Improving the detection of behavioral health conditions through positive and unlabeled learning: opioid use disorder

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Background

Opioid use disorder (OUD) is a chronic behavioral health condition marked by prolonged opioid use that leads to significant distress or impairment of brain structure and function.[1] The opioid crisis continues to be a significant public health problem worldwide.[2] Globally, opioid use disorders afflict over 16 million people, including more than 2.1 million individuals in the US alone.[3] Additionally, opioids contribute to more than 120,000 deaths annually worldwide.[1,4] In 2020, 91,799 drug overdose deaths occurred in the US, with opioids contributing to 74.8% of all those deaths.[5,6]

Accurately detecting and estimating behavioral health conditions, such as OUD, is crucial for identifying at-risk individuals, determining treatment needs, tracking prevention and intervention efforts, and finding treatment-naive individuals for clinical trials. With increased data availability and improved machine learning (ML) frameworks, researchers have recently started applying ML models to healthcare data to analyze various aspects of the opioid crisis.[7] Nevertheless, underdiagnosis and undercoding of these conditions in electronic health records (EHRs) and claims data are common,[8] with this missing data potentially compromising the reliability of analytics and inferences drawn from EHRs.

Our study employs a novel Positive and Unlabeled (PU) machine learning method to estimate the probability of an individual patient having OUD and the overall prevalence of OUD among individuals who have been exposed to at least one opioid in their lifetime. Furthermore, we examine differences in OUD diagnosis versus our imputed estimates across US states using administrative claims data. Since the Selected Completely At Random (SCAR) assumption is often not valid in healthcare data due to the fact that coded cases may not be true representatives of undetected cases (e.g., severe cases may more likely to generate a healthcare encounter), we applied our novel PU learning algorithm, "*Positive Unlabeled Learning Selected Not At Random (PULSNAR)*," to estimate the proportion of OUD among undetected individuals. PULSNAR can also generate a calibrated estimate of the probability that each patient has a given condition, assuming other patient healthcare data (i.e., conditions, procedures, drugs) are correlated with the condition of interest. The full details of our PU learning algorithm are available in a preprint.[9]

Methods

This study utilized the Merative MarketScan commercial claims and encounters database from 2003-2021, comprising 48,043,595 individuals exposed to at least one of 36 opioids over the time span of enrollment (e.g., morphine, oxycodone). Out of those

exposed, we selected a random sample of 1,000,000 individuals for this study. An OUD phenotype was defined by the presence of the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes F11*, T40.2*, T50.7* and International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 304.0*, 304.7*, 305.5*. If one of these codes was present in a person's data, the person was labeled as class 1 (positive); otherwise, class 0 (unlabeled). The analysis included 24,535 distinct covariates, comprising sex and three categories of features: *condition_occurence, drug_era, and ancestor terms*.

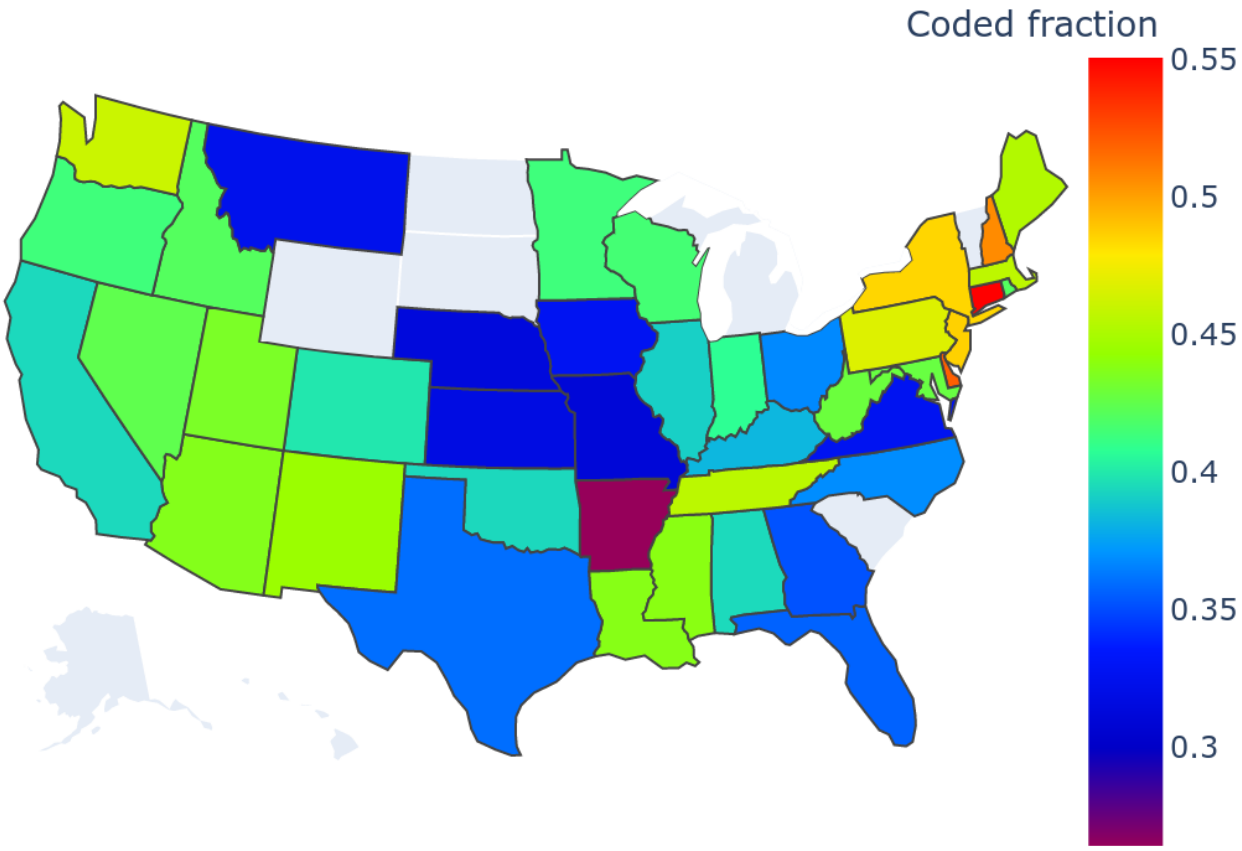

Figure 1: Fraction of coded OUD by state. Due to MarketScan license restrictions, data for South Carolina were excluded from the figure. Also, data for states PR, HI, VT, ND, DC, AK, WY, and SD were not included due to the smaller sample size. Coded fraction=coded/(coded+imputed). State-level diagnosis of OUD ranges from 26.4-55.0%.

Given that OUD cases are not SCAR, we applied the PULSNAR algorithm for analysis. The PULSNAR algorithm used the class 1 probability of examples predicted by the XGBoost[10] method to estimate the proportion (α) of uncoded OUD examples. After obtaining the estimated α, we applied isotonic calibration to calibrate the probabilities of uncoded examples. Subsequently, these calibrated probabilities were used to determine the fraction of coded OUD cases and estimate OUD prevalence among opioid users by US state.

Results

In the random sample of 1,000,000 patients with at least one opioid prescription fill, PULSNAR estimated 5.3% (53,144) of patients have OUD, compared to the 2.0% (20,079) with a recorded OUD diagnosis. The top 5 features that XGBoost used to classify a record were: *naloxone (drug), chronic pain (condition), buprenorphine (drug), drug-related disorder, and mental disorder (condition).* Sex was included in the model, but its contribution in discriminating between positive and unlabeled examples was relatively low. The coded OUD proportions for males and females were 0.43 and 0.38, respectively, suggesting females are less likely to have their OUD recognized through a coded diagnosis. The proportion of coded OUD cases per state ranged from 26.4% to 55.0% (Figure 1). When considering both coded and imputed OUD cases with at least one opioid prescription fill, the estimated fraction having OUD ranged from 2.2% to 7.9% across US states (Figure 2).

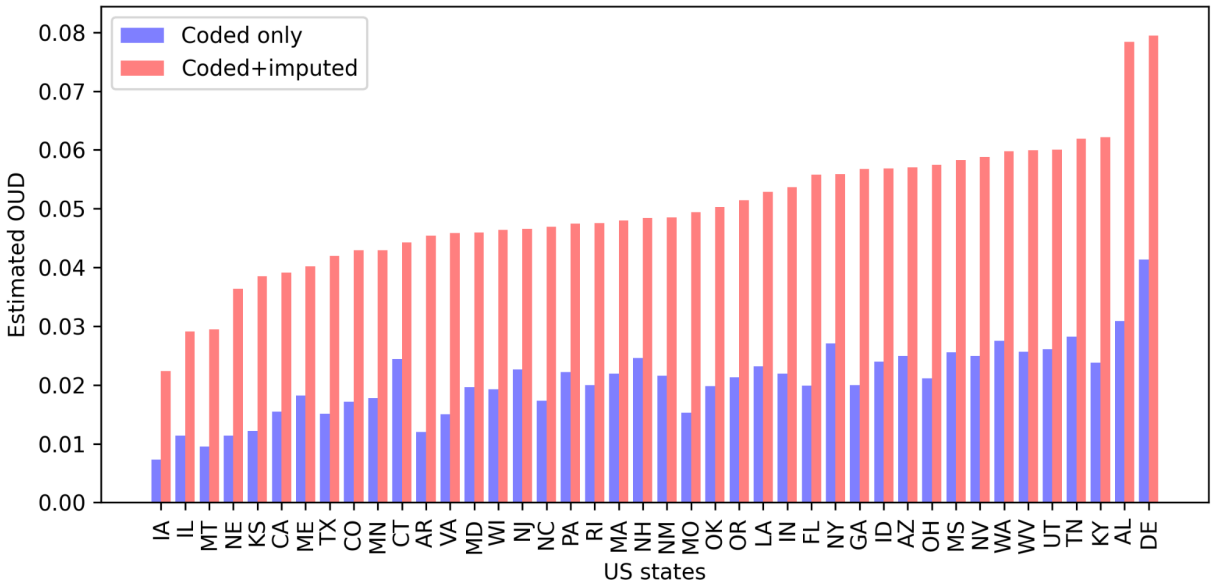

Figure 2: Estimated OUD among opioid users (ever). Coded plus imputed OUD fraction among those who had at least one opioid prescription fill ranged 2.2%-7.9% across US states. Some states were excluded, as described in Figure 1.

Discussion and Conclusion

Accurately estimating the prevalence of undiagnosed/unreported behavioral health conditions can have significant implications for public health, screening efforts, identifying health disparities, and mitigating the negative impacts of these conditions. Notably, OUD is more likely missed in females than males. It is also sobering that out of 1M randomly selected individuals across the US with opioid exposure, 2% have a coded OUD diagnosis, and an estimated 3.3% have unrecognized OUD, for a total of 1 in 19 people exposed to opioids. That coded OUD fraction varies between 26-55% across different US states raises questions about differences in access to care and documentation practices. A limitation of this current model is it did not use opioid dosage, which, if incorporated, could increase model performance. It also remains as future work to validate our detection of unrecognized OUD through chart review or other means. This was done successfully in our prior work with self-harm in Veterans Health Administration EHR data, where PULSNAR was effective in providing a calibrated

estimate of lifetime self-harm.[11] Importantly, as we showed with self-harm, OHDSI comparative effectiveness studies can be performed using imputed phenotypes,[12] and calibrated estimates enable phenotype definitions with targeted sensitivity and specificity. The utilization of the PULSNAR algorithm in estimating the prevalence of unrecognized OUD presents an opportunity to strengthen public health interventions, drive effective screening programs, make a positive impact on population well-being, and identify suitable candidates for participation in clinical trials of OUD who have not yet undergone treatment.

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