Using Machine Learning Techniques to Identify Key Risk Factors for Diabetes and Undiagnosed Diabetes

Avraham Adler

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Abstract

This paper reviews a wide selection of machine learning models built to predict both the presence of diabetes and the presence of undiagnosed diabetes using eight years of National Health and Nutrition Examination Survey (NHANES) data. Models are tuned and compared via their Brier Scores. The most relevant variables of the best performing models are then compared. A Support Vector Machine with a linear kernel performed best for predicting diabetes, returning a Brier score of 0.0654 and an AUROC of 0.9235 on the test set. An elastic net regression performed best for predicting undiagnosed diabetes with a Brier score of 0.0294 and an AUROC of 0.9439 on the test set. Similar features appear prominently in the models for both sets of models. Blood osmolality, family history, the prevalence of various compounds, and hypertension are key indicators for all diabetes risk. For undiagnosed diabetes in particular, there are ethnicity or genetic components which arise as strong correlates as well.

Keywords: Machine Learning; Classification; Diabetes; Unbalanced Data; Brier Score

Contents

Introduction 2

NHANES Data 3

Variable Description 4

Target Variables 4

Gender 6

Blood Sugar 6

Demographics 6

Income 6

Body measurements 7

Hypertension 7
Introduction

Diabetes is a chronic and lifelong disease with many health risks. According to the American Diabetes Association (ADA) [1], it:

...poses a significant financial burden to individuals and society. It is estimated that the annual cost of diagnosed diabetes in 2017 was $327 billion, including $237 billion in direct medical costs and $90 billion in reduced productivity.

There are a few types of diabetes of which the most common is type-2 diabetes [2]. This is when the human body develops a resistance to insulin over time.
leading to elevated blood sugars [3], eventually causing heart, organ, and neural complications—if not outright failure [4], [5]. In 2010, a study published in The Lancet estimated that screening can reduce diabetes-related complications, increase the number of quality-adjusted life-years, and prevent a significant number of simulated deaths, with early onset screening being more cost-effective than later [6].

The actual diagnosis of diabetes is relatively straightforward using either fasting plasma glucose (FPG) or hemoglobin A1C levels [7]. The FPG measures the blood sugar level at a point in time. The A1C levels reflect the average sugar in the blood over a three-month period [8].

Diabetes diagnosis using machine learning is not a new problem; there exists a body of research related to indicators of Type-2 diabetes. A proprietary implementation of decision trees on over 22,000 records from Iranian hospitals between 2009 and 2011 was developed by [9]. [10] built a gradient-boosted machine model on a proprietary dataset of 200,000 records of 13,000 Canadian patient data obtained from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN). [11] used classic machine learning techniques such as artificial neural networks, random forests, and K-means clustering to develop a predictive model relating various medical characteristics with diabetes using the formerly public-access Pima Indians dataset.

This paper will use data from the National Health and Nutrition Examination Survey (NHANES) to build a predictive model for diabetes. What this study attempts beyond previous analyses of NHANES data, such as [12] and [13], is to build a second model to specifically predict undiagnosed type-2 diabetes and compare the significant predictors between the two models. Logically, correlates of undiagnosed diabetes may prove especially valuable for early detection.

The remainder of this paper is organized as follows. First, the NHANES dataset will be described. Following will be a description of feature selection based on a concomitant literature review. Thereafter will be a description of the general data preparation with sections depicting an overview of each model. More detail about specific implementations may be found as comments in the code appendix. Afterwards, the models will be tested against the holdout set. The last section of the paper will be a reprise of any findings and suggestions for further research. The body of the paper will be followed by two appendices. The first will display statistical tables and figures of secondary interest, and the second will contain the R [14] code used to perform the analyses. The final element of the paper will be the reference list.

**NHANES Data**

Among the many projects of The Center for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS) is the National Health and Nutrition Examination Survey (NHANES). This is:
a program of studies designed to assess the health and nutritional sta-
tus of adults and children in the United States. The survey is unique
in that it combines interviews and physical examinations... The
NHANES interview includes demographic, socioeconomic, dietary,
and health-related questions. The examination component consists of
medical, dental, and physiological measurements, as well as laboratory
tests administered by highly trained medical personnel [15].

The study comprises hundreds of questions and tests from each of thousands
of respondents. Most of the questions are grouped in individual files and must
be cross-referenced with both the general demographic data as well as findings
from other tests. For example, the diabetes questionnaire is separate from the
lab results for A1C or glucose.

The benefit of using the NHANES data is that there are many features which may
be investigated for their relationship to diabetes. However, this very flexibility
has a drawback in the combinatorial nature of the possibilities. A reasonable
balance of records, fields, and constructed features will be necessary. To include
all available data would be both impractical and intractable. Earlier studies
[12], [13], [16] have identified variables related to diabetes including the expected
body mass index (BMI), age, family history, and hypertension. This study
will augment these prior-identified variables with other judgmentally selected
variables to provide a wider universe to analyze.

The NHANES data has been collected in two-year cycles since 1999. However,
there have been a number of changes in both the data collected and the variable
names. For this study the data collected will be that of the four cycles spanning
2011–2018. This is a reasonable balance between volume of data and selection of
features. While this prevents some possible potentially valuable metrics—such as
waist-to-hip ratio (WHR) or iron metabolism—it allows for 39,156 records in the
initial dataset, as opposed to many fewer if limited to 2017–2018. After cleaning
and munging the data, however, the final data set has only 10,329 records which
both fit the desired characteristics and have sufficient features. Much of this
reduction is due to the NHANES policy of only performing laboratory work on
a subset of all interviewed. Reviewing prior literature and the data, 32 features
were selected against which to train the models. Some of these will be expanded
into dummy variables for models which require them.

Variable Description

Target Variables

There are two simultaneous modeling exercises which will be performed for each
algorithm—the first will train a model to detect the presence of diabetes and
the second will train a model for the presence of undiagnosed diabetes. Every
model will be trained, validated, and tested identically but on slightly different
extracts of the data sets as explained below.
Diabetes

The first target is defined similar to [17]:

1. If a patient answered “yes” to the question “Have you ever been ever been told by a doctor or health professional that you have diabetes or sugar diabetes?”
2. If a patient’s lab work exceeds the accepted thresholds for diabetes as per [7]:
   1. Fasting plasma glucose (FPG) level of 126 mg/dL or greater
   2. Glycohemoglobin (A1C) level of 6.5% or greater

Using the results from the diabetes survey questions and lab work, each observation will be tagged as either “diabetic” or “non-diabetic.” Among the 10,329 records, there are 8,245 patients without diabetes and 2,084 with diabetes.

Undiagnosed Diabetes

The second target is defined for cases where the blood sugar or A1C threshold was breached but the answer to part 1. above was not “Yes.” This includes cases of “I don’t remember,” “Borderline,” or “No.” The object of this modeling exercise is to identify predictors or correlates for diabetics who have not as yet been diagnosed. The desire is to identify if there are any correlates which stand out from those already diagnosed and thus more likely to have sought treatment. Therefore, the training set for predicting undiagnosed diabetes will remove all observations with diagnosed diabetes. The hypothesis is leaving these observations in would train for what causes someone to get diagnosed and not for correlates for diabetes prior to any medical or dietary interventions. Therefore, the 1,486 patients with diagnosed diabetes will be removed from the data, leaving 598 positives against the 8,245 patients without diabetes at all. As the two data sets are no longer identical, model comparisons may only be made within each target and not between them.

PreDiabetes

The existing literature is conflicted when it comes to classification of prediabetes. These are people whose FPG level falls on the range between 100 mg/DL and 125 mg/DL, or whose A1C either falls between 5.7% and 6.4% or exhibited a 10% increase. The scheme in [17] only focuses on diabetes. In [12], two schemes are used: one where prediabetes is grouped with diabetes and one where it is not. A similar technique was used by [13] where the first scheme trained for true diabetics and the second stage removed those considered positive for the first stage and trained for prediabetes.\(^1\) For the purposes of this study, prediabetes

\(^1\)There appears to be a contradiction in [13] in that their first stage considers either a “yes” answer or a FPG of 126 mg/dL or greater to be diagnosed diabetes. They remove the diagnosed diabetes from the dataset, but say that those who answer “no” but have a FPG of 126+ mg/dL are undiagnosed and are maintained in the dataset. As these are people with actual diabetes and not prediabetes, consistency implies they too should have been removed.
will not be grouped with diabetes.

**Class Imbalance**

Both modeling exercises suffer from class imbalance. Where the target is all patients with diabetes, the negative-to-positive ratio is approximately 4:1. Where the target is undiagnosed diabetes, the negative-to-positive ratio is approximately 14:1. There are many ways to address class imbalance. These include artificial sampling methods, applying case weights, and implementing a cost function among many others. The interested reader is directed to chapter 16 of [18] and to [19] for a more complete approach. In this analysis, the effects of class imbalance will be ameliorated by the use of a strictly proper scoring metric, which will be discussed in the appropriate section.

**Gender**

As the focus of this investigation is Type-2 diabetes, the data will exclude pregnant women and people below the age of 20 to remove possible confusions with Type-1 or gestational diabetes [12]. Women whose pregnancy status is missing will be considered not pregnant.

**Blood Sugar**

Counter-intuitively, the values for FPG and A1C will not be included in the training data. These are not predictors of diabetes; rather, they define diabetes. This approach is consistent with [12] and [13], but is not consistent with [10] or [16] who use glycemic values in their models.

**Demographics**

Race and ethnicity have been shown to be related to diabetes [13]. This stands to reason for a disease with genetic components. Similarly, family history, where known, is a valuable indicator. This study will use the enhanced racial and ethnic profile implemented by NHANES in 2011 which separated Asians from non-Hispanic whites [20].

**Income**

The NHANES data measures income via categorical data. Moreover, there is overlap between some of the categories. While categories—even ordered—can be analyzed using modern techniques and software, it is easier to convert the data to numerical values. This also allows for easier imputation of the missing values. As the original data was converted into ranges to begin with, it will be reconverted to numeric using the midpoint of each range. For the categories representing the simple cutoff at $20,000 the lower category will use $15,000 and from the data for the second stage.
the higher category will use $60,000—the rounded median of the median US
incomes over the eight year experience period [21].

Body measurements
A suite of measurements will be included in the initial feature set. It is expected
that BMI will remain one of the significant factors. While the waist-to-hip
ratio (WHR) is also a known measurement of interest, NHANES only started
capturing hip circumference in the 2017–2018 cycle.

Hypertension
The presence of hypertension is defined as per the 2017 revision by the American
College of Cardiology and the American Heart Association [22]. This lowered
the thresholds for hypertension to 130 mmHg for the systolic pressure and 80
mmHg for the diastolic pressure. Also, anyone actively taking blood pressure
medication is considered to be be hypertensive even if their readings are below
the thresholds—similar to the definition of diabetes. When there is more than
one measurement in the data, the measurements will be averaged and that
average used for identification [22, Sec. 4.1].

Hyperlipidemia
Unlike with diabetes or hypertension, the targets for hyperlipidemia are not
fixed but depend on the presence of other positive of negative risk factors [23],
Table 4. Therefore, instead of a logical indicator for hyperlipidemia, individual
values for high-density lipoproteins (HDL)—the “good” cholesterol, low-density
lipoproteins (LDL), and triglycerides will be analyzed, although [9] did not
consider triglycerides.

Smoking
Some studies have shown a relationship between smoking and an increased
prevalence for type-2 diabetes [16]. The serum level of cotinine will be used as a
proxy for smoking and second-hand smoke exposure, as cotinine has the longer
half-life of the two primary metabolites of nicotine [24].

Blood Measurements
As diabetes is measured by the level of sugar in the blood, many of the variables
from the NHANES standard blood assay, such as blood sodium, potassium, and
calcium, will be investigated for their relationship with diabetes.
Model Preparation

Training and Testing

Approximately 25% of the data for each modeling exercise—all diabetes and undiagnosed diabetes—will be set aside as a testing set against which the “best-tuned” models will be compared. This will be done prior to any missing data imputation to prevent leakage of the test data into the training data. The split will attempt to maintain the same ratio of diabetics to non-diabetics in both training and testing sets.

Missing Data Imputation

Missing numeric variables will be imputed using a bagged tree method. This is where a tree-based model is built for each predictor based on the other predictors in the training set. This is a more powerful than a k-nearest-neighbors approach and also does not require centering and scaling of the data. This training-data based imputation model will be used to impute missing data in the test sets.

Categorical Variables

Some of the models do not handle categorical variables well. For these models, dummy variables will be created. Other models, specifically tree-based models, may do better when categorical variables are not converted to binary, as their splitting performs more efficiently when treated as a single variable [18], Ch 14, [25, Sec. 57]. The training and testing sets will have both formats. As these both represent the same underlying data, models which use either as input may be properly compared one with the other.

Tuning and Testing Metrics

The metric used to tune the hyperparameters—which will also be the primary metric used to compare across the models—is the Brier score [26]. The Brier score is a strictly proper scoring metric [27], [28], which means that it finds its optimal value solely at the true probabilities [29]. One of the benefits of using a strictly proper scoring metric for evaluation is that it is much less affected by imbalanced data [30] as it is a probabilistic measure and not a threshold measure [31]. For the binary classification problem, the Brier score simplifies to the mean squared error between the predicted probability and the actual event coded as 0 if it did not occur or 1 if it did [32].

Other metrics which will be calculated and displayed include the area under the ROC (AUROC), the area under the precision-recall curve (AUPRC) using the interpolation method of [33], accuracy, balanced accuracy, precision, recall, F score, and the Matthews correlation coefficient. Most of these metrics are well-known in machine learning but two deserve more explanation in light of the unbalanced nature of the classes.
**Balanced accuracy** is the arithmetic mean of sensitivity (recall) and specificity. Thus, it is the mean of the ratio of true positives to all positives and true negatives to all negatives. In cases where the decision boundary puts all predictions on the majority side there will either be no false positives or no false negatives, making one ratio will be 1 and the other 0. The balanced accuracy in this case will be 50%, notwithstanding the prevalence of the majority class [34].

The **Matthews correlation coefficient** (MCC) is a single metric which combines all four quadrants of the confusion matrix into a single score ranging between -1 and 1 [35]. First introduced by Matthews [36], it can also be viewed as a correlation measure between the the observations and the predictions. Mathematically:

$$
MCC = \frac{TP \cdot TN - FP \cdot FN}{\sqrt{(TP + FP) \cdot (TP + FN) \cdot (TN + FP) \cdot (TN + FN)}}
$$

where $TP$, $TN$, $FP$, and $FN$ are the true positive, true negative, false positive, and false negative counts respectively. In cases where the selection is completely random, such as all the observations being predicted as the same class, the convention is to set the denominator to 1 which lets the fraction equal 0 as well.

**Hyperparameter Tuning**

A five times repeated ten-fold cross-validation (CV) method will be used to tune the hyperparameters for each model. This is where the average of five different ten-fold CVs are used to select the tuning parameters. This is not the same as fifty-fold CV although fifty models are run. This allows for the reduced bias of ten fold CV and a further reduced variance around the metrics due to the repeats. As the Brier metric is optimized through minimization, reducing the process variance around metrics of order of 0.05 should help better identify optimal parameter sets. The **caret** package for R [37] will be used to train and test models for which it has interfaces. Otherwise, models will use their native packages.

**Feature Selection**

All models will start with the full feature set and most will undergo feature selection. Some models, such as the elastic net, have built-in feature selection. Those which do not may undergo a reverse recursive feature elimination where the model starts saturated and then algorithmically removes features. Some models do not have the implementation to undergo feature elimination; this will be noted in the model description sections.

**Predictive Models**

The models which will be investigated are:
• Regression
  – Logistic regression with reverse recursive feature elimination
  – Logistic regression with step-wise AIC feature elimination
  – Elastic Net regression
• Linear Discriminant Analysis (LDA)
  – LDA with reverse recursive feature elimination
• Support Vector Machines (SVM)
  – SVM with a linear kernel on all features
• Naive Bayes (NB)
  – NB with with reverse recursive feature elimination
• Neural Networks
  – Multilayer perceptron using Keras and Tensorflow
• Decision Trees
  – CART
  – C5.0
• Ensemble Methods
  – Random Forest using the ranger package
  – Extreme Gradient Boosting using XGBoost
  – Random Forest using LightGBM
  – Extreme Gradient Boosting using LightGBM

Regression
Logistic regression will be used with three kinds of feature reduction techniques. The first, and most general, is based on a simple wrapper loop which starts at the fully saturated model and removes predictors based on their (lack of) importance [37]. This is a technique useful for many model families.

The second feature selection technique used will be based on the model’s Akaike information criterion (AIC). This is a likelihood-based metric which reflects how close the model is to a theoretical “best” model, which may or may not be in the set of models reviewed [38] Ch. 6.4. The model starts fully saturated and then algorithmically removes or adds predictors based on how they reduce the AIC of the model, as for AIC, the lower the score, the better.

The third technique is to use an linear elastic net model. This is a blend between ridge and lasso regression. The lasso portion of the net can truly eliminate variables and the ridge portion of the net can drive variables close together or asymptotically close to zero [39], [40].

Linear Discriminant Analysis
Linear discriminant analysis (LDA) will be tried with recursive feature elimination. In the binary case, LDA works under the assumption that there is a linear boundary between two normally-distributed random variables [41] Ch. 4.3.
Support Vector Machines (SVM)

Support Vector Machines (SVM) theoretically operate by “boosting” the problem into a high-enough dimensionality that a separating hyperplane may be found. This plane, when projected back into the dimensionality of the feature space, may be highly non-linear. In practice, however, the kernel trick is used to calculate the needed metrics without having to calculate any of the n-dimensional distances [41] Ch. 12.3.

Unfortunately, the recursive feature elimination routines are not implemented for the SVM in the caret framework for R. While there has been research in implementing such processes for SVM in biogenetics [42], the model here will be trained on all the features. The linear kernel outperformed the radial basis function kernel in all attempts on this data set so the latter will not be shown.

Naïve Bayes

Generally, naïve Bayes (NB) does better than expected in classification problems but the expectation here is muted. The uncorrelated assumptions may be too big of a jump for this dataset; moreover, NB tends to perform poorly with unbalanced data due to a bias which reduces the weights for underrepresented classes [43]. The recursive elimination wrapper in the caret package will be used here for feature elimination. The implementation for NB uses the area under the ROC curve to decide variable importance.

Neural Networks

Neural networks are well-established predictive modeling methods which, through today’s computing power, have evolved into deep learning techniques. This analysis leverages the Keras [44] and Tensorflow [45] deep learning implementations. More advanced neural network techniques, such as convolutional or recurrent neural networks, are geared towards data with multiple dimensions such as the temporal or spatial. Here, the data is treated as singularly dimensional, so dense neural network connections will be used. Also, instead of implementing a specialized Brier score for the Keras/Tensorflow framework, the log-loss function—which is also a strictly proper scoring metric—will be used for tuning. The best models will still be compared via their Brier score performance on the testing set.

Decision Trees

The first decision tree will be a classification and regression tree (CART). One of the benefits of a single CART is that it can be plotted. It is unlikely to be the best model, but it will demonstrate the built-in feature selection by having fewer than 32 nodes.
As seen in the dendrograms above, The CART for predicting diabetes focuses on age, waist size, family history, blood sodium levels, LDL cholesterol, and blood osmolality as the more important variables. The CART for undiagnosed diabetes is overwhelmed by the imbalance and simply assigns everything to the larger class.

A more sophisticated classification tree-building technique is that of C5.0, an upgrade to Quinlan’s C4.5 [46]. Here, the method has the ability to winnow the features. It also can enhance the tree structure by allowing a rules-based model to be the node and not just a value. The best fitting C5.0 trees did not prune any features and used a rules-based method, so there is no dendrogram for either the diabetes model or the undiagnosed diabetes model.

**Random Forest**

Random forest is a decision tree based method which uses an ensemble of trees to reduce the propensity to overfit. It is similar to bagging in that the final results are based on a collection of bootstrapped trees fit to a random sampling of the data. It improves on bagging by using a random set of features to decide on each split [41] Ch 15, [47]. This section uses the random forest implementation found in the ranger [48] package for R. It also implements the feature elimination routine of [49]. This adds a regularization penalty to the splitting routine with the intention of preventing deeper trees which overfit the training data.

**Extreme Gradient Boosting**

Boosted trees are another decision tree based ensemble method. Unlike bagged trees and random forests, boosted trees work by repeatedly training a tree against the errors from a prior iteration [41] Ch. 10. The extreme gradient boosting
algorithm (XGB) is a particularly efficient implementation of boosted trees [50]. Two types of booster—the weak learners used in each iteration training against the errors—will be used: a linear-type learner akin to a penalized regression and a tree-type learner akin to a CART.

**LightGBM**

The LightGBM software package is an implementation of boosted decision trees with a number of design differences from the XGB implementation. For example, it grows the tree leaf-wise (vertically) over level-wise (horizontally). There are other design choices which make it especially suitable for large data [51]. A random forest ensemble, a boosted tree, and a piecewise linear gradient boosted tree will be built for each target. This last is similar to the LightGBM boosted tree and XGBoost, but instead of each node being a constant, each node is itself a linear model [52].

**Results**

To compare the results of a model’s ability to predict versus its ability to learn, and to observe if there is severe overfitting, it is customary to show the model’s training statistics and not only its testing statistics. These statistics may be found in the statistical appendix.
Predicting Diabetes

Performance

Table 1: Results for Predicting Diabetes

| Model                  | Brier | AUPRC | AUROC  | Acc  | BalAcc | MCC   | Precision | Recall | F     |
|------------------------|-------|-------|--------|------|--------|-------|-----------|--------|-------|
| SVM                    | 0.06540 | 0.85685 | 0.92347 | 0.91441 | 0.82233 | 0.71798 | 0.87879 | 0.66795 | 0.75900 |
| Logistic Red.          | 0.06596 | 0.85770 | 0.93005 | 0.91208 | 0.82876 | 0.71229 | 0.84670 | 0.68906 | 0.75979 |
| Logistic Step          | 0.06651 | 0.85574 | 0.93076 | 0.91441 | 0.83524 | 0.72090 | 0.84722 | 0.70250 | 0.76840 |
| Elastic Net            | 0.06652 | 0.85598 | 0.93079 | 0.91441 | 0.83452 | 0.72070 | 0.84884 | 0.70058 | 0.76761 |
| LGBM: Isl LinTree      | 0.07094 | 0.84365 | 0.93069 | 0.90511 | 0.80718 | 0.68507 | 0.85025 | 0.64209 | 0.73224 |
| LDA                    | 0.07436 | 0.84387 | 0.93050 | 0.89969 | 0.76578 | 0.66381 | 0.93377 | 0.54127 | 0.65530 |
| XGB: Tree              | 0.07536 | 0.82283 | 0.92700 | 0.89620 | 0.79372 | 0.65493 | 0.82025 | 0.62188 | 0.70742 |
| LGBM: Boost Tree       | 0.07832 | 0.81295 | 0.91952 | 0.89311 | 0.80253 | 0.64997 | 0.78291 | 0.65067 | 0.71069 |
| XGB: Linear            | 0.08034 | 0.80300 | 0.92116 | 0.88962 | 0.78816 | 0.63410 | 0.78922 | 0.61804 | 0.69322 |
| C5.0                   | 0.09144 | 0.78577 | 0.91470 | 0.87994 | 0.77492 | 0.60199 | 0.75545 | 0.58985 | 0.66809 |
| Rand F. Red.           | 0.09728 | 0.73473 | 0.89473 | 0.86897 | 0.71913 | 0.54909 | 0.80731 | 0.46641 | 0.59124 |
| LGBM: RandF            | 0.11348 | 0.64706 | 0.86470 | 0.84508 | 0.66345 | 0.44130 | 0.73913 | 0.35893 | 0.48320 |
| CART                   | 0.12011 | 0.57015 | 0.80614 | 0.84314 | 0.67658 | 0.44558 | 0.69463 | 0.39731 | 0.50549 |
| Naive Bayes Red.       | 0.13238 | 0.47178 | 0.79966 | 0.90713 | 0.61244 | 0.29253 | 0.54182 | 0.28539 | 0.37437 |
| RF/TP DenseNN          | 0.20964 | 0.20113 | 0.50984 | 0.79822 | 0.50800 | 0.00000 | NA       | NA     | NA     |

The table above compares the performance of the 15 trained models. All models, with the exception of the dense neural network, improved on the “no-information rate” (NIR) accuracy of 0.7982. The top four models performed very similarly in all metrics and outperformed the others in almost all metrics. It is interesting that the top performing models are all some form of linear model. The three logistic models are linear in sigmoid space and the SVM is linear in a hyperspace. Logistic models being superior to other models in the cases of class imbalance was also noted by Menardi & Torelli [19, p. 22]. Linear discriminant analysis did not perform as well. While it is linear in the sense that it searches for a linear boundary, it assumes that the variables being separated have Gaussian behavior which does seem to be the case here. The next best set of models are the various flavors of gradient boosted trees, random forests, and trailing them the non-ensemble based trees. The naïve Bayes classifier provides barely any gain over selecting the majority class 100% of the time and the dense neural network does not learn anything at all.

Important Variables

As the best performing model is a SVM, there is no actual model formula which can be displayed. In general, predictive models outside the realm of regressions often do not have direct formulaic representation. One measure used to compare variables in predictive models is called variable importance (VI). While the mathematics of calculating this variable differs for every model family, it allows for comparison across models—albeit imperfect [53]. Focusing on the four best-performing models helps reduce complexities. The VI of the three linear regression models is based on the absolute value of the t-statistic for the predictors, and for the SVM model it is based on the AUROC.
Table 2: Diabetes Prediction: Variable Importance

| SVM | Red. Logit | StepAIC Logit | ENet |
|-----|-----------|---------------|------|
| Age | Osmolality| Age           | Sodium |
| Waist| Sodium   | Waist         | Osmolality |
| Osmolality| UreaNitrogen| Osmolality | FamHist.Yes |
| Hypertension.Yes| FamHist.Yes| Hypertension.Yes | Ethnicity.White |
| BMI | Age       | BMI           | UreaNitrogen |
| Triglycerides| Ethnicity.White| Triglycerides | Hypertension.Yes |
| UreaNitrogen| Waist | UreaNitrogen | Albumin |
| HDL | Hypertension.Yes | HDL | Phosphorus |
| Weight| LDL | Weight | Calcium |
| ArmC | LegLen | ArmC | Gender.Female |
| Albumin| Phosphorus| Albumin | Ethnicity.Hispanic |
| Alk.Phosphate| Asp.Aminotransferase| Alk.Phosphate | Bilirubin |

In the table above, the variables are listed in order of their importance within each model. It is clear that the most important features correlated with diabetes include age, blood osmolality, blood sodium, waist size/BMI or both, family history, hypertension, and cholesterol. The second-best model is the logistic regression that underwent recursive feature reduction. Therefore, the important variables and the direction of their influence can be seen directly from the model formula.

Table 3: Reduced Logit Model

|                      | Estimate | Std. Error | z value | Pr(>|z|) |
|----------------------|----------|------------|---------|---------|
| (Intercept)          | -20.000  | 2.616      | -7.647  | 0.000   |
| Osmolality           | 1.549    | 0.052      | 29.504  | 0.000   |
| Sodium               | -2.934   | 0.100      | -29.394 | 0.000   |
| UreaNitrogen         | -0.521   | 0.020      | -26.541 | 0.000   |
| FamHist.Yes          | -1.081   | 0.132      | -8.166  | 0.000   |
| Age                  | 0.027    | 0.003      | 8.371   | 0.000   |
| Ethnicity.White      | -0.836   | 0.094      | -8.890  | 0.000   |
| Waist                | 0.025    | 0.003      | 9.400   | 0.000   |
| Hypertension.Yes     | 0.527    | 0.101      | 5.198   | 0.000   |
| LDL                  | -0.006   | 0.001      | -5.151  | 0.000   |
| LegLen               | -0.042   | 0.012      | -3.599  | 0.000   |
| Phosphorus           | 0.275    | 0.080      | 3.455   | 0.001   |
Increased blood osmolality and decreasing sodium and nitrogen levels have the highest z-values. Dr. Valentine Burroughs, Director of Endocrinology, Diabetes and Metabolism for Montefiore Nyack Hospital, explained that what is occurring is that the larger sugar molecules are lodging in the blood, pushing out the smaller sodium and nitrogen compounds, making the blood thicker as well [54].

Comparison with Prior Studies

The models reviewed here compare favorably with others built on NHANES data, although it must be recognized that different years may have been used for these studies. The study in [12] used NHANES data from 1999–2004. Their best performing model for detecting any diabetes, also a SVM, had an AUROC of 0.8347. As seen in Table 1, twelve of the models in this study exceeded that score.

The study in [13] did not use a holdout set to test the effectiveness of their model. Rather, they used downsampling to create a balanced sample from the data and split that 80/20 to validate their models. They then used ten-fold cross-validation of the entire dataset to evaluate the model’s performance, which returned an AUROC of 0.962. For comparison, the average AUROC over ten-fold cross-validation of the entire dataset for the best-performing SVM model was 0.921. This AUROC is based on the original distribution of observations in the training set, of course.

Predicting Undiagnosed Diabetes

Performance

| Model         | Brier   | AUROC  | AUROC | Acc  | BalAcc | MCC  | Precision | Recall | F     |
|---------------|---------|--------|--------|------|--------|------|-----------|--------|-------|
| Elastic Net   | 0.02937 | 0.74101| 0.94315| 0.96471| 0.80805| 0.69002| 0.81982   | 0.61074| 0.70080|
| Logistic Step | 0.02941 | 0.74548| 0.94332| 0.96471| 0.79429| 0.68579| 0.81786   | 0.59732| 0.67331|
| Logistic Red. | 0.02993 | 0.73691| 0.93733| 0.96109| 0.76735| 0.64839| 0.81818   | 0.54346| 0.65233|
| SVM           | 0.03027 | 0.73284| 0.93808| 0.96244| 0.80864| 0.67776| 0.77049   | 0.63087| 0.69373|
| LDA           | 0.03465 | 0.72782| 0.94107| 0.95430| 0.68909| 0.55712| 0.86364   | 0.38255| 0.53023|
| LGBM: Bst LinTree | 0.03508 | 0.67523| 0.92807| 0.95982| 0.73510| 0.61659| 0.84524   | 0.47651| 0.69944|
| XGB: Tree     | 0.03784 | 0.63129| 0.91049| 0.95339| 0.66861| 0.54772| 0.83884   | 0.38255| 0.52535|
| LGBM: Boost Tree | 0.03789 | 0.63029| 0.90994| 0.95249| 0.66812| 0.53870| 0.81429   | 0.38255| 0.52055|
| XGB: Linear   | 0.04184 | 0.57441| 0.89965| 0.94751| 0.64498| 0.46674| 0.80000   | 0.29530| 0.43137|
| C5.0          | 0.04922 | 0.52163| 0.88758| 0.94118| 0.56376| 0.34634| 1.00000   | 0.12752| 0.22019|
| Rand F. Red.  | 0.05013 | 0.43340| 0.87286| 0.93891| 0.54068| 0.29606| 1.00000   | 0.09396| 0.17178|
| LGBM: RandF   | 0.05473 | 0.38638| 0.84009| 0.93030| 0.52626| 0.16222| 0.52941   | 0.06040| 0.10843|
| Naive Bayes Red. | 0.05919 | 0.18254| 0.76421| 0.93258| 0.50000| 0.00000| NA        | NA     | NA     |
| CART          | 0.06288 | 0.06742| 0.50000| 0.93258| 0.50000| 0.00000| NA        | NA     | NA     |
| K/TF DenseNN  | 0.14567 | 0.07291| 0.49612| 0.93258| 0.50000| 0.00000| NA        | NA     | NA     |

Developing a successful model for undiagnosed diabetes proved more difficult. This is almost certainly due to the gross imbalance within the classes. Not
unexpectedly, the same group of four models proved themselves superior to the remainder.

**Important Variables**

Table 5: Undiagnosed Diabetes Prediction: Variable Importance

| ENet            | Red. Logit  | StepAIC Logit | SVM  |
|-----------------|-------------|---------------|------|
| Sodium          | Osmolality  | Waist         | Waist|
| Osmolality      | Sodium      | Age           | Age  |
| UreaNitrogen    | UreaNitrogen| Triglycerides | Triglycerides |
| Ethnicity.Asian | NA          | BMI           | BMI  |
| Gender.Female   | NA          | Osmolality    | Osmolality |
| Hypertension.Yes| NA          | Hypertension.Yes | Hypertension.Yes |
| FamHist.Yes     | NA          | HDL           | HDL  |
| Potassium       | NA          | ArmC          | ArmC |
| Protein         | NA          | Weight        | Weight |
| Calcium         | NA          | Alk.Phosphate | Alk.Phosphate |
| Ethnicity.White | NA          | UricAcid      | UricAcid |
| Albumin         | NA          | Asp.Aminotransferase | Asp.Aminotransferase |

In the table above, the variables are listed in order of their importance within each model. The variables are similar to those for the all-diabetes model but there is less emphasis on body measurements and more on gender and ethnic variables.

For undiagnosed diabetes, the best performing model is the elastic net with $\alpha = 1$ and $\lambda = 0$. In other words, a pure ridge regression. Therefore, there is no expectation that features will be completely eliminated; however, their coefficients may be driven to 0. While there is no simple formulaic representation of the elastic net, there is a plotting method which shows how the variables behave as the penalties change.
Variables above the 0-line, such as 7, 34, and 19, are positively correlated with an increased risk of undiagnosed diabetes. Variables below 0, such as 11, 4, and 29 are inversely correlated with that risk. The further to the left these variables “break away” from the horizontal axis, the more important they are at that level of regularization. As the graph traverses towards the right, more variables are allowed in the model. Therefore, the importance of any variable may change—or even switch direction—if other, possibly confounding, variables are now explicitly modeled.

The best-performing model did not eliminate any of the variables—it is the rightmost point in the above plot. However, we can still see that as the model developed, there are no variables which switch direction but there are those that change their slope and become more or less “important.” The twelve most important variables of the final model, six positively correlated and six negatively correlated, are shown in the table below.
Table 6: Key Variables in ENet for Undiagnosed Diabetes

| VarNum | Name               | Correlation |
|--------|--------------------|-------------|
| 7      | Osmolality         | +           |
| 34     | Ethnicity.Asian    | +           |
| 19     | Hypertension.Yes   | +           |
| 27     | FamHist.Yes        | +           |
| 14     | Protein            | +           |
| 12     | Bilirubin          | +           |
| 11     | Sodium             | -           |
| 4      | UreaNitrogen       | -           |
| 29     | Gender.Female      | -           |
| 10     | Potassium          | -           |
| 13     | Calcium            | -           |
| 32     | Ethnicity.White    | -           |

An interesting observation from the graph is the behavior of variable 19—hypertension. At first, it is a significant positive indicator of undiagnosed diabetes. However, as more variables enter the model, variable 34—Asian ethnicity—overtakes it in importance. With the elastic net, the magnitude of \( \lambda \) determines the intensity of the feature selection. The optimization procedure adjusts the lasso penalty \( \lambda \) and the ridge penalty \( \alpha \) to find the best model. Investigating the details of the optimization routine, hypertension enters the model early on, when \( \lambda \) is relatively large. It entered the model together with blood osmolality and only three other variables preceded them in importance: waist size, age, and triglycerides. Asian ethnicity enters the model after 15 variables, at which point hypertension’s coefficient is the second largest magnitude in absolute value after osmolality. However, at the optimal model with all variables included, hypertension’s magnitude is eclipsed by Asian ethnicity. Apparently, as other variables enter the model, they assume some of the predictive burden of hypertension and it, in and of itself, has less overall importance.

**Conclusions and Next Steps**

Using eight years of data from NHANES allows for the training of accurate predictive models of type-2 diabetes. The family of linear models performed better than those based on Gaussian assumptions or trees, likely due to the imbalance of the data. The models in this study compare very favorably to those of [12] and are similar in magnitude to those of [13] without having to change the empirical distribution of the data through artificial resampling. The correlates most relevant for predicting diabetes are age, weight, family history, various blood components, cholesterol, and hypertension.
Focusing on the prediction of undiagnosed type-2 diabetes, the correlates are similar, but give more weight to gender and ethnicity, such as Asian being positively correlated and non-Hispanic whites and females being negatively correlated. Remembering the dictum that “correlation is not causation,” and with the lessons of Simpson’s paradox in mind, it would be unwise to state that this is proof of a biological component in women or white males which is absent in Asians. The correlation may simply be who has better access to medical care, as there may be a preponderance of white males diagnosed with diabetes and thus absent from this data. However, the study does suggest that someone with a family history of type-2 diabetes, active hypertension, high blood osmolality, or low blood sodium would be wise to discuss investigating their blood sugar and A1C levels with their physician.

A remaining disappointment is that the multilayer perceptron did not learn anything in either modeling exercise. This may be due to the imbalance or another structural issue with the data. Future research in this topic should include testing the effects of artificial balancing on some of these models, although that appears to be of less appeal to the statistician than it is to the data scientist. Statisticians, such as [55] and [56], look at rebalancing the data with a jaundiced eye. This is in contrast to the approach of more the data science-aligned, such as [18], [57], and the writings on popular data science portals such as towardsdatascience.com [58] and KDnuggets [59]. These sources consider rebalancing the data to be an acceptable, if not first step, in addressing class imbalance.

Another area of future research would be to address the imbalance through Bayesian methods. By creating a hierarchical Bayesian model with reasonable priors on the probabilities of the positive and negative classes, a more accurate model using the full joint distribution may be obtained [60] Ch. 16.
Statistical Appendix

Training Statistics

Table 7: Training (Learning) Results for Predicting Diabetes

| Model                | Brier  | AUPRC  | AUROC  | Acc  | BalAcc | MCC   | Precision | Recall | F    |
|----------------------|--------|--------|--------|------|--------|-------|-----------|--------|------|
| LGBM: Boost Tree     | 0.04986| 0.92195| 0.9624 | 0.93443| 0.86116| 0.78724| 0.92099   | 0.73832| 0.81960|
| LGBM: LinTree        | 0.06267| 0.87886| 0.9425 | 0.91881| 0.82436| 0.73276| 0.90679   | 0.66003| 0.76798|
| Logistic Step        | 0.06912| 0.84601| 0.9265 | 0.90861| 0.81272| 0.69778| 0.86137   | 0.65195| 0.74217|
| SYM                  | 0.06977| 0.84140| 0.9169 | 0.90987| 0.79755| 0.70074| 0.91788   | 0.68871| 0.73111|
| Logistic Red.        | 0.07409| 0.84033| 0.9215 | 0.90874| 0.81219| 0.69835| 0.86497   | 0.65032| 0.74132|
| Elastic Net          | 0.07052| 0.84124| 0.9236 | 0.90799| 0.81061| 0.69563| 0.86336   | 0.64735| 0.73904|
| XGB: Tree            | 0.07890| 0.81057| 0.9169 | 0.89550| 0.74548| 0.65036| 0.83548   | 0.60103| 0.69388|
| LDA                  | 0.08004| 0.82589| 0.9218 | 0.90343| 0.75059| 0.64001| 0.92976   | 0.51110| 0.65086|
| XGB: Linear          | 0.08818| 0.77756| 0.90669| 0.88414| 0.76598| 0.69790| 0.80132   | 0.56789| 0.66381|
| C5.0                 | 0.09513| 0.76284| 0.90123| 0.88106| 0.76931| 0.60241| 0.77373   | 0.58196| 0.66346|
| LGBM: RandF          | 0.10271| 0.73592| 0.89718| 0.86498| 0.69455| 0.52465| 0.83968   | 0.48883| 0.54991|
| Rand F. Red.         | 0.10275| 0.69963| 0.87580| 0.86051| 0.69585| 0.50833| 0.79212   | 0.41982| 0.54742|
| CART                 | 0.11016| 0.51410| 0.77105| 0.82892| 0.64629| 0.38299| 0.65179   | 0.33859| 0.44421|
| Naive Bayes Red.     | 0.11465| 0.47006| 0.78878| 0.80870| 0.60551| 0.28736| 0.59647   | 0.26486| 0.35790|
| K/TF DenseNN         | 0.20566| 0.19687| 0.49518| 0.79824| 0.50000| 0.00000| NA        | 0.00000| NA    |

What should be noted here is the behavior of the LightGBM tree models. Their training errors are lower than the best-performing models on the test set, and much lower than their own performance on the test set. This is an example of overfitting. It may be that deliberately limiting the training performance of these models to prevent overfitting may return better results on the true holdout set.

Table 8: Training (Learning) Results for Predicting Undiagnosed Diabetes

| Model                | Brier  | AUPRC  | AUROC  | Acc  | BalAcc | MCC   | Precision | Recall | F    |
|----------------------|--------|--------|--------|------|--------|-------|-----------|--------|------|
| LGBM: Boost Tree     | 0.02283| 0.87434| 0.98174| 0.96970| 0.79466| 0.74128| 0.94604   | 0.58575| 0.72352|
| LGBM: Boost Tree     | 0.02142| 0.86998| 0.98144| 0.96502| 0.75714| 0.68233| 0.93927   | 0.51670| 0.66667|
| Logistic Step        | 0.02720| 0.78165| 0.95431| 0.96594| 0.79170| 0.69758| 0.86319   | 0.59020| 0.70106|
| Logistic Red.        | 0.02785| 0.77153| 0.94406| 0.96563| 0.78223| 0.69179| 0.88053   | 0.57056| 0.69747|
| SYM                  | 0.02538| 0.76747| 0.94770| 0.96520| 0.80307| 0.69610| 0.82897   | 0.61556| 0.70442|
| Elastic Net          | 0.02855| 0.76623| 0.94947| 0.96451| 0.78411| 0.68419| 0.85692   | 0.57546| 0.68593|
| LDA                  | 0.03421| 0.76204| 0.94670| 0.95607| 0.69410| 0.57774| 0.90824   | 0.39110| 0.53442|
| XGB: Tree            | 0.03857| 0.62558| 0.91674| 0.95176| 0.68798| 0.53266| 0.80617   | 0.38291| 0.51508|
| LGBM: RandF          | 0.04074| 0.66951| 0.92136| 0.94903| 0.61628| 0.45147| 0.92920   | 0.23385| 0.37867|
| XGB: Linear          | 0.04707| 0.48434| 0.87795| 0.94316| 0.60368| 0.39375| 0.81018   | 0.21105| 0.33233|
| C5.0                 | 0.05202| 0.45552| 0.85026| 0.93879| 0.55365| 0.29352| 0.90097   | 0.10820| 0.19494|
| Rand F. Red.         | 0.05310| 0.37470| 0.82704| 0.95581| 0.52504| 0.21186| 0.89826   | 0.05922| 0.11433|
| Naive Bayes Red.     | 0.06102| 0.13725| 0.71806| 0.93216| 0.49992| -0.00104| 0.00000   | 0.00000| NaN    |
| CART                 | 0.06236| 0.11744| 0.56752| 0.93216| 0.51664| 0.08201| 0.48522   | 0.03606| 0.12210|
| K/TF DenseNN         | 0.14586| 0.06831| 0.50273| 0.93231| 0.50000| 0.00000| NA        | 0.00000| NA    |
ROC and PR

While neither the area under the ROC curve (AUROC) nor the area under the PR curve (AUPRC) are proper scoring metrics, they are both widely used for classification models. The AUROC in particular has a weakness when the data is unbalanced. This weakness stems from the AUROC’s dependence on both the true positive and true negative rate. In cases where the true positive rate is poor, the metric may still return good values if dominated by the performance of the true negative class. The AUPRC is less prone to this distortion as both precision and recall have only true positive in their numerator. Therefore if the positive class is much smaller, poor performance will not be overwhelmed by excellent performance on the negative class [61]. Nevertheless, it is customary to return not only the single area under the curve values but also the ROC and PR curve plots.

Predicting Diabetes

SVM: ROC
AUC = 0.9234695

SVM: PRC
AUC = 0.8568497
Predicting Undiagnosed Diabetes

**ENet: ROC**

AUC = 0.9439348

**FPR**

Sensitivity

0.0 0.4 0.8

0.0 0.6

**ENET: PRC**

AUC = 0.747054

**Recall**

Precision

0.0 0.4 0.8

0.0 0.6

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