Real-World Economic Benefit of Administering Naloxone Among Patients with High- and Low-Dose Opioid Overdose

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Background

Consequences of Prescription Opioid Misuse in the United States

- 9.3 million people in the United States reported prescription opioid misuse in 2020.[1]
- 2.3 million individuals were estimated to have opioid use disorders in 2020.[1]
- 68,630 Americans died from an opioid overdose in 2020, including 56,516 overdose deaths involving synthetic opioids (primarily fentanyl) and 16,416 overdose deaths involving prescription opioids.[2]
- Prescription opioid overdose costs the United States $78.5 billion a year.[3]
- According to a recent study conducted by a healthcare improvement company, opioid overdoses account for more than $11 billion in annual hospital costs nationwide.[4]

Opioid Dose and Overdose Risk

- According to Centers for Disease Control and Prevention (CDC) guidelines for prescribing opioids, clinicians should be cautious when considering high-dose opioid prescriptions ≥50 morphine milligram equivalents (MME) per day.[5]
- Although most patients receiving opioid therapy are prescribed low to moderate doses, high doses of opioids are indicated in conditions such as sickle cell disease, back pain, cancer, and palliative care.[6-7]
- Several studies have found a significantly increased risk of inadvertent prescription opioid overdose, starting at dosages above 20 MME per day.[8-10]
- Although higher opioid doses are associated with increased risk of opioid overdose death, more than 40% of prescription opioid overdose deaths occurred in individuals prescribed low-dose opioids (<50 MME per day).[8-9]

Naloxone

- Naloxone is a medication that can rapidly reverse an opioid overdose and restore normal breathing.
- Current opioid prescription guidelines recommend co-prescribing naloxone to patients at risk for opioid overdose.[11]

Objectives

A US healthcare claims database was analyzed to identify low-dose opioid overdose patients (LDOOP) and high-dose opioid overdose patients (HDOOP) from 2016-2019.

Our study assessed:

- Rates of low- and high-dose prescription opioid overdose by state and payor (overall, commercial, Medicare, and Medicaid).
- Characteristics of LDOOP and HDOOP by payor.
- Rates of naloxone administration at index event among LDOOP and HDOOP by payor.
- Total healthcare costs for LDOOP and HDOOP treated with and without naloxone at index event by payor.

Methods

Study Design

- A retrospective cohort study.

Data Source

- Optum's Clinformatics® Data Mart (CDM) that is derived from administrative health claims for members of large Commercial, Medicare Advantage, and Managed Medicaid health plans.[12]

Patient Inclusion Criteria

- Adult patients (≥18 years old) with both an opioid prescription and an opioid overdose index event (first opioid overdose claim date) occurring between January 1, 2016 and December 31, 2019.
  - LDOOP cohort: opioid overdose patients with at least one low-dose prescription opioid (<50 MME per day) filled within the year and/or on the opioid overdose index event date.
  - HDOOP cohort: opioid overdose patients with at least one high-dose opioid prescription (≥50 MME per day) filled within the year and/or on the opioid overdose index event date.
  - Opioid prescriptions classified as low- or high-dose based on CDC prescription guidelines.[5]
- 12-month continuous medical and drug plan enrollment pre- and post-index (2 years of continuous coverage in total).

Analysis

- LDOOP and HDOOP rates were analyzed by insurance coverage (commercial, Medicare, and Medicare), state, comorbidities, healthcare costs for index event, and total costs with and without naloxone administration at index event. Patient comorbidities were characterized using the Charlson Comorbidities Index (CCI).
- International Classification of Disease (ICD)-9-CM and ICD-10-CM codes (opioid overdose diagnosis) and National Drug Codes (opioid prescription) were used to search claims.

Results

Figure 1. Characteristics of Prescription Opioid Overdose Patients by Payor

	LDOOP				HDOOP			
	Overall n=10,665	Commercial n=1,315 (12.33%)	Medicare n=3,996 (37.47%)	Medicaid n=5,354 (50.20%)	Overall n=6,833	Commercial n=698 (10.21%)	Medicare n=3,528 (51.63%)	Medicaid n=2,607 (38.15%)
Age (SD)	53 (17)	43 (16)	67 (12)	45 (14)	57 (14)	47 (15)	64 (10)	49 (13)
Gender								
Female	6,581 (61.71%)	749 (56.96%)	2,711 (67.84%)	2,233 (41.71%)	4,044 (59.18%)	395 (56.59%)	2,076 (58.84%)	1,573 (60.34%)
Male	4,804 (38.29%)	566 (43.04%)	1,285 (32.16%)	3,121 (58.29%)	2,789 (40.82%)	303 (43.41%)	1,452 (41.16%)	1,034 (39.66%)
Race								
Caucasian	6,383 (59.85%)	890 (67.68%)	2,501 (62.59%)	2,992 (55.88%)	4,225 (61.83%)	499 (71.49%)	2,356 (66.78%)	1,370 (52.55%)
African American	1,437 (13.47%)	103 (7.83%)	526 (13.16%)	808 (15.09%)	789 (11.55%)	48 (6.88%)	402 (11.39%)	339 (13.00%)
Hispanic	666 (6.24%)	137 (10.42%)	386 (9.66%)	143 (2.67%)	374 (5.47%)	59 (8.45%)	254 (7.20%)	61 (2.34%)
Asian	107 (1.00%)	27 (2.05%)	55 (1.38%)	25 (0.47%)	68 (1.00%)	15 (2.15%)	44 (1.25%)	9 (0.35%)
Other	2,072 (19.43%)	158 (12.02%)	528 (13.21%)	1,386 (25.89%)	1,377 (20.15%)	77 (11.03%)	472 (13.38%)	828 (31.76%)
CCI score, mean	2.30	1.43	3.66	1.49	2.88	1.95	3.71	2.00
At least one CCI comorbidity	7,352 (68.94%)	719 (54.68%)	3,591 (89.86%)	3,042 (56.82%)	5,383 (78.78%)	461 (66.05%)	3,173 (89.94%)	1,749 (67.09%)

Rates by state

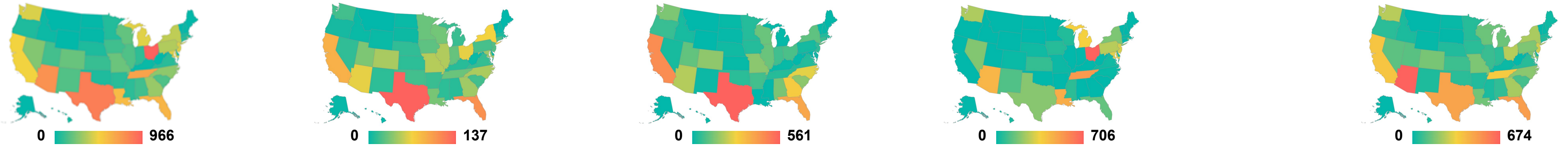


Figure 2. Comorbidities Among Prescription Opioid Overdose Patients by Payor

Figure 3. Administration of Naloxone Among Prescription Opioid Overdose Patients, At-Index

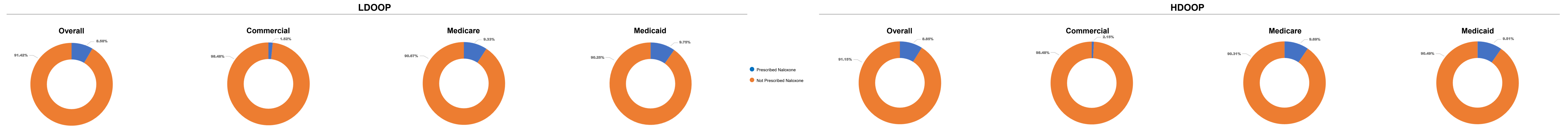
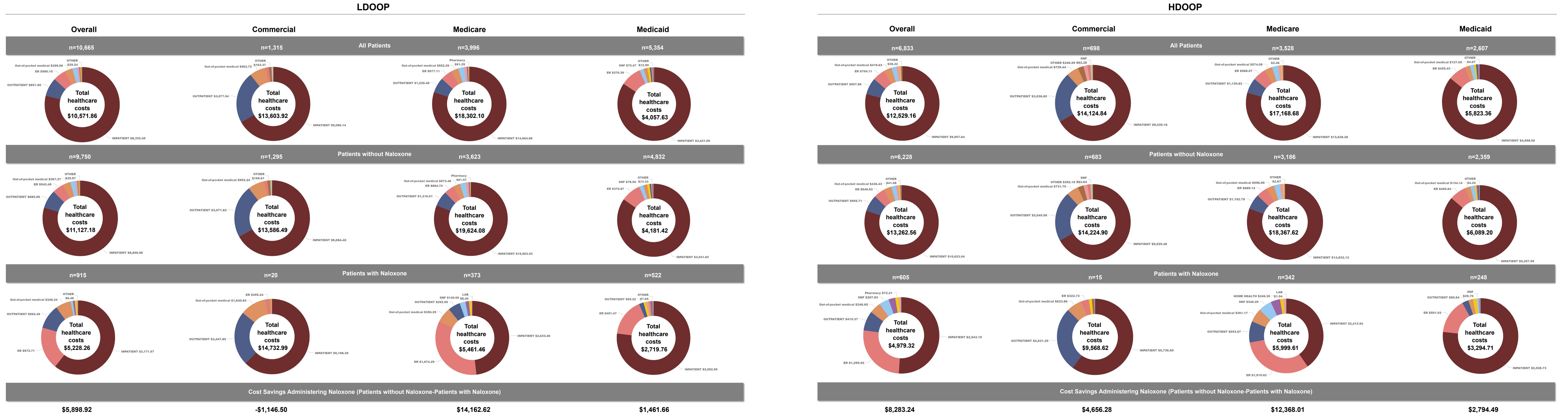


Figure 4. Inflation-Adjusted Costs Associated with Treatment of Opioid Overdose (At-Index Event)



Key Findings

Patient Characteristics

- 10,665 low-dose prescription opioid overdose patients and 6,833 high dose prescription opioid overdose patients were identified between 2016 and 2019.
- The average age of the LDOOP cohort was 53 years (SD±17), with the highest average age among the Medicare population (67), followed by those with Medicaid (45) and commercial insurance (43). LDOOP were mostly female (61.71%), Caucasian (59.85%), and covered by Medicaid (50.20%). States with the highest LDOOP rates were TX (9.06%), OH (7.99%), AZ (6.65%), TN (6.64%), and FL (5.70%).
- The average age of the HDOOP cohort was 57 years (SD±14), with the highest average age among the Medicare population (64), followed by those with Medicaid (49) and commercial insurance (47). The majority of HDOOP were female (59.18%), Caucasian (61.83%), and insured by Medicare (51.63%). States with the highest number of HDOOP included AZ (9.86%), FL (8.58%), TX (7.90%), TN (6.37%), and CA (5.58%).

Comorbidities among LOORCP and non-LOORCP

- Overall, more than two-thirds (68.94%) of LDOOP and more than three-quarters (78.78%) of HDOOP had at least one comorbidity.
- Average Charlson Comorbidity Index (CCI) scores were higher among HDOOP (2.88) than LDOOP (2.30). Medicare patients were the sickest individuals among both HDOOP (3.71) and LDOOP (3.66). In the HDOOP cohort, the Medicaid (2.00) and commercial insurance (1.95) groups had similar average CCI scores. This trend was also observed among the Medicaid (1.49) commercial insurance (1.43) groups within the LDOOP cohort.
- The most common CCI comorbidities among the overall LDOOP cohort were chronic pulmonary disease (41.49%), diabetes with chronic complications (33.84%), congestive heart failure (26.26%), peripheral vascular disease (21.03%), renal disease (20.10%), and mild liver disease (20.03%). Medicare patients were most likely to suffer from chronic pulmonary disease (42.97%), diabetes with chronic complications (41.30%), and congestive heart failure (35.59%), while chronic pulmonary disease (41.68%, 33.24%), diabetes with chronic complications (27.61%, 22.95%), and mild liver disease (25.84%, 22.11%) were the most common comorbidities among Medicaid and commercially insured patients, respectively.
- The most common CCI comorbidities among the overall HDOOP cohort were chronic pulmonary disease (49.92%), congestive heart failure (28.94%), peripheral vascular disease (22.35%), myocardial infarction (12.60%), cerebrovascular disease (9.40%), and diabetes with chronic complications (2.45%). Chronic pulmonary disease (38.39%, 45.51%, 42.48%), congestive heart failure (19.09%, 35.17%, 20.24%), and peripheral vascular disease (14.32%, 27.77%, 14.64%) were the top three most common comorbidities among commercial, Medicare, and Medicaid patients, respectively.

Naloxone Use and Healthcare Utilization

- Only 8.58% of LDOOP received naloxone at index event, with commercial patients receiving naloxone at a much lower rate (1.52%) than Medicare (9.33%) or Medicaid (9.75%) patients.
- In the HDOOP cohort, 8.85% of patients received naloxone at index event, with Medicaid (9.51%) and Medicare (9.69%) patients receiving naloxone at a much higher rate than commercial patients (2.15%).
- Among LDOOP who received naloxone at index event, 96.39% needed emergency care, 26.23% received inpatient treatment, and 10.49% required advanced medical care. Among those in the LDOOP cohort not administered naloxone, 87.50% needed emergency care, nearly half (49.09%) received inpatient treatment, and one-quarter (25.44%) required advanced medical care.
- Among HDOOP who were provided naloxone, 97.36% needed emergency care, 32.40% were admitted for inpatient treatment, and 16.03% required advanced medical care. Among those in the HDOOP cohort not treated with naloxone, 87.67% needed emergency care, 57.93% received inpatient treatment, and 34.36% required advanced medical care.
- Average index event costs were higher among HDOOP ($12,529.16) than LDOOP ($10,571.86), and costs were noticeably different among the 3 payors. Total costs for LDOOP with commercial insurance ($13,603.92) and Medicare ($18,302.10) were much higher than for those with Medicaid ($4,057.63), while a similar trend was observed among HDOOP with Medicare ($17,168.68) and commercial patients ($14,124.84) showing much higher average costs than the Medicaid ($5,823.36) cohort.
- Total at-index costs for LDOOP treated with naloxone were $5,228.26, compared to $11,127.18 for LDOOP without naloxone. HDOOP treated with naloxone had index event costs of $4,979.32, while HDOOP without naloxone had costs of $13,262.56.
- Based on the total medical costs differences between patients treated with and without naloxone, we estimate that 100,000 LDOOP provided with naloxone at the index event will result in ~$1.41 billion savings to Medicare plans and ~$146 million in savings for Medicaid. Cost savings for commercial insurance payors cannot be assessed due to the low number of patients receiving naloxone in the LDOOP cohort (n=20).
- A conservative estimate of 100,000 HDOOP index events shows naloxone treatment can yield cost savings of ~$1.23 billion for Medicare ~$279 million for Medicaid. Commercial insurance cost savings cannot be assessed due to the low number of patients receiving naloxone in the LDOOP cohort (n=15).

Limitations

- Inherent limitations of claims data analysis include the possibility of incomplete, inaccurate, or missing data. Undetected coding errors could have resulted in the misidentification of LDOOP and HDOOP.
- Our use of claims data only allowed for analysis of dispensed prescriptions and diagnoses if a claim was filed. Opioid overdose events and medication dispensing that occurred outside of medical channels are not captured in the data used in this study.
- Prescription opioid exposure was determined by claims associated with the filling of an opioid prescription and based on the assumption that patients took the prescribed opioid as instructed. In some cases, the actual dosage of opioid exposure may have differed from what was prescribed.
- Switching from high- to low-dose opioids during the patient pathway likely contributed to opioid overdose in some identified patients, as variability in opioid dose has been shown to be associated with an increased risk of opioid overdose.[13]
- This study presents prescription opioid overdose rates only. Although we limited our cohort population to individuals with both an opioid prescription and an opioid overdose diagnosis, we cannot rule out the possibility that some of our observed prescription opioid overdoses were attributed to the use of illicit opioids.
- Analysis was restricted to a defined study window with a minimum continuous enrollment of 365 days, both pre- and post-index dates. Due to this continuous enrollment constraint, our study did not address overdose-induced deaths at the index event.
- Calculated at-index costs were conservative because they do not account for any subsequent overdose events and associated medical encounters for treatment occurring within the same year.
- One needs to use caution and consider the implications of smaller sample size in some of the groups while interpreting these study results.

Conclusions

- Our study provides previously unavailable information on LDOOP and HDOOP rates broken down by payor types (overall, commercial, Medicare, and Medicaid), patient characteristics, and comorbidities.
- LDOOP and HDOOP demonstrated significant economic burden to the U.S. healthcare system and payors of commercial, Medicare, and Medicaid plans.
- Overall, the HDOOP cohort had higher average index event total costs than the LDOOP group. These cost differences are likely due to the higher rates of underlying comorbidities among HDOOP and their greater need for more costly services, such as inpatient treatment and advanced medical care.
- Although naloxone use greatly reduced medical costs and healthcare utilization following a prescription opioid overdose, this medication remains grossly under-dispensed among LDOOP and HDOOP. This lack of naloxone utilization is especially alarming, given that almost all prescription opioid overdose patients continue to receive prescription opioids after a nonfatal overdose.[14]
- Given increasingly constrained healthcare budgets, higher rates of naloxone co-prescribing may help reduce the economic burden associated with treating LDOOP and HDOOP.
- Our findings may serve as a useful resource for policymakers, researchers, and payors to further evaluate the real-world benefits of naloxone among LDOOP and HDOOP populations.

Future Research

- Our findings justify the need for further studies to assess the real-world clinical outcomes and other benefits of naloxone among LDOOP and HDOOP.
- Future research should explore the relationship between naloxone use, lower medical costs, and decreased utilization of healthcare resources among LDOOP and HDOOP.
- Additional studies are needed to assess the benefits of naloxone co-prescribing among LDOOP and HDOOP, using data from states that have implemented co-prescribing policies.
- Reasons behind under-utilization of naloxone at index event among LOODP and HOODP needs further investigation.

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