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Using RWD in the Form of EHR Data to Predict Adverse Events and Outcomes

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ABSTRACT

The paper discusses a method for using a large set of electronic health record (EHR) data to predict adverse drug event outcomes for patients undergoing drug therapies. Combining rigorous data science principles with subject matter expertise, the research developed machine learning models to predict targeted outcomes related to anticoagulant therapy. The first objective of the work was to create a patient-level risk score for a specific negative outcome, a bleeding event. The research tested predictive models using support vector machine, random forest, logistic regression and neural network methods. The research merged external determinants of health data, including Social Determinants of Health (SDoH), with the EHR data which enhanced predictive capabilities. Practical implementations to improve patient safety and quality of live are discussed.

INTRODUCTION

Adverse drug events (ADEs) disproportionality impact older adults and are potentially preventable 50% of the time.[1] One research study reported that **one in six senior admissions** to a hospital was due to an adverse drug event.[2] A recent clinical journal publication highlights the need for a predictive tool to help identify risks ahead of an emergent need for acute care.[3]

Another recent publication referenced that 13% of avoidable 30-day readmissions were due to ADEs and more than 90% were confirmed to be preventable.[4] Health systems can prospectively use ADE prevention to achieve performance at or below peer Excess Readmission Ratios (ERRs) for Hospital Readmissions Reduction Program (HRRP) categories under the Center for Medicare Services (CMS). For a multi-hospital system with a CMS penalty rate between 0.5% and 1%, achieving these ERR rates could reduce penalty rates by more than 80% and reduce both CMS and commercial penalties by millions of dollars.

In 60+ customer discovery interviews to find technology that addresses ADEs using machine learning and EHR data, the authors did not discover a prevalent solution or toolset available to hospitals and health systems to counter ADEs. **The project work described herein seeks to create a methodology for predicting individual patient risk of an ADE using clinical and SDoH data combined with machine learning.** The value proposition of the current project work is threefold for health systems: 1) improving patient safety for the powerful intrinsic value, for improving population health, and for value based care and quality initiatives; 2) reducing readmissions; and 3) focusing care management resources on the most actionable cases.

GOALS

The project objectives were: 1) to predictively model individual patient risk of a major bleeding event using EHR data, SDoH data and machine learning; 2) to assess the variables of importance globally impacting risk; and 3) to produce individual risk factors at a patient level to enable prescriptive action to mitigate patient risk. As a result, the expectation was to produce a proof-of-concept model for real-time risk assessment for health system operations. Additionally, the analytics would produce insights for a current snapshot of the population.

APPROACH

The project sought to forecast the risk of a major bleed event, including intracranial, urinary tract or GI bleeding, looking three months forward. The project scientists used EHR data to produce both the features (input variables) and outcomes for the ADE model. Model features included demographic data, service locations visited, length of medical records with health system, counts of encounters, diagnoses, procedures, medications, insurance type, and vitals. Table 1 provides a high-level summary of feature types and examples of those features. For ICD codes, CPT codes and medications, indicator vectors were created when a code or medication occurred in a specific fraction of records.

Feature Type	Example Features
Demographic data	Age, sex, smoking status, drug use, marital status, race
Service locations visited	Counts of visits for each location within health system visited within past two years
Measures related to patient visit counts	Length of medical records with health system, frequency of visits, time since last visit
Health system encounters	Counts of general and specific encounters (inpatient, outpatient, imaging, etc.)
Diagnoses and procedures	Specific codes, hierarchical roll-ups, and bag-of-words representation of descriptions
Medications	Generic names and medication classes
Insurance type	Commercial, Medicare, Medicaid, self-pay, etc. …
Vitals and labs	Summary stats of results (mean, median, standard deviation, min, max), slope of means over time, and frequencies taken for vitals like heart rate

Table 1: High-level view of feature types and examples of features used in the predictive model

The project scientists also utilized an NLP technique known as bag-of-words to create features from diagnosis and procedure descriptions. This produced more than 1,000 new features for the input matrix. Despite also including diagnosis codes and procedure codes into modeling, these NLP-informed description "roll-ups" were some of the most informative features to ADE modeling, showing evidence that they capture information that the granularity of diagnosis codes alone can miss.

After creating the clinically based model, the project scientists expanded the feature set to include SDoH to gauge predictive improvement. These features included measures related to transportation, reliability, income, wealth, credit and debt.

To support assessing individual patient risk, as part of the approach, the project scientists took advantage of a new algorithm on the back-end of modeling to isolate specific risk factors for individual patients. **Whereas many machine learning classifier models focus on producing variables of importance for the *population*, this technology allows the insight into the biggest risk and anti-risk factors for *individuals* in an automated fashion.** Having the individual risk factors facilitates personalized intervention to help avert negative outcomes for patients at high-risk of a bleeding event.

RESULTS

The model type with the highest performance was the random forest, which had an AUC of 0.809 (95% CI = 0.796 - 0.821). Of the 34,000+ patients included in the model, the rate of occurrence of a major bleed event was 1.03%. Using a random forest model, the project scientists isolated segments of the population with more than a 6X higher risk rate of bleeding that the general population. Risk scores ranged from zero (lowest risk) to one (highest risk). Table 2 shows stratifications of bleed risk score, the corresponding actual bleed rate within the thresholds shown, and the positive (bleed) and negative (non-bleed) outcomes within each bracket.

Predicted Bleed Risk Score	Actual Bleed Rate	Positives (bleed events) in Threshold	Negatives (no bleed events) in Threshold
.8 to 1	6.9%	17	274
.6 to .8	4.31%	28	1063
.4 to .6	2.37%	41	3056
.2 to .4	.74%	16	3752
0 to .2	.12%	7	4289

Table 2: Stratification of predicted bleeding risk compared to the actual bleed rate and positive and negative outcomes

Globally, the top four types of features that were most influential were: 1) the procedures discovered through NLP; 2) the diagnoses discovered through NLP; 3) medications; and 4) patient vitals. For instance, the appearance of anti-hypertensive drugs within a patients' historic record was important to discriminating a bleed versus non-bleed outcome. Figure 1 shows a depiction of the percent occurrences of a bleed or no-bleed outcome as a function of the amount of antihypertensive medication prescribed. The figure highlights the area of increased risk. This is just one of many factors contributing to the risk score, and, in reality, many factors combine nonlinearly to ultimately produce the score, which is the power of machine learning modeling.

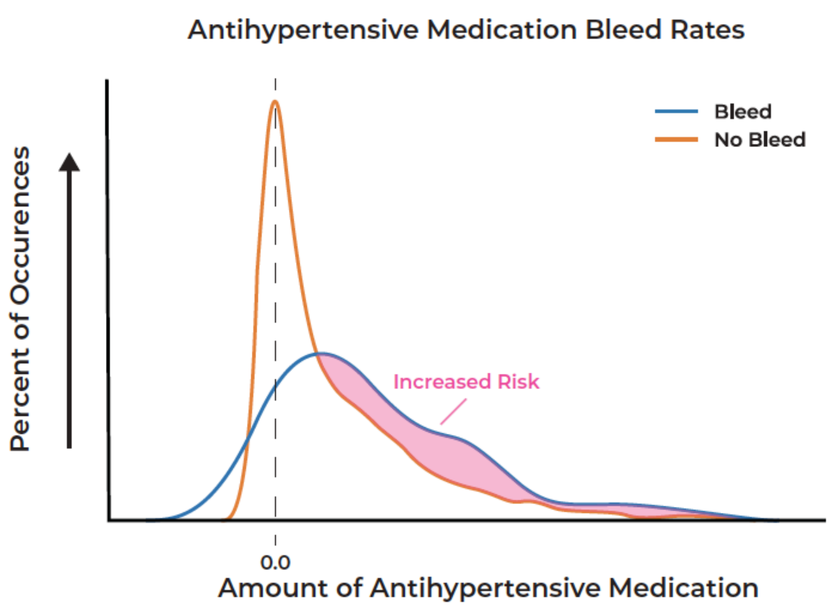

Figure 1: Example of a feature of importance contributing to differentiated risk in the population

The predictive algorithm included the capability to produce risk and anti-risk factors for any given patient. For example, Figure 2 shows factors impacting a patient with a high risk of a bleed event. The top three risk factors noted were the previous occurrence of a GI hemorrhage, digestive system issues and the total length of time between blood pressure recordings. The top three anti-risk factors were the patient's recorded minimum heart rate, the frequency of O2 saturation labs and the maximum heart rate. Being able to produce patient risk and anti-risk factors algorithmically can help mold a personalized preventative course of action.

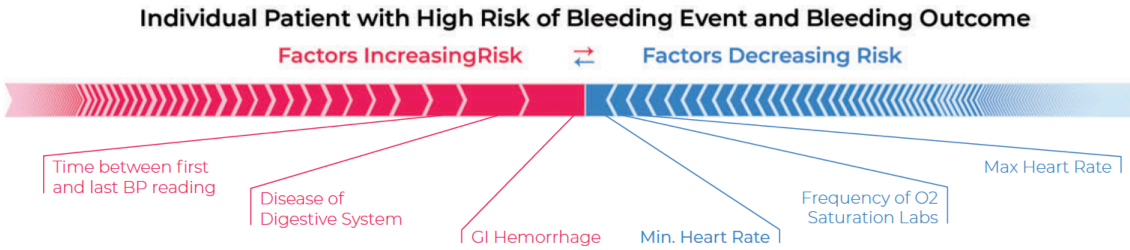

Figure 2: Example of individual patient risk and anti-risk factors produced through machine learning

In addition to using EHR data, the project team also used a pilot set of SDoH to test social determinant influence on predicting an adverse event. The data was at a zip+4 granularity, about half of a city block, and spanned five zip codes that overlapped a substantial portion of the patient base. The features included 27 factors ranging from bill-paying behavior to expected longevity (from an actuarial sense) to housing stability. **For the tested population, adding these SDoH factors improved predictive accuracy by 8%.**

DISCUSSION

The project team successfully satisfied the project goals with a machine learning model for predicting individual patient risk of bleeding when undergoing therapeutic treatment of anticoagulants. Within the project framework, the results provided a current snapshot of the state of risk for the patient population as well as the variables of importance influencing that risk, both at the global and patient level. The methodology created presents a framework to expand to other drug classes where risks for adverse drug events may exist.

Incorporating SDoH improved the predictive power of the model. Based on the success, continued work will integrate much fuller, broader sets of social determinants into the project efforts. Currently, the project team is developing indicators for influential factors like social isolation and food security.

Conversations with pharmacists and physicians throughout the model development helped dynamically improve the model applicability. As results became available, the project incorporated subject matter experts to get feedback and refine the model to assess it for prospective implementation. In one refinement, for instance, the model excluded patients treated with heparin from the model. In another refinement, the model was configured to produce risk rankings by molecule. Subject matter experts helped to present risk factors for individual patients in a way that helped discover whether or not an adverse event may be preventable. These subject matter expertise interactions are critical to make predictions relevant to operational practices.

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