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Deep Learning Solutions for Classifying Patients on Opioid Use

S118: Detecting and Examining Patterns in Data: Applications for Combating Opioid Abuse and Adverse Events

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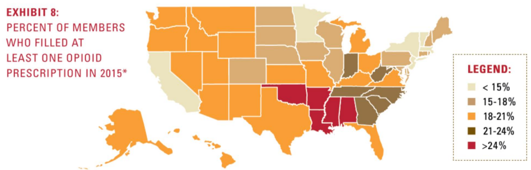
MAYO CLINIC

Disclosure

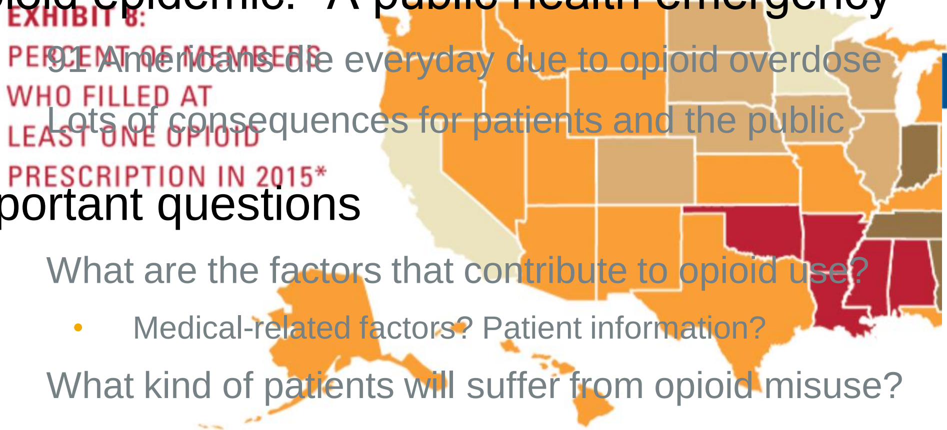
All authors have no relevant relationships with commercial interests to disclose.

Opioid Epidemic

- Opioids: Painkiller with high usage
  - 7% adults in US took opioids in last 30 days

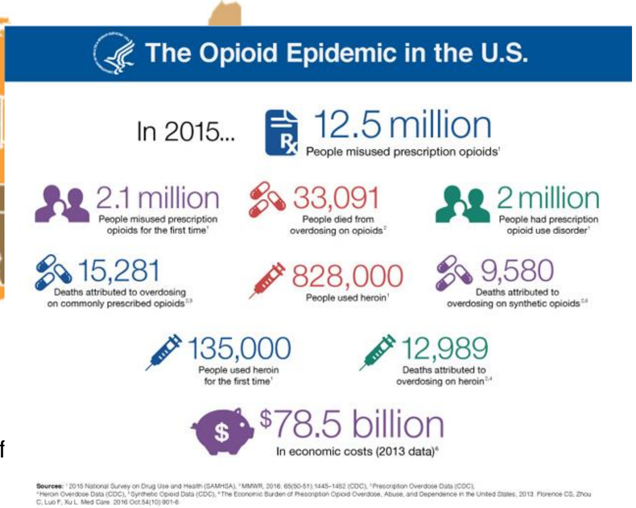


- Opioid epidemic: “A public health emergency”
  - 91 Americans die everyday due to opioid overdose
  - Lots of consequences for patients and the public



- Important questions
  - What are the factors that contribute to opioid use?
    - Medical-related factors? Patient information?
  - What kind of patients will suffer from opioid misuse?
    - Accurate prediction and proper intervention?
    - Prediction and intervention at early stage?

https://www.bcbs.com/the-health-of-america/reports/americas-opioid-epidemic-and-its-ef

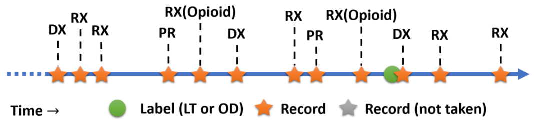


https://www.hhs.gov/opioids/about-the-epidemic/index.html

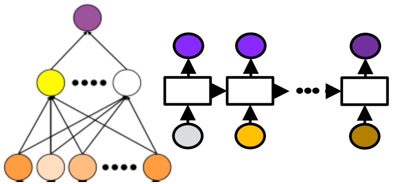
Opioid Usage Study

- Existing work on opioid usage study
  - [Hooten et al., 2015; Clarke et al., 2014; Thielke et al., 2017; etc]
- Data: Static features only (e.g., demographics, diagnoses/drug use history)
  Data: Large-scale temporal EHR data from multiple chart tables
- Task: Identifying risk factors and indicators
  Task: Classifying dependent users, making early prediction, identifying factors
- Method: Multivariate logistic regression & p-value test
  Method: Powerful and scalable deep learning models & model investigations

Large-scale Temporal EHR Data



Several Simulated Settings
(e.g., Early Prediction, Hidden Factor Finding)

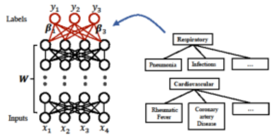


Deep Learning Models

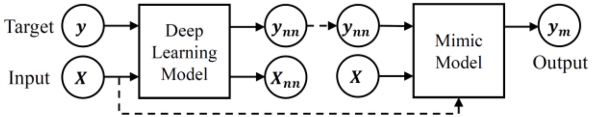
Deep learning for opioid usage study is promising!

Deep Learning for Health Care

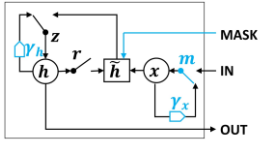
- Deep Computational Phenotyping
  - [Che et al., KDD 2015]



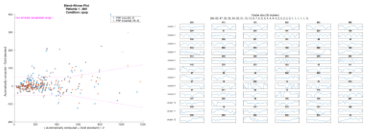
- Interpretable Deep Models
  - [Che et al., AMIA 2016]



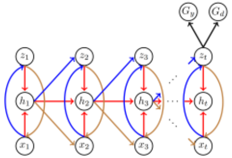
- Deep Models for EHRs with Missing Values
  - [Che et al., arXiv 2016]



- Anomaly Detection
  - [Nilanon et al., CinC 2016]



- Variational Adversarial Deep Domain Adaptation
  - [Purushotham et al., ICLR 2016]



Data & Task

- Data source: Rochester Epidemiology Project (REP)
  - > 140,000 people
  - Covered 98.7% of the population in Olmsted County, MN
  - > 50 years of history
- Two classification tasks
  - Predict whether an opioid user will become a long-term user or short-term user
  - Predict if a long-term opioid user will be opioid-dependent
  - Identify factors and indicators in these two tasks
- Preliminary study [Hooten et al., 2015]
  - Same data source, ~300 patients, 1-year record, characteristics exploration

Data Processing – Cohort Selection

- Obtain outpatient drug prescriptions
  - Mayo Clinic & Olmsted Medical Center
  - Study period: Jan 1th, 2003 to March 31, 2016
  - Define analgesic prescriptions by RxNorm 2016 version
    - NDF-RT class code C8834 (Opioid Analgesics), or
    - Ingredient code 10689 (Tramadol) or 352362 (Acetaminophen/Tramadol)
  - Handle duplicated prescription data
    - Only keep the last prescription if the same drug is prescribed within 30 mins
- Determine cohorts
  - With authorization on the use of medical records
  - Ensure clean label
    - Exclude patients with prescriptions 6 months prior to first prescriptions within study period
  - **N = 102,166 patients**

Data Processing – Group Identification

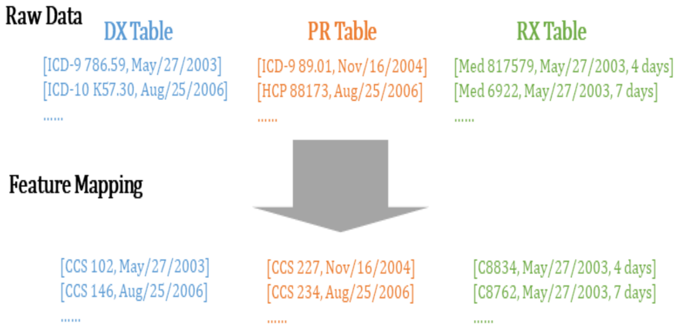
- Label all patients into 3 groups
  - Short-term user (**ST**) and Long-term user (**LT**)
    - Similar definition used by the CONSORT study
    - Long-term user:
      - Episodes of opioid prescriptions >90 days, and
      - With >120 days supply or with >10 prescriptions
  - Opioid-dependent user (**OD**)
    - Subset of LT patients
    - Identified by the diagnosis of "opioid dependence" from their problem lists by Mayo NLP group
    - *Not all OD patients are explicitly diagnosed.*
  - Data characteristics matches preliminary studies

Short-Term (ST)		Long-Term (LT)		Opioid-Dependent (OD)	
#	%	#	%	#	% of LT
80,596	78.89%	21,570	21.11%	749	3.47%

Method – Feature Extraction

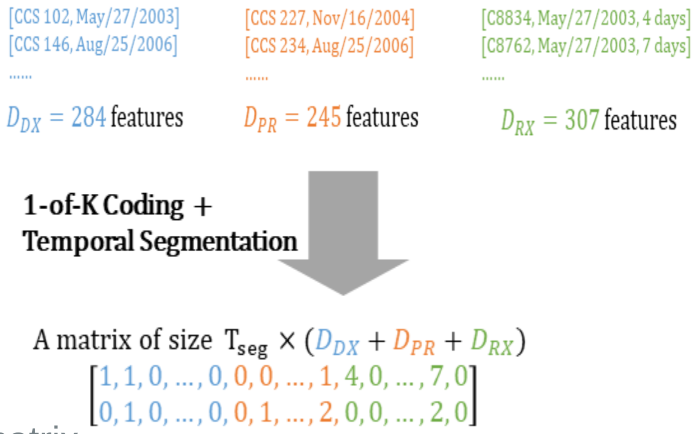
- Features from 3 chart tables
  - Diagnosis records (**DX**): ICD-9, ICD-10, HICDA code ⇒ CCS code
  - Procedure and service records (**PR**): ICD-9, ICD-10, CPT/HCPCS code ⇒ CCS code
  - Prescription records (**RX**): RxNorm ingredient code ⇒ NDF-RT class code
  - Features to use: *time step*, *code*, and *duration (for RX only)*.
- **Feature mapping** is required
  - Raw code records are sparse
  - Coding system are different for different time/sites

Table	DX	PR	RX
# of records	56,229,157	46,386,740	8,102,477
# of raw codes	43,438	18,984	2,460
# of mapped codes	284	245	307



Method – Handling Temporal Data

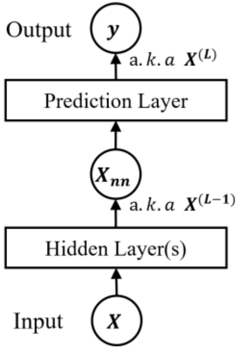
- Make extracted features suitable for models
- **1-of-K (one-hot) encoding**
  - Convert each record into a fixed-length vector of size D
  - A prescription of m days is converted to $[0, \ldots, m, \ldots, 0]$
- **Temporal sum-pooling** *Get fixed-length input*
  - Sum up all records of one patient into a vector of size D
  - Data can be used in any model
- **Temporal segmentation** *Keep temporal info*
  - Take sum-pooling for every year and stack them into a matrix
  - Data matrix is of size T x D, where T may be different
  - Data can be used in RNN model



Method – Deep Learning Predictive Models

- Two different deep learning models

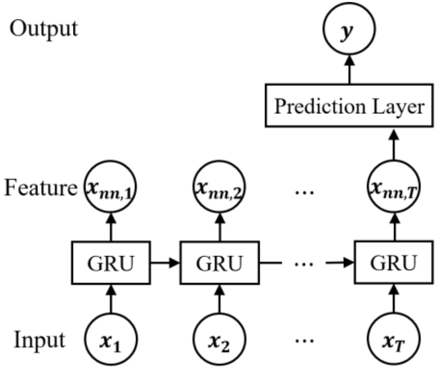
DNN: Multilayer feedforward network



$$x^{(l)} = f\left(W^{(l)} x^{(l-1)} + b^{(l)}\right)$$

$$y = x^{(L)}$$

RNN: Recurrent neural network with Long Short-Term Memory (LSTM)



$$c_t, h_t = f(x_{t-1}, h_{t-1}, c_{t-1})$$

$$x_{nn,t} = c_t \qquad y = \sigma(W x_{nn,T} + b)$$

Method – Other Baselines

- Three commonly used models are compared
  - Logistic Regression (LR)
  - Support Vector Machine (SVM)
  - Random Forest (RF)
- Implementation details
  - L1 penalty is applied in LR and SVM with hyperparameter tuning
  - Default setting of RF is used to avoid overfitting
  - Implemented in Python with scikit-learn package
- Can train and test efficiently on a desktop (no need for GPU!)

Model	DNN	RNN	LR	SVM	RF
Model Size (KB)	1,878	9,320	21	23	2,282

Discussion – Experiment Settings

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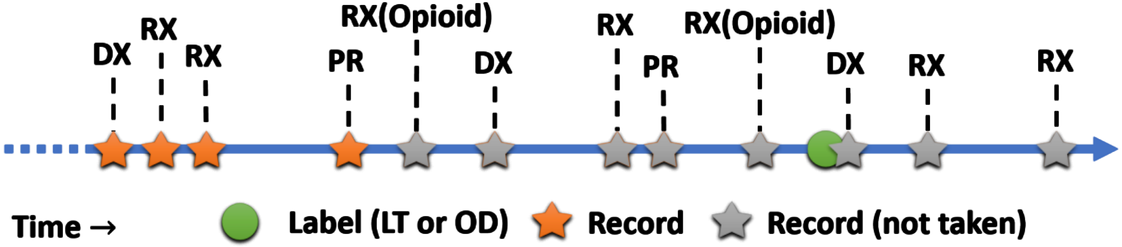
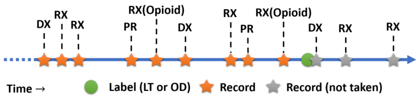
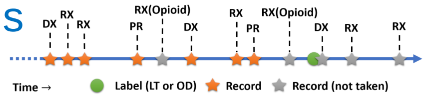


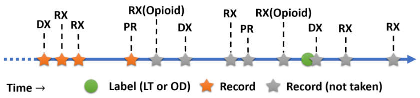
- Three simulated settings
  - **Setting A**: Take all medical records before the labeling time
    - Ideal case with most input features and best prediction performance



  - **Setting B**: same as Setting A, excluding analgesics prescriptions
    - Try to find hidden indicators / factors

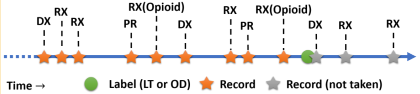


  - **Setting C**: Take all medical records before the first opioid prescription
    - Demonstrate early prediction capacity

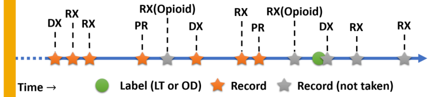


Discussion – ST-LT Results

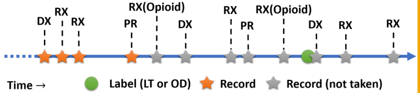
- Setting A

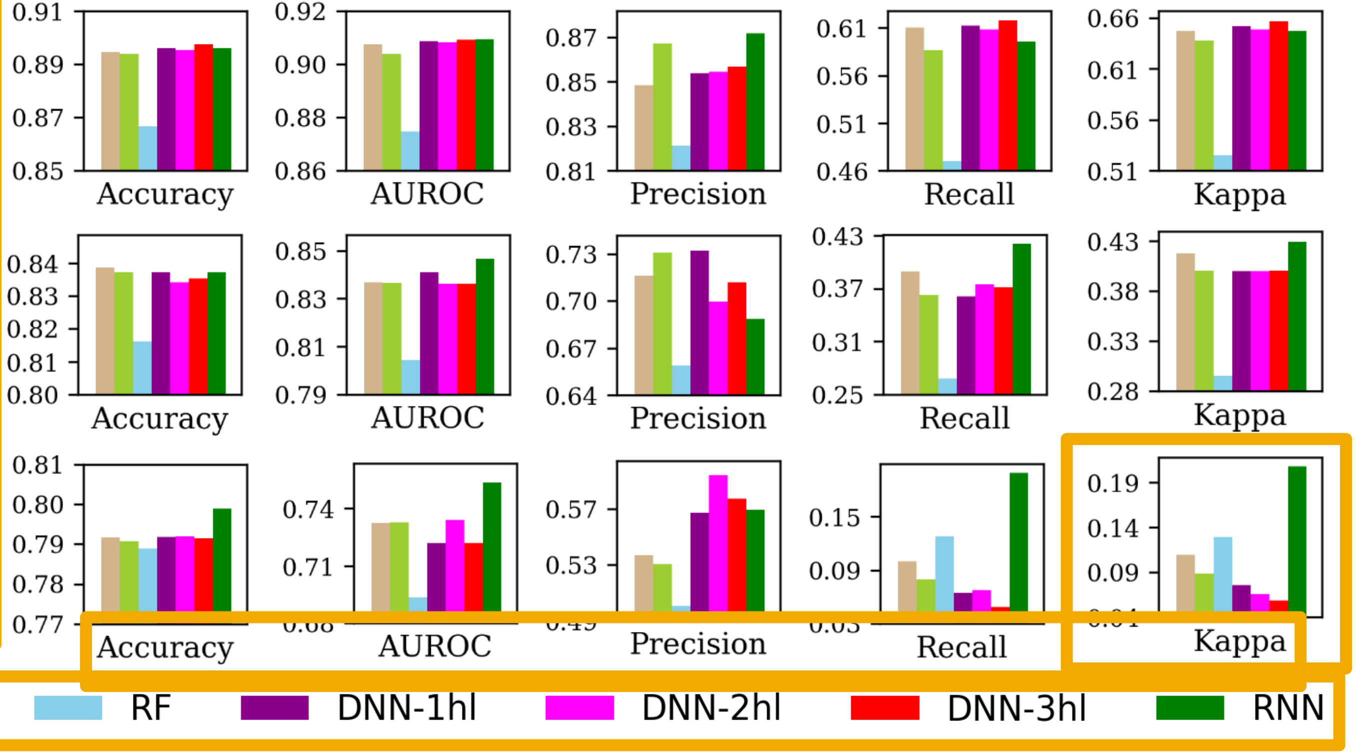


- Setting B



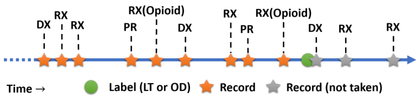
- Setting C





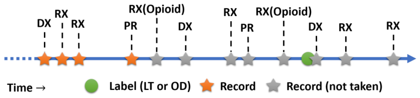
Discussion – LT-OD Results

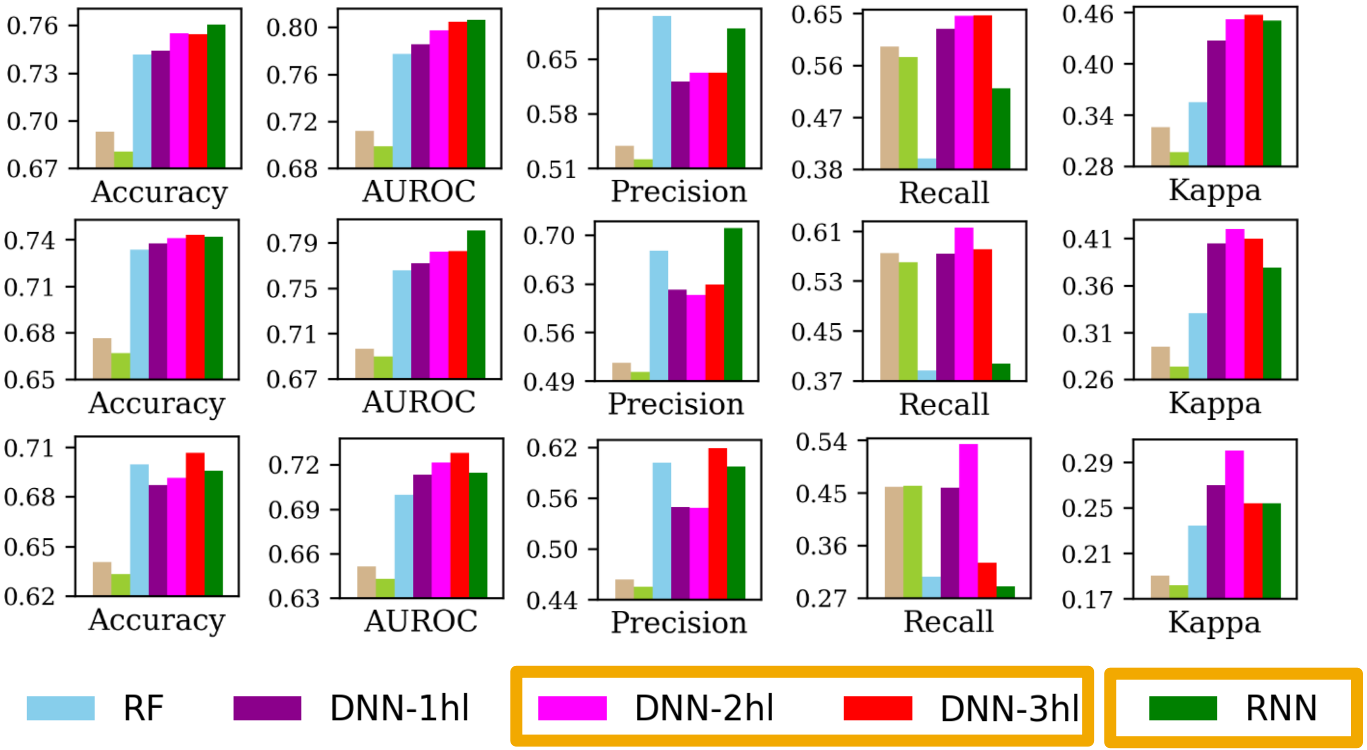
- Setting A



- Setting B

- Setting C





Discussion – Feature Investigation Method

- Equation of prediction results in DNN

$$y = \sigma\left(\boldsymbol{W}^{(L)} f^{(L-1)}\left(\cdots \boldsymbol{W}^{(2)} f^{(1)}\left(\boldsymbol{W}^{(1)} x + b^{(1)}\right) + b^{(2)} \cdots\right) + b^{(L)}\right)$$

- Estimation on input feature importance in DNN

$$I = \boldsymbol{W}^{(L-1)} Bn^{(L-1)} \left(\cdots \boldsymbol{W}^{(2)} Bn^{(2)} \left(\boldsymbol{W}^{(1)} Bn^{(1)}\right)\right) \in \mathbb{R}^{1\times D}$$

  - d-th number in I is the importance score for d-th input feature
  - Absolute value indicates the strength
  - Sign indicates whether it's positively or negatively relevant
  - This is only a rough estimation, without considering
    - Feature dependencies in data
    - Bias term and non-linearity in models

Discussion – Feature Investigation Results

Table / Code		Features for ST-LT Task	*I*
RX	C8834	Opioid Analgesics	0.2287
RX	C8890	Amphetamine-like Stimulants	0.0843
RX	C8838	Non-opioid Analgesics	0.0802
PR	CCS 227	Other Diagnostic Procedures	0.0272
DX	CCS 258	Other Screening	0.0218
RX	C4859	Salicylates, Antirheumatic	0.0204
DX	CCS 203	Osteoarthritis	0.0185
DX	CCS 205	Spondylosis	0.0179
DX	CCS 98	Essential Hypertension	0.0126

Table / Code		Features for LT-OD Task	*I*
RX	C8834	Opioid Analgesics	0.7784
DX	CCS 661	Substance-related Disorders	0.6186
PR	CCS 182	Mammography	0.3481
DX	CCS 663	Substance Abuse/Mental Health History	0.3248
DX	CCS 258	Other Screening	0.2948
PR	CCS 228	Prophylactic Vaccinations/Inoculations	0.2796
DX	CCS 651	Anxiety Disorders	0.2785
RX	C8864	Anticonvulsants	0.2626
RX	C8860	Benzodiazepine Derivatives	0.2382

Summary

- Summary
  - A deep learning solution for opioid use study with promising results
  - Showcase of applying deep learning models in practical clinical studies with large-scale data
- Future work
  - Handle incomplete data and noisy features / labels
  - Incorporate numerical and unstructured data
  - Further investigate important indicators / factors
  - Capture temporal evolutions of opioid users and help prescription making
- Contact
  - Mayo NLP Group, Medical Informatics
  - USC Melady Lab

Thank you!

Email me at:
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Terms

- **RxNorm**: US-specific terminology in medicine that contains all medications available on US market
- **CONSORT**: Consortium to Study Opioid Risks and Trends, supported by the National Institute of Drug Abuse
- **ICD-9/10**: International Classification of Diseases, 9th/10th version
- **HICDA**: Hospital International Classification of Diseases Adapted (Mayo adaptation of ICD-8)
- **CPT/HCPCS**: Healthcare Common Procedure Coding System based on Current Procedural Terminology
- **CCS**: Clinical Classifications Software, a uniform and standardized coding system based on ICD-9 into a smaller number of clinically meaningful categories
- **NDF-RT**: National Drug File - Reference Terminology
- **Bn**: Batch normalization, a technique used in deep learning by normalizing the activations of neural network layer at each batch.