**System Description**

*Opioid-Abuse Binary Classifier*

Created: 06/23/2023 by Tom Lever

Updated: 07/04/2023 by Srimann Ramachandruni

**Context: Previous Research**

Opioids are a class of medications that medical providers prescribe to patients to alleviate severe symptoms such as constipation, respiratory distress, and more commonly pain. Common types of opioids include oxycodone, hydrocodone, morphine, and methadone. Although these medications can be effective, they may also result in adverse drug effects, of most concern to be dependence, abuse, and poisoning. Not only do these conditions result in more than 130 deaths of Americans daily, they also generate significant financial and resource burdens on the healthcare system. Given that 91.8 million (37.8%) civilian non-institutionalized adults in the United States consumed prescription opioids in 2015 and 13.5 million (5.5%) of them had some form of opioid misuse, knowledge of which individuals are at an increased susceptibly to these conditions is essential for responsible management of pain and symptoms (Han et al., 2015). Unfortunately, due to these risks coupled with limited understanding and patient self-reporting along with other factors, many providers report a lack of confidence in the prescribing of opioids with this regard. To support providers in clinical decision making, statistical methods and machine learning techniques can be leveraged that identify patterns and risk factors of aberrant drug-related behavior (ADRB) of opioids from vast amounts of electronic health record (EHR) data. These models can help predict which individuals are at an increased susceptibility to dependence, abuse, and poisoning, allowing providers to tailor their prescribing practices and interventions accordingly. By utilizing these tools, medical providers can strike a balance between effectively managing pain and symptoms while prioritizing patient safety and mitigating the negative consequences of opioid use.

Currently, there are two main statistical methods used to identify individuals at an increased susceptibility for ADRB and their associated risk factors: self-reported questionnaires/assessments and machine learning algorithms. The former include tools such as the Opioid Risk Tool (ORT), Screener and Opioid Assessment for Patients with Pain, and the Current Opioid Misuse Measure, which have been developed with physician input and implemented into current EHR systems. These tools work by asking patients a series of questions about their medical history, pain, and use of opioids. The most popular of these tools is the ORT, a 10-item questionnaire that medical providers can administer to assess the risk for opioid-related ADRB. Despite its accessibility and promising potential, the ORT, in addition to the other self-reported tools, has relatively poor evidence of its accuracy and consists of items that rather more generally predict substance use disorder (SUD). Adaptations to the ORT and related tools, while improvements in accuracy, acknowledge limitations in self-reported error and evaluation of subjects at a single point in time.

Machine learning algorithms, on the other hand, do not rely on self-reported measures but rather analyze EHR data, including everything from demographics to diagnoses, to predict an individual’s risk for opioid-related ADRB as well as their risk factors. Studied have utilized a range of machine learning algorithms for this purpose, including logistic regression, decision trees, random forest, deep neural networks (DNN’s), and recurrent neural networks (RNN’s), among others. While they generally have comparable if not better performance than the previously mentioned class of tools, RNN’s stand out as a popular and effective method in the identification of individuals at increased vulnerability to opioid-related ADRB’s. RNN’s, in contrast to other common traditional machine learning algorithms, generally account for temporal variations in medications, diagnoses, etc. and therefore are better in capturing how the risk of opioid-related ADRBs changes over time.

For example, Che et al. were able to achieve AUC scores of 0.80 using an RNN to classify opioid users into long-term users, short-term users, and opioid-dependent patients. Dong et al. and Dong et al. improved upon this with the incorporation of LSTM’s and bidirectional layers to address limitations of RNN’s such as vanishing and exploding gradients. These applications of RNN’s improved upon the performances of their counterpart ML algorithms that did not take into account temporal dependencies of medications, procedures, conditions, etc. It is still important to recognize, however, that there are still challenges to these models, notably interpretability. Although these methods and architectural choices certainly divide most of the current research, further specifications such as the population of focus, target classes, and feature selection truly distinguish the works within this field.

With regards to the population of focus, many risk assessment tools have focused on predicting opioid-related ADRB either prior to after prescription of an opioid. The COMM, for example, identify if a patient currently on an opioid prescription is at high risk of developing opioid-related ADRB’s. Similarly, many of the machine learning applications select the first incident of an ADRB as the target encounter, thereby allowing changes during the course of prescription to serve as features. On the other hand, the ORT and SOAPP serves as prescreening assessment that informs providers whether it is safe for a patient experiencing chronic non-malignant pain to start on an opioid medication. There are relatively fewer machine learning studies, however, that focus on the same patient population of individuals who are being evaluated prior to starting an opioid medication. This serves as a crucial gap in research, as although both approaches are relevant, identifying prior to prescription can most importantly prevent the need for opioid tapering.

The term ADRB encompasses several adverse drug reactions, the most commonly of which are studied are opioid poisoning, abuse, and dependence. Opioid poisoning, or more commonly referred to as an overdose, involves the excessive intake of opioids and subsequent inhibition of the central nervous system. Opioid dependence, on the other hand, describes a physical dependence on opioids that requires continued use to alleviate pain. This makes it more challenging to predict than opioid poisoning, as the symptoms may not be as obvious. While opioid abuse and dependence may be utilized interchangeably in the literature, there is a meaningful distinction between the two in that opioid abuse is distinguishes less by physiological need and more by improper use. Furthermore, opioid abuse can sometimes precede opioid dependency and dependency can be over/under reported due its complexity. Importantly, these distinctions inform that, although these conditions may share similar origins and effects, it may provide useful to examine conditions separately and under more scrutiny to understand their nuances, thereby improving performances of statistical method that attempt to predict them.

Due to the similar natures of different opioid-related ADRB’s, their risk factors and predictors are also generally consistent. The ORT consist of 10-questions regarding history of substance abuse, age, sexual abuse, and presence of psychiatric disease. Other screening assessment tools such as the SOAPP also share these criterions, mainly substance abuse history, medication-related behaviors, and psychiatric behaviors. Similarly, some machine learning applications have focused on a fewer number of features for prediction, commonly examining depression, alcoholism, immunization history, and medications such as natural Opium Alkaloids and phenylpiperidine derivatives. (Beaver, Burek, & Shakeria, 2022). The vast majority, however, have taken a more encompassing approach with over hundred features. In spite of this, they commonly share the features listed above, primarily pain, opioid prescriptions, dependence, and other analgesic medications.

**Opportunity Opioid-Abuse Binary Classifier Will Address**

In this paper, we aim to improve upon the general objective of the ORT of predicting the probability that a patient will exhibit an opioid-related ADRB prior to any prescription of opioids. This prediction of prior to prescription is especially relevant as it prevents the need for opioid tapering after an individual has begun an opioid medication. Opioid tapering, while a logical intervention, can paradoxically worsen pain, function, and psychiatric symptoms due to protracted abstinence syndrome. Importantly, however, we will specifically focus on the predicting of opioid abuse due to its capability of initiating dependence and the complexity of opioid dependency diagnoses. Furthermore, this project will extend our population of focus to all individuals without malignant pain who are being considered for opioid medication. How? We intend on implementing an LSTM RNN model trained on NIH researcher workbench EHR data that is able to capture the essential, temporal dependencies. In addition, as previously mentioned, we will employ a time series factor analysis to provide further potential performance and interpretability, a common challenge in such models. Ultimately, this statistical tool attempts to serve as a clinical decision making support system for providers so that they can more safely prescribe opioids to patients.

We intend Opioid-Abuse Binary Classifier to mobilize NIH researcher workbench EHR data. We intend Opioid-Abuse Binary Classifier to serve as a modern, easy-to-use building block for further research. Such research includes relating essential, temporal dependencies (between what and what?) to accurate predictions of probabilities of opioid abuse. Such research includes applying cutting-edge technologies like LSTM RNN’s and factor analysis to predicting probabilities of opioid abuse.

Ultimately, Opioid-Abuse Binary Classifier will serve as a clinical decision making support system for providers so that they can more safely prescribe opioids to patients.

**What Opioid-Abuse Binary Classifier Will Do**

Opioid-Abuse Binary Classifier will be a system that a Requester may use to submit a Patient and receive a prediction of the probability that a patient will exhibit an opioid-related ADRB prior to any prescription of opioids.

**Iterations Of Development**

At the end of Iteration…

1. Opioid-Abuse Binary Classifier will be as described in “What Opioid-Abuse Binary Classifier Will Do”.