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## Patterns of prescription opioid use prior to self-reported heroin initiation

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### Abstract

**Objectives:** To determine the association between self-reported heroin initiation and patterns of prescription opioid use.

**Methods:** Using linked Oregon Medicaid, prescription drug monitoring program (PDMP), and Treatment Episodes Data Set data, we conducted a case-control study of individuals reporting heroin initiation between 2015 and 2017 during treatment intake. PDMP data provided prescription opioid use patterns, including long-term prescription opioid therapy, in the year prior to self-reported heroin initiation. Four controls were matched to each case on aggregate prescription opioid use and demographics.

**Results:** About half (49%) of individuals who reported heroin initiation filled an opioid in the year prior to initiation. Individuals who initiated heroin (n=306) were more likely to receive prescriptions from multiple prescribers (24% vs 18%, p=0.007) and pharmacies (12% vs 5%, p<0.001) compared with matched controls (n=1,224). Long-term opioid therapy (13% vs 14%, p=0.74) was uncommon and did not differ between groups.

**Conclusions:** Although prescription opioid use commonly preceded self-reported heroin initiation, long-term opioid therapy was not common. Although this study did not find an association between opioid discontinuation and heroin initiation, sample size and follow-up limitations preclude definitive conclusions. Efforts to limit prescription opioids should continue to evaluate for unintended harms.

### Keywords

heroin; prescription opioids; opioid use disorder

## Introduction

A hallmark of the opioid crisis has been its close relationship with prescription opioids which have risen in parallel with overdose deaths over the last decade. Efforts to improve opioid prescribing have resulted in reduced opioid utilization (Guy et al., 2019) and contributed to an attenuation in prescription opioid-involved overdose rates (Ahmad et al., 2018). Between 2010 and 2017, overdose deaths involving prescription opioids (natural or semi-synthetic opioids) increased 26% (Hedegaard et al., 2018). However, heroin-related deaths increased five-fold during this time and now outnumber deaths from prescription opioids (Hedegaard et al., 2018); much of this increase likely driven by fentanyl exposure.

More than 80% of people who use heroin report initiating with prescription opioids (Jones, 2013; Cicero et al., 2014). The sharp rise in heroin-involved deaths coupled with declining prescription opioid use has prompted speculation that efforts to limit prescription opioids may cause patients to seek illicit opioids such as heroin (Compton et al., 2016). Although prescription opioid misuse commonly precedes heroin initiation, the hypothesis that limits placed on prescription opioids hasten the transition to heroin is not strongly supported by evidence. A few studies suggest that the 2010 abuse-deterrent reformulation of long-acting oxycodone led some individuals to substitute with other opioids including heroin (Cicero et al., 2012; Cicero and Ellis, 2015; Powell et al., 2019). However, other patterns of prescription opioid use preceding transition to heroin have yet to be explored.

Our objective was to compare prescription opioid utilization patterns in the year preceding self-reported heroin initiation for Oregon Medicaid beneficiaries admitted to any publicly funded treatment facility reporting a heroin-involved opioid use disorder (OUD).

## Methods

Our analysis used linked data from Oregon's Medicaid administrative claims, Prescription Drug Monitoring Program (PDMP), and Treatment Episode Data Set (TEDS) from 2014 to 2017. Details of the Medicaid - PDMP linkage have been previously described (Hartung et al., 2017; Deyo et al., 2019). Briefly, Medicaid data are linked to PDMP using a probabilistic linkage on last name, first name, date of birth, and ZIP code using LinkKing (v7.1) software. TEDS data are collected by states and maintained by the Substance Abuse and Mental Health Services Administration to track admissions (TEDS-A) to publicly funded substance use treatment facilities. For each admission, TEDS includes individual-level information describing substances used, routes of administration, frequency of use, and age of first use as well as demographics, treatment-related characteristics (e.g. level of care), and Medicaid ID if applicable. In Oregon, TEDS-A data are reported through the Oregon Health Authority's (OHA) Measures & Outcomes Tracking System (MOTS). Although Oregon's MOTS did not report to TEDS between 2015 and 2017 because of certain variable reporting deficiencies, for admissions with complete reporting and valid Medicaid IDs, OHA was able to create a deterministic linkage between the MOTS TEDS-A data and the clients Medicaid ID.

For each individual with a heroin-involved TEDS admission, we defined a heroin initiation date (heroin index date) as an individual's birth date during the year they indicated first heroin use using the 'age at first use' (from TEDS-A data) and date of birth (from Medicaid data) variables. For individuals with a heroin index date between January 1, 2015 and December 31, 2017 we then characterized prescription opioid fills in the 365 days preceding the heroin index date using PDMP data. Oregon's PDMP was established in 2012 and includes controlled substance prescription dispensing records for all Oregon residents.

Among heroin initiators with one or more opioid prescriptions, we compared prescription opioid and benzodiazepine use to a control group of Medicaid beneficiaries using prescription opioids who did not have a TEDS treatment admission. For each heroin initiator dispensed a prescription opioid, we first selected a pool of candidate controls who were matched on patient age (5-year increments using Medicaid data), sex (Medicaid data), and urban/rural residence (Medicaid data). Of those candidate controls, we then computed their annual PDMP opioid use that preceded the matched case index data and randomly selected four controls who were matched to each case on total morphine milligram equivalents (MME) in the year  $\pm$  25%. We compared the frequency, type, and dosing of opioid prescriptions, prescriptions from multiple prescribers or filled at multiple pharmacies (4 in year), and benzodiazepine use using data derived from Oregon's PDMP. Finally, we characterized the frequency of discontinuation of long-term opioid therapy. We defined long-term use as 90 or more days of continuous prescription opioid use without a gap. We considered discontinuation as having a 45-day period of no opioid dispensing following this continuous use period. We used conditional logistic regression to assess the statistical significance ( $p < .05$ ) between heroin initiating cases and matched controls.

This study was approved by the Oregon Health & Science University Institutional Review Board.

## Results

Of 10,538 patients admitted to treatment for OUD involving heroin between 2015 and 2017, 624 individuals reported initiating heroin use during this period. Among these individuals, 314 reported daily use of heroin (50%), 307 injected (49%), and 375 also used stimulants (60%). In the year preceding the heroin index date, 309 (49%) filled one or more opioid prescription. Of the 309 individuals with an opioid prescription, we identified four matched controls for 306 individuals for a total of 1,224 controls. Three individuals had no equivalent match for patient age (5-year increments), sex, urban/rural residence, and annual prescription opioid use and were excluded from the analysis. As shown in the Table, 46% of cases and controls were age 20–29, 58% were female, and 46% lived in a rural area.

Relative to the matched controls, individuals initiating heroin had similar rates of high-dose use ( $>90$  MME, 7% vs 7%) and long-acting opioid use (8% vs 6%) in the year prior. Individuals initiating heroin had greater use of multiple prescribers (24% vs 18%,  $p=0.007$ ), multiple pharmacies (12% vs 5%,  $p<.0001$ ), and benzodiazepines (24% vs 15%,  $p<0.001$ ). Buprenorphine prescriptions were also more common among the heroin initiators relative to controls (5% vs 1%,  $p<.001$ ).

The proportions of individuals with long-term opioid therapy (13% vs 14%,  $p=0.74$ ) and subsequent discontinuation (41% vs 44%,  $p=0.54$ ) were similar.

## Discussion

To our knowledge, this is the first study to quantify patterns of prescription opioid preceding self-reported heroin initiation. Half of individuals admitted to a treatment facility for OUD involving heroin were prescribed an opioid in the year preceding their self-reported heroin initiation. Among those prescribed an opioid, individuals initiating heroin were more likely to exhibit indicators of misuse or diversion through use of multiple prescribers or pharmacies. However, long-term opioid use was relatively uncommon (~10%) and similar between groups. While discontinuation of long-term opioid therapy prior to heroin initiation was common, it did not differ from those prescribed long-term prescription opioids who did not initiate heroin.

Some qualitative studies suggest that supply side prescription opioid limitations may hasten heroin initiation for some (Mars et al., 2014), yet, quantitative patient-level data describing the trajectory from prescription opioid misuse to heroin use are limited. A single longitudinal study of 362 individuals with misuse of prescription opioids found that 27 reported initiation of heroin (7.5%) over a 36-month period (2.8% per year) and use of prescription opioids to self-medicate a medical problem was associated with a lower risk of transition (Carlson et al., 2016). This is consistent with our study which finds no relationship between long-term opioid use and heroin initiation.

This study has limitations. Our cases were derived from treatment-seeking individuals in Oregon who were identified in Oregon's TEDS treatment database. From 2015 to 2017, Oregon TEDS data were omitted from the National SAMHSA TEDS Admissions reports because of suboptimal reporting by treatment facilities (SAMHSA, 2017). Consequently, study cases identified may not be generalizable to individuals receiving treatment in underreporting facilities in Oregon and elsewhere. Moreover, our sample may not be representative of people who use heroin and do not enter treatment. Ultimately, the sample in our study reflects a very small proportion (<3%) of the total number of people who entered treatment with a heroin use disorder and even a smaller proportion of the estimated 13,000 adults in Oregon who reported heroin use in the past year (SAMHSA, 2019). Our assessment of opioid prescription patterns may be insufficient for a number of reasons. First, our estimate of the date of heroin initiation was based on individual self-report of age at first use and is likely subject to recall bias of an uncertain direction. The odds of buprenorphine use, although uncommon (~5%), was 6-fold higher among heroin initiators relative to controls which suggests some heroin initiators were already being treated for an OUD. Second, we only evaluated prescription patterns in the year immediately preceding the estimated heroin initiation date and therefore were unable to ascertain longer-term patterns of use developing over several years. Finally, PDMP-assessed prescription opioid use is likely confined to opioids prescribed for legitimate medical conditions, and we were unable to assess prescription opioid use acquired through non-medical sources (e.g. diverted through family or friends).

## Conclusions

Similar to other studies, we found that prescription opioid use was common among individuals who reported initiating heroin. Although long-term opioid therapy was uncommon (13%), individuals who reported heroin initiation were more likely to have prescriptions for benzodiazepines, buprenorphine, and have multiple prescribers or pharmacies. Rates of discontinuation of long-term therapy among individuals initiating heroin were similar to the control group, but the overall sample was small and conclusions remain uncertain. Although the harms of long-term opioid therapy are well-described (Chou et al., 2015), emerging evidence is beginning to suggest risks associated with discontinuation or disruption of long-term therapy (Glanz et al., 2019; James et al., 2019; Mark and Parish, 2019). A retrospective cohort study of chronic pain patients on long-term opioid therapy in one primary care clinic found that discontinuation of opioid therapy was associated with a nearly 3-fold increase in the risk of an overdose death (James et al., 2019). A study among Medicaid recipients in Vermont who discontinued long-term opioid therapy found that a shorter time to discontinuation was associated with elevated rates of opioid-related adverse events (Mark and Parish, 2019). There remains an urgent need to identify factors that predict transition to heroin as well as delineate the adverse sequelae of rapid or forced de-escalation of chronic opioid therapy.

## Conflicts of Interest and Source of Funding:

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**Table.**

Patient Characteristics and Prescription Opioid Dispensing Patterns Among People who Use Heroin and Matched Controls.

Dispensing Pattern	Heroin Initiator <i>N</i> =1306	Controls <i>N</i> =1,224	Odds Ratio (95% CI)	p-value
<b>Demographics from Medicaid data</b>				
Age Groups				
19 years	21 (7%)	84 (7%)	NA	NA
20–29 years	141 (46%)	564 (46%)	NA	NA
30–49 years	129 (42%)	516 (42%)	NA	NA
50 years	15 (5%)	60 (5%)	NA	NA
Sex (Female)	176 (58%)	704 (58%)	NA	NA
Rural	141 (46%)	564 (46%)	NA	NA
<b>Controlled Substance Dispensings from PDMP</b>				
Average number of fills per person (SD)	6.2 (7.7 SD)	5.9 (7.7 SD)	1.03 (1.00, 1.06)	0.04
Average days with an opioid available	64 (107 SD)	64 (110 SD)	1.00 (0.99, 1.00)	0.14
Average MME per day	43 (39 SD)	45 (36 SD)	1.00 (0.99, 1.00)	0.21
Any prescription >90 MME per day (%)	20 (7%)	88 (7%)	0.87 (0.48, 1.57)	0.64
Any long-acting/extended release opioid	24 (8%)	76 (6%)	0.74 (0.44, 1.26)	0.27
Multiple pharmacy 4	38 (12%)	70 (5%)	2.66 (1.68, 4.21)	<0.001
Multiple prescriber 4	74 (24%)	223 (18%)	1.63 (1.14, 2.32)	0.007
Benzodiazepine use	73 (24%)	178 (15%)	1.84 (1.35, 2.50)	< 0.001
Benzodiazepine/opioid overlap	47 (15%)	147 (12%)	1.41 (0.95, 2.10)	0.09
Buprenorphine Use (N, %)	15 (5%)	12 (1%)	6.49 (2.72, 15.46)	<0.001
Long-term use (90 days)	39 (13%)	161 (14%)	0.89 (0.46, 1.72)	0.74
Discontinuation of long-term use	16/39 (41%)	74/161 (44%)	0.81 (0.43, 1.54)	0.54

NA is not applicable because variables used for matching, MME is morphine milligram equivalents, SD is standard deviation