ORIGINAL RESEARCH ARTICLE

Demographic, Clinical, and Prescribing Characteristics Associated with Future Opioid Use in an Opioid-Naive Population in an Integrated Health System

David M Mosen, PhD, MPH[1]; A Gabriela Rosales, MS[1]; Rajasekhara Mummadi, MD, MPH[2]; Weiming Hu, MS[1]; Neon Brooks, PhD[1]

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ABSTRACT

Introduction: Health systems and prescribers need additional tools to reduce the risk of opioid dependence, abuse, and overdose. Identifying opioid-naive individuals who are at risk of opioid dependence could allow for the development of needed interventions.

Methods: We conducted a retrospective cohort analysis of 23,804 adults in an integrated health system who had received a first opioid prescription between 2010 and 2015. We compared the demographic, clinical, and prescribing characteristics of individuals who later received a third opioid dispense at least 27 days later, indicating long-term opioid use, with those who did not.

Results: The strongest predictors of continued opioid use were an initial prescription dosage of 90 morphine milligram equivalence or more; prescription of extended-release opioids, rather than short-release; and being prescribed outside of a hospital setting. Patients with a third prescription were also more likely to be older than 45 years, white, and non-Hispanic and to have physical comorbidities or prior substance abuse or mental health diagnoses.

Discussion: Our findings are largely consistent with prior research but provide new insight into differences in continued opioid use by opioid type, prescribing location, ethnicity, and comorbidities. Together with previous research, our data support a pattern of higher opioid use among older adults but higher rates of diagnosed opioid abuse among younger adults.

Conclusions: By identifying population characteristics associated with continued opioid use following a first prescription, our data pave the way for quality improvement interventions that target individuals who are at higher risk of opioid dependence.

BACKGROUND

Over the past 30 years, opioid prescribing in the US has increased substantially. The number of prescriptions nearly tripled from 76 million in 1991 to more than 210 million in 2010.[1] Since 2012, the number of opioid prescriptions has slowly declined; the number stood at about 191 million in 2017.[2] Although the prescribing decline is good news, opioid abuse and addiction continue to take a heavy toll. Between 1999 and 2017, overdose deaths in the US due to prescription opioids increased 6-fold.[3] Nearly 218,000 people died in the US from overdoses related to prescription opioids over that time period.[1] Overdoses involving opioids caused more than 47,000 deaths in 2017, and 36% of those deaths (about 17,000) involved prescription opioids.[4,5]

These statistics document a crisis that has destroyed individual lives and damaged families and communities. In 2016, the CDC released a Guideline for Prescribing Opioids for Chronic Pain, which recommended that prescribers limit the use, duration, and potency of prescribed opioids for adults seen in primary care.[6] In 2017, the US Department of Health and Human Services declared the opioid crisis a public health emergency.[7] As federal agencies have moved to curb the crisis, health care systems have come under increased pressure to more tightly control opioid prescribing.

To prevent future opioid addiction among those who are not currently using opioids (ie, naive populations), health systems need to identify patient characteristics associated with future opioid use disorder. Such information can help systems develop interventions to provide additional support and outreach to those who are most at risk of addiction. Several previous studies have identified individual patient demographics (eg, male gender,[8,9] younger age,[8-10] receiving public insurance[11,12]), clinical conditions (eg, previous mental health diagnoses,[8,9,13,14] previous substance abuse), and prescribing characteristics (eg, more days of supply,[8,9,15] higher daily dose[10,15], extended duration of opioid release[16-18]) associated with future opioid use or with diagnosis of opioid use disorder. However, analyses that use a population-based approach examining an entire cohort of patients over time to identify patient-level characteristics associated with future use are limited. Moreover, limited studies of this kind have been conducted within integrated health care systems where more comprehensive clinical information is available (eg, clinical comorbidities). Also, few studies have looked at a third prescription of opioids shortly after an index prescription, which can be a "leading indicator" and have strong predictive power for long-term use.

Author Affiliations

[1] Kaiser Permanente Center for Health Research, Portland, OR

[2] Kaiser Permanente Northwest Quality Management and Systems, Portland, OR

Corresponding Author

David Mosen, PhD, MPH (david.m.mosen@kpchr.org)

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In this study, we examined the independent associations of demographic, clinical, and prescribing characteristics with future opioid use among all naive (first-time) users in Kaiser Permanente Northwest (KPNW), an integrated group model health maintenance organization serving more than 626,000 members in Oregon and southwestern Washington. By studying the characteristics associated with continued opioid use using a cohort-based approach within an integrated health system, we will be able to better identify characteristics associated with long-term use that can be used to create new predictive models. These models can help health systems identify individuals who are most likely to be at risk for future long-term opioid use and dependence and target additional support and resources toward these individuals.

METHODS

We conducted a retrospective cohort analysis of 23,804 patients who meet the following inclusion criteria: 1) adults (age 18 and older) with at least one opioid prescription (eg, oxycodone, hydrocodone, tramadol) between January 1, 2010 and September 30, 2015 (index prescription) who 2) did not have an opioid prescription 6 months prior to the index prescription (opioid naive). Patients with cancer diagnoses (any type) or who were receiving hospice care were excluded. These criteria were based on previous research defining opioid-naive populations.[19] Data needed for the analyses were identified through KPNW's electronic health record. Opioid medications included only those filled at KPNW pharmacies. The quality lead for specialty care for Northwest Permanente, KPNW's physician group, was closely involved with the development and execution of this analysis. The primary intent of the analysis was quality improvement oriented, with the results used to inform future initiatives by identifying factors that predict risk for future opioid use among the naive population. The analysis was reviewed and approved by the KPNW Institutional Review Board.

Measures and analyses

The primary outcome measure was whether a patient received a third prescription of opioids at least 27 days after index prescription (yes vs no). The rationale for the outcome was 2-fold. First, previous research has demonstrated that each additional opioid prescription has predictive power for future opioid dependence,[20] but few studies have examined factors associated with a third prescription, which may have strong predictive power for future use. Second, the rationale for at least 27 days to third dispense was that it is a reasonable time period in which to consume the index and second opioid prescriptions for patients filling a third prescription and that the majority of third dispenses occurred 27 or more days after the index prescription.

Predictor Measures: Demographic, Clinical, and Prescribing Characteristics

Predictor measures in this analysis included demographic, clinical, and prescribing characteristics available from KPNW's electronic health record. The selection of these measures was based on previous published research.[8-10, 15-18]

Demographic measures included age category (< 45, > 45 and < 65, > 65), sex (male, female), race (white, non-white), and Hispanic ethnicity (Hispanic, non-Hispanic). We also examined whether individuals had Medicaid insurance (yes vs no) and Medicare insurance (yes vs no).

Clinical characteristics included the Charlson Co-morbidity Index (CCI, 0 vs 1+), a measure of clinical comorbidities in the year prior to index prescription,[21,22] any prior substance abuse diagnosis (yes vs no), and any prior mental health diagnosis (yes vs no). The look-back period to assess substance abuse and prior mental health diagnosis was a far as KPNW membership existed.

Prescribing characteristics included prescribing location (hospital, outpatient, other location [eg, specialty care]), type of opioid (extended/long release vs short release), and total morphine milligram equivalents (MME) dosage for index prescription (MME > 90 vs MME < 90). This was one of the first studies we are aware of that compared prescribing location of opioids for index fill as a predictor for long-term use of opioid medications.

Statistical Analysis

We conducted univariate descriptive analyses comparing the population who received a third prescription with those who did not on each of the characteristics listed above using γ^2 analyses at baseline. Next, we conducted multivariable logistic regression to determine which characteristics best predicted receiving a third prescription when controlling for the other characteristics. The final model was estimated using logistic regression with stepwise variable selection, from those variables compared at baseline, to develop the most parsimonious statistical model.

RESULTS

Of the 23,804 patients who received a first opioid prescription during our study period, 8,762 (36.8%) received a third prescription at least 27 days later. Table 1 presents univariate descriptive characteristics among those who did and did not receive a third prescription. Except for sex and Medicaid insurance status, all demographic, clinical, and prescribing characteristics were associated with whether a patient received a third prescription.

Table 2 presents the final multivariable logistic model of predictor measures associated with having a third prescription of opioid medications, after stepwise variable selection. Those who received a third prescription were significantly more likely to be in the older age categories, white, and non-Hispanic. They were also significantly more likely to have a CCI score of 1 or higher, including prior substance abuse and mental health diagnoses. Patients prescribed in the hospital were significantly less likely to receive a third prescription than those prescribed in other settings (eg, specialty care). Last, there was no difference between rates of receiving a third prescription in outpatient as compared with other settings. Those receiving extended-release prescriptions and dosages above 90 MME were significantly more likely to receive a third prescription than those who received short-release prescriptions or lower dosages.

DISCUSSION

In one of the first studies examining predictors of opioid use in a population-based cohort from an integrated health system, we identified several demographic, clinical, and prescribing characteristics that were associated with a third opioid prescription within 27 or more days of a patient's first opioid prescription. These findings provide new insights about characteristics that could contribute to chronic opioid use. These data can be used to develop innovative provider-based interventions for individuals at high risk of developing a pattern of chronic opioid use.

The strongest predictors of receiving a third prescription were characteristics of the initial prescription. Consistent with many previous studies that found associations between opioid dosage and chronic use or abuse/dependence,[10,12,15] we found that patients who received doses above 90 MME were three times more likely to have a third prescription than those who were prescribed lower doses. We also found that those prescribed extended-release opioids were 1.53 times more likely to receive a third prescription than those prescribed short-release opioids. Although few previous studies have examined differences in long-term use based on type of opioid prescription, one previous study based on a large commercial claims database found a stronger relationship between short-acting opioids and later opioid misuse than between long-acting opioids and later opioid misuse. This difference may be due to different outcome variables: Short-acting opioids may put patients at a higher risk of misuse, whereas long-acting opioids may be more associated with prolonged use.

Our study was also the first to show a lower rate of continued use among patients prescribed opioids in a hospital setting compared with other prescribing settings. This may be because of high awareness among hospital providers of the need to prescribe low opioid pill counts following inpatient surgical procedures; lower pill counts have been associated with lower long-term opioid use.[23]

In our cohort, older age was associated with higher likelihood of a third prescription. At first glance, this finding may appear to be in conflict with previous reports of lower risk of opioid abuse and dependence among older age groups.[8-10, 13] However, 2 other studies that have focused on prolonged opioid use, rather than misuse or abuse, also found higher rates of continued use among older adults.[12,15] Together, these data paint a picture in which younger adults who are prescribed opioids may be more at risk of misuse, whereas older adults are more likely to become chronic prescription users under the guidance of their doctors.[14]

Our study also adds to the sound body of literature demonstrating that individuals with a past history of substance abuse or mental health diagnoses are more at risk for long-term use of opioids.[10,12,13] Additionally, we found that patients with a CCI score of 1 or higher were significantly more likely to get a third prescription. This is consistent with another study that found a relationship between CCI and chronic opioid therapy.[12] In contrast, the few studies examining the relationship between CCI and opioid abuse or dependence have reported mixed results.[10,13]

Although studies have consistently found that white race is associated with higher risk of chronic opioid use or dependence, findings about the relationship with Hispanic ethnicity have been more mixed. Whereas some studies have found higher rates of misuse among Hispanic populations,[13,14] we found that Hispanic patients were less likely to receive a third prescription. This is consistent with a previous study that showed that Hispanic ethnicity was associated with lower likelihood of filling an opioid prescription,[11] possibly due to problems with cost and access among lower-income Hispanic populations. We also found no differences by sex in patients' likelihood to continue using opioids, whereas some past studies have found higher rates of chronic use or reported misuse among women.[14,15]

These results provide preliminary evidence of the characteristics associated with continued opioid use among naive users. This evidence can be used to develop more refined predictive risk models that could identify patients most in need of additional resources and support, including quality improvement interventions, to reduce their likelihood of chronic opioid use or misuse. Future research could also examine whether tailoring interventions to individuals with specific demographic, clinical, or prescribing characteristics could prevent future opioid dependence. For example, individuals with a past history of substance abuse may benefit from different interventions than older adults with multiple physical comorbidities. Similarly, prescribing

location and prescribing characteristics could be used to tailor interventions appropriately for individuals with different medical histories and reasons for using opioids.

More research is needed to develop and evaluate effective provider-based interventions with a focus on naive opioid users with the goal of reducing future opioid dependence. These interventions should use predictive models and other tools, such as identifying outliers, to maximize the effectiveness of limited resources and improve outcomes for patients who are most at risk. Our results suggest that KPNW pharmacists could be a key component of such interventions, using this information to select alternate medications to opioids and to connect with patients' primary care clinicians to better manage and coordinate care.

One limitation of this study was that it only includes data from patients first dispensed opioids between 2010 and 2015. Opioid use was declining during this period and continues to decline through the present day. However, the factors associated with long-term opioid use are likely similar between this time frame and the present. A second limitation is that this analysis occurred in an integrated health system in the Pacific Northwest; therefore, results may not be generalizable to the larger US population. Last, this analysis only included opioid prescriptions filled in KPNW pharmacies; the associations of patient characteristics with the third prescription of opioids may not be the same in prescribing locations outside of KPNW.

CONCLUSION

In a population-based cohort of 23,804 naive opioid users, prescribing characteristics (dosage, extended vs short release, and prescribing location) most strongly predicted continued opioid use, as measured by a third prescription at least 27 days after the initial prescription. We also identified key clinical and demographic factors associated with continued use. These findings could be used to inform quality improvement interventions for preventing opioid dependence. Such innovative quality improvement approaches should involve collaboration with KPNW pharmacists and primary care physicians to prescribe alternate medications to opioids and better manage and coordinate care. ❖

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