An Updated View on the Initial Opioid Prescription Characteristics and Pain Etiologies That Influence Long-Term Opioid Use Among Opioid Naïve Patients

EPH55

Allen M. Smith, PharmD and Bradley C. Martin, PharmD, PhD

[1]Division of Pharmaceutical Evaluation and Policy, University of Arkansas for Medical Sciences, 4301 W. Markham St., Little Rock, AR, 72205, USA

BACKGROUND

Two papers from **Shah et al. (2017)** explored the association between **long-term opioid use** (**LTOU**) and characteristics of the **initial opioid prescription** and **pain etiologies** among **opioid-naïve subjects** using administrative claims data between **2006-2015**.[1, 2]

- **LTOU probability** at **1** & **3** years ↑ w/ **each additional day** of supplied opioid after the **3rd day supplied of the initial opioid prescription**.[3]

However, 2006-2015 was largely characterized by **escalating opioid prescribing** with relatively **high rates** of **LTOU** and it is **unclear if the same relationships between days supplied and LTOU persist in this contemporary era** with lower rates of opioid prescribing .[2, 3]

Using claims data between **2016-2020**, the objective of the present study was to investigate the **association** between **LTOU** among **opioid-naïve subjects** and characteristics of the **initial opioid prescription (IOP)** and **pain etiology**

METHODS

Data Source

- This study utilized a **10% random subject sample** obtained from the **IQVIA PharMetrics®Plus for Academics database** from **2016-2020**.[4]

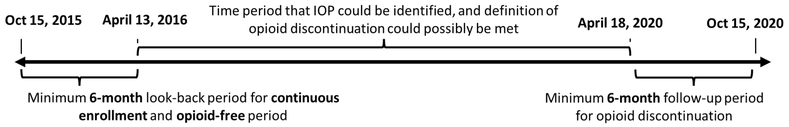
Study Subjects

- All persons who had:
  - **i. ≥ 1 opioid analgesic prescriptions** between April 13, 2016 and April 18, 2020.
  - **ii. ≥ 180 days of continuous enrollment** prior to **IOP.**
  - **iii. ≥ 180 days without an opioid prescription** prior to **IOP.**
  - **iv. ≥ 14 years old** at the time **IOP** was dispensed.

Opioid discontinuation/subject follow-up

- **Opioid discontinuation: ≥180 days continuous enrollment** without opioid Rx from the end date of most recent opioid Rx assessed.
- **Follow-up**: IOP dispense date until whichever of the following first occurs: 1) opioid discontinuation, 2) reach study end date (Oct. 15th, 2020), 3) health plan disenrollment

Study Timeframe



Pain Etiology

- **Categories:** (i) Trauma and Surgery, (ii) Trauma, (iii) Surgery, (iv) Burn, (v) Childbirth, (vi) Dental procedure, (vii) Chronic pain, (viii) Non-chronic pain, (ix) Other inpatient admission, (x) Other Emergency Department (ED) visit, and (xi) Unknown etiology
- Assessed **7 days** prior to/including IOP date (exception: 6 mo prior for chronic pain)
- Adopted ICD-9-CM definitions from Shah et al. and converted to ICD-10-CM.[2, 5]

IOP characteristics[2]

- **Days' supply categories:** (i) 1-2, (ii) 3-4, (iii) 5-7, (iv) 8-10, (v) 11-14, (vi) 15-21, (vii) ≥ 22
- **Mean daily morphine milligram equivalents (MME) categories:** (i) 0-24, (ii) 25-49, (iii) 50-89, (iv) ≥ 90
- **IOP type dispensed:** (i) Long-acting, (ii) Other Schedule II Short-acting, (iii) Oxycodone Short-acting, (iv) Hydrocodone Short-acting, (v) Schedule III-IV, and (vi) Tramadol

Analysis

- **Kaplan Meier Curves:** Accounted for subject censoring and determined the median time to opioid discontinuation
  - Stratified 1-year LTOU probability by pain etiology, IOP type, and days' supply
- **Multivariate cox-proportional hazards regressions:** Hazard ratios were calculated for days' supply (ref: 1-2 days), average daily MME (ref: 0-24), IOP type (ref: Schedule III-IV), and pain etiology (ref: surgery)
  - Hazard ratios from Shah et al. (2017) included for comparison
  - Additionally explored association between days' supply and LTOU likelihood stratified by opioid type and pain etiology

RESULTS

A total of 578,403 individuals were included, of which 416,772 (72.06%) met opioid discontinuation criteria, 4,186 (0.72%) continued opioid use for ≥ 365 days, and 161,631 (27.94%) were censored.

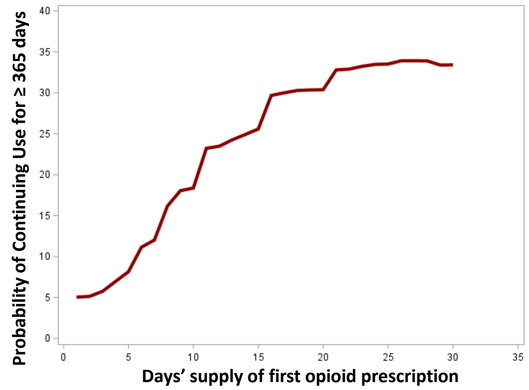
Kaplan-Meier estimate: Overall **5.05%** of subjects had LTOU at 1 year

Days' supply for initial opioid prescription for individuals with < 365 days of opioid use and for individuals with ≥ 365 days of opioid use.

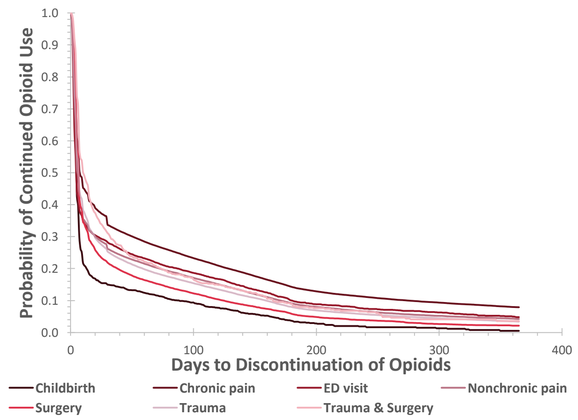
	Current study (2024)[a]		Shah et al. (2017)[a]	
CHARACTERISTICS	Persons w/ < 365 days of opioid use (n = 574,217; 99.28%)[a]	Persons w/ ≥ 365 days of opioid use (n = 4,186; 0.72%)[a]	Persons w/ < 365 days of opioid use (n = 1,320,883; 97.56%)[a]	Persons w/ ≥ 365 days of opioid use (n = 33,019; 2.44%)[a]
DAYS' SUPPLY OF 1st PRESCRIPTION, n (%)				
1-2	121,123 (21.09%)	254 (6.07%)	274,601 (20.79%)	2,580 (7.81%)
3-4	208,489 (36.31%)	544 (13.00%)	490,737 (37.15%)	5,266 (15.95%)
5-7	178,065 (31.01%)	1,017 (24.30%)	363,181 (27.50%)	7,336 (22.22%)
8-10	31,751 (5.53%)	392 (9.36%)	99,417 (7.53%)	4,040 (12.24%)
11-14	5,208 (0.91%)	100 (2.39%)	15,331 (1.16%)	1,056 (3.20%)
15-21	12,581 (2.19%)	400 (9.56%)	39,205 (2.97%)	3,638 (11.02%)
≥ 22	17,000 (2.96%)	1,479 (35.33%)	38,411 (2.91%)	9,103 (27.57%)

[a] Stratified by subjects who continued opioid use for ≥ 365 days and subjects who discontinued opioids < 365 days. Censored subjects were included in the opioid discontinuation group.

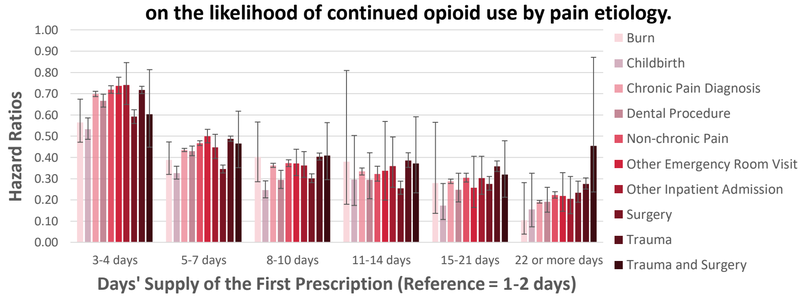
Likelihood of continued opioids use for ≥ 365 days among opioid-naïve subjects stratified by IOP days' supply, expressed in daily increments from 1-30



Kaplan-Meier estimates of LTOU likelihood at 1 year by Pain Etiology



Interaction of pain etiology with days' supply, representing the impact of day's supply on the likelihood of continued opioid use by pain etiology.



Adjusted hazard ratios of IOP characteristics and pain etiologies on likelihood of opioid discontinuation

	HAZARD RATIO (95% CI)	
CHARACTERISTICS	Current study (2024) n = 578,403	Shah et al. (2017) n = 1,353,902
DAYS' SUPPLY OF FIRST PRESCRIPTION (REF=1-2 DAYS)		
3-4	0.66 (0.65-0.66)	0.70 (0.70-0.71)
5-7	0.41 (0.41-0.41)	0.48 (0.47-0.48)
8-10	0.33 (0.33-0.34)	0.37 (0.37-0.38)
11-14	0.30 (0.29-0.31)	0.32 (0.31-0.33)
15-21	0.26 (0.26-0.27)	0.29 (0.28-0.29)
≥ 22	0.17 (0.17-0.18)	0.20 (0.19-0.20)
INDICATION FOR OPIOID PRESCRIPTION (REF=SURGERY)		
TRAUMA AND SURGERY	0.82 (0.77-0.87)	0.91 (0.90-0.92)
TRAUMA	0.86 (0.84-0.87)	0.84 (0.83-0.84)
BURN	0.98 (0.91-1.05)	0.96 (0.92-1.00)
CHILDBIRTH	1.09 (1.05-1.12)	1.11 (1.10-1.13)
DENTAL PROCEDURE	0.98 (0.95-1.00)	0.90 (0.88-0.91)
CHRONIC NON-CANCER PAIN	0.84 (0.83-0.85)	0.77 (0.77-0.78)
NON-CHRONIC PAIN	0.90 (0.89-0.92)	0.85 (0.84-0.86)
OTHER INPATIENT ADMISSION	0.89 (0.85-0.92)	0.82 (0.79-0.85)
OTHER EMERGENCY DEPARTMENT VISIT	0.87 (0.84-0.89)	0.92 (0.91-0.94)
UNKNOWN INDICATION	0.98 (0.97-1.00)	0.92 (0.92-0.93)
CHOICE OF FIRST OPIOID PRESCRIPTION (REF=SCHEDULE III-IV)		
LONG-ACTING OPIOID	0.73 (0.67-0.79)	0.79 (0.77-0.82)
SCHEDULE TWO SHORT-ACTING OPIOID	0.90 (0.87-0.93)	0.93 (0.92-0.95)
SHORT-ACTING OXYCODONE	1.02 (1.01-1.03)	0.97 (0.96-0.98)
SHORT-ACTING HYDROCODONE	1.02 (1.01-1.04)	0.95 (0.95-0.96)
TRAMADOL	0.93 (0.91-0.94)	0.89 (0.89-0.90)
AVERAGE DAILY DOSE OF FIRST PRESCRIPTION IN MME (REF=0-24 MME)		
25-49	1.01 (1.01-1.02)	0.97 (0.96-0.97)
50-89	1.02 (1.01-1.03)	0.95 (0.94-0.95)
≥ 90	0.93 (0.91-0.95)	0.91 (0.91-0.92)

REF = Reference category for the variable, CI = Confidence Intervals.

[a]Hazard ratios < 1 indicate higher probability of continued opioid use; hazard ratios > 1 indicate higher probability of opioid discontinuation.

CONCLUSION

- ✓ **Fewer persons were initially prescribed opioids for extended periods and/or transitioned to LTOU compared to older Shah et al. (2017) studies[3, 4]**
- ✓ **However, receiving an initial opioid prescription with a long days' supplied confers the nearly same excessive risk of LTOU as was originally described in Shah et al. (2017) when prescribed opioid use was generally increasing.**
  - ✓ **The initial days' supply of opioids remained the strongest factor associated with opioid discontinuation**
  - ✓ **Both studies show that LTOU likelihood monotonically increases with incremental increases in days' supplied.**
- ✓ **To further reduce the probability of LTOU, it is particularly important to ensure that clinicians continue to exercise caution when initiating opioid therapy, treating patients with the lowest opioid days' supply needed.**

References

1. Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. MMWR Morb Mortal Wkly Rep. 2017;66(10):265-269. doi:10.15585/mmwr.mm6610a1
2. Shah A, Hayes CJ, Martin BC. Factors Influencing Long-Term Opioid Use Among Opioid Naive Patients: An Examination of Initial Prescription Characteristics and Pain Etiologies. J Pain. 2017;18(11):1374-1383. doi:10.1016/j.jpain.2017.06.010
3. Moncrieff T, Moncrieff J. A comparison of opioid prescription trends in England and the United States from 2008 to 2020. Int J Risk Saf Med. 2023;34(3):287-291. doi: 10.3233/JRS-220040. PMID: 37154185.
4. IQVIA. IQVIA PharMetrics® Plus. https://www.iqvia.com/library/fact-sheets/iqvia-pharmetrics-plus. Published online 2022.
5. Agency for Healthcare Research and Quality. AHRQ Quality Indicators. https://qualityindicators.ahrq.gov/resources/toolkits. Published online 2022.