					<0.001*
< 7 tabs	183 (49)	3 (9)	3 (11)	17 (4)	-
8 - 15 tabs	172 (46)	26 (76)	17 (65)	215 (50)	-
16 - 30 tabs	14 (4)	4 (12)	5 (19)	123 (29)	-
> 30 tabs	1 (.2)	1 (3)	1 (4)	72 (17)	-

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