



# Development of a machine learning algorithm for early detection of opioid use disorder

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## Abstract

**Background:** Opioid use disorder (OUD) affects an estimated 16 million people worldwide. The diagnosis of OUD is commonly delayed or missed altogether. We aimed to test the utility of machine learning in creating a prediction model and algorithm for early diagnosis of OUD.

**Subjects and methods:** We analyzed data gathered in a commercial claim database from January 1, 2006, to December 31, 2018 of 10 million medical insurance claims from 550 000 patient records. We compiled 436 predictor candidates, divided to six feature groups - demographics, chronic conditions, diagnosis and procedures features, medication features, medical costs, and episode counts. We employed the Word2Vec algorithm and the Gradient Boosting trees algorithm for the analysis.

**Results:** The c-statistic for the model was 0.959, with a sensitivity of 0.85 and specificity of 0.882. Positive Predictive Value (PPV) was 0.362 and Negative Predictive Value (NPV) was 0.998. Significant differences between positive OUD- and negative OUD- controls were in the mean annual amount of opioid use days, number of overlaps in opioid prescriptions per year, mean annual opioid prescriptions, and annual benzodiazepine and muscle relaxant prescriptions. Notable differences were the count of intervertebral disc disorder-related complaints per year, post laminectomy syndrome diagnosed per year, and pain disorders diagnosis per year. Significant differences were also found in the episodes and costs categories.

**Conclusions:** The new algorithm offers a mean 14.4 months reduction in time to diagnosis of OUD, at potential saving in further morbidity, medical cost, addictions and mortality.

## KEYWORDS

algorithm, big data analytics, diagnosis, machine learning, Opioid use disorder

**Abbreviations:** CCW, Chronic Condition Data Warehouse; IDF, Inverse Document Frequency; OUD, Opioid use disorder.

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## 1 | INTRODUCTION

Opioid use disorder (OUD) is the chronic use of opioids, causing significant clinical distress or impairment. OUD affects an estimated 16 million people worldwide, and 2 million in the United States<sup>1,2</sup> at very high cost.<sup>2,3</sup> The diagnosis of OUD is based on the American Psychiatric Association DSM-5 and includes a desire to obtain and take opioids independent of consequences.<sup>4,5</sup> OUD causes approximately 12 000 annual deaths worldwide<sup>6</sup> and is more prevalent among men between 40 and 50 years of age.

OUD is defined as opioid consumption at repeated occurrence within 12 months, with two or more of eleven defining problems (Textbox). Six or more positive items among the diagnostic criteria indicate a severe condition. The signs and symptoms of OUD include drug-seeking behavior, legal or social ramifications due to opioid use, subsequent adverse health outcomes and multiple opioid prescriptions from different clinicians. Furthermore, various medical complications from the use of opioids include opioid cravings, increased opioid usage over time, and symptoms of opioid withdrawal with stopping opioids.

The 11 defining problems.<sup>2</sup> are presented in the Box 1:

The actual prevalence of opioid use disorder may be much higher than the diagnosed numbers quoted above, as only a subset of those with OUD have had their disorder recognized by a medical professional. Due to the immense effects of OUD on health and well-being and its high mortality rates, it is essential to diagnose the condition as early and effectively as possible, so that treatment can be initiated.<sup>7</sup> A careful review of the literature has failed to identify a study that calculated the delay in diagnosis of OUD.

The objective of the present study was to test the utility of machine learning, applied to big data in creating a prediction model and algorithm for early diagnosis of OUD, and for identification of the typical delay in diagnosis. Within this objective, our aim was to

### BOX 1 Defining problems of OUD.

1. Continued use despite worsening physical or psychological health
2. Continued use leading to social and interpersonal consequences
3. Decreased social or recreational activities
4. Difficulty fulfilling professional duties at school or work
5. Excessive time to obtain opioids, or recover from taking them
6. A tendency to take more than intended
7. The individual has cravings
8. The individual is unable to decrease the amount used
9. Tolerance
10. Continued use despite it being physically dangerous
11. Withdrawal

identify patients at high risk for OUD before OUD has been fully developed and diagnosed, in order to be able to offer them early prevention and interventions.

## 2 | MATERIALS AND METHODS

### 2.1 | Data Set

This study utilized a commercial claims database of a large American health maintenance organization of over 20 million patients, between January 2006, and December 2018. The medical claims database contains data on medical insurance claims for reimbursement purposes, as well as personal diagnoses according to the International Classification of Diseases, Ninth Revision, Clinical Modification (*ICD-9-CM*) and International Classification of Diseases, Tenth Revision, Clinical Modification (*ICD-10-CM*) diagnosis and procedure codes, and details of pharmacy purchases.

### 2.2 | Study population and definitions

This study analyzed a sample of 10 million medical insurance claims recorded in patient records from the medical reports claim database. Inclusion criteria were patients who purchased at least one medication from the opioid class for example after trauma or medical procedures, excluding codeine (Appendix). The threshold for diagnosis of OUD was at least 2 of the 11 defining problems. Patients diagnosed with cancer or assigned palliative care were excluded as were patients with missing data from the 11 defining problems. Index date for the case group was defined as the date of the diagnosis of opioid use disorder (30 *ICD-9-CM* and *ICD-10-CM* codes for OUD, see Appendix). After employing these inclusion and exclusion criteria, the study group included 550 000 patient records. For the control group we included all other patients and the index date was the date of the last available entry in the database, either a diagnosis or a pharmacy purchase. The observation window consisted of all data available before the index date, while patients who had less than three months of claims records prior to index date were excluded.

### 2.3 | Prediction model construction and evaluation

Within the observation window of each patient, we used age, sex, *ICD-9-CM* and *ICD-10-CM* diagnostic codes and National Institutes of Health's RxCUI (RxCUI) medication codes, and the claims for clinical encounters and costs found in that period for features creation. *ICD-9-CM* and *ICD-10-CM* codes were used either directly as diagnostic information in some of the features, or by CCS mapping in other features in order to aggregate codes according to medical reasoning. For medication coding, an NDC to RxCUI mapping was done according to NIH conversion tables.

We manually compiled 436 predictor candidates informed by key published peer review papers that describe the characteristics of subjects with OUD<sup>1-4</sup>. A sample of these predictors is presented in Table 1 and their diagnostic codes are displayed in the Appendix. The Results section presents the main predictors. These candidate predictors were divided by medical reasoning to six feature groups - demographics, chronic conditions, diagnosis and procedures features, medication features, medical costs and number of episode counts.

Chronic conditions status was calculated from the claims data using the Center for Medicare and Medicaid Services' Chronic Condition Data Warehouse (CCW) algorithm.<sup>8</sup>

Initially, inspired by the well-known Word2vec algorithm<sup>9</sup> (a natural language processing methods which assigns for each word in a sentence a vector representation), we created an embedding representation (ie we converted medical codes into vector representations) for each medical code. The idea was to treat a patient's set of medical codes as if it was a sentence consisting of words.

Next, code embeddings were summed into patient-level vector representations in two different architectures. First, all code embeddings in a patient's history were summed to form a single patient-level vector. Second, all code embeddings were summed per patient to patient-level vectors. During both processes, two types of weights were added per code. The first was Inverse Document Frequency (IDF), which grants higher impact to less frequent codes than frequent ones and thus reduces the impact of frequently used administrative codes

for example. The second was a temporal weighting function (TWF), which takes into consideration the time interval between the code's date and the prediction date. In that way recent codes have more impact than previous ones. The results of this process constituted a vector with a length of 100 representing each component of the data - diagnoses, procedures, and medications.

We treated the prediction of OUD risk as a binary classification problem. For the analysis, we used the Gradient Boosting trees algorithm (XGBoost implementation).<sup>9,10</sup>

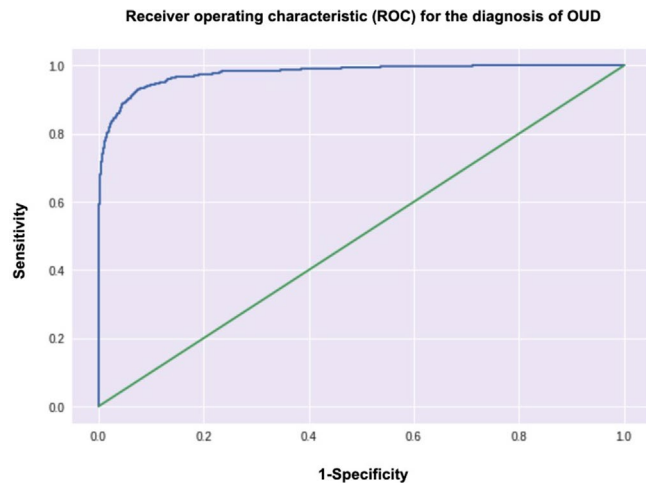
Employment of the Gradient Boosting Trees algorithm is a Machine-Learning technique where several decision trees are fitted to the data in a stepwise manner where each newly fitted tree is dependent on the previous ones, and thus an ensemble model is gradually fitted so that the prediction loss function is minimized using gradient descent. We tuned the maximum depth of a tree, the minimum child weight and gamma, as well as the learning rate and the number of trees constructed in the model.

We randomly divided the cohort into training (development and evaluation of the algorithm's prediction performance) and testing (evaluating algorithm's prediction performance) samples in a ratio of 70:30 (70% train and 30% test). The model was trained using the training set, and hyper-parameters were optimized using a fourfold cross-validation procedure. The fourfold cross validation was implemented on the training data only.

In addition, we used a filter method for feature selection. All features with a correlation coefficient above 0.9 with another feature

**TABLE 1** A sample of mean differences and significance of clinical features between cases and control independent groups

Feature groups	Feature	Cases Group- OUD positive (n = 3239)	Control group- OUD negative (n = 126,881)	Significant P value
Medication features	Number of annual opioid prescriptions	3.66 [±5.75]	0.64 [±1.81]	<.0001
	Days of opioid treatment (per year)	87.63 [±144.58]	11.96 [±47.52]	<.0001
	Overlapping opioid prescriptions (per year)	10.70 [±23.19]	1.76 [±10.13]	<.0001
	Longest consecutive opioid prescription period (average)	126.27 [±319.15]	28.84 [±156.13]	<.0001
	Nonopioid analgesics prescriptions (per year)	2.59 [±4.06]	0.72 [±1.59]	<.0001
	Benzodiazepine prescriptions (per year)	1.78 [±3.43]	0.48 [±1.56]	<.0001
Diagnosis and Procedures	Intervertebral disc disorder events (per year)	0.94 [±2.58]	0.22 [±0.96]	<.0001
	Pain disorders diagnosis (per year)	0.41 [±1.58]	0.04 [±0.39]	<.0001
	Post laminectomy syndrome	0.28 [±1.35]	0.02 [±0.30]	<.0001
Episodes and Costs	ER visits (per year)	0.82 [±1.74]	0.31 [±0.60]	<.0001
	Outpatient visits (per year)	14.80 [±14.04]	10.19 [±9.53]	<.0001
	Total costs (in dollars per year)	31 242.8 [±78 000.7]	16 266 [±30 471.7]	<.0001
	Inpatient ER costs (in dollars per year)	14 981.8 [±67 426.4]	6873.4 [±19 780.5]	<.0001



**FIGURE 1** Receiver operating characteristic (ROC) curve for the diagnosis of OUD. Area under the curve (AUC) for is 0.959

(only one from the couple) were excluded. This step was implemented on the training data, and then the same selected features were used in the test data. Furthermore, all features that had a normal distribution were normalized using the z-score formula (with the mean and standard deviation of the train set).

## 2.4 | Statistical analysis

We compared the patient characteristics by overdose status and by training, testing, and validation sample with unpaired, independent 2-tailed t test,  $\chi^2$  test and analysis of variance, or corresponding nonparametric tests, as appropriate. All analyses were performed using Python, version 3.7 (Python Software Foundation Inc, Beaverton, OR).

## 3 | RESULTS

### 3.1 | Patient Characteristics

Beneficiaries in the training ( $n = 104\,357$ ) and testing ( $n = 26\,094$ ) samples had similar characteristics and outcome distributions. The mean [SD] age was 47.4 [15.5] years with 40.3% female patients in the control group and 53.6 [16.7] in the case patients.

Factors from all six feature groups significantly varied between the case and control groups of patients (Table 1). Positive cases constituted 2.53% of the training population and 2.53% in the test population.

Notable examples of differences between positive OUD- cases group patients and the negative OUD- control group in univariate analysis were the mean annual number of opioid use days [87.63 vs 11.96,  $P < .00001$ ], number of overlaps in opioid prescriptions per year [10.70 vs 1.76,  $P < .00001$ ], the average annual opioid prescriptions [3.66 vs 0.64,  $P < .00001$ ], average annual benzodiazepine

prescriptions [1.78 vs 0.48,  $P < .00001$ ] and average muscle relaxants prescriptions per year [0.61 vs 0.15,  $P < .00001$ ].

In the Diagnosis and Procedures feature group, notable differences were the count of intervertebral disc disorder related complaints per year [0.94 vs 0.22,  $P < .00001$ ] and chronic pain-related complaints per year [0.41 vs 0.04,  $P < .00001$ ].

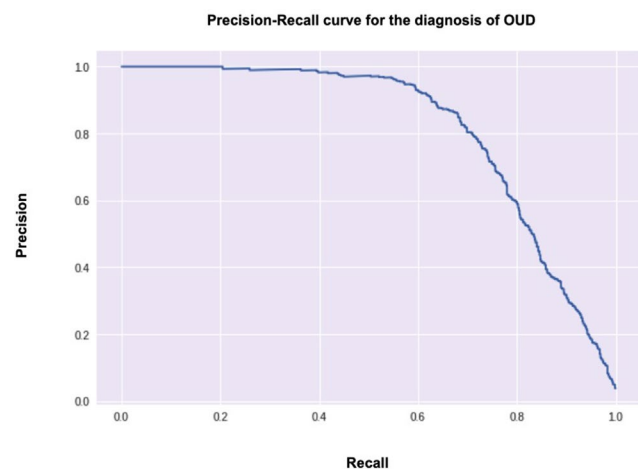
Significant differences were also found in the Episodes and Costs categories: OUD patients had more outpatient visits [14.80 vs 10.19,  $p$  value  $< 0.0001$ ], ER visits [0.82 vs 0.31,  $P < .00001$ ], total costs [31242.8 vs 16266.4,  $P < .0001$ ] and inpatient ER costs [14981.8 vs 6873.4,  $p$  value  $< 0.0001$ ].

Figure 1 summarizes the results of the Gradient Boosting trees model: The c-statistic for the model was 0.959, with a sensitivity of 0.85 and specificity of 0.882. Positive Predictive Value (PPV) was 0.362 and Negative Predictive Value (NPV) was 0.998. For the top 1 percentile of patients identified by our model, PPV was 0.80. Notable features contributing to the model were hypertension and hyperlipidemia as a comorbidity, as well as patient age and the number of hypertensive crisis events.

After implementation of the model, we used the fitted model weights for assessments of the time our algorithms identified a patient as OUD positive, before a formal diagnosis was made by a physician. For that end, we calculated the predicted OUD probability for each patient, while cutting out data from the model in incrementing three month time windows, and determined the time point at which the OUD probability passed our preassigned threshold. Using this method, our algorithm identified OUD in a mean 14.4 months before formal diagnosis (Figure 2).

## 4 | DISCUSSION

Abuse of prescription opioids is a major public health issue, with increasing numbers of subjects meeting the criteria of OUD, at a huge price of mortality, morbidity, and social burden.<sup>1,2,5</sup> While major



**FIGURE 2** Precision-Recall curve for the diagnosis of OUD. Chen, T., Guestrin, C. 2016XGBoost: a scalable tree boosting system. KDD conference 2016

studies acknowledge that the true prevalence of affected individuals is much larger than recognized by medical authorities due to major under diagnosis, it is not known, even among diagnosed patients who are served medically and diagnosed, how much delay occurs in diagnosis and initiation of treatments. Early diagnosis is critical due to the serious consequences of OUD and the fact that loss of time contributes to increased morbidity, mortality, as well as social burden, family damage, and crime rate.<sup>1,2,5</sup>

In the USA recent studies have shown a 50% increase in prevalence of prescription opioid use disorder from 0.6% to 0.9% during 10 years between 2003-2013, and 73% increase in drug overdose rate from 4.5/100000 to 7.8/100000.<sup>10</sup>

Several efforts have been published in attempts to predict individuals at risk of developing opioid dependence at the time of initial opioid prescription. Using a large commercial insurance claim database, Cochran and colleagues identified several risk factors for developing OUD, including male gender, history of more days of supply of opioids, greater rates of psychiatric disorders, utilization of more medical and psychiatric services, and prescribed more concomitant medications.<sup>8</sup> Mathematical modeling successfully predicted 79.5% of OUD diagnosed cases within two years.

Calcaterra and colleagues created a model to predict the risk of chronic opioid therapy among 1457 hospitalized patients who were not on chronic opioid therapy prior to their hospitalization<sup>11</sup> Their model, which included 13 covariates, predicted 79% of future chronic opioid therapy, and 78% of those not on chronic opioid therapy.

Using machine learning for prediction of sustained opioid prescription after spine surgery among 2737 patients, 9.9% of them exhibited sustained receipt of opioid prescription. Variables contributing to the model's predictive power included male gender, multilevel surgery, myelopathy, tobacco use, insurance status (Medicaid, Medicare), duration of preoperative opioid use, and concomitant medications. The most important predictors of sustained postoperative opioid prescription were preoperative opioid duration, antidepressant use, tobacco use and Medicaid insurance.<sup>12\</sup>

Hastings and colleagues used state government administrative data and machine learning to predict the risk of future opioid dependence, abuse or poisoning at the time of initial prescription. Prior nonopioid prescriptions, medical history, incarceration and demographic were identified as strong predictors.<sup>13</sup> Mojtabai and colleagues assessed the prevalence and correlates of self-reported misuse of prescribed opioids by analyzing 31 068 adults participating in the National Survey on Drug Use and Health from 2015-2016. Prescribed opioid misuse was most strongly correlated with co-occurring misuse of opioids without prescription, misuse of benzodiazepines, other drug use disorders, history of illegal activity, and psychological distress.<sup>14</sup>

Ellis and colleagues presented prediction of opioid dependence from electronic health records with machine learning.<sup>15</sup> The top machine learning classifier achieved a mean area under the receiver operating characteristics curve of 92%, with associations with

diagnoses, prescriptions and procedures prior to diagnoses of substance dependence. The authors believe their predictive model may help in identifying subjects at risk for drug dependence.<sup>15</sup>

Different from traditional statistics, machine learning considers large numbers of predictors by combining them in nonlinear and highly interactive computational methods. In the model construction phase of the forest algorithm, for example, the model automatically generates decision trees which aim at identifying success rates of treatment. The model's performance is tested by using 90% of the data for construction, and the remaining 10% for examination of its performance. This process is repeated 10 times by dividing the derivation set into new and different learning and testing subsets. The model created through these steps could then be applied on a new and previously unused data.<sup>9,16-18</sup>

Medical claims data offer unique challenges and possibilities. On the one hand, claims data are limited to diagnosis, procedures and pharmaceutical structured data, without laboratory data or physician notes that are unique to Electronic Medical Records (EMR) data. On the other hand, as EMR data in the US are limited and dispersed among different providers, the scale of the claims data are much bigger than any other available EMR data, and conclusions and implementations derived from claims data using big data mathematical machine learning may be implemented in much broader scopes, with higher relevance to population health.

Our algorithm has demonstrated very high sensitivity and specificity for identifying OUD over a year before formal diagnosis was made, at a cost of relatively low TPV. First, we must acknowledge the fact that OUD was relatively rare in our data, identifying less than 2.5% of cases, and hence almost a 10-fold increase in PPV is significant. Second, our aim was to offer physicians and case-managers an assessment tool, where, as a first step, a questionnaire will be sent to high-probability patients identified by the algorithm, for further evaluation. In that setting, choosing a high sensitivity over low PPV is preferred.

This study has several limitations. The first limitation is the use of claims data. Claims data are restricted to billable elements in the patient's medical history, often without a clinical context and reasoning. As the DSM-5 OUD diagnostic criteria rely heavily on aberrant behaviors whereas other key information may not be included in claims data, the reliance of our model on the billable ICD9 and ICD10 codes prevents us from assessing the correctness of the diagnosis, mitigating the well-known problem of under diagnosis of OUD. Although we had more than 3200 diagnosed patients, under-diagnosis is probably reflected in the performance of the model, demonstrating a low PPV and high NPV. However, this does not introduce an error in diagnosis but rather relatively low sensitivity. Future studies should contrast billing data with other forms of EMR data. Because American EMR data are limited and dispersed among different providers, the much bigger scale of the claim data than any other available EMR data, may increase the overall detection rate of early identification of OUD.

In terms of the practicing physician and patient, our present analysis suggests that with this algorithm, OUD may be diagnosed on

average 14.4 months earlier than it is diagnosed clinically, at substantial saving of morbidity, suffering, and medical cost.

The way this new algorithm can be optimally utilized is that, when a patient reaches the algorithm threshold for being at risk for OUD, a warning message will be sent electronically to the physician, who will initiate an investigation of the specific context of the individual, in order to hasten the establishment of diagnosis and initiate management and therapy when appropriate.

## DATA SHARING AND DATA ACCESSIBILITY STATEMENT

The data presented in the manuscript will be shared upon request two years after publication request, pending agreement by the health fund.

## ACKNOWLEDGEMENT

Diagnostic Robotics Inc develops algorithms related to health care. The particular topic of OUD did not have a commercial interest or purpose.

## DISCLOSURES

ZS, KR, MB, ML, BE, PG are employed by Diagnostic Robotics. LK, GK do not have any conflict of interest to declare.

## AUTHOR CONTRIBUTIONS

ZS: Conceptualized, co-wrote first draft, interpreted results. KR: Obtained data, oversaw the process. GE, GM, MB, ML, BE, PG: performed the machine learning analyses. LK: Clinical and public health interpretation. GK: Clin interpretation, co-wrote first draft.

## ETHICAL STATEMENT

All data were anonymous and exempted from ethical approval by the health fund owning the data who consented to its use in this research project.

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## APPENDIX

**TABLE 1 - XGBOOST MODEL PARAMETERS:**

Following a fourfold cross-validation hyperparameter tuning, optimal hyperparameters were:

Learning rate:0.1

Max depth = 6,

Min childweight = 3

Number of estimators:250

Gamma = 0

Positive weight scaling:  $(\text{length}(y_{\text{train}}) - (\text{sum}(y_{\text{train}})) / \text{sum}(y_{\text{train}}))$

Opioid Use Disorder		
ICD-10 Codes	ICD-9 Codes	
F11.1, F11.10, F11.12, F11.120, F11.121, F11.122, F11.129, F11.14, F11.15, F11.18, F11.19, F11.2, F11.20, F11.21, F11.22, F11.23, F11.24, F11.25, F11.28, F11.29, T40.3X1A, T40.3X2A, T40.3X3A, T40.3X4A	305.5, 305.50, 305.51, 305.52, 305.53, 304.0, 304.7, 304.70, 304.71, 304.72, 304.73, E850.1, E935.1, 965.02	
RXCUI Drug Codes	Methadone	
6813, 218 337		
RXCUI Drug Codes - Inclusion Criteria for Opioid Use Disorder		
RXCUI Codes	RxNorm Class	
352 362, 1819, 1841, 3290, 22 713, 4337, 3423, 484 259, 6754, 6761, 7052, 7238, 1 545 902, 1 806 700, 7676, 7804, 7894, 8001, 8119, 8354, 8785, 787 390, 10 597, 10 689	Opioids	
International Classification of Diseases Codes - Exclusion Criteria		
ICD-10 Codes	ICD-9 Codes	Description
C00-C26, C30-C41, C43-C58, C60-C96, C7A, C7B	140-165, 170-176, 179-209 excluding benign neoplasms under 209.x (209.4, 209.5, and 209.6)	Cancer Diagnosis Codes
Z51.5	V662, V667	Encounter for palliative care
International Classification of Diseases Codes - Comorbidities		
ICD-10 Codes	ICD-9 Codes	Description
F14.1, F14.2, F14.9, F16.1, F16.2, F16.9	291.0, 303, 304.2, 304.4, 304.5, 304.8, 304.9, 305.7, 305.3	psychoactive substances use or dependence
F55		Abuse of nonpsychoactive substances
F10.1, F10.2, F10.9	303, 305.0	Alcohol use or dependence
F17.2	305.1	Tobacco/ Nicotine use or dependence
F12.1, F12.2, F12.9	304.3, 305.2	Cannabis use or dependence
F20-F29	295, 297	nonmood psychotic disorders
F30-F39	296	Mood (affective) disorders
F40-F48	300, 309	Nonpsychotic mental disorders
F50, F51, F53	307.4, 307.5	Behavioral syndromes
F60	301	Personality disorders
F63	312	Impulse disorders
F10.24	291	Alcohol induced mental disorders
	292	Drug induced psychotic disorders
G43	346	Migraine
M54.4, M54.5, M54.8, M54.9	724	Back pain
M797	729.1	Fibromyalgia
G44, R51	339	Headache

(Continues)

## APPENDIX (Continued)

International Classification of Diseases Codes - Comorbidities		
ICD-10 Codes	ICD-9 Codes	Description
K590.0	E9352, 564.00, 564.09	Opioid adverse effects
T400, T401, T402, T404, T406	965.00, 965.01, 965.09	Poisoning by opioids and narcotics
T39, T42, T43, T505, T506, T508, T509, T519	965, 966, 967, 968, 969, 970, 971, 972, 973, 975, 977, 980	Other drug/ substance-related overdose
M43, M45, M46, M47, M48, M50, M51, M53, M54, M6788, M961	721-724	Diseases of the musculoskeletal system and connective tissue
B02.22, B02.23, F45.41, F45.42, G45.41, G45.42, G50.0, G54.6, G56.40, G57.70, G58.9, G89.0, G89.4, G90.519, G90.529, G90.59	053.12, 053.13, 307.80, 307.89, 337.20, 337.21, 337.22, 337.29, 338.0, 338.4, 350.1, 353.6, 354.4, 355.71, 355.9	Pain disorders
G89.12, G89.18, G89.21, G89.22, G89.28	338.12, 338.18, 338.21, 338.22, 338.28	Postoperative pain
G89.11	338.11	Pain due to trauma
M26.6	524.60, 524.61, 524.62, 524.63, 524.69	Temporomandibular Joint Disorders
M15, M16, M17, M19	715.00, 715.04, 715.09, 715.11-715.15, 715.17, 715.25, 715.16, 715.26, 715.80, 715.89, 715.90	Osteoarthritis
B20, Z21	42, V08	HIV
K8020, K8021, K8070, K8071, N200, N201, N202, N209	574.20, 574.21, 574.90, 574.91, 592.0, 592.1, 592.9	Kidney or gallbladder stones
	617, 625.2, 625.4, 625.5, 625.8, 629.89, 629.9	Menstrual or genital pain
M40, M41	737.30, 737.32, 737.34, 737.39, 737.43	Scoliosis
M45	720.0	Ankylosing spondylitis
M46	720.1	Spinal enthesopathy
M47	721.0	Spondylosis
M10.0	274	Gout
M11.0	712.8	Hydroxyapatite Deposition Disease
G60, G61, M79.2	340, 341, 356, 357, 729.2	Neuropathies

ICD-9 = International Classification of Diseases, Ninth Revision

ICD-10 = International Classification of Diseases, Tenth Revision

## Generic Drug Code Number associated with Opioid Use Disorder

RXCUI Codes	RxNorm Class
25 480, 187 832, 1 101 333	Gabapentinoids
2101, 2410, 21 949, 6845, 7715	Muscle Relaxants
94, 17 698, 704, 722, 47 111, 42 347, 19 895, 2556, 2597, 3247, 734 064, 3332, 3634, 3638, 72 625, 321 988, 2 119 365, 4493, 42 355, 5691, 5979 6011, 6465, 6646, 29 434, 446 248, 6929, 588 250, 30 031, 15 996, 30 121, 31 565, 7394, 7500 7531, 7674, 32 937, 8123, 8886, 35 242, 60 842, 36 437, 258 326, 38 252, 38 382, 10 734, 10 737, 10 834, 10 898, 39 786, 1 086 769, 11 196, 1 455 099	Antidepressants

(Continues)



## APPENDIX (Continued)

Current Procedural Terminology (CPT) Codes Associated with Opioid Dependence	
CPT Codes	Procedure
20 610, 20 605, 20 600, 27 096, 20 552, 23 350, 27 093, 64 450, 64 640	Joints and Bursa – Injection or Aspiration
20 550, 20 551, 20 552, 20 553	Tendons, Ligaments, and Muscle Injections
64 405, 64 450, 64 418, 64 420, 64 421, 64 425, 64 400, 64 505, 64 510, 64 517, 64 520, 64 530, 64 455	Nerve blocks
62 321, 62 323, 64 479, 64 480, 64 483, 64 484	Epidural Steroid Injections (ESI)
64 490, 64 491, 64 492, 64 493, 64 494, 64 495	Facet Joint Procedures
64 633, 64 634, 64 635, 20 552, 27 096, 64 450, 64 635, 64 640	Radiofrequency Ablation (RFA)
22 510, 22 511, 22 512, 22 513, 22 514, 22 515	Vertebroplasty/ Kyphoplasty
63 650, 63 655, 62 291, 62 290	Neurostimulation
95 874, 64 616, 64 614, 64 615, 20 526	Botulinum Toxin Injections
97 813, 97 810, 98 925, 98 926, 98 927, 98 928, 98 929, 97 110, 97 530	Noninvasive chronic pain treatment
27 447, 47 600, 47 605, 47 610, 27 130, 19 301, 19 302, 19 303, 19 180, 47 562, 47 563, 47 564, 44 950, 44 960, 59 510, 59 514, 59 515	Surgeries associated with chronic opioid use
80 305, 80 306, 80 307	Presumptive drug testing
G0283	Transcutaneous Electrical Nerve Stimulation
97 112	Neuromuscular reeducation