Predicting Diabetic Readmission Rates: Moving Beyond HbA1c

Article ·	January 2017	
DOI: 10.190	80/CTBEB.2017.07.555715	
CITATION	S	READS
0		1,444
1 autho	p.	
1 autilo	1.	
	Damian Mingle	
T	SwitchPoint Ventures	
	12 PUBLICATIONS 4 CITATIONS	
	SEE PROFILE	
Some o	f the authors of this publication are also working on these related projects:	
Project	Applied Machine Learning for Diabetes Mellitus View project	
Project	Hepatitis Prognosis Using Machine Learning View project	

Predicting Diabetic Readmission Rates: Moving Beyond HbA1c

Damian Mingle WPC Healthcare, Nashville, USA

Corresponding author: Damian Mingle, Chief Data Scientist, WPC Healthcare, 1802 Williamson Court,

Brentwood, TN 37027, USA

Email: dmingle@wpchealthcare.com

Abstract

Hospital readmission is considered an effective measurement of care provided within healthcare. Being able to risk identify patients facing a high likelihood of unplanned hospital readmission in the next 30-days could allow for further investigation and possibly prevent the readmission. Current models, such as LACE, sacrifice accuracy in order to allow for end-users to have a straight forward and simple experience. This study acknowledges that while HbA1c is important, it may not be critical in predicting readmissions. It also investigates the hypothesis that using machine learning on a wide feature, making use of model diversity, and blending prediction will improve the accuracy of readmission risk predictions compared with existing techniques. A dataset originally containing 100,000 admissions and 56 features was used to evaluate the hypothesis. The results from the study are encouraging and can help healthcare providers improve inpatient diabetic care.

Keywords: Predictive modeling, 30-day readmission, hospital readmission, type 2 diabetes, diabetes mellitus

1. Introduction

A survey conducted by the Agency for Healthcare Research and Quality (AHRQ) found that in the year 2011 more than 3.3 million patients were readmitted in the United States within 30-days of being discharged. Over \$250 million was spent on treatment of readmitted diabetic patients in 2011 (Hines et al., 2014). Current practice to identify at-risk diabetic patients are subjective: a clinician will assess the patient and decide what the appropriate care plan is for that individual. Research has shown that these subjective methods for determining readmission are slightly better than random guessing (Allaudeen et al., 2011). However, there are tools to objectively score readmission risk, such as LACE (van Walraven et al., 2010). These objective tools are seen to be useful because end-users can make these calculations manually and offer improved accuracy over subjective techniques.

Machine learning models can be used to create objective models which then can be used to measure risk (Mingle, 2015). These models are more complex, but may be able to create more accurate risk predictions that should lead to improved diabetic patient outcomes.

This study investigates the hypothesis that advanced machine learning techniques can make use of a wide set of clinical features to improve diabetic readmission risk prediction over simpler objective measures like LACE while reducing hospital cost. An existing dataset and algorithms are used to test this hypothesis.

2. Background and Related Work

Many healthcare providers in the U.S. use LACE to identify at-risk patients. At its core LACE is a logistic regression model that makes use of a small set of features. LACE itself was derived from a set of 4812 patients, and validated on 1,000,000 patients using patient records from 2004 to 2008 (van Walraven et al., 2010).

In addition, numerous previous studies have analyzed the risk factors that predict readmission rates of diabetic patients. However, much of the research is focused on subsets of diabetic populations and solutions are derived from a smaller sample size than this study. In some cases, the results were based on demographic and socioeconomic factors that influence readmission rates (Jiang et al., 2003). In some cases, the models are unspecific in target and focus on general readmission for all-cause (Hosseinzadeh, 2013). Our study considers data that covers demographic, clinical procedure-related and diagnostic-related features, as well as medication information for all ages to predict readmissions for diabetic patients within a 30-day window. We provide comprehensive results on features and the model performance is superior to those currently in use. Our goal was not an analysis of readmission cost as this is well documented by other researchers.

In our judgment, our work is the first of its kind structuring a machine learning framework, which analyses all age groups specifically for the diabetic population and unplanned readmissions within a 30-day window. Our study uses a considerably larger dataset which is more balanced when comparing to previous works. Accordingly, our results appear to be more reflective of the problem of unplanned readmissions within 30-days of discharge for diabetics of all ages within the United States.

Other studies have not documented the typical performance metrics of machine learning classifiers. Our machine learning framework solves a general problem for diabetic patients who discharge from the hospital and as a single comprehensive solution can be easily implemented.

In addition to addressing the above gaps in the research, this work coves methods to identify potential modifiable risk factors leading to readmission rates. Machine learning identification of likelihood of readmission is the foundational step to understanding and developing protocols for better inpatient diabetes care. Our primary aim to have the results presented in this study be the baseline for any future work to compare.

3. Materials and Methods

3.1. Data Assembly

We performed a secondary analysis of a multicenter prospective cohort study conducted between 1999-2008. The study involved patients discharged to the community from 130 hospitals. The data is provided by the Center for Clinical and Translational Research, Virginia Commonwealth University and is a de-identified abstract of the Health Facts database (Cerner Corporation, Kansas City, MO). This data was used to test the hypotheses that

machine learning could predict the likelihood of readmission within the next 30-days for a diabetic patient. The data represents 10 years (1999-2008) of clinical care at 130 hospitals and integrated delivery networks through the United States: Midwest (18 hospitals), Northeast (58), South (28), and West (16). Most of the hospitals (78) have bed size between 100 and 499, 38 hospitals have bed size less than 100, and bed size of 14 hospitals is greater than 500. The dataset contains 50 features representing patient encounters: patient demographics, admission details, diagnoses and procedures (in ICD-9-CM format), laboratory data, and pharmacy data. Strack et al., 2014 originally pulled the dataset to meet the following criteria:

- (1) It is an inpatient encounter (a hospital admission).
- (2) It is a "diabetic" encounter; that is, one during which any kind of diabetes was entered into the system as a diagnosis.
- (3) The length of stay was at least 1 day and at most 14 days.
- (4) Laboratory tests were performed during the encounter.
- (5) Medications were administered during the encounter.

In total, there were 101,766 encounters available for analysis that satisfy these criteria. Each encounter was labelled with one of three classes ("<30", ">30", "NO") based on whether the patient was readmitted within 30 days ("<30"), readmitted in more than 30 days (">=30"), or did not have a recorded readmission ("NO"). Further information about the dataset can be found at http://www.cioslab.vcu.edu/.

Table 1: List of features and their descriptions in the initial dataset (data is available at VCU Data Mining and Biomedical Informatics (http://www.cioslab.vcu.edu/)).

Feature name	Description and values	% missing	
Race	Values: African American , Asian, Caucasian, Hispanic, and Other	2%	
Gender	Values: female, male, unknown/invalid	0%	
Age	Grouped in 10-year intervals: [0-10),[10-20),,[90,100)	0%	
Weight	Weight in pounds	97%	
Admission type	Integer corresponding to 9 distinct values	0%	
Discharge disposition	Integer identifier corresponding to 29 distinct values	0%	
Admission source	Integer identifier corresponding to 21 distinct values	0%	
Time in hospital	Integer number of days between admission and discharge	0%	
Payer code	Integer identifier corresponding to 23 distinct values	52%	
Medical specialty	Integer identifier of a specialty of the admitting physician, corresponding to 894 distinct values	53%	
Number of lab procedures	Number of lab tests performed during the encounter	0%	
Number of procedures			

Number of medications	Number of distinct generic names administered during the encounter	
Number of outpatient	Number of outpatient visits of the patient in the	0%
visits	year preceding the encounter	070
Number of emergency	Number of emergency visits of the patient in the	0%
visits	year preceding the encounter	070
	umber of inpatient Number of inpatient visits of the patient in the	
visits Number of inpatient visits of the patient visits year preceding the encounter		0%
Diagnosis 1	The primary diagnosis	0%
Diagnosis 2	Secondary diagnosis	0%
Diagnosis 3	Additional secondary diagnosis	1%
Number of diagnosis	Number of diagnoses entered to the system	0%
Glucose serum test	Indicates the range of the result or if the test was	0%
result	not taken	0/0
A1c test result	Indicates the range of the result or if the test was	0%
AIC lest result	not taken. Values: ">8" if the result was greater	0%
	than 8%, ">7" if the results was greater than 7%	
	but less than 8%, "normal" if the result was less	
Change of madications	than 7%, and empty if not measured.	00/
Change of medications	Indicates if there was a change in diabetic	0%
	medications (could be dosage or generic name).	
D: 1	Values: "change" and "no change"	00/
Diabetes medications	Indicates if there was any diabetic medication	0%
245 - 5	prescribed. Values: "yes" and "no".	00/
24 features for	For the generic names: metformin, repaglinide,	0%
medications	nateglinide, chlorpropamide, glimepiride,	
	acetohexamide, glipizide, glyburide, tolbutamide,	
	pioglitazone, rosiglitazone, acarbose, miglitol,	
	troglitazone, tolazamide, examide, sitagliptin,	
	insulin, glyburide-metformin, glipizide-	
	metformin, glimepiride-piglitazone, the feature	
	indicates whether the drug was prescribed or	
	there was a change in the dosage. Values: "up" if	
	the dosage was increased during the encounter,	
	"down" if the dosage was decreased, "steady" if	
	the dosage did not change, and "no' if the drug	
	was not prescribed.	
Readmitted within 30-	Days to inpatient readmission. Values: "1" if the	0%
days	patient was readmitted in less than 30 days and	
	"0" for no record of readmission.	

3.2. Data pre-processing

The original dataset was not ideally suited for a machine learning approach. In particular, we removed the "encounter ID" and "patient nbr" to avoid overfitting the model. Additionally, it would have been useful to have actual age and actual weight of the patient. While there were techniques used to work around these issues, none proved useful in testing.

One of the more significant changes was enriching the dataset with "diagnosis groups":

Table 2: Values for diagnosis in the final dataset. In the analysis, groups that covered less than 3.5% of encounters were grouped into the "other" category.

Group name	ICD-9 Codes	Descriptions
Circulatory	390-459,785	Diseases of the circulatory system
Respiratory	460-519,786	Diseases of the respiratory system
Digestive	520-579,787	Diseases of the digestive system
Diabetes	250.xx	Diabetes mellitus
Injury	800-999	Injury and poisoning
Musculoskeletal	710-739	Diseases of the musculoskeletal
		system and connective tissue
Genitourinary	580-629,788	Diseases of the genitourinary system
Neoplasms	140-239	Neoplasms
	780,781,784,790-799	Other symptoms, signs, and ill-defined conditions
	240-279, excluding 250	Endocrine, nutritional, and metabolic diseases and immunity disorders, without diabetes
	680-709,782	Diseases of the skin and subcutaneous tissue
	001-139	Infectious and parasitic diseases
Other	290-319	Mental disorders
	E-V	External causes of injury an supplemental classification
	280-289	Diseases of the blood and blood- forming organs
	320-359	Disease of the nervous system
	630-679	Complications of pregnancy,
		childbirth, and the puerperium
	360=389	Diseases of the sense organs
	740-759	Congenital anomalies

Finally, since this study is concerned with readmissions of patients with diabetes mellitus within a 30-day period from hospital discharge, we relabeled the target variable "1" for encounters that were marked "<30" and "0" otherwise.

3.3. Preliminary Analysis and the Final Dataset.

Our analysis demonstrates that there are unique diabetic readmission profiles within the following age groups:

Age Group	Description		
[0-30)	From 0 to 29 years old		
[30-70)	From 30 to 69 years old		
[70-100)	From 70 to 99 years old		

We are making the original dataset inclusive with data augmentation and enrichment available (https://www.researchgate.net/publication/312493339 Diabetic 30-Day Unplanned Readmission by Age Group). Each of the groups has its own set of unique characteristics that we utilized when building our machine learning framework.

3.4. Machine Learning Methods.

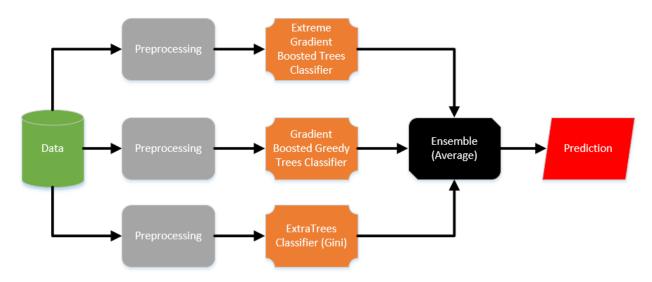
A. Classification

Identification of high-risk diabetic patients was posed as the problem of classifying whether a patient would be readmitted within 30-days of being discharged. Best practice is to make use of several machine learning algorithms, which is part of this study. Prior to training the classification algorithms, we randomly split our dataset into two distinct sets — the training and the test set. The training and test set consisted of 75% and 25% of the data. The parameters of each algorithm were chosen based on the classification performance evaluated by 10-fold cross-validation on the training set. The performance of all algorithms was evaluated on the test set.

Each age group was treated as a subset of the entire available diabetic population, however the final models for each age group are viewed as independent of each other.

The configuration for the [0-30) age group was uniquely created within the machine learning model framework to optimize understanding from the diabetic profile of this patient population.

Figure 1: Machine learning configuration for age group [0-30)



The data represented in the graph above is all the patient encounters that meet the single criteria of age, [00-30). The data is treated as three distinct datasets and preprocessing is completed with a

single model as the focus. As each model experiences each diabetic patient encounter, it will make a prediction that will be stored until an ensemble is created. The models include:

- (1) Extreme Gradient Boosted Trees we made use of ordinal encoding of categorical variables and missing value imputations.
- (2) Gradient Boosted Greedy Trees Classifier we implemented One-Hot Encoding, univariate credibility estimates with ElasticNet, category count, missing value imputations, search for differences, and search for ratios.
- (3) ExtraTrees Classifier (Gini) we utilized One-Hot Encoding, univariate credibility estimates with ElasticNet, missing value imputations, search for differences, and search for ratios.

The ensemble of all models for [0-30) was averaged using the following

$$A = \frac{1}{n} \times \sum_{i=1}^{n} x_i$$

where A equals average, n equals the number of models being averaged, and x_i equals the predicted probability of each patient encountered. Other important measures for this ensemble are:

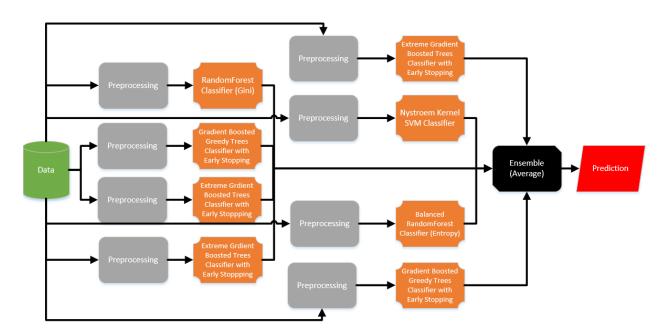
Table 3: Summary of measures for configuration for [0-30)

Measure	Value
F1 Score	0.4213
Sensitivity	0.4978
False Positive Rate	0.1081
Specificity	0.8919
Precision	0.3651
Negative Predictive Value	0.9343
Accuracy	0.8481
Matthews Correlation Coefficient	0.3416

Configuration for [30-70)

The machine learning framework produced a model for the [30-70) age group, which is the most complex of three age groups. There was a total of 8 different models averaged together to produce a final output.

Figure 2:Machine learning configuration for age group [30-70) with 10-fold cross-validation.



Although a few of the 8 models seem the same, there are unique preprocessing steps with each model, along with Grid Search, to create a different perspective of the same machine learning task.

- (1) RandomForest Classifier(Gini) we utilized ordinal encoding of categorical variables, a converter for text mining, auto-tuned word N-Gram text modeler using token occurrences, and missing values imputation.
- (2) Extreme Gradient Boosted Trees Classifier with Early Stopping we performed ordinal encoding of categorical variables, converter for text mining, auto-tuned word N-gram text modeler using token occurrences, missing values imputed.
- (3) Nystroem Kernel SVM Classifier we constructed One-Hot Encoding, converter for text mining, auto-tuned word N-gram text modeler using token occurrences, transform on the link function scale, standardized, missing value imputation, Ridit.
- (4) Balanced RandomForest Classifier (Entropy) we made use of ordinal encoding of categorical variables, category count, converter for text mining, auto-tuned word-ngram text modeler using token occurrences, missing values imputed.
- (5) Gradient Boosted Trees Classifier with Early Stopping We developed ordinal encoding of categorical variables, category count, converter for text mining, auto-tuned word-N-gram text modeler using token occurrences, missing values imputed.
- (6) Gradient Boosted Greedy Trees Classifier with Early Stopping We performed One-Hot Encoding | Univariate credibility estimates with ElasticNet | Category Count | Converter for Text Mining | Auto-Tuned Word N-Gram Text Modeler using token occurrences | Missing Values Imputed | Balanced ExtraTrees Classifier (Gini) | Search for differences | Search for ratios | Gradient Boosted Greedy Trees Classifier with Early Stopping

- (7) Extreme Gradient Boosted Trees Classifier with Early Stopping we used Ordinal encoding of categorical variables | Category Count | Converter for Text Mining | Auto-Tuned Word N-Gram Text Modeler using token occurrences | Missing Values Imputed | Balanced ExtraTrees Classifier (Gini) | Search for differences | eXtreme Gradient Boosted Trees Classifier with Early Stopping
- (8) Extreme Gradient Boosted Classifier with Early Stopping We used Ordinal encoding of categorical variables | Matrix of word-grams occurrences | Pairwise Cosine Similarity | Converter for Text Mining | Auto-Tuned Word N-Gram Text Modeler using token occurrences | Missing Values Imputed | eXtreme Gradient Boosted Trees Classifier with Early Stopping

The ensemble method to average the 8 predicted probabilities for each diabetic patient by encounter is the same as the [0-30) equation.

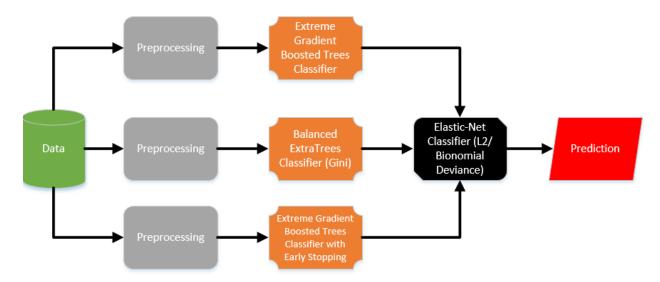
Below are other important measures for this age group:

Table 4: Summary of measures for configuration for [30-70) with 10-fold cross-validation.

Measure	Value
F1 Score	0.3001
Sensitivity	0.4363
False Positive Rate	0.1738
Specificity	0.8262
Precision	0.2288
Negative Predictive Value	0.9254
Accuracy	0.785
Matthews Correlation Coefficient	0.2012

Our machine learning framework produced another set of 3 models that captured well the underlying data pattern for age group [70-100). Although it is the same number of models as [00-30), the models themselves are different.

Figure 3: Machine learning configuration for age group [70-100)



Tree top models resulted in the best model performance of those we tested. The below models demonstrate the preprocessing that was completed before sending as input to the models themselves.

- (1) Balanced ExtraTrees Classifier (Gin) we used One-Hot Encoding | Univariate credibility estimates with ElasticNet | Converter for Text Mining | Auto-Tuned Word N-Gram Text Modeler using token occurrences | Missing Values Imputed | Balanced ExtraTrees Classifier (Gini) | Search for differences | Search for ratios | Balanced RandomForest Classifier (Gini)
- (2) Extreme Gradient Boosted Trees Classifier with Early Stopping we used ordinal encoding of categorical variables | Category Count | Converter for Text Mining | Auto-Tuned Word N-Gram Text Modeler using token occurrences | Missing Values Imputed | Balanced ExtraTrees Classifier (Gini) | Search for differences | eXtreme Gradient Boosted Trees Classifier with Early Stopping
- (3) Extreme Gradient Boosted Trees Classifier with Early Stopping we used ordinal encoding of categorical variables | Matrix of word-grams occurrences | Pairwise Cosine Similarity | Converter for Text Mining | Auto-Tuned Word N-Gram Text Modeler using token occurrences | Missing Values Imputed | eXtreme Gradient Boosted Trees Classifier with Early Stopping

Unique to this final model was the concept of meta-model approach - to use model outputs of 1,2, and 3 for the [70-100) age group as input into an Elastic-Net Classifier (L1/ Binomial Deviance). This type of classifier is based on block coordinate descent. Elastic Net is an extension of logistic regression where the optimizer makes an attempt to find a parsimonious model by having a preference for simpler models. In this context, simpler is defined as having coefficients with smaller absolute values as well as fewer non-zero coefficients. In practice, this helps the model deal with co-linear variables and can also produce models that are less prone

to overfitting and generalize better to new data. Elastic-Net is useful in machine learning problems where there are multiple features that are correlated with one another.

For completeness, we provide the additional important measures and their corresponding values to compare with the other final models produced for age groups [00-30), [30-70), and [70-100):

Table 5: Summary of measures for configuration for [30-70) with 10-fold cross-validation

Measure	Value
F1 Score	0.2694
Sensitivity	0.4902
False Positive Rate	0.2889
Specificity	0.7111
Precision	0.1857
Negative Predictive Value	0.9121
Accuracy	0.6849
Matthews Correlation Coefficient	0.1403

B. Feature Analysis

In our study we decided to augment and enrich the original features in an effort to maximize the signal provided in each age group. We implemented several engineered features that we either gained intuition about through the initial study of the data or through the domain expertise of clinicians. While this table does not represent all that can be done with this data, it does represent what we studied:

Table 6: List of engineered features and their descriptions in the construction of machine learning models (data is available at Research Gate (http://www.ResearchGate/doi.com)).

Feature name	Description and values
Add_outpatient_inpatient	Adding together the number of
	outpatient and inpatient values
Div_emergency_labeProcedures_medications	Dividing the number of emergency visits
	by the sum of lab procedures and
	medications
Diag_1_name	Short text descriptions for ICD-9 codes
	for primary diagnosis
G_mult_outpatient_inpatient	Multiply encounter values for
	"outpatient" and "inpatient"
G_labProcedures_medications	Concatenating the number of lab
	procedures with the number of
	medications
G_averageDiag	Arithmetic mean of numeric values:
	diag_1, diag_2, and diag_3. In the event

of an alpha-numeric diag code the	
remaining values will be averaged.	
Short text description for admit type.	
Binary values for 1 of 8 admit types.	
Concatenated values from "Time In	
Hospital" and "Medical Specialty"	
A row-wise count of the number of	
missing values for a specific encounter.	
Concatenated values from "A1Cresult"	
and "Medical Specialty"	
Concatenated values from "medical	
specialty" and "Discharge"	
Concatenated values from "Race" and	
"Discharge	
Concatenated values from "Discharge"	
and "Time In Hospital"	
Short text description of admission	
source	
Short text descriptions for ICD-9 codes	
for secondary diagnosis	
Short text descriptions for ICD-9 codes	
for additional secondary diagnosis	

Because various machine learning models induce learning from a variety of perspectives (information-based, similarity-based, probability-based, error-based), it was important to select features that provided the greatest context for each machine learning model. In our case, feature selection proved to be significant in improving model performance in all three age groups for diabetic patients. No age group had the exact same feature importance ascribed to the same top 5 features. As can be seen below in Tables 8-10, items in bold are unique within the top 5 ranked features across all models.

The final model for the age group [0-30) worked with over 74 features. We ranked the top 5 features for this model by informativeness how informative they are relative to the other features of that age group. (Mingle, 2017). The "Number of emergency" feature and the feature engineered by dividing the number of emergency visits by the sum of lab procedures plus medications were both unique among all three models:

Table 7: Ranked list of features for age group [00-30)

Rank_1	Rank_2	Rank_3	Rank_4	Rank_5
Number	Add	Diagnosis	Number Emergency	Divide Emergency by the
Inpatient	Outpatient	Code 1		sum of Lab Procedures
	and			and Medications

Inpatient		
values		
together		

In the case of the age group [30-70) final model, we worked with 79 features that shared the same features as the [70-100] age group

Table 8: Ranked list of features for age group [30-70)

Rank_1	Rank_2	Rank_3	Rank_4	Rank_5
Number	Add Outpatient and	Medical	Diagnos	Discharge Disposition
Inpatient	Inpatient values	Specialty	is Code	Description
	together	Concatenated	1	
		with Discharge		
		Code		

Like the age group [00-30), the age group [70-100) resulted in two unique features ranking in the top 5 out of 79 features. They were the concatenation of discharge disposition with time in hospital and concatenation of race with discharge disposition:

Table 9: Ranked list of features for age group [70-100)

Rank_1	Rank_2	Rank_3	Rank_4	Rank_5
Medical Specialty	Discharge	Race	Discharge	Number Inpatient
Concatenated	Concatenated	Concatenated	Disposition	
with Discharge	with Time in	with	Description	
Code	Hospital	Discharge		

It is significant that all models did not utilize "A1c" results from patients when making a predication for unplanned hospital readmissions. In our study we see that only very few clinicians perform the measurement of HbA1c (18.4%) in the inpatient setting. Many researchers suggest that further attention to the HbA1c by a clinician before a diabetic patient is discharged from the hospital may prove helpful in patient outcomes and lower cost of inpatient care (Strack et al., 2014). In our study, we aimed to develop learning models that could be predictive without the HbA1c measurement, the primary reason being clinician judgment and hospital protocols vary greatly.

3.5. Evaluation Method

Each algorithm was evaluated using a 10-fold stratified cross-validation. Cross-validation is an evaluation technique where the dataset is randomly but evenly distributed into a number of fold (this study, 10). The learning algorithm is trained on all but one of the folds

and tested on the held-out fold. This repeated for each possible holdout fold. Stratified cross-validation attempts to preserve the class distribution between folds so that each fold is representative of the date full dataset. The process of cross-validation is repeated ten times to ensure that particular random initialization does not bias the overall result.

All algorithms were evaluated using the area-under-the-curve (AUC), which is equivalent to the c-statistic in this binary classification scenario. The AUC is the probability that a randomly chosen positive instance (this study, "<30" represented as "1") ranks higher than a randomly chosen negative one (this study, "0"). An AUC of 0.5 or less indicates that the algorithm is not better than a random guess while an AUC of 1.0 indicates perfect classification. Previous research in readmission risk has achieved AUCs between 0.5 and 0.7.

AUC is a graphical plot that illustrates the performance of a binary classifier system as its discrimination threshold is varied. It is created by plotting the fraction of true positives out of the positives vs the fraction of false positives out of the negatives, at various threshold settings. TPR is also known as sensitivity, and FPR is one minus the specificity or true negative rate.

In all cases our machine learning models are compared to the LACE index AUC, calculated by comprising a threshold of each index value to the true positive and false positives achieved by that threshold.

3.6. LACE Index Scoring Tool for Risk Assessment of Hospital Readmission

LACE is seen as the current in-use solution for readmissions for the U.S. One considerable benefit to LACE is the interpretability of the index itself. While many hospitals use the index in a computer assisted way, manual calculation is certainly possible. Further work is required to identify additional factors that may increase the discrimination or accuracy of the index. LACE is known to have limitations in that it was derived over a small sample size which may prevent it from being useful in the hospitals population if they do not overlap.

There are four steps to calculating the LACE Score Risk of Readmission (van Walraven et al., 2010):

STEP 1: Length of stay (including day of admission and discharge) days

Length of stay (days)	Score
1	+1
2	+2
3	+3
4-6	+4
7-13	+5
14 or more	+7

STEP 2: Acuity of Admission

If you can answer "yes" to the question," Was the patient admitted to the hospital via the emergency department?" then you can add "3" to the LACE Score from step 1.

STEP 3: Comorbidities

The patient may have multiple comorbidities. If the total score in this section is between 0 and 3 then "3" should be added to the LACE Score. If the score is ≥ 4 than "5" is added to the LACE Score. Additional information about what is meant by these conditions is in Appendix A.

Condition	Score
Previous myocardial infarction	+1
Cerebrovascular disease	+1
Peripheral vascular disease	+1
Diabetes without complications	+1
Congestive heart failure	+2
Diabetes with end organ damage	+2
Chronic pulmonary disease	+2
Mild liver or renal disease	+2
Any tumor (including lymphoma or leukemia)	+2
Dementia	+3
Connective tissue disease	+3
AIDS	+4
Moderate or severe liver or renal disease	+4
Metastatic solid tumor	+6

STEP 4: Emergency Department Visits

Determine how many times the patient has visited an emergency department in the six months prior to admission (not including the emergency department visit immediately

preceding the current admission) and ad that figure to the LACE score. However, in cases where the visits are => 4 then add only "4" to the LACE score.

Once LACE steps 1 through 4 are complete, then total the score. If in total a patient receives a LACE Score of \geq 10 then the patient is labeled "high risk for readmission." LACE attempts to lessen the burden for clinicians by requiring only a very few number of features that can be found within a patient's record. The non-condition specific nature of LACE, as it relates to diabetes mellitus and its simple approach, renders the result slightly better than random.

Cost Analysis

It is well known that hospital readmissions are costly to the healthcare system. Research shows that the cost of readmission of diabetes mellitus and its complications is \$251 million for 23,700 total readmissions. Hence the cost per readmission is approximately equal to \$10,591 (Hines et al., 2014). In this secondary analysis the average length of stay for the diabetic patient encounter is 4.396 days, leading us to believe the cost for one-day admission is considered to be \$2,409.

This is of particular importance to develop costing models around the benefit of having a proper machine learning solution delivered to hospital clinicians in a low-tech way. By establishing a one-day review of a patient before actual discharge there could be risk-reward trade-off that would be appealing to many healthcare settings.

4. Results and Discussion

The results from performing 10-fold cross-validation are presented in Table 8:

Table 10: Comparison of model performance

Age Group	Model Description	AUC
[0-30)	Ensemble Average	0.79
[30-70)	Ensemble Average	0.70
[70-100)	Meta Model (Elastic Net)	0.65
All Age Groups	LACE	0.56

In conclusion, while providers of care may make the decision not to obtain a measurement of HbA1c for patients with diabetes mellitus during the stay at the hospital, there exist other useful predictors of readmission rates that may prove valuable in the development of strategies to reduce readmission rates and associated costs for the care of these individuals. Our machine learning approach yielded a 26% improvement using over 100,000 patient encounters from 130 U.S. hospitals over a 10-year period compared to LACE, which was derived from 4,800 patients over a 4-year period.

5. Conclusion and Future work

Our research suggests that applying a machine learning approach to a larger feature set as well as novel approaches to model diversity and model blending can improve on simpler readmission models such as LACE, potentially improving patient outcomes and lowering inpatient cost to hospitals. The highest performing models were those developed around age groups rather than a general "all" age group.

This study targets diabetic patients only; however, we believe this early work sets the stage for further research to improve the accuracy of readmission risk for other top health conditions like heart disease, Schizophrenia, COPD, etc. An improved dataset, one that includes other critical features such as age, weight, and lab values, could prove valuable and are worth further study. Additional discovery may exist in modeling by condition group name (circulatory, respiratory, diabetes) as a primary condition. Also, suggesting a "next step" in transitions of care (home health, SNF, rehab facility) for a patient's optimal outcome may prove useful within healthcare.

Conflict of Interests

The authors declare that they have no conflict of interests.

Acknowledgment

The authors thank Cerner Corp. and the VCU cent for Clinical and Translation Research for the data used in the study. The authors appreciate the information available through organizations such as American Diabetes Association, International Diabetes Federation, and the Juvenile Diabetes Research Foundation. The authors thank WPC Healthcare for supporting this study.

References

- 1. Allaudeen, N., Schnipper, J. L., Orav, E. J., Wachter, R. M., & Vidyarthi, A. R. (2011). Inability of providers to predict unplanned readmissions. *Journal of general internal medicine*, *26*(7), 771-776.
- 2. Blondel, M., Seki, K., & Uehara, K. (2013). Block coordinate descent algorithms for large-scale sparse multiclass classification. *Machine learning*, *93*(1), 31-52.
- 3. Britton, K. A., Aggarwal, V., Chen, A. Y., Alexander, K. P., Amsterdam, E., Fraulo, E., ... & Roe, M. T. (2011). No association between hemoglobin A1c and in-hospital mortality in patients with diabetes and acute myocardial infarction. *American heart journal*, *161*(4), 657-663.
- 4. Chen, T., & He, T. (2015). Higgs boson discovery with boosted trees. In *Cowan et al., editor, JMLR: Workshop and Conference Proceedings* (No. 42, pp. 69-80).
- 5. Forsythe, C. E. (2014). Predictive Risk Modelling for Hospital Readmissions.
- 6. Friedman, B., & Basu, J. (2004). The rate and cost of hospital readmissions for preventable conditions. *Medical Care Research and Review*, *61*(2), 225-240.
- 7. Friedman, J., Hastie, T., & Tibshirani, R. (2001). *The elements of statistical learning* (Vol. 1). Springer, Berlin: Springer series in statistics.

- 8. Geiss, L. S., Pan, L., Cadwell, B., Gregg, E. W., Benjamin, S. M., & Engelgau, M. M. (2006). Changes in incidence of diabetes in US adults, 1997–2003. *American journal of preventive medicine*, *30*(5), 371-377.
- 9. Geurts, P., Ernst, D., & Wehenkel, L. (2006). Extremely randomized trees. *Machine learning*, 63(1), 3-42.
- 10. Halkos, M. E., Puskas, J. D., Lattouf, O. M., Kilgo, P., Kerendi, F., Song, H. K., ... & Thourani, V. H. (2008). Elevated preoperative hemoglobin A1c level is predictive of adverse events after coronary artery bypass surgery. *The Journal of thoracic and cardiovascular surgery*, *136*(3), 631-640.
- 11. Hines, A. L., Barrett, M. L., Jiang, H. J., & Steiner, C. A. (2014). Conditions with the largest number of adult hospital readmissions by payer, 2011.
- 12. Hines, A. L., Barrett, M. L., Jiang, H. J., & Steiner, C. A. (2014). Conditions with the largest number of adult hospital readmissions by payer, 2011.
- 13. Hosseinzadeh, A., Izadi, M. T., Verma, A., Precup, D., & Buckeridge, D. L. (2013, June). Assessing the Predictability of Hospital Readmission Using Machine Learning. In *IAAI*.
- 14. Howell, S., Coory, M., Martin, J., & Duckett, S. (2009). Using routine inpatient data to identify patients at risk of hospital readmission. *BMC Health Services Research*, 9(1), 1.
- 15. Jiang, H. J., Stryer, D., Friedman, B., & Andrews, R. (2003). Multiple hospitalizations for patients with diabetes. *Diabetes care*, *26*(5), 1421-1426.
- 16. Kim, H., Ross, J. S., Melkus, G. D., Zhao, Z., & Boockvar, K. (2010). Scheduled and unscheduled hospital readmissions among diabetes patients. *The American journal of managed care*, *16*(10), 760.
- 17. Levetan, C. S., Passaro, M., Jablonski, K., Kass, M., & Ratner, R. E. (1998). Unrecognized diabetes among hospitalized patients. *Diabetes Care*, *21*(2), 246-249.
- 18. Lichman. M. (2013). UCI machine learning repository.
- 19. Mingle, D. (2015). A Discriminative feature space for detecting and recognizing Pathologies of the vertebral column. *International Journal of Biomedical Data Mining*, *04*(01). doi:10.4172/2090-4924.1000114
- 20. Mingle, D. (2017). Controlling Informative Features for Improved Accuracy and Faster Predictions in Omentum Cancer Models. *Curr Trends Biomedical Eng & Biosci*, 1(2). doi:CTBEB.MS.ID.555559
- 21. Pittas, A. G., Siegel, R. D., & Lau, J. (2004). Insulin therapy for critically ill hospitalized patients: a meta-analysis of randomized controlled trials. *Archives of internal medicine*, *164*(18), 2005-2011.
- 22. Shah, R. V., Altman, R. K., Park, M. Y., Zilinski, J., Leyton-Mange, J., Orencole, M., ... & Das, R. (2012). Usefulness of Hemoglobin A 1c to Predict Outcome After Cardiac Resynchronization Therapy in Patients With Diabetes Mellitus and Heart Failure. *The American journal of cardiology*, 110(5), 683-688.
- 23. Siegelaar, S. E., Hoekstra, J. B., & DeVries, J. H. (2011). Special considerations for the diabetic patient in the ICU; targets for treatment and risks of hypoglycaemia. *Best Practice & Research Clinical Endocrinology & Metabolism*, *25*(5), 825-834.

- 24. Silverstein, M. D., Qin, H., Mercer, S. Q., Fong, J., & Haydar, Z. (2008, October). Risk factors for 30-day hospital readmission in patients? 65 years of age. In *Baylor University Medical Center*. *Proceedings* (Vol. 21, No. 4, p. 363). Baylor University Medical Center.
- 25. Stolker, J. M., Spertus, J. A., McGuire, D. K., Lind, M., Tang, F., Jones, P. G., ... & Kosiborod, M. (2012). Relationship between glycosylated hemoglobin assessment and glucose therapy intensification in patients with diabetes hospitalized for acute myocardial infarction. *Diabetes Care*, *35*(5), 991-993.
- 26. Strack, B., DeShazo, J. P., Gennings, C., Olmo, J. L., Ventura, S., Cios, K. J., & Clore, J. N. (2014). Impact of HbA1c measurement on hospital readmission rates: analysis of 70,000 clinical database patient records. *BioMed research international*, 2014.
- 27. Umpierrez, G. E., Isaacs, S. D., Bazargan, N., You, X., Thaler, L. M., & Kitabchi, A. E. (2002). Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *The Journal of Clinical Endocrinology & Metabolism*, *87*(3), 978-982.
- 28. van Walraven, C., Dhalla, I. A., Bell, C., Etchells, E., Stiell, I. G., Zarnke, K., ... & Forster, A. J. (2010). Derivation and validation of an index to predict early death or unplanned readmission after discharge from hospital to the community. *Canadian Medical Association Journal*, 182(6), 551-557.
- 29. Vinik, R., & Clements, J. (2011). Management of the hyperglycemic inpatient: tips, tools, and protocols for the clinician. *Hospital Practice*, *39*(2), 40-46.
- 30. Williams, C., & Seeger, M. (2001). Using the Nyström method to speed up kernel machines. In *Proceedings of the 14th annual conference on neural information processing systems* (No. EPFL-CONF-161322, pp. 682-688).

Appendix A

Table 11: List of conditions, definitions, and notes for LACE comorbidities

Condition	Definition and/or notes
Previous myocardial infarction	Any previous definite or probable myocardial infarction
Cerebrovascular disease	Any previous stroke or transient ischemic attack (TIA)
Peripheral vascular disease	Intermittent claudication, previous surgery or stenting, gangrene or acute ischemia, untreated abdominal or thoracic aortic aneurysm
Diabetes without microvascular complications	No retinopathy, nephropathy or neuropathy
Congestive heart failure	Any patient with symptomatic CHF whose symptoms have responded to appropriate medications

Diabetes with end organ damage	Diabetes with retinopathy, nephropathy or neuropathy
Chronic pulmonary disease	??
Mild liver or renal disease	Cirrhosis but no portal hypertension (i.e., no varices, no ascites) OR chronic hepatitis Chronic Renal Disease
Any tumor (including	Solid tumors must have been treated within the last 5 years;
lymphoma or leukemia)	includes chronic lymphocytic leukemia (CLL) and polycythemia vera (PV)_
Dementia	Any cognitive deficit??
Connective tissue disease	Systemic lupus erythematosus (SLE), polymyositis, mixed
	connective tissue disease, moderate to severe rheumatoid arthritis, and polymyalgia rheumatica
AIDS	AIDS-defining opportunistic infection or CD4 < 200
Moderate or severe liver or	Cirrhosis with portal hypertension (e.g., ascites or variceal
renal disease	bleeding)
	End stage Renal Disease, Hemodialysis or Peritoneal Dialysis
Metastatic solid tumor	Any metastatic tumor