A Comparison of Definitive Urine Drug Test Results for Illicit Drugs in a Sample of People With Chronic Pain Prescribed Opioids to those Not Prescribed Opioids





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Introduction

Opioid prescribing has decreased dramatically over the past decade, and yet drug overdose deaths continue to climb.^{1,2} Changing views about management of chronic pain with opioids have been reflected in shifting guidelines, policy and rules, and are driven by a desire to reckon with the societal problems of opioid misuse, addiction, diversion, overdose and death. In part, sparing people with chronic pain exposure to opioids is motivated by a desire to protect vulnerable people from the possibility of setting in motion misuse or unhealthy use of opioids and/or addiction. Whether these policies have been a success or failure is a matter of debate; in any event, the number of people with chronic pain treated with opioids has decreased to levels unseen since the early 1990s.¹

We set out to compare urine drug test (UDT) results from people with chronic pain not prescribed opioids to those prescribed opioids. We examined a large sample of people treated in pain management practices who underwent UDT with liquid chromatography-tandem mass spectrometry (LC-MS/MS) technology. We eliminated sub-groups of subjects who, it may be argued, might be best treated without opioids, while safer alternatives are trialed (e.g. patients with a history of substance use disorder), to drill down to the group in whom the reasons for foregoing opioids may be less obvious and more a reflection of present policy. Describing the influence of opioid prescribing on the frequency of UDT findings for illicit drugs may help those interested in understanding whether present policies are indeed protecting people with chronic pain from opioid misuse or whether it is resulting in dangerous self-treatment at a time when the drug supply of illicit and counterfeit opioids are tainted with lethal fentanyl, fentanyl analogues, and other excipients that can cause harm. People who think they are purchasing a legal opioid with which they are familiar from an illicit source might well be purchasing a lethal dose of fentanyl.

Methods

- Retrospective study of liquid chromatography-dual mass spectrometry (LC-MS/MS) UDT results examined specimens obtained between January 1, 2019 December 31, 2021, from patients receiving treatment in pain management practices.
- 188,796 unique specimens from Millennium Health's proprietary UDT database. (Figure 1)
- Out of the 188,796 total urine specimens, 147,222 (78.29%) were from patients reported to be prescribed at least one of the following drugs at the time of the sampling: fentanyl, codeine, hydrocodone, hydromorphone, oxymorphone, morphine, oxycodone, and tramadol.
- We evaluated positivity in the 188,796 specimens for four illicit substances; these were chosen because they are the four drugs known to contribute most to overdose deaths.² The following drugs and/or drug classes were tested based on the ordering clinician's determination of medical necessity (drug and metabolites tested in parentheses): cocaine (benzoylecgonine), fentanyl (fentanyl, norfentanyl), heroin (6-monoacetylmorphine), and methamphetamine.
- If any parent analyte or metabolite was detected, the drug of interest was considered positive for that specimen. We excluded positive results for medications that contained these active ingredients that were reported by clinicians to be currently prescribed to patients.
- We used Poisson Generalized Estimation Equations to fit marginal regression models for the four illicit drug positivity rates while accounting for the longitudinal sampling of patients. The main factor of interest was prescription opioid status. Sex, age, payor group, US census location and collection year were also added as covariates.
- The study protocol was approved by the Aspire Independent Review Board and includes a waiver of consent for the use of deidentified data. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Figure 1. UDT Specimen Selection Workflow ection of specimens with Unique urine specimens from Random selection of n SUD diagnosis, methado que urine specimens betw Patients must have at lea patients in pain management specimens collected durin 00 years of age and with eith 60,000 unique patients buprenorphine prescrip practices collected betwee nale/female gender recorde (n=188,796 specimen the study period (n=231,932 specimens 2019 and 2021 n=54,484 patients

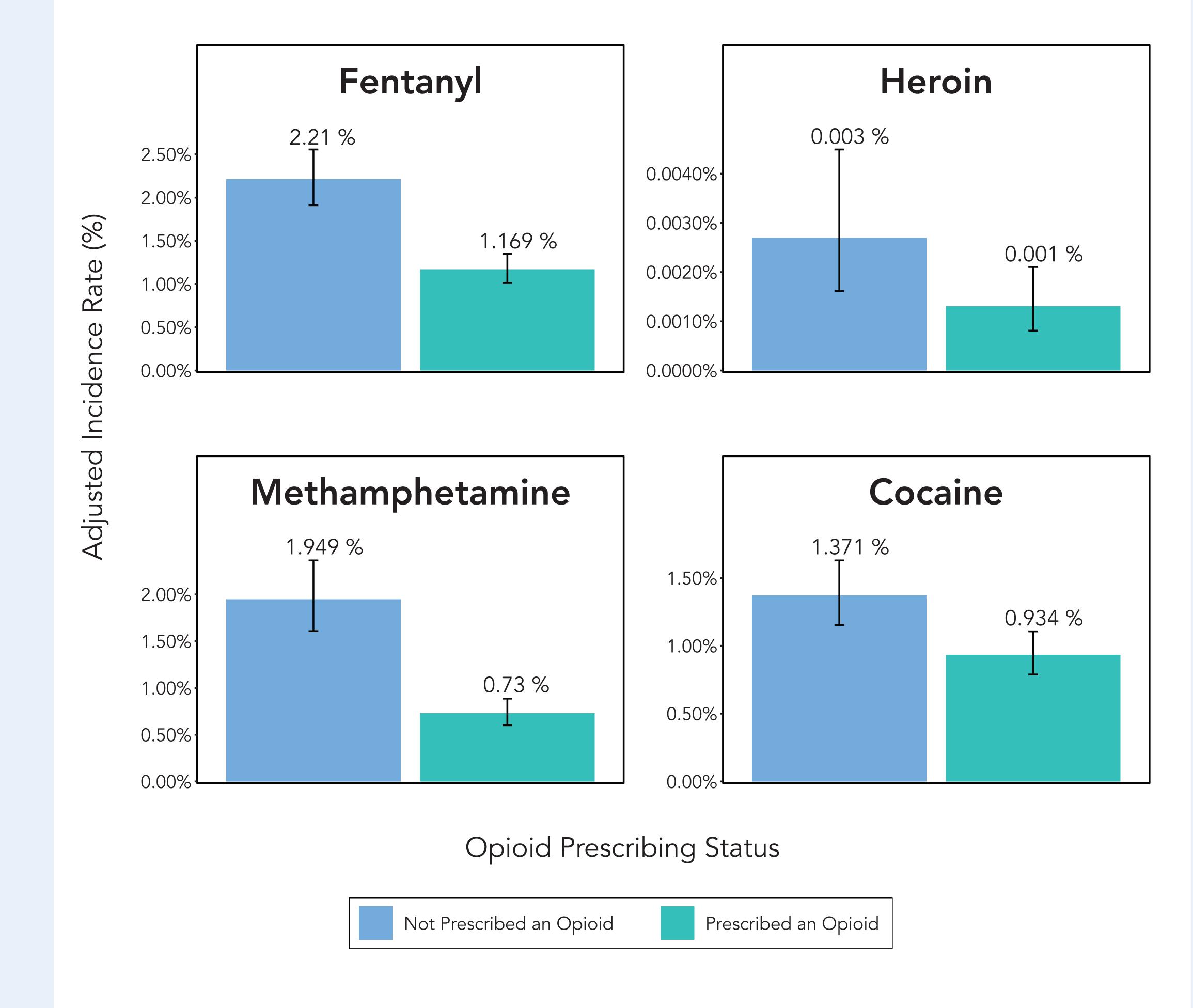
Table 1. Characteristics of UDT Specimens Tested in a Pain Management Setting Between January 1, 2019, and December 31, 2021

| Characteristic | Specimens | Characteristic | Specimens | |
|------------------------|---------------------------|---------------------------------|-----------------|--|
| Total | 188,796 (54,484 Patients) | U.S. Census Division | | |
| Sex | | East North Central | 22,744 (12.0%) | |
| Female | 110,861 (58.7%) | East South Central | 11,599 (6.1%) | |
| Male | 77,952 (41.3%) | New England | 2,926 (1.5%) | |
| Age | | Mid Atlantic | 10,186 (5.4%) | |
| Median Age [IQR] | 58[18] | South Atlantic | 45,822 (24.3%) | |
| 18-24 | 907 (0.5%) | West North Central 3,809 (2.0%) | | |
| 25-34 | 9,403 (5.0%) | West South Central | 17,036 (9.0%) | |
| 35-44 | 23,919 (12.7%) | Mountain | 54,064 (28.6%) | |
| 45-54 | 38,067 (20.2%) | Pacific | 20,641 (10.9%) | |
| 55+ | 116,518 (61.7%) | Prescribed Opioid, no. (%) | | |
| Payor Group | | Opioid Group | 147,722 (78.2%) | |
| TBD | 16,538 (8.8%) | Codeine | 4,587 (2.4%) | |
| Private insurance | 60,818 (32.2%) | Hydrocodone | 65,315 (34.6%) | |
| Workers Comp_liability | 8,123 (4.3%) | Hydromorphone | 15,105 (8.0%) | |
| Medicaid | 32,310 (17.1%) | Oxycodone | 62,500 (33.1%) | |
| Medicare | 69,915 (37.0%) | Oxymorphone | 265 (0.1%) | |
| Uninsured | 1,111 (0.6%) | Morphine | 19,259 (10.2%) | |
| Collection Year | | Tramadol | 19,259 (10.2%) | |
| 2019 | 58,855 (31.2%) | Fentanyl | 3,197 (1.7%) | |
| 2020 | 55,348 (29.3%) | | | |
| 2021 | 74,622 (39.5%) | | | |

Results

- ICD-10 diagnosis codes associated with substance use disorders (SUD) were found in 11.4% of the patients. Methadone (2.2%) and buprenorphine (7.5%) were found in the medication listings provided by the ordering physician.
- After removal of these patients, 54,848 patients contributed 181,796 total specimens, a mean of 3.1 specimens per patient. (Figure 1)
- The population was mostly female (58.7%). The median patient age was 58 years old at collection and 61.7% were 55 years or older.
 The specimens were relatively evenly distributed for each collection year (29.3-39.5%). 64.9% of patient specimens were collected in the East North Central, South Atlantic or Mountain divisions. (Table 1)
- 78.29% of patients were reported to be prescribed at least one of the eight opioids at the time of their first specimen, most commonly hydrocodone (34.6%) and oxycodone (33.1%). (Table 1)
- From 2019 to 2021, illicit positivity rates for heroin, fentanyl, cocaine and methamphetamine were lower in the population prescribed an opioid compared to those not prescribed an opioid.
- Those prescribed an opioid were 47% less likely to be positive for illicit fentanyl, 52% less likely to be positive for heroin,
 63% less likely to be positive for methamphetamine, and 32% less likely to be positive for cocaine (all significant at p<0.001). (Table 2, Figure 2)

Figure 2. Marginal Incidence Rates for Opioid Prescribing Status



Adjusted Incidence Rates represents the marginal predicted rates for Opioid Prescribing Status (yes or no) from each of the four GEE Poisson regression models. Each model shows the illicit drug positivity to be higher in the population that was not prescribed an opioid (p<0.05).

Table 2. GEE Poisson adjusted Incidence Rate Ratios (aIRR) with Robust 95% CI Estimates

| Table Model Coefficients (IRR +/- 95% CI) SUD, buprenorphine Rx and Methadone Rx specimens removed** | | | | | | |
|---|----------------------|-----------------------|----------------------|--------------------|--|--|
| Terms | Fentanyl | Heroin | Methamphetamine | Cocaine | | |
| Intercept | 0.03 [0.02-0.04] *** | 0.00 [0.00-0.01] *** | 0.06 [0.04-0.10] *** | 0.02 [0.01-0.03] * | | |
| Prescribed Opioids (Re | | | | | | |
| Yes | 0.53 [0.48-0.58] *** | 0.48 [0.34-0.69] *** | 0.37 [0.34-0.42] *** | 0.68 [0.61-0.76] * | | |
| Discrete Age (Referenc | | | | | | |
| 25-34 | 0.98 [0.62-1.55] | 2.69 [0.64-11.35] | 0.95 [0.63-1.41] | 1.16 [0.66-2.06] | | |
| 35-44 | 1.04 [0.67-1.62] | 1.06 [0.25-4.53] | 0.67 [0.45-0.99] * | 1.09 [0.62-1.92] | | |
| 45-54 | 0.77 [0.49-1.20] | 0.70 [0.16-2.98] | 0.60 [0.40-0.89] * | 1.10 [0.63-1.92] | | |
| 55+ | 0.54 [0.35-0.85] ** | 0.35 [0.08-1.51] | 0.37 [0.25-0.54] *** | 0.74 [0.42-1.30] | | |
| Sex (Reference = Fema | le) | | | | | |
| Male | 1.20 [1.10-1.31] *** | 2.17 [1.59-2.97] *** | 1.30 [1.18-1.44] *** | 1.97 [1.79-2.18] * | | |
| Payor Group (Referenc | e = Medicaid) | | | | | |
| Medicare | 0.70 [0.61-0.79] *** | 0.43 [0.27-0.70] *** | 0.48 [0.42-0.56] *** | 0.38 [0.33-0.45] * | | |
| Private insurance | 0.67 [0.59-0.75] *** | 0.34 [0.22-0.52] *** | 0.32 [0.28-0.37] *** | 0.37 [0.32-0.42] * | | |
| TBD | 0.56 [0.47-0.67] *** | 1.32 [0.86-2.02] | 0.92 [0.78-1.08] | 0.51 [0.43-0.62] * | | |
| Uninsured | 0.76 [0.47-1.23] | 1.97 [0.72-5.37] | 0.76 [0.45-1.28] | 0.87 [0.59-1.27] | | |
| Workers Comp_liability | 0.33 [0.24-0.45] *** | 0.22 [0.07-0.70] * | 0.38 [0.27-0.55] *** | 0.45 [0.36-0.57] * | | |
| US Census Division (Re | ference = East North | Central) | | | | |
| East South Central | 0.77 [0.59-0.99] * | 0.90 [0.25-3.22] | 0.78 [0.59-1.03] | 0.96 [0.73-1.27] | | |
| Mid Atlantic | 1.70 [1.37-2.13] *** | 2.59 [1.10-6.12] * | 0.77 [0.57-1.05] | 2.34 [1.89-2.90] * | | |
| Mountain | 1.41 [1.21-1.64] *** | 2.70 [1.43-5.07] ** | 1.34 [1.14-1.57] *** | 0.66 [0.54-0.79] * | | |
| New England | 2.06 [1.46-2.89] *** | 1.12 [0.14-8.83] | 0.26 [0.08-0.80] * | 1.93 [1.32-2.82] * | | |
| Pacific | 1.50 [1.24-1.81] *** | 7.26 [3.62-14.55] *** | 1.71 [1.41-2.07] *** | 0.86 [0.68-1.08] | | |
| South Atlantic | 1.47 [1.25-1.72] *** | 1.39 [0.68-2.82] | 0.79 [0.66-0.95] * | 1.96 [1.65-2.32] * | | |
| West North Central | 1.12 [0.78-1.60] | 0.00 [0.00-0.00] *** | 1.01 [0.71-1.43] | 0.34 [0.17-0.66] * | | |
| West South Central | 1.10 [0.88-1.37] | 2.18 [0.89-5.36] | 0.76 [0.58-0.99] * | 1.30 [1.03-1.64] * | | |
| Collection Year (Refere | nce = 2019) | | | | | |
| 2020 | 1.22 [1.09-1.37] *** | 1.11 [0.75-1.63] | 0.79 [0.70-0.90] *** | 0.87 [0.77-0.99] * | | |
| 2021 | 1.23 [1.10-1.36] *** | 0.96 [0.66-1.40] | 0.68 [0.60-0.77] *** | 1.08 [0.96-1.21] | | |

Conclusion

The results of this study suggest that people with chronic pain who are not prescribed opioid medications are more likely to have UDT results positive for illicit drugs than those prescribed opioid medications. It is unclear what the actual clinical circumstances and motives of people with pain who use illegally obtained drugs are from a database such as this one. Is their use of these drugs the result of desperation to relieve pain and other symptoms? Or is their unsanctioned use a manifestation of a substance use disorder? Based on our analysis, avoiding opioid prescribing does not automatically translate to less drug use on the part of people with chronic pain – at a time when self-medication using street opioids has perhaps never been more dangerous. Instead, safe opioid prescribing processes might be preferred wherein the hope would be that adequate comfort and pain management with needed safeguards might help a subset of people with chronic pain avoid desperate and dangerous attempts to self-treat.

References

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