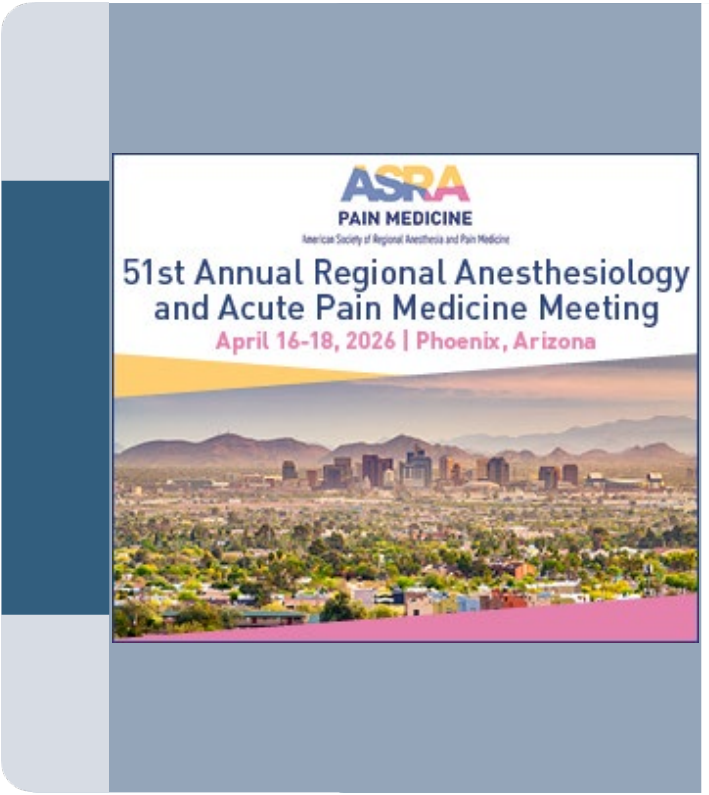




Characteristics of Initial Opioid Prescriptions and Risk of New Persistent Opioid Use and OUD: US Commercial/Medicare Populations

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BACKGROUND

- Opioids remain widely prescribed for post-surgical acute pain despite the significant risks of misuse, dependency, and addiction.
- New persistent opioid use (NPOU) after surgery occurs when a patient is prescribed opioids for short-term post-surgical acute pain but then continues to fill opioid prescriptions beyond the period in which their acute pain should resolve.¹
- NPOU is a major concern, associated with higher risk of long-term complications, increased healthcare resource utilization, opioid use disorder (OUD), and mortality.
- OUD is a chronic condition characterized by the problematic pattern of opioid use, leading to significant health impairment, reduced quality of life, and substantial burdens on healthcare systems and society.²
- Given long-term opioid use often stems from short-term opioid prescriptions for acute pain and considering the significant impacts of NPOU and OUD on patients, there is a critical need to better understand how characteristics of the initial opioid prescriptions impact the risk of NPOU and OUD.^{3,4}

OBJECTIVES

- To evaluate the relationship between characteristics of the initial opioid prescription (e.g., days' supply) and risk of NPOU among opioid-naïve post-surgical patients with acute pain in the Commercial/Medicare populations.
- Additionally, to analyze the impact of days' supply of the initial opioid prescription on the incidence of OUD.

METHODS

- A retrospective, longitudinal, observational study was conducted using the Merative MarketScan Commercial and Medicare databases. The study period was from January 1, 2015, through June 30, 2024.
- Opioid naïve adult patients (aged ≥18 years) who were prescribed an opioid medication (date of earliest treatment = index date) between January 1, 2016, and June 30, 2023, either within 14 days before or 30 days after a major surgical procedure for the management of post-surgical acute pain and without a cancer diagnosis in the 12-month period prior to index date were included in the analysis.
 - Opioid naïve was defined as no pharmacy or medical claim for an opioid and no medical claim for OUD (based on ICD-10-CM diagnosis codes for opioid abuse [F11.1*] or opioid dependence [F11.2*]) in the 12-month period prior to index date.
 - Patients were also required to have at least 12 months of continuous enrollment prior to and following the index date.
- Days' supply and daily dose (defined by morphine milligram equivalent [MME]/day) of the initial opioid prescription were assessed.
 - Daily dose was categorized into low (<36MME/day), medium (36-<120MME/day), and high (≥120MME/day).
- The incidence of NPOU was estimated; NPOU was defined as an opioid prescription between 90-180 days after the initial prescription, stratified by days' supply and daily dose of the initial opioid prescription.⁵
- The incidence of OUD was evaluated based on ICD-10-CM diagnosis codes from the index date through the earlier of disenrollment or end of the study period and stratified by days' supply.
- Descriptive analyses were performed for all outcomes. A multivariable logistic regression model was utilized to evaluate the association between the days' supply and daily dose of the initial opioid prescription and the incidence of NPOU, adjusting for potential confounding variables.
- Deidentified administrative claims data were used; therefore, institutional review board approval was not required.

RESULTS

Population and Patient Characteristics

- 1,223,995 opioid-naïve patients in the MarketScan Commercial/Medicare population were prescribed opioids for post-surgical acute pain.
- Patient demographics, clinical, and surgical characteristics are described in **Table 1**.

Table 1. Patient Characteristics

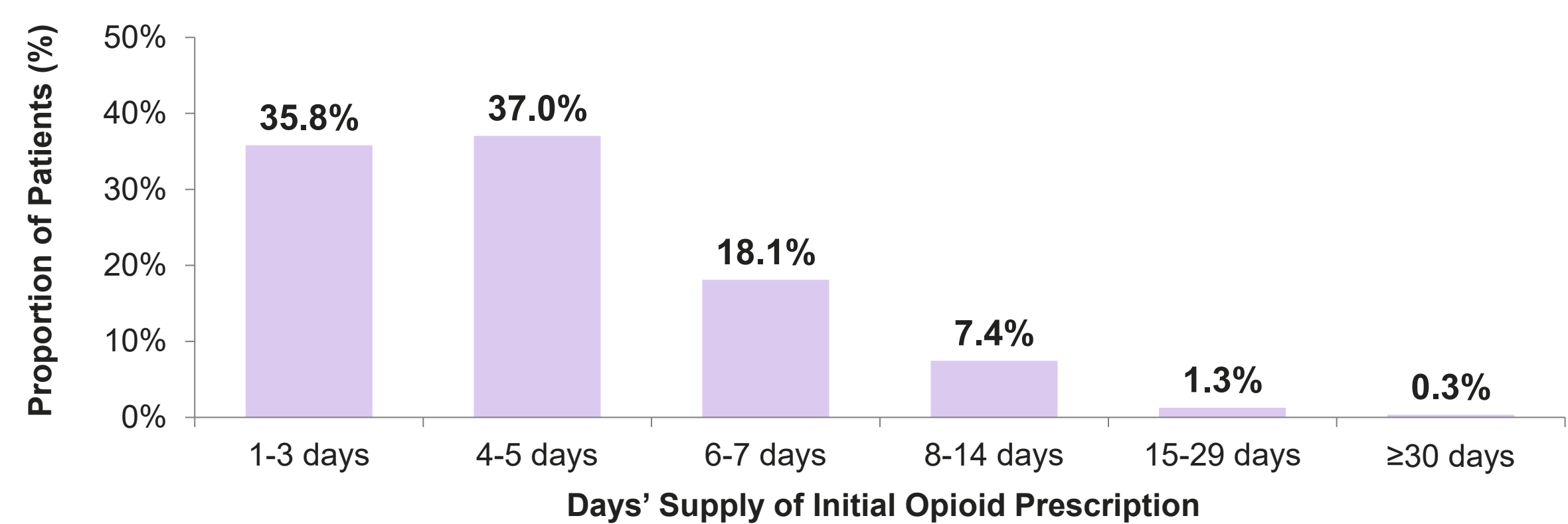
Characteristic	N = 1,223,995
Age (years), mean (SD)	46.7 (14.9)
Male, n (%)	501,549 (41.0)
Payer, n (%)	
Commercial	1,116,242 (91.2)
Medicare	107,753 (8.8)
DCCI, mean (SD)	0.42 (0.94)
Most Common Clinical Conditions ^a , n (%)	
Hypertension	345,929 (28.3)
Obesity	238,480 (19.5)
Osteoarthritis	209,706 (17.1)
Hypercholesterolemia	167,822 (13.7)
Anxiety	163,847 (13.4)
Sleep disorders	150,468 (12.3)
Diabetes	120,123 (9.8)
Depression	116,434 (9.5)
Tobacco use ^b	84,533 (6.9)
Surgery Type ^a , n (%)	
Orthopedic	518,997 (42.7)
General	290,255 (23.7)
Gynecologic and Male Reproductive	234,797 (19.2)
ENT	87,526 (7.2)
Plastic	75,215 (6.1)
Cardiothoracic	34,511 (2.8)
Neurosurgery	22,854 (1.9)
Ophthalmologic	17,187 (1.4)
Urologic	10,701 (0.9)
Other	3,135 (0.3)

^a Categories are not mutually exclusive. ^b Includes current or history of tobacco use. ENT, ear, nose, and throat; N: number of participants; n: number of participants in the specified category; SD: standard deviation.

Characteristics of Initial Opioid Prescriptions

- The mean (standard deviation [SD]) days' supply of the initial opioid prescription was 4.9 (3.1) days, with 91% of patients receiving ≤7 days and 36% receiving brief prescriptions of 1–3-days (**Figure 1**).
- Among patients with a calculable MME, the mean (SD) daily dose of the initial prescription was 48.4 (26.1) MME/day, with 31% and 67% of patients receiving a low and medium daily dose, respectively.

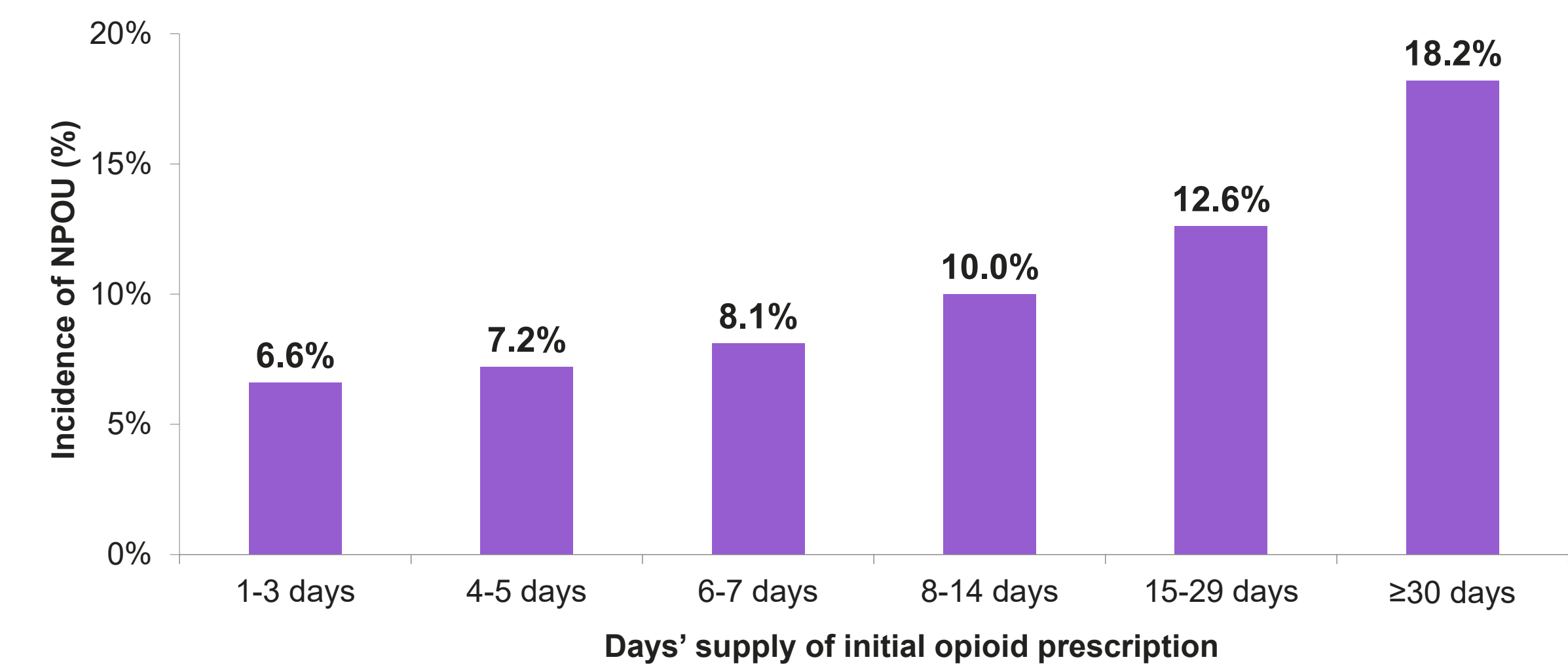
Figure 1. Distribution of Days' Supply of Initial Opioid Prescription



New Persistent Opioid Use

- The incidence NPOU increased substantially with longer days' supply of initial opioid prescription.
- Brief opioid prescriptions of 1-3 days had a 6.6% incidence of NPOU, which increased to 7.2% for 4-5 days' supply and 8.1% for 6-7 days' supply (**Figure 2**).
 - Overall, opioid prescriptions of ≤7 days had a 7.1% incidence of NPOU.

Figure 2. Incidence of NPOU Stratified by Days' Supply of Initial Opioid Prescription



- The incidence of NPOU was 7.2% among individuals prescribed low daily doses of initial opioids, increasing to 7.5% for medium daily doses and 9.9% for high daily doses.
- When adjusting for covariates, each additional day of initial opioid prescription significantly increased the odds of NPOU by 3.5% (OR 1.035 [95% CI: 1.033-1.037]; p<0.001) (**Table 2**).
 - A medium daily dose of initial opioid prescription increased the odds of NPOU by 4% (OR 1.04 [95% CI: 1.03-1.06]; p<0.001) compared to a low daily dose.

Table 2. Multivariate Logistic Regression Analysis: Association Between Days' Supply and Daily Dose of Initial Opioid Prescription Characteristics and Risk of New Persistent Opioid Use

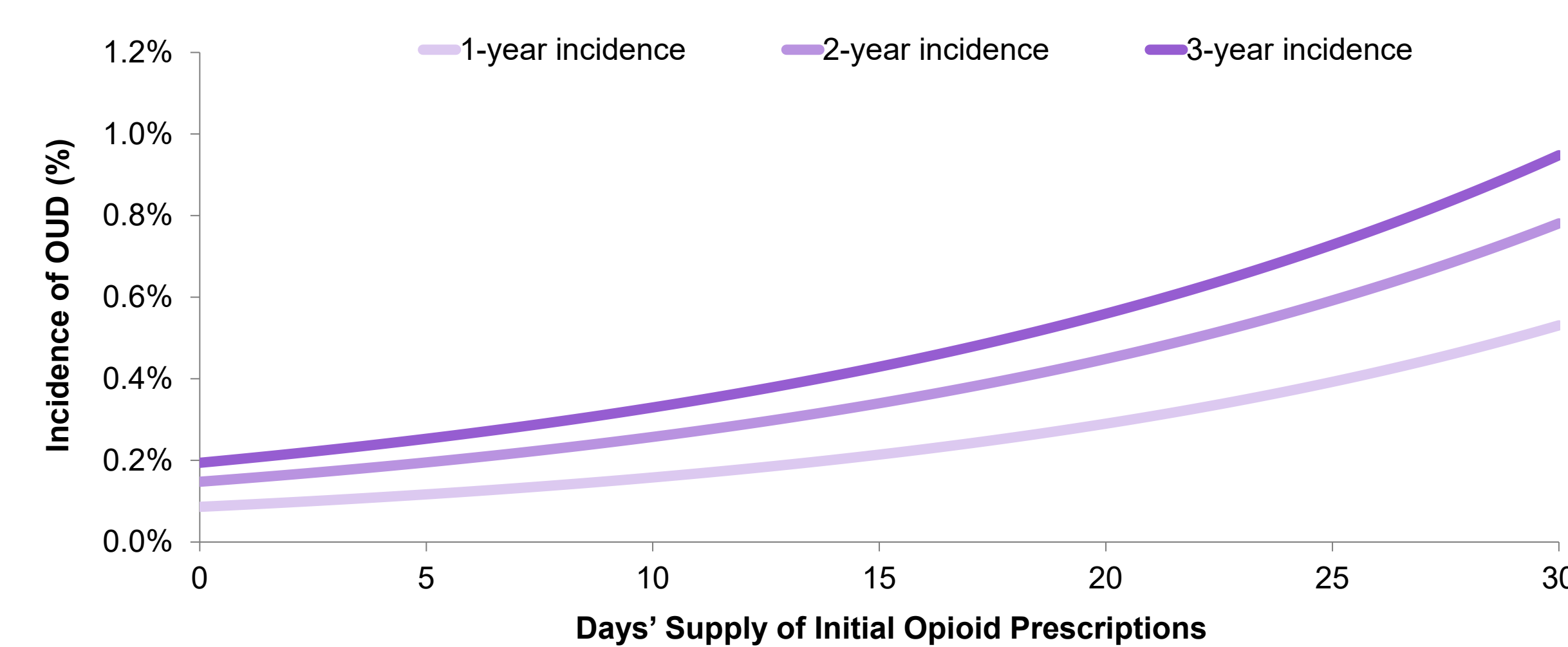
Characteristic	Odds Ratio (95% CI)	P Value
Days' Supply (1-day)	1.04 (1.03-1.04)	<0.001
Daily Dose (MME/day)		
Low (<36 MME/day)	1 [Reference]	-
Medium (36-<120 MME/day)	1.04 (1.03-1.06)	<0.001
High (≥120 MME/day)	1.32 (1.26-1.38)	<0.001
Age		
18-24	1 [Reference]	-
25-34	0.89 (0.86-0.93)	<0.001
35-45	1.09 (1.05-1.12)	<0.001
45-54	1.31 (1.27-1.35)	<0.001
55-65	1.51 (1.47-1.56)	<0.001
≥65	1.42 (1.37-1.47)	<0.001
Female	1.08 (1.06-1.10)	<0.001
Deyo Charlson Comorbidity Index	1.13 (1.12-1.13)	<0.001
Clinical comorbid conditions		
Anxiety	1.18 (1.15-1.20)	<0.001
Depression	1.19 (1.17-1.22)	<0.001
Obesity	1.12 (1.11-1.14)	<0.001
Hypertension	1.18 (1.16-1.20)	<0.001
Sleep disorders	1.20 (1.17-1.22)	<0.001
Substance abuse ^a	1.28 (1.22-1.34)	<0.001
Tobacco use ^a	1.28 (1.25-1.31)	<0.001

^a Includes current or history of substance abuse/tobacco use. CI, confidence interval; MME, morphine milligram equivalent.

Opioid Use Disorder

- The 1-, 2-, and 3-year cumulative incidence of OUD also increased with longer days' supply of initial opioid prescription (**Figure 3**).
- Even brief prescriptions of 1-3 days had a 1-, 2-, and 3-year cumulative OUD incidence of 0.10%, 0.17%, and 0.23%, respectively.

Figure 3. Cumulative Incidence of OUD Stratified by Days' Supply of Initial Opioid Prescription



LIMITATIONS

- This study identified opioid-naïve patients identified through the absence of pharmacy or medical claims for an opioid and OUD diagnosis during the 12 months prior to index date, however, patients could have had a claim for an opioid outside the study period.
- This study included patients without a documented diagnosis of OUD in the 12 months prior to the index date. However, it is possible that some patients may have had a diagnosis outside the study period or remained clinically undiagnosed
- The incidence of OUD was assessed using specific ICD-10 codes from claims data. This approach does not capture patients diagnosed through other methods or those exhibiting OUD symptoms without a clinical diagnosis, likely leading to an underestimation of the true incidence of OUD.
- The MarketScan Commercial and Medicare datasets are convenience samples comprised of people with employer sponsored health insurance and people with Medicare Advantage and Medicare Supplemental insurance plans; therefore, there may be limitations associated with generalizing results to the general population.

DISCUSSION

- Short-duration opioid prescriptions for post-surgical acute pain are associated with a substantial risk of NPOU and OUD, with the risk increasing with each additional days' supply of the initial prescription.
 - Even brief opioid prescriptions of just 1-3 days pose a notable risk of NPOU and OUD, underscoring the need to eliminate opioid exposure.
 - Further, even low daily doses (<36MME/day) of opioids have a profound risk of NPOU, which increases significantly with a medium daily dose.
- Based on the findings of this study, approximately 1 in 15 patients prescribed a brief opioid prescriptions (1-3 days) may develop NPOU, while around 1 in 417 patients may be diagnosed with OUD within 3-years of opioid exposure.
- Given the high volume of post-surgical opioid prescribing for acute pain in the US, NPOU and OUD affect a substantial number of individuals, resulting in significant implications for patients, the healthcare systems, and society at large.

CONCLUSIONS

- These findings highlight the significant risk associated with even short duration and/or low doses of opioid prescriptions in developing NPOU and OUD. They underscore the importance of prioritizing effective and safe non-opioid analgesics for managing post-surgical acute pain.

References

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