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MEDICAID PRIOR AUTHORIZATION AND OPIOID MEDICATION ABUSE AND OVERDOSE

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Abstract

Objectives: The US opioid medication epidemic has resulted in serious health consequences for patients. Formulary management tools adopted by payers, specifically prior authorization policies (PA), may lower rates of opioid medication abuse and overdose. We compared rates of opioid abuse and overdose among enrollees in plans that varied in their use of PA from High (required PA for 17–74 opioids), Low (required PA for 1 opioid), to No PA policies for opioid medications.

Study Design: Retrospective cohort study of patients initiating opioid treatment in Pennsylvania Medicaid from 2010 to 2012.

Methods: Generalized linear models with generalized estimating equations were employed to assess relationships between presence of PA policies and opioid medication abuse and overdose, as measured in Medicaid claims data, adjusting for demographics, comorbid health conditions, benzodiazepine/muscle relaxant use, and emergency department use.

Results: The study cohort included 297,634 enrollees, with a total of 382,828 opioid treatment episodes. Compared to plans with no PA, enrollees in High PA (Adjusted Rate Ratio [ARR]=0.89, 95% CI=0.85–0.93, $p<0.001$) and Low PA plans (ARR=0.93, 95%CI=0.87–1.00, $p=0.04$) had lower rates of abuse. Enrollees in the Low PA plan had a lower rate of overdose than those within plans with No PA (ARR=0.75, 95% CI=0.59–0.95, $p=0.02$). High PA plan enrollees were also less likely than No PA enrollees to experience overdose, but this association was not statistically significant (ARR=0.88, 95% CI=0.76–1.02, $p=0.08$).

Conclusions: Enrollees within Medicaid plans that utilize PA policies appear to have lower rates of abuse and overdose following initiation of opioid medication treatment.

Précis:

Enrollees in Medicaid plans employing prior authorization policies for opioid medications may have lower rates of opioid medication abuse and overdose.

Keywords

Opioid overdose; opioid abuse; prior authorization; Medicaid

Introduction

The US opioid medication epidemic has led to serious effects on public health, including opioid-related overdoses and mortality.[1,2] Perhaps the largest system-level investment in the US to address abuse and prevent overdose has been Prescription Drug Monitoring Programs,[3–5] which have shown mixed results for protecting patient health.[3,6,7] Another system-level intervention is a lock-in program, wherein patients who exceed filling pattern thresholds are limited to specific providers/pharmacies to receive future opioid medications,[8] which programs have shown some promise for improving medication monitoring and reducing diversion.[9] Formulary management tools may represent a valuable set of interventions payers can employ to control opioid medication consumption, deter shopping behaviors, and improve quality and safety.[10]

One specific formulary management tool that may be used to address the opioid crisis is *prior authorization* (PA). PA is a requirement placed on some medications by payers that requires verification that the medication is necessary and/or patients meet medical criteria for use.[11] An extensive body of literature has shown cost saving benefits of PA policies for a variety of medications (often expensive name brand drugs),[12,13] but limited research has been conducted on their impact on patient-related opioid and quality of care outcomes.[14–16] PA policies applied in public or commercial health insurance plans frequently result in reductions in medication use,[17–20] but often this result is accomplished by placing administrative burdens on clinicians.[21]

Medicaid programs serving low-income populations have federally allowable copayments mandating minimal out-of-pocket costs that can be charged to enrollees.[22] Medicaid programs are therefore particularly reliant on PA policies as opposed to other formulary management tools that use cost-sharing to influence demand. Research has shown approximately one-quarter of Medicaid patients who regularly use opioid medications (>90 days) are engaged in problematic opioid consumption behaviors,[23] and Medicaid enrollees on average receive more than double the total annual opioid dose compared to the privately insured.[24] To date, 19 states' Medicaid programs have required PA for long-acting opioids, and studies show these policies can reduce long-acting opioid fills.[14,16] The extent to which PA policies can help reduce the problematic opioid-related outcomes of abuse and drug overdose is unknown. We hypothesized enrollees within Medicaid fee-for service (FFS) programs and managed care plans employing PA policies for opioid medications would have lower rates of: (1) abuse and (2) opioid medication overdose compared to patients enrolled in Medicaid plans without PA. Understanding potential associations between PA and abuse and overdose may provide health systems and payers with an additional tool to address problematic opioid-related outcomes.

Methods

Design

This investigation was a retrospective cohort study that utilized Pennsylvania Medicaid data from 2010 to 2012. The Pennsylvania Medicaid program is among the largest in the US in both expenditures and enrollment, and Pennsylvania's healthcare utilization and access[25] and statewide demographic profile (with the exception of lower rates of Hispanics)[26] are similar to those seen across the nation. Pennsylvania has the 8th highest overdose rate in the US, and opioid prescribing rates are consistently above national averages.[27,28] We obtained Pennsylvania Medicaid data directly from the Pennsylvania Department of Human Services (PADHS) for all FFS and managed care enrollees.

We used Medicaid enrollment data and pharmacy/medical claims to establish an analytic cohort of Medicaid enrollees who initiated a new opioid medication not used for addiction treatment (Appendix 1). We included patients in the study cohort that were between 18–64 years of age, not dually eligible for Medicare (given we could not capture medication use for those >64 years/dually eligible), without previous cancer treatment, not in long-term care for ≥90 days, and not receiving hospice services (as opioid use patterns would likely differ for

these groups). We identified the index opioid exposure event as patients' first oral, transdermal, or submucosal opioid medication fill.

To identify new episodes of opioid medication treatment, we excluded individuals from the cohort that possessed a record of filling any opioid medication, had an opioid use disorder, or experienced an opioid medication overdose in the six months prior to the index opioid fill. This step in the cohort construction allowed us to create a "clean" baseline period for patients before they were exposed to opioid medications and potentially developed abuse or experienced overdose. Lapses in fills following the index fill greater than six months ended patients' eligible treatment episodes. We selected a 6-month gap in fills to end the episode to be consistent with prior studies validating this approach in behavioral health populations.[29] We examined numbers of patient episodes by plan PA status, and no major differences were detected (results not shown). This study was designated exempt by the University of Pittsburgh Institutional Review Board.

Variables

Outcomes.—We identified opioid medication abuse following previously published approaches[30,31] using International Classification of Diseases, 9th Edition (ICD-9)[32] coding classifications and pharmacy claims. After the index fill, enrollees who had any code for an opioid use disorder (ICD9 304.0, 304.00, 304.01, 304.02, 304.03, 304.7, 304.70, 304.71, 304.72, 304.73, 305.5, 305.50, 305.51, 305.52, 305.53) or opioid medication poisoning (ICD-9 965.00 [opium poisoning], 965.02 [methadone poisoning], 965.09 [opiate poisoning-not elsewhere classified], E.850.1 [accidental methadone poisoning], and E.850.2 [accidental opioid poisoning- not elsewhere classified])[33] and had any overlapping fill for a opioid pain medication were categorized as having abuse (no abuse=0, abuse=1).[30,31] Patients meeting this definition of abuse have been observed to have both heightened overdose risk[34] and to have serious behavioral, mental, and/or physical health problems.[30,31] We recognize this definition of abuse does not match the *Diagnostic and Statistical Manual for Mental Disorders*; we chose to employ this term given its previous use in the literature.[30,31]

The opioid overdose indicator used in this analysis followed previously established methods for identifying prescription opioid overdose using International Classification of Disease, 9th edition (ICD-9)[32] codes within claims data.[33] The overdose indicator occurred after the index opioid fill, was comprised of opioid medication poisoning codes (ICD-9 965.00, 965.02, 965.09, E.850.1, E.850.2), and was dichotomized (no overdose=0, overdose=1). These codes capture non-fatal and fatal overdose events resulting in hospitalization, emergency department visits, and /or other medical care. We do not capture overdose events outside of the healthcare system, which events may have largely been untreated within Pennsylvania given the limited and variable availability of naloxone to public safety and prehospital healthcare professionals during the study years. We acknowledge that abuse and overdose are both constructed using poisoning claims, and that there is some overlap between these measures; however, we chose this approach (i.e., not removing the poisoning codes from the abuse indicator) to remain consistent with the previous literature.

PA indicator.—Specification of plans in Pennsylvania Medicaid with PA took place in partnership with the Bureau of Managed Care within PADHS. Officials from the Bureau provided FFS PA information as well as contacted all managed care plans (N=8) via email requesting historical formulary medication management policy information between January 1, 2010 and December 31, 2012. Qualitative responses were transferred into a data tracking template. Given the variation in use of PA across plans in our study data, we followed an ordinal classification approach for categorization of policies similar to those previously employed in the literature.[35] One insurance plan was labeled *Low PA* (required PA for 1 opioid); 2 plans were labeled *High PA* (required PA for 17–74 opioids), and 6 plans were labeled *No PA* based on number of generic, name brand, and combination product medications subjected to PA (Table 1). PA policies were active before or on the first day of our study observation period (1/1/2010), thus limiting our ability to compare differences between plans across time. We therefore conducted a cross-sectional comparison of enrollees across plan types.

Covariates—Covariates were measured in the enrollees' baseline periods. Demographic covariates included in the model were age (18–29, 30–39, 40–49, 50–64 years), sex, race/ethnicity (white, black, Hispanic, other), Medicaid eligibility category (General Assistance, Supplemental Security Income, Temporary Assistance for Needy Families), Medicaid plan type (fee-for- service, managed care organization), and urban/rural county of residence (coded using RuralUrban Continuum Codes[36,37]).

We likewise included measures of comorbidity in the models, which were also measured at baseline. Specific comorbidities included: alcohol use disorders (abuse/dependence), non-opioid drug use disorders (abuse/dependence [e.g., cocaine, marijuana] not including NEC codes [i.e., Not Elsewhere Classified], which clinicians may have used in lieu of opioid use disorder codes), several indicators for mental health disorders (adjustment, anxiety, mood, personality, miscellaneous), separate indicators for pain diagnoses (back, neck, arthritis/joint, headache/migraine), and HIV/AIDS.[38] We included in the model a modified Elixhauser comorbidity index, an indicator that used ICD codes to measure patient comorbidity within administrative claims data from hospitals and physician services. This indicator was modified by removing comorbidities described above that we included as individual covariates. Emergency department use was also included in the model (ED; ≥1 visit[s]=1, <1 visit=0).

We included morphine milligram equivalents (MME) following the index fill but before the occurrence of abuse or overdose. MME was constructed by converting total within-episode opioid supply into morphine equivalents, dividing by days supplied, and coding into 4 levels: ≥100 MME/day, 50-<100 MME/day, 20-<50 MME/day, <20 MME/day.[39] Indicators of medication use that are known correlates with abuse/overdose were also added as covariates in the model, which included any use of benzodiazepines and muscle relaxants in the baseline period. Covariates were all categorical with the exception of the Elixhauser index, which was a count indicator, and age, which was ordinal.

Analyses

With the exception of descriptive demographic characteristics that were calculated at the person-level for patients enrolled in the 3 PA plan types, analyses for this study were conducted at the episode-level. Our modeling strategy needed to account for two features of our data: heterogeneity in the duration of opioid use across episodes and some enrollees having multiple episodes. The importance of accounting for episode-level events for individual enrollees is based on the dynamic nature of patient behaviors and health status across time, which can alter an individual's risk. We therefore employed generalized linear models with generalized estimating equations (GEE) using log link function and Poisson distribution where follow-up length (day) was treated as offset in the model, and the exchangeable covariance structure was employed to account for standard error correlation. These models therefore were able to account for greater exposure to opioids and PA policies within episode and greater numbers of episodes. These models were applied to examine the association between the outcome variables of opioid medication (1) abuse and (2) overdose and the predictor variable of PA adjusted for all covariates described above. We also report abuse and overdose rates with 95% confidence intervals by PA type adjusted for all covariates and offset log length of episode. All analyses were conducted with SAS 9.4.[40]

In an alternative model specification, we estimated both the abuse and overdose outcome analyses using a propensity score matching approach wherein we matched individuals in the High and Low PA plans to those in No PA plans. Results showed no substantive differences; therefore, we chose to present the adjusted GEE results instead of the matched sample for the purpose of simplicity and to maximize our sample size included in the analyses.

Results

The analytic cohort included 297,634 individual plan enrollees, with a total of 382,828 opioid treatment episodes. Enrollees within the cohort typically had multiple opioid treatment episodes, with most patients having an average of 2 episodes (median=1; results not shown). Table 2 presents descriptive patient-level demographic and episode-level health and medication use characteristics. The largest proportions of patients were 18–29 years of age (n=140,876; 47.3%) and were female (n=212,209; 71.3%). The largest proportional differences among PA plans were for race and rural/urban living location. White enrollees were most prominent in High PA plans (77.2%, n=79,965), and Black (47.9%, n=15,950) and Hispanic (31.2%, n=10,386) enrollees were most prominent in the Low PA plan. Most Low (99.9%; n=33,226) and No PA (95.1%; n=152,913) enrollees lived in urban locations compared to 63.7% (n=65,948) of High PA plan enrollees.

The most common level of opioid consumption within episodes (60.9–68.6%) was 20–49.9 MMEs/day following the index opioid fill. Unadjusted rate of abuse within episodes was 3.46 for High PA plans, 2.36 for the Low PA plan, and 3.39 for the No PA plans after the index opioid medication fill. Unadjusted rate of overdose in episodes was 0.26 in High PA plans, 0.19 for the Low PA plan, and 0.29 in No PA plans after the index fill (Table 3).

Results of the GEE analyses adjusted for demographic and health status differences across plan types demonstrated individuals in High PA plans were 11% less likely to develop

opioid medication abuse after their index opioid medication fill compared to those within plans with No PA (95% CI=0.85–0.93, $p<0.001$). Enrollment in the Low PA plan was also associated with a 7% lower rate of developing opioid medication abuse after the opioid medication index fill (95% CI=0.87–1.00, $p=0.04$) relative to No PA. In terms of the relationship between PA and overdose, enrollment in the Low PA plan was associated with a 25% lower rate of experiencing an overdose following the index opioid medication fill (95% CI=0.59–0.95, $p=0.02$). There was a non-significant 12% reduction in (95% CI=0.76–1.02, $p=0.08$) in overdose for enrollees in High PA plans. We recognize that the High PA plans had the highest unadjusted rate of abuse, but after adjustment, the No PA plan was the highest. To identify which set of covariates influenced this change, we re-estimated our model adding blocks of variables to the model in a stepwise fashion (e.g., block 1=abuse, overdose, and MME; block 2=demographics; block 3=mental/behavioral health and co-occurring health conditions [i.e., pain, Elixhauser Index]). Results showed adding the demographic block resulted in the change. We also re-estimated the GEE analyses without the MME covariate to examine its influence on model outcomes. The magnitude/direction of all effects were unchanged removing MME.

Table 5 reports adjusted rates based on the GEE analyses for abuse and overdose per person days (where 452.1 [SD=299.2] was the average number of per person follow-up days for subjects in the cohort). The adjusted rates of abuse were 2.49% for High PA plans, 2.58% for the Low PA plan, and 2.76% for No PA plans per average person days. The adjusted rate of overdose was 0.21% for High PA plans, 0.17% for the Low PA plan, and 0.23% for No PA plans per average person days.

Discussion

The opioid medication epidemic has brought to the forefront of healthcare practice and policy the need to identify and intervene with patients engaged in abuse and at-risk for overdose. Policy-level efforts that limit access to opioid medications and influence patient/prescriber behaviors have the potential to make an important impact for reducing negative patient outcomes. We analyzed data from Medicaid enrollees who developed opioid pain medication abuse or experienced overdose after initiating opioid treatment who were within plans that operated PA policies compared to plans that did not. Our findings showed a minority of plans implemented PA policies (3/9 plans), and there was substantial variation in the number of medications within plans subjected to PA policies (range=1–74).

Enrollment in High and Low PA plans was associated with modestly lower adjusted rates of opioid medication abuse, and enrollment in the Low PA plan was associated with lower adjusted rates of overdose. These results are consistent with previously published studies that have examined the effect of PA on opioid medication fills. Specifically, our findings that PA was associated with 7 to 11% (<0.05) lower rates for abuse and 12 ($p=0.08$) to 25% ($p=0.02$) lower rates for overdose are consistent with studies that have reported 8 to 19% reductions in long- acting opioid medication fills among enrollees in plans that utilized PA policies.[14,15]

A central point of importance for our findings is they advance previous studies reporting reductions in long-acting opioid medication fills, which outcome metric has limited ability to differentiate between patients with problematic use and those who may benefit from opioid medications. Assessing only fills as an outcome also cannot disentangle patient and prescriber behavior. Accordingly—evaluating benefit of PA policies by changes in abuse and overdose more effectively discriminates reductions in potential repercussions of opioid use—perhaps demonstrating an outcome especially relevant to combatting the national opioid epidemic. Further, reductions in abuse, for example, could have valuable ramifications for health systems, payers, and prescriber stakeholders as patients with opioid use disorders have higher healthcare needs, utilization, and costs.[41]

Future research should seek to extend our findings by examining the effect of PA within an analytical framework capable of examining both within and between group differences over time. Such studies should seek account for legitimate pain management needs of patients. In particular, while abuse and overdose are both important outcomes for patient safety and health, future studies should examine potentially unintended consequences of PA plans on patients, such as under-treatment of painful conditions[42] or transition to heroin use.[2] If future research continues to provide support for PA, broader implementation of these policies may necessitate streamlined and automated approaches to minimize disruption to medical/pharmacy workflow.[21]

Limitations

These findings should be viewed in light of certain limitations. First, while we recognize strengths of our study include possessing actual PA information from Medicaid plans, having complete FFS and managed care data, and Pennsylvania being similar to other programs in the nation with respect to healthcare utilization, access,[25] and demographics;[26] it nonetheless represents one state in the US. Second, the last year for our data was 2012, and some analyses have shown reductions in opioid abuse and diversion in more recent years.[43] Furthermore, the larger Medicaid landscape has evolved since this date, including the expansion of Medicaid through the Affordable Care Act in Pennsylvania as in many other states. Studies conducted with more recent data may yield different estimates as a result of these changes. PADHS also recently implemented additional restrictions on opioids,[44,45] that may yield even greater benefit. However, these policies went into effect after our study period ended so we were unable to evaluate them. Third, we used a simple and straightforward approach to categorizing PA schemes (High, Low, and No based on the number of products subject to PA). It is possible our data collection method did not capture other aspects of these policies such as the ease of use that may influence prescribing behavior. It is also possible that we did not capture information on all plan features or policies that may influence opioid prescribing and use. In light of this, we recognize our characterization of the policies may not capture the full range of interventions plans may have had in place. We note, however, that enrollees with evidence of opioid medication misuse have an equal possibility of enrollment in the state Medicaid agency operated lock-in program. Fourth, while the abuse measure is one of the more common and valid indicators in the field,[46] it has the potential to misclassify individuals engaged legitimate use of opioids. Moreover, while we have been able to adjust for a number of patient-level characteristics in

our analyses that could have introduced bias into our findings, other individual- level factors and regional variation in our outcomes could have influenced study outcomes. Future research should seek to employ quasi-experimental designs with comparison groups, such as difference-in-differences analyses, to help better understand the impact of PA. Last, we recognize opioid use disorders are likely under-coded within claims data[47] and claims data do not account for cash payments to prescribers/pharmacies, which could influence observed associations were these data available.[48]

Conclusion

This study examined associations between PA requirements and developing abuse or experiencing an opioid medication overdose following an index opioid medication fill for Medicaid enrollees. These findings extend previous research by demonstrating improved outcomes among patients within PA plans in terms of lower rates of abuse and overdose. Future research should seek to extend these findings within more rigorous causal designs/ analyses and among other Medicaid and commercial payer data to continue building evidence for PA policies reducing problematic opioid behaviors and consequences.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Take-Away Points:

Health insurance payers can implement policies to help curb the opioid epidemic. This retrospective cohort study of Pennsylvania Medicaid data examined associations between Medicaid plans that utilized prior authorization policies for opioid medications and enrollees: (1) developing opioid medication abuse or (2) experiencing overdose.

- Enrollees within plans that subjected opioid medications to prior authorization policies had lower rates of opioid medication abuse and overdose after initiating opioid medication treatment.
- Future research should work to extend these findings in order to support systematic and large scale implementation of prior authorization policies for opioid medications.

Table 1.

Summary Description of Prior Authorization by Plan

Plan	N of medications subject to prior authorization [a]	Earliest date of implementation [b]
Low prior authorization plan		
Plan A	1 [c]	1/2010
High prior authorization plans		
Plan B	17	<2010
Plan C	74	<2010
No Prior authorization plans		
Plans D-I	None	Not applicable

[a] Number (N) of medications includes generic, name brand, and combination products

[b] date represents first date reported for any medication subjected to PA requirement

[c] the single medication was OxyContin.

Table 2.

Demographic, Behavioral Health Characteristics, and Comorbidities by Level of Prior Authorization

Characteristics	Total n (%)	High Prior Authorization n (%)	Low prior authorization n (%)	No prior authorization n (%)
Patient Level [a]	297,634 (100.0)	103,587 (34.8)	33,270 (11.2)	160,777 (54.0)
Demographics				
Age, y				
18–29	140,876 (47.3)	50,946 (49.2)	13,619 (40.9)	76,311 (47.5)
30–39	66,258 (22.3)	23,366 (22.6)	7,188 (21.6)	35,704 (22.2)
40–49	47,584 (16.0)	15,696 (15.2)	6,130 (18.4)	25,758 (16.0)
50–64	42,916 (14.4)	13,579 (13.1)	6,333 (19.0)	23,004 (14.3)
Female	212,209 (71.3)	73,891 (71.3)	23,568 (70.8)	114,750 (71.4)
Race				
White	167,175 (56.2)	79,965 (77.2)	5,418 (16.3)	81,792 (50.9)
Black	83,874 (28.2)	14,641 (14.1)	15,950 (47.9)	53,283 (33.1)
Hispanic	35,885 (12.1)	6,416 (6.2)	10,386 (31.2)	19,083 (11.9)
Other	10,700 (3.6)	2,565 (2.5)	1,516 (4.6)	6,619 (4.1)
Urban	252,087 (84.7)	65,948 (63.7)	33,226 (99.9)	152,913 (95.1)
Type of eligibility				
GA	32,256 (10.8)	9,162 (8.8)	5,075 (15.3)	18,019 (11.2)
SSI	86,785 (29.2)	31,167 (30.1)	10,702 (32.2)	44,916 (27.9)
TANF	178,593 (60.0)	63,258 (61.1)	17,493 (52.6)	97,842 (60.9)
Medicaid region				
Region 1	54,475 (18.3)	13,233 (12.8)	112 (0.3)	41,130 (25.6)
Region 2	38,602 (13.0)	36,791 (35.5)	74 (0.2)	1,737 (1.1)
Region 3	26,861 (9.0)	23,346 (22.5)	8 (0.0)	3,507 (2.2)
Region 4	104,890 (35.2)	8,780 (8.5)	33,044 (99.3)	63,066 (39.2)
Region 5	72,806 (24.5)	21,437 (20.7)	32 (0.1)	51,337 (31.9)
Episode-level [b] **(N=382,828)**				
Behavioral and Mental Health				
Alcohol use disorder	9,973 (2.6)	3,342 (2.6)	978 (2.3)	5,653 (2.7)
Drug use disorder	8,795 (2.3)	2,383 (1.8)	1,058(2.5)	5,354 (2.5)
Adjustment disorders	8,509 (2.2)	3,274 (2.5)	810 (1.9)	4,425 (2.1)
Anxiety disorders	39,604 (10.4)	13,958 (10.8)	4,102 (9.5)	21,544 (10.2)
Mood disorders	84,437 (22.1)	28,332 (21.9)	10,970 (25.5)	45,135 (21.4)
Personality disorders	2,034 (0.5)	847 (0.7)	109 (0.3)	1,078 (0.5)
Miscellaneous mental health disorders	12,082 (3.2)	3,957 (3.1)	1,522 (3.5)	6,603 (3.1)
Painful Conditions and Healthcare Utilization				

Characteristics	Total n (%)	High Prior Authorization n (%)	Low prior authorization n (%)	No prior authorization n (%)
Back pain	67,346 (17.6)	22,971 (17.8)	8,294 (19.3)	36,081 (17.1)
Neck pain	23,822 (6.2)	8,246 (6.4)	2,738 (6.4)	12,838 (6.1)
HIV/AIDS	3,525 (0.9)	495 (0.4)	878 (2.0)	2,152 (1.0)
Arthritis/joint pain	76,691 (20.0)	25,312 (19.6)	9,468 (22.0)	41,911 (19.9)
Headache/migraine pain	15,514 (4.1)	5,722 (4.4)	1,380 (3.2)	8,412 (4.0)
ED visit	180,045 (47.0)	59,237 (45.8)	20,528 (47.7)	100,280 (47.6)
Medication Use				
Benzodiazepine use	55,986 (14.6)	18,287 (14.2)	7,317 (17.0)	30,383 (14.4)
Muscle relaxant use	36,597 (9.6)	12,555 (9.7)	4,484 (10.4)	19,558 (9.3)
Comorbidity				
Elixhauser index[c]	1.12 (1.62)	1.07 (1.57)	1.42 (1.84)	1.09 (1.59)

[a]Measured at the person level, N=297,634;

[b]Measured at the event-level, N=382,828;

[c]mean (standard deviation)

Table 3.

Post-Index Fill Unadjusted Rates of Abuse, [a] Overdose, [a] and Morphine Milligram Equivalents (MME) [b] by Prior Authorization Type [c]

Indicator	No prior authorization	Low Prior Authorization	High Prior Authorization
Abuse	3.39	2.36	3.46
Overdose	0.29	0.19	0.26
MME/Day			
<20	17.0	21.8	15.4
20–49.9	67.9	60.9	68.6
50–99.9	12.6	14.8	13.4
>100	2.5	2.6	2.6

[a] Abuse and overdose rates are calculated after the index fill.

[b] Morphine milligram equivalents are calculated after the index fill and before abuse and overdose occur.

[c] Analyses conducted at the episode-level.

Table 4.

Generalized Estimating Equation Estimates for Opioid Abuse [a] and Overdose [b] Adjusted for All Covariates and Offset by Log Length of Episode [c]

	Abuse		Overdose	
Predictor	**ARR (95% CI) [d]**	***p* [e]**	**ARR (95% CI)**	***p***
Prior authorization (reference =No prior authorization)				
Low	0.93 (0.87–1.00)	0.04	0.75 (0.59–0.95)	0.02
High	0.89 (0.85–0.93)	<.001	0.88 (0.76–1.02)	0.08
Categorical MME [f], MME/day (reference=<20)				
20–49.9	1.05 (1.00–1.10)	0.06	0.97 (0.82–1.16)	0.77
50–99.9	1.17 (1.10–1.25)	<.001	1.42 (1.15–1.75)	0.001
≥100	2.12 (1.97–2.28)	<.001	2.58 (2.04–3.27)	<.001
Demographics				
Race (reference=Other)				
White	2.12 (1.86–2.42)	<.001	1.41 (0.92–2.16)	0.11
Black	0.92 (0.80–1.05)	0.21	0.90 (0.58–1.40)	0.65
Hispanic	0.81 (0.70–0.93)	0.004	0.62 (0.38–1.01)	0.06
Female	0.70 (0.67–0.73)	<.001	0.87 (0.75–1.00)	0.04
Age, y	0.86 (0.85–0.88)	<.001	0.99 (0.93–1.05)	0.73
Urban	1.13 (1.07–1.19)	<.001	1.33 (1.10–1.62)	0.004
Eligibility type (reference=Temporary Assistance for Needy Families)				
General assistance	1.77 (1.67–1.86)	<.001	1.58 (1.28–1.94)	<.001
Supplemental Security Income	0.94 (0.90–0.98)	0.005	1.26 (1.08–1.48)	0.004
Mental/behavioral health				
Alcohol abuse/dependence	1.42 (1.32–1.54)	<.001	1.47 (1.14–1.90)	0.003
Non-opioid drug use disorder	2.08 (1.92–2.24)	<.001	1.26 (0.92–1.71)	0.15
Adjustment disorders	1.12 (1.01–1.23)	0.03	1.11 (0.81–1.53)	0.51
Anxiety disorders	1.21 (1.16–1.27)	<.001	1.26 (1.07–1.48)	0.005
Mood disorders	1.41 (1.35–1.48)	<.001	1.29 (1.12–1.50)	<.001
Personality disorders	0.97 (0.83–1.13)	0.69	0.87 (0.50–1.52)	0.63
Miscellaneous mental health disorders	1.05 (0.96–1.14)	0.31	1.01 (0.74–1.38)	0.95
Painful conditions and healthcare utilization				
Back pain	1.26 (1.21–1.31)	<.001	1.29 (1.12–1.49)	<.001
Neck pain	1.06 (1.00–1.12)	0.04	1.17 (0.98–1.41)	0.08
HIV/AIDS	1.68 (1.45–1.94)	<.001	1.04 (0.59–1.85)	0.89
Arthritis/joint pain	0.95 (0.91–0.99)	0.01	1.13 (0.99–1.30)	0.07

	Abuse		Overdose	
Predictor	**ARR (95% CI)** [d]	***p*** [e]	**ARR (95% CI)**	***p***
Headache/migraine pain	0.95 (0.88–1.02)	0.17	0.99 (0.77–1.28)	0.96
Health services/comorbidity				
ED visit	1.28 (1.23–1.33)	<.001	1.43 (1.25–1.63)	<.001
Medication use				
Benzodiazepine use	1.73 (1.66–1.81)	<.001	2.12 (1.82–2.46)	<.001
Muscle relaxant use	1.18 (1.13–1.24)	<.001	1.40 (1.20–1.64)	<.001
Comorbidity				
Elixhauser comorbidity index	0.94 (0.92–0.95)	<.001	1.06 (1.02–1.10)	0.004

[a] Number of abuse events is 12,631

[b] number of overdose events is 1,024

[c] Analyses conducted at the episode-level.

[d] ARR=adjusted rate ratio, CI=confidence interval;

[e] *p*=probability value;

[f] MME/day observed before abuse or overdose.

Table 5.

Abuse and Overdose Rate with 95% Confidence Interval by Prior Authorization Adjusted Rate Ratio for All Covariates and Offset by Log Length of Episode (Day) [a, b]

Indicator	ARR [b]	(95% CI)
Abuse		
High PA	2.49	(2.35–2.62)
Low PA	2.58	(2.40–2.76)
No PA	2.76	(2.67–2.89)
Overdose		
High PA	0.21	(0.17–0.25)
Low PA	0.17	(0.14–0.22)
No PA	0.23	(0.20–0.27)

[a] Average number of follow-up days for subjects=452.1 (SD=299.2). ARR=Adjusted Rate Ratio.

[b] Analyses conducted at the episode-level.