Machine Learning Approaches for Type 2 Diabetes Prediction and Care Management

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Abstract

Prediction of diabetes and its various complications has been studied in a number of settings, but a comprehensive overview of problem setting for diabetes prediction and care management has not been addressed in the literature. In this document we seek to remedy this omission in literature with an encompassing overview of diabetes complication prediction as well as situating this problem in the context of real world healthcare management. We illustrate various problems encountered in real world clinical scenarios via our own experience with building and deploying such models. In this manuscript we illustrate a Machine Learning (ML) framework for addressing the problem of predicting Type 2 Diabetes Mellitus (T2DM) together with a solution for risk stratification, intervention and management. These ML models align with how physicians think about disease management and mitigation, which comprises these four steps: Identify, Stratify, Engage, Measure.

Introduction

Diabetes Mellitus (DM) is a group of metabolic disorders mainly caused by abnormal insulin secretion and/or action, resulting in elevated blood glucose levels (hyperglycemia) and impaired metabolism of carbohydrates, fats and proteins [1]. DM affects more than 463 million adults worldwide, and its prevalence is projected grow to 578 million by 2030 and 700 million by 2045. Its rapid rise is thought to be the result of a complex interplay of socioeconomic, demographic, environmental and genetic factors, including rising levels of obesity, unhealthy diets and widespread physical inactivity [2].

Diabetes has serious implications on individuals and health systems. Diabetes can cause numerous debilitating health complications, such as coronary artery disease, peripheral arterial disease, stroke, diabetic neuropathy, nephropathy and retinopathy [1]. Globally, 11.3% of deaths are due to diabetes. An estimated USD 760 billion is spent on treating diabetes, with over 50% of that spent on treating its complications. By 2045, this cost is projected to rise to USD 845 billion [2].

The good news is that the risk of diabetes and its complications can be reduced with therapies and lifestyle interventions, especially if the risks are detected early. A healthy diet and physically active lifestyle are some of the most important preventive factors for T2DM. There are many opportunities for ML to aid in early detection and intervention of T2DM, including predicting the risk of pre-diabetes, diabetes, and diabetic complications, identifying risk factors for T2DM, and optimizing interventions for effective management and follow-up.

Literature Review

A large and diverse body of research exists on the applications of ML for diabetes. [1] provides a comprehensive review of the 103 articles published in the five years spanning July 2011 to July 2016, which can be classified in the following five broad categories: Biomarkers Identification and Prediction of DM (including Diagnostic and Predictive Markers, use of biomarkers for Prediction of DM), Diabetic Complications, Drugs and Therapies, Genetic Background and Environment and Health Care Management. For our purpose identification of diagnostic biomarkers, and diabetic complications are most relevant on the descriptive side. On the predictive side, the most relevant aspects of literature are (a) predicting T2DM and its complications, and (b) identify risk factors, especially controllable risk factors that can be used to design appropriate interventions.

Prediction of DM

The research on Prediction of DM constitutes diverse set of problem formulations, data sets, features and ML techniques applied to diabetes. The DM prediction problem can be framed in several ways. A summary of standard problem formulations is given in Table 1.

Problem Formulation	**Reference**
Predict blood glucose level or glycemic status	[3]–[6]
Predict risk of diabetes (regression producing a probability)	[7]
Predict current pre-diabetes and/or diabetes (classification)	[8]–[17]
Predict onset of diabetes in a future time window	[18]–[20]
Predict progression from normoglycemia to prediabetes, normoglycemia to T2DM, prediabetes to T2DM	[21]
Generate association rules that predict diabetes and reveal risk factors	[22]–[24]
Predict death in diabetic patients	[25]
Predict comorbidities of diabetes (not necessarily complications due to diabetes)	[26]

Table 1: Problem formulation for diabetes prediction

These studies explored different feature spaces, depending on the data sets available, intended use case, or research question. Thus, in most cases it is not possible to compare the predictive performance or the efficacy of the models across studies and settings. Many studies included the common risk factors for diabetes, including demographics (age and gender), family history of diabetes and BMI. In some cases (e.g. [10], [15]) lifestyle data were incorporated, such as smoking, alcohol consumption, coffee consumption, exercise, work stress and food preferences. Where medical records were available, diagnosis codes, prescriptions, labs (those most common being glucose and lipids) and vitals were commonly used. However, some studies (e.g. [9]) intentionally excluded labs or other medical data, as the intended use was to screen for diabetes in the least invasive way possible.

Some studies explored more interesting feature spaces. [8] constructed patient trajectories in terms of sequences of comorbidities (as indicated by diagnosis codes) to predict diabetes risk. [3] used salivary electrochemical parameters such as pH, redox potential, conductivity and concentration of sodium, potassium and calcium to predict fasting blood glucose. Anthropometric measures such as waist circumference, height, weight and BMI were used by several studies. In [5], the authors not only used the most extensive list of anthropometric measures, including circumferences at 8 body sites and 25 ratios of those, they also predicted fasting blood glucose using only these anthropometric measures. [26] used temporal patterns in EHR data, which are heterogeneous and irregularly sampled in the time domain.

Most diabetes prediction problems were framed as classification problems, with logistic regression, Naïve Bayes, support vector machines (SVMs), decision trees, random forests and artificial neural networks being the most commonly used ML techniques amongst these studies. While there is no clear winner, SVMs and tree-based models tend to outperform other models in side-by-side comparisons. It should however be noted that many of these studies do not employ gradient descent-based models for model building and comparison. Although the studies are not comparable, most models achieved AUC above 0.7, with a few models reaching 0.9. More complex models like ensembles of Bayesian models [21], Probabilistic Neural Networks [12] and LDA-MWSVM [17] did not necessarily outperform simpler models, and in some cases even underperformed them.

[7] developed models that produced consistent estimates of probability of diabetes using k nearest neighbors (kNN), bagged nearest neighbors (bNN), random forest (RF) regressors and random forest classifiers. The results demonstrated a trade-off where kNN and bNN produced more accurate probability estimates, while RF regressors and classifiers produced higher classification accuracy.

Prediction of Diabetic Complications

Several studies have been conducted on ML techniques to predict complications associated with diabetes, using different data sets and methods. A survey of literature for prediction of diabetic complications is given in Table 2.

Diabetes Complication	**Reference**
Cardiovascular Disease	[27], [28]
Coronary Heart Disease	[29]
Depression	[30]
Hypoglycemia	[27], [28], [31]–[33]
Ketoacidosis	[27], [28]
Liver Cancer	[34]
Microalbuminuria	[27], [28]
Nephropathy	[35], [36]
Neuropathy	[27], [28], [37]–[39]
Proteinuria	[27], [28]
Retinopathy	[27], [28], [40]–[49]
Maculopathy / macular edema	[50], [51]

Table 2: Diabetes complication prediction literature survey

The table also illustrates that diabetes complications are a large heterogeneous category covering different medical conditions, and thus a wide variety of data sets, features and ML techniques were used. Literature survey also revealed that there is a sparsity of studies within each diabetic complication. This makes cross-comparison rather difficult. The exception to sparsity is diabetic retinopathy which appears to be the most widely studied complication in the list.

Most of these studies used commonly available clinical data such as demographics, labs and diagnoses. Genetic data were combined with clinical data in the prediction of diabetic nephropathy in [35], [36]. Ewing tests were used in the prediction of cardiac autonomic neuropathy (CAN) [37], [38]. Self-monitored blood glucose (SMBG) and professional continuous glucose monitoring (PCGM) data were used to predict hypoglycemia [31]–[33]. Fundus images [42], [44]–[48], [50], [51] were most commonly used to predict diabetic retinopathy (including maculopathy), but clinical records [40], [43], tear fluid proteomics [41], [42] and images of the tongue [49] were also used.

Prediction of Non-Compliance

[52] developed ML models to predict intentional insulin omission in patients with T1DM, which happens often in adolescent females who omit or restrict insulin doses in order to lose weight.

ML Design

Work by Lagani et al. [27], [28] serves as a useful reference for the design of the ML system described in the current manuscript. The various aspects of their approach which are similar to the approach we take are as follows: (a) identifying the minimal feature set for each risk event (in their case, one of seven

diabetic complications), (b) developing models to predict future risk events, (c) applying the models to score a different population than the one the models were trained on, and (d) making the models easy to use via a web-based graphical user interface.

They developed a two-stage framework combining feature selection with regression to predict the risk (probability) for a specified diabetic complication (e.g., onset of microalbuminuria) at a future time (e.g. next 24 months). Four feature selection techniques – Survival Max-Min Parent Children, Lasso Cox Regression, Bayesian Variable Selection and Forward and Univariate Selection – were evaluated in combination with five regression techniques – Cox Regression, Ridge Cox Regression, Accelerated Failure Time, Random Survival Forest and Support Vector Machine Censored Regression. The best combination for each risk event (diabetic complication) was selected as the final model. Different models were found to be the best performer for each diabetic complication, and the number of features used ranged from 5 to 10. For example, the best model for predicting hypoglycemia was linear SVM with 5 features, while the best model for ketoacidosis was Ridge Cox Regression with 10 features.

Although the models were trained on data sets collected in the 1980's from American and Canadian patients, they were tested on contemporary European patients, demonstrating their transferability to new cohorts. Results were further improved by calibrating on the new data using Cox regression, while conserving the original predictive signatures.

Missing data is a practical issue when deploying risk prediction models on a new cohort of patients from a different EHR data source. Lagani et al. developed a missing information module that estimated the *distribution* of missing values based on other available features, using Bayesian Networks. The survival function for each risk event was then computed as the average of the original survival functions with the imputed values plugged in, weighted by the probabilities of the imputed values.

Once the models were trained, a web-based interface was developed where clinicians could select the type of risk, enter the minimal feature set for a patient (Figure 1), and get the predicted risks (probabilities) for that patient at different time horizons (Figure 2).

Although the framework was used to develop risk prediction models for diabetic complications, it can be generalized for other risk events such as the onset of pre-diabetes or diabetes. Other feature selection and regression techniques can also be used as candidate models, in addition to or in place of those used by Lagani et al.

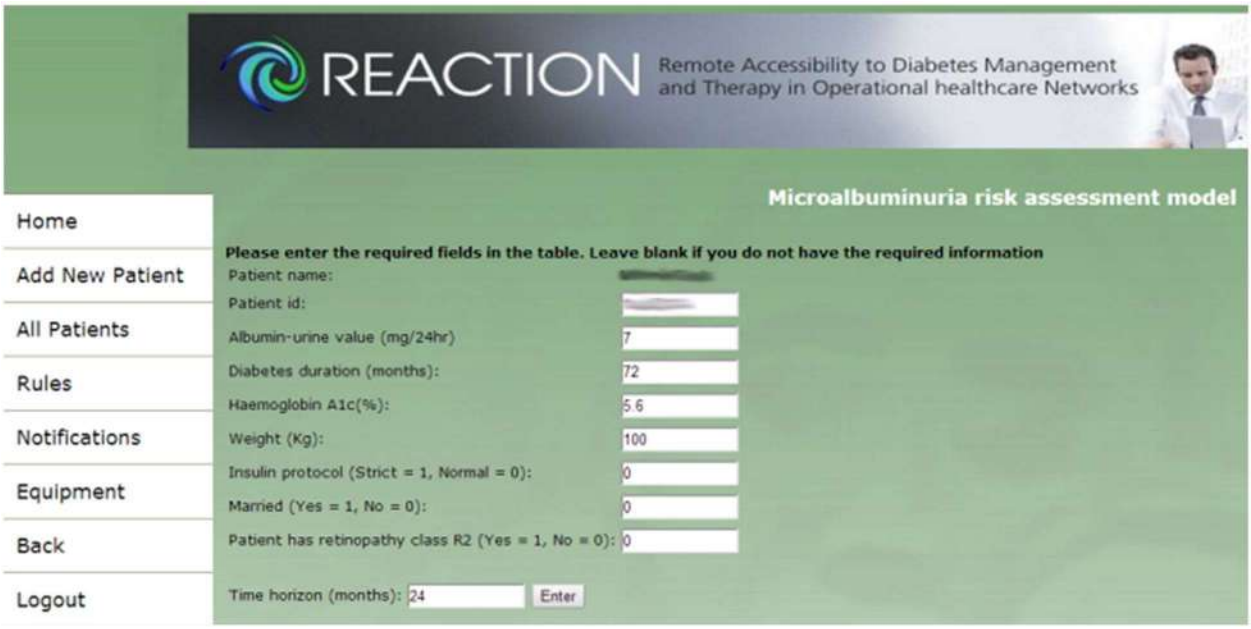


Figure 1. REACTION platform providing a microalbuminuria risk assessment tool based on 7 predictive features [28].

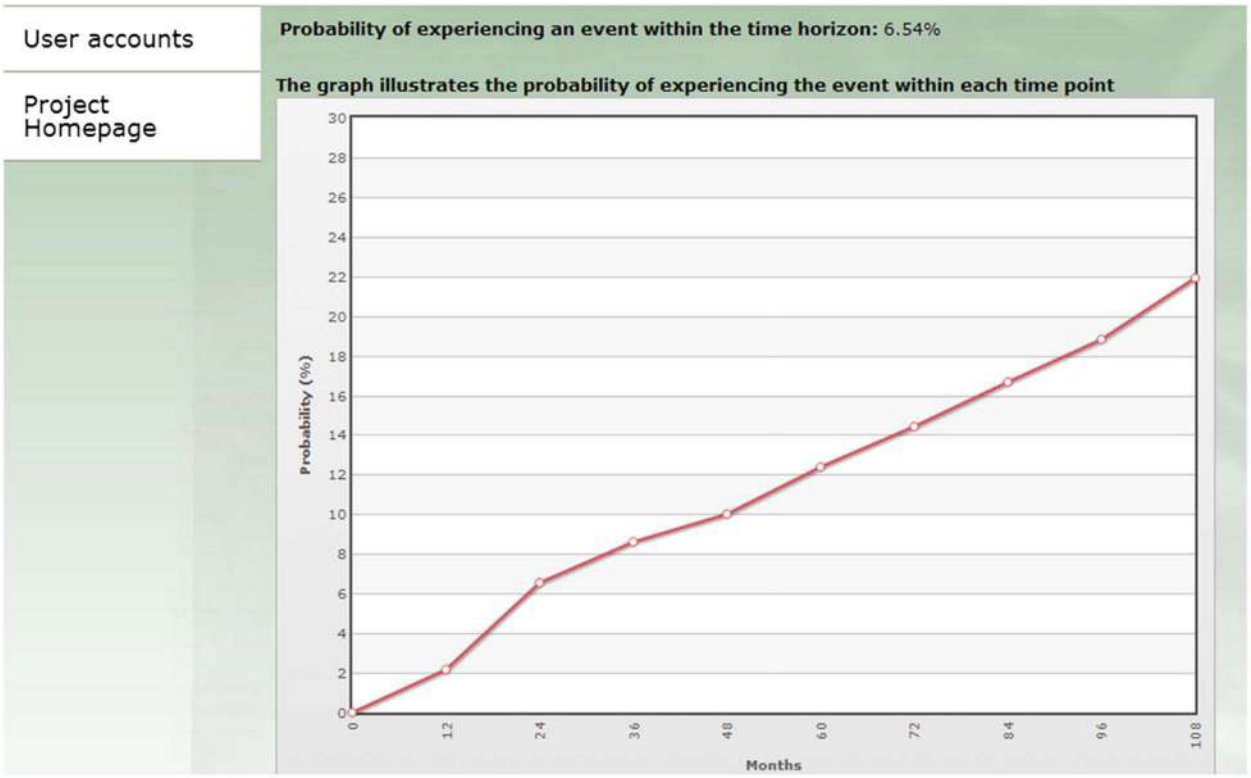


Figure 2. REACTION platform showing microalbuminuria risk assessment for a given individual [28].

DM ED Utilization

Studies on ED utilization are mainly focused on identifying factors affecting ED usage of all patients in general, DM patients or across specific subgroups such as the Ambulatory Care Sensitive Condition[1] (ACSC) population [53], Hispanic and African American with diabetes [54], patients with severely uncontrolled T2DM (A1C > 10%) [55] or patients with both schizophrenia and diabetes [56]. The main difference among these studies is often the cohort criteria and the features used which will be discussed later. We considered two main bodies of literature, one focusing on all-cause ED usage and the other on DM-related ED usage. Studies on all-cause ED usage centered around understanding patients with at least one occurrence of ED use [54], [57]–[59] or those who are frequent ED users [53], [60]–[68] while DM-related ED usage studies covered DM-related ED visits in general [55], [56], ED visits relating to hypoglycemia [69]–[73] or both hypoglycemia and hyperglycemia [74]. All of the studies were framed at the patient level except for 2, which carried out the prediction at the ED visit level [56], [70]. Binary classification was most commonly used, some studies used multi-class classification [54], [56], [59], [67] and only 1 study carried out regression on the number of visits to the ED in a 12-month period [75].

Studies predicting ED usage had differing definitions of their target variable. All-cause ED usage predictions were defined with respect to a specific time frame, with a period of 12 months being the most common while studies on DM-related ED usage typically did not have a time frame. Studies in all-cause ED usage typically involves predicting the patients with $\geq x$ ED visits in the next 12 months (x can range from 1 – 17, with 4 being the most common) [53], [57], [58], [60]–[66]. The cutoff x, was commonly determined by reviewing the distribution of ED visits and setting it based on the percentage of patients to target. Some studies created multiple models, one for each cutoff value and compared their performances before selecting a suitable cutoff [60], [62], [67]. Other studies stratified patients into 3 classes of low (0 visits), medium (1 visit) and high frequency of use ($\geq$ 2 visits) [54], [59], [67]. DM-related (in general (E11) or relating to hypoglycemia (E11.64) or hyperglycemia (E11.65, E11.0, E11.1)) ED usage problems that were framed at the visit level aimed at predicting which of the ED visits were DM related among all other visits [56], [70] with the use case of identifying the relevant predictors of ED utilization whereas those at the patient level predicted whether patients will have any DM-related ED visits in the future [55], [69], [71], [73], [74].

All-cause ED usage studies which specified their cohort criteria included patients with at least 1 ED visit and considered ED visits that were made on consecutive days as the same episode by counting them only once [53], [67]. DM-related ED visit studies excluded patients who were pregnant, newly diagnosed with T2DM, type 1 diabetic and had life expectancies of < 12 months [55] while studies on Hypoglycemia-related ED visits applied stricter cohort definitions. Patients without diabetes, having type 1 diabetes or gestational diabetes as well as those with deliberate overdose of diabetes medications were excluded [69], [70], [72]. ED visits having secondary discharge diagnoses for hypoglycemia were also excluded since such events might have occurred during the ED encounter itself and is not the primary reason of the encounter [69]. ED episodes that occurred within 3 days after a prior event were excluded to avoid double counting [70]. Lastly, patients on lifestyle modifications alone were excluded while those who received at least one oral hypoglycaemic agent or insulin therapy (for more than 7 days) 3 months prior to the visit were included to ensure that the event can be attributed to the use of anti-diabetic agents [70], [71].

[1] ACSC refer to chronic conditions which can be managed effectively through primary care services and includes high blood pressure, diabetes, angina, asthma, COPD, CHF, etc.

Demographics, socioeconomic indicators, comorbidity, healthcare utilization, diabetes condition and treatment factors were found to be predictors of ED utilization. In terms of demographics, females [54], [60], [63], [64], [70], [71], younger (18 – 44) and older age groups (> 65) [53], [54], [57], [59], [60], [64], [70], [74], Hispanic, Black and African American [54], [56], [63], [64] were found to have higher ED utilization. Patients with less education [54], [65], [66], lower income [57], [59], [61], [65], [74], who are single parents, single or divorced [65] and those who are insured, especially with Medicaid or Medicare [63], [64], [68] are more likely to visit the ED. Patients with a history of substance abuse, mental illness [53], [57], [62], [63], [66], [68] or greater number of comorbidities [53], [59], [61]–[63], [65]–[67] were associated with all-cause ED visits. In terms of utilization, most studies found that prior ED or hospital utilization were predictive of future ED visits [53], [60], [63], [66], [67], [69]. However, while all-cause ED visit studies reported that having a usual source of care [64]–[66], [68] and high utilization of other medical services (ambulatory care visits, specialist or physician visits) [63]–[66] increase the likelihood of ED usage, one DM-related ED visit study disagreed and suggested that having a usual source of care and more primary care visits reduces the probability of hyperglycemia or hypoglycemia ED use [74]. Most of the studies found that having a longer duration of diabetes [57], [73], diabetic complications [54], [59], [71] and higher HbA1C measurements [73] contributes to ED usage. In terms of treatment, patients who require insulin or oral hypoglycaemic medications were more likely to visit the ED [54], [57], [69], [71], [73]. Specific hypoglycaemic medications such as Sulfonylurea [72] were found to increase the likelihood of hypoglycemia related ED visits while [71] reported the following diabetes-related medications, metformin, thiazolidinedione and dipeptidyl peptidase-4 inhibitor have helped to decrease hypoglycemia related ED visits. [71] also found that non-diabetes-related medications like NSAIDs, benzodiazepines, fluoroquinolones, warfarin, and trimethoprim led to increased hypoglycemia related ED visits while having a systolic blood pressure between 90-150 mmHg and a heart rate of > 110 bpm served as protective factors. Lastly, although there was no consensus on the directionality of ED use in terms of the distance between the patient's home and hospital, it was considered to be a significant factor [60], [66], [67].

The most common ML technique to model ED utilization was Logistic Regression [53], [57]–[62], [65], [68], [74] while other studies used Decision Tree, Support Vector Machine, Random Forest, and Adaboost [58], [67], [69] for classification whereas the study which performed regression made use of Negative Binomial regression [75]. Of the few studies which specified their model performance, all-cause ED usage predictions had AUC values ranging from 0.786 - 0.960 whereas DM-related ED usage predictions had AUC values between 0.759 - 0.830.

An interesting finding mentioned in a few studies predicting frequent all-cause ED usage was that most frequent users in a given year will not remain as a frequent user in the following year: patients with ≥ 4 visits in a year have only 28 - 38% probability of being a frequent user in the next year [60], [64]. Of note, [64] also discussed predictions of chronic frequent users (frequent users over consecutive years), highest frequency users (> 20 visits in a year) and multiple ED users (treated at ≥ 5 EDs in a year) in the literature in addition to frequent ED users. Lastly, [72] shared how the use of multiple data sources, namely hospital episode statistics and patient administration system in addition to ambulance electronic records have helped to increase the number of ED episodes that were identified by 79.4%.

DM Visit Non-Compliance (All/DM patients)

Most of the literature surrounding visit compliance were around predictors of no-show, self-reported reasons of no-show (gathered through surveys and interviews with patients), effect of no-show on health outcomes which includes elevated A1C levels [76], [77] and significantly higher mean systolic blood pressure [78], and interventions to reduce no-show such as appointment reminders and patient education [79]. While the literature on visit compliance in general and those specific to DM have a lot in common, the main difference would be that studies specific to DM included DM related variables such as the time since the patient had DM or its complications, the patient's diabetes treatment type and intensity, and the patient's A1C measurements [80]–[82]. On the other hand, studies on visit compliance in general tend to include features such as the clinic type, medical specialty, healthcare provider as well as referral source [83]–[89]. No-show prediction was framed either at the appointment level or the patient level and binary classification was performed in all the studies (although it is possible to approach the problem using regression on the no-show rates).

Studies predicting no-show behavior had varied definitions of no-show. Those that predicted no-show at the appointment level considered no-show either as scheduled appointments that were missed (excluding any cancelled appointments) [84], [85], [88] or more commonly any missed appointments or late cancellations [90], [91]. Late cancellations were defined as cancellations that were made on the day of the appointment [92] or within 24 hours of the appointment time [86], [87]. On the other hand, in studies that modelled the problem at the patient level, greater variation was observed in how no-show was quantified. Definitions include the inability to visit a physician within 2 months after a missed appointment [80], missing more than one appointment within a pre-defined period, having no record of A1C measurements in the past 12-15 months [93] or whether a patient had missed more than 30% of appointments in a year [81]. Studies which specified their cohort criteria excluded patients that showed up without any prior appointment [89] as well as same-day appointments or appointments scheduled within 24/48 hours before the actual appointment [88], [91] since such appointments are most likely to be kept.

Determinants of no-show include patient demographics, comorbidities, treatment type, medication adherence, medical provider, patient appointment history and appointment characteristics. Characteristics of patients that are more likely to no-show include younger patients [84], [86], [87], [90], [91], [93], males [84], [90], smokers [93], patients with depressive symptoms [80]–[82] or psychiatric diagnoses [84], patients having greater co-payment for outpatient appointments [81] as well as those belonging to minority racial, ethnic, financial or insurance groups [81], [84], [93]. Those having higher comorbidity scores [81], those with family members or are married [84] or those who are not proficient in English [86] were less likely to no-show. Pharmacologic treatment of diabetes (as opposed to treatment only based on diet) and poor medication refill adherence [81] were associated with an increased risk of no-show while patients with intensive insulin therapy (> 2 insulin injections daily) and those who carry out daily self-monitoring of blood glucose were less likely to no-show. As for provider characteristics, patients with clinicians having greater expertise were less likely to no-show [84]. Multiple studies found that the risk of no-show increases with the duration between when the appointment was made and the actual appointment date [84], [86], [87], [90], [91], [94]. Also, if the patient has multiple appointments on the same day or if the appointment was a follow up, the probability of no-show is reduced [91]. Although no directional effects were mentioned for the following variables, they were found to be significant no-show predictors as well: amount of co-payment due [92], amount of diabetic medications a patient had left

[94], the number of previous no-shows [84], [86], [89], the number of previous appointments [84], whether the appointment was rescheduled [92], if past kept appointments were on the same day of week as the current appointment [94], the appointment length [92] as well as patient engagements such as the number of calls and whether a phone reminder was provided [92].

In terms of machine learning algorithms employed, Logistic Regression was most commonly used [80]–[82], [86], [88], [91], [92], [94]. Others such as [83] used Logistic Regression, Support Vector Machine and Recursive Partitioning, [85] used a hybrid probabilistic model based on Logistic Regression and Bayesian Inference while [89] used a Gradient Boosting Machine. Prediction performance of the models ranged from AUC values of 0.710 to as high as 0.958.

Although many factors were found to be significant in no-show prediction, factors complicating predictions include patients who switched clinic without prior notice and extreme weather or traffic conditions which prevented appointments from being kept [84], [94]. In addition, there could be underlying causes of no-show that might be hard to detect from the data, these are self-reported reasons from patients such as forgetting the appointment, competing priorities or conflicts, the patient's health status, appointment scheduling problems or financial problems [84]. [91] included a discussion on ways to encode the appointment attendance history of patients. While common representations include describing attendance history as a rate or using the outcome of the most recent appointment, the paper proposed representing patient histories using binary sequences (e.g. a sequence of 100 indicates that a patient had a total of 3 appointments, missed the most recent appointment and showed up for the previous 2) and computing the conditional probability of no-show on the next appointment given the sequence from past appointments based on the existing sequences observed in the data. The study capped the sequence length at 10 since the represented number of appointments for each sequence degraded once it exceeds 10. An advantage of this method would be that it is capable of adjusting for the recency of past attendance. For instance, the no-show probability calculated for a patient with sequence 0000011111 which attended the 5 most recent appointments was 0.197 while a patient with sequence 1111100000 which missed the 5 most recent appointments has a no-show probability of 0.547.

DM Medication Non-Adherence

Past studies on medication adherence were focused on the factors influencing medication adherence, patient-perceived barriers to adherence such as fear of side effects or embarrassment of insulin injection in public [95]–[98], outcomes of poor medication adherence which includes higher HbA1c levels, onset of diabetes complications, increased risk of morbidity and mortality and increased costs from outpatient care, emergency department visits and hospitalization [97]–[99]. Lastly, there were also discussions around strategies to improve adherence such as reducing medication complexity, providing better patient education, improving communication with health care providers, reminder systems and reducing out-of-pocket costs for patients [97]–[101]. All of the literature that were reviewed covered patients with T2DM that are on oral antihyperglycemic drugs (OAD) and/or insulin except for [102], [103] which excluded patients on insulin, [104], [105] which focused on patients newly initiating statins and [106] which includes patients who filled a prescription for a statin, antihypertensive, or oral antidiabetic. Medication adherence prediction was framed at the patient level and it could be either on a single medication or multiple medications. Medication adherence is made up of two separate components, compliance (the degree to which a patient takes medication as prescribed which includes filling prescriptions, taking medication on time or administering the right amount of injections) and persistence (the duration from initiation to

discontinuation of therapy) [95], [97], [107]. Binary classification or multi-class classification is typically performed for predictions on compliance while survival models were used for predicting persistence.

There exists a wide variety of compliance measures such as (1) biological measurements of therapeutic outcomes (blood glucose levels, urinary glucose levels or glycosylated hemoglobin concentration) which are more sensitive but can be invasive [97], (2) self-reported measures (generic for medication adherence in chronic conditions: Morisky Medication Adherence Scale (MMAS), Medication Adherence Rating Scale (MARS) or diabetes specific: Diabetes Self-Care Inventory (SCI), Summary of Diabetes Self-Care Activities (SDSCA)) which are often inaccurate and subjective [99], [108], (3) pill counts which requires patients to return their pill bottles and are time intensive [101], [107], [108], (4) Medication Event Monitoring System (MEWS) which does electronic monitoring of the time and frequency of bottle openings on pill bottles fitted with microprocessors [107], [108]. Despite being able to provide a precise measurement, MEWS is expensive and requires significant time and effort to implement. A widely used method that is objective and suitable for measuring adherence over large populations would be utilizing (5) pharmacy or medical records to compute measures such as the Medication Possession Ratio (MPR) or the Proportion of Days Covered (PDC) which are reported in terms of the percentage of time in which a patient has medication available [95], [97], [99], [107]–[109]. These measures do not directly measure medication consumption behavior but rather they measure medication collecting behavior. Lastly, (6) measures suitable for insulin adherence such as the Ecological Momentary Assessment (EMA) and computerized logbooks were also introduced in [108].

MPR and PDC are the most widely used measures in the domain and thus require further elaboration. It should be noted that there are some caveats when measuring non-compliance for insulin. This is so because the daily dosage is dependent on the blood glucose level. In contrast, OAD doses are fixed, so the PDC/MPR measures are more accurate. The key variables required for computing both measures are the drug name, the date filled and the number of days of supply. MPR refers to the total number of days' supply in a time period divided by the number of days in the time period and while PDC is similar to MPR, it considers the days that are covered (number of days patient has access to medication) instead of the total days supplied (number of days of medication the patient has on hand). Although a time frame of 1 year is typically used [102], [103], [110], [111], a much shorter time frame of 3 months was also observed [101] and patients are considered as adherent if their MPR or PDC $\geq x\%$ and non-adherent otherwise (x is most commonly fixed at 80% [97], [98], [101], [102], [110], [112], a cut-off at 90% was also used in [103]). While binary classification is conventionally used, [113] split PDC into 6 categories (PDC <20%, 20%≤PDC<40%, 40%≤PDC<60%, 60%≤PDC<80%, 80%≤PDC<100%, and PDC=100%) and carried out multi-class classification.

A disadvantage of MPR is that it tends to overestimate adherence in some cases, for example, patients who routinely refill their medications ahead of time will have overlapping days supplied, causing their MPR to exceed 100%. PDC on the other hand will shift the overlapping prescription to begin the day after the patient has completed his medication from the previous fill and this guarantees that PDC will not exceed 100%. In terms of handling multiple medications when using PDC, [111] first calculated the average PDC of each of the prescriptions within each oral hypoglycemic class and subsequently computed the group mean of the averages. Other approaches include [113] which required only 1 medication to be available to the patient for a day to be considered as covered while [114] defined a stricter approach in which all medications have to be available to be considered as covered. Unlike PDC, MPR is not as flexible and the only way to calculate MPR for multiple medications would be to take an average of the MPR of

each drug. Furthermore, skewed values will be produced upon computing the average should the MPR of any of the drugs exceed 100% [114]. Given the advantages that PDC has over MPR, it is becoming the preferred measure of compliance [114].

A methodology that has been gaining traction in medication adherence is Group-Based Trajectory Modelling (GBTM) which is able to capture the dynamic patterns of medication adherence over time as compared to a single static measure of adherence like PDC or MPR. For example, it is possible for patients with initial consistent use but poor subsequent use, poor initial use and consistent subsequent use or intermittent adherence throughout to share the same PDC value. GBTM provides an alternative method for representing long-term medication adherence that accounts for the fluid nature of adherence and it can be used to segment groups of patients with similar adherence patterns, analyze how adherence patterns change across time, predict adherence by fitting models with the trajectory groups as labels or even as variables in subsequent predictions (risk of hospitalization or ED visits) [106], [115]–[117].

First, monthly measures of adherence (e.g. PDC≥80%) for each patient over some pre-defined period, known as trajectories are calculated. The trajectories, along with a set of covariates are fitted into a mixture model which is used to identify subgroups of patients with similar trajectories, summarized by a set of polynomial functions of the covariates that were determined through maximum likelihood estimation using a quasi-Newton procedure [105], [118], [119]. GBTM then gives an approximate trajectory curve for each group, estimates the probability of group membership for each patient and assigns them to the group for which they have the highest membership probability. The most common adherence trajectory groups identified in the literature were (1) consistent, high adherence, (2) early and consistent adherence, (3) declining adherence, and (4) initial non-adherence followed by a slight increase in adherence [115]. The advantages of GBTM are being able to capture changes in adherence as well as customize interventions based on adherence trajectory memberships [115]. However, GBTM requires a longer observational period of at least 6-12 months, is more complicated to implement and measuring adherence of multiple medications is challenging and less researched upon [116].

Although most of the literature were focused on the compliance aspect of medication adherence, a few discussed persistence as well. Predictions on persistence could be framed as a binary classification problem on whether a patient persists with treatment after 1 year [107] or as a survival model to predict the time from initiation to discontinuation of medication [97], [112], where discontinuation is defined as a gap of more than x days without any available drug supply (x is commonly fixed between 30-90 days) [98]. In [112], the case in which a patient switched to a different medication within the same drug class was also considered as a discontinuation.

Studies which specified their cohort criteria included patients that are diagnosed with T2DM and having at least 1 prescription of an OAD for at least 6-12 months prior to the prediction [102], [103], [120]. Some studies excluded patients receiving insulin, pramlintide, or exenatide prescriptions alone or those only on dietary treatments [102], [103], [111] while [103], [111], [121] excluded patients with < 2 OAD fills which includes patients with primary non-adherence that never filled their initial prescription. Additionally, patients with type 1 diabetes [121], gestational diabetes [111], [116], a new T2DM diagnosis [120], a life expectancy of < 1 year [120], Metformin use due to polycystic ovary syndrome [111], [116] as well as evidence of prolonged institution (their medications will be administered by nurses or caregivers) [111], [116] were excluded. In some cases, patients receiving their medication by mail were also excluded since the distribution of PDC for such patients will be different from that of patients that collect their medication

from the pharmacy [105]. Lastly, [106], [117] adjusted the PDC/MPR denominator to account for the days in which the patient was hospitalized.

Predictors of medication compliance include patient demographics, socioeconomic indicators, comorbidity, healthcare utilization, diabetes condition, treatment burden, and treatment-related beliefs. Characteristics of patients with lower medication compliance include younger patients (25 - 44 years old) [99], [101], [105], [112], [115], [116], [121]–[123], non-whites [101], [115], [116], those who are obese [97], professionally active [99], [115], [121] or with lack of support from their family members [97], [99], [100], [121], as well as those with lower income [97], [101], [105], [121], lower educational level [105], [115] or those with depression, alcohol abuse or drug abuse [100], [110], [115], [120]. Patients with more comorbidities were less compliant [102], [112], [115], [123], while [113] found that those with a longer duration of hypertension or dyslipidemia were associated with higher medication compliance. Patients with a higher number of past hospitalizations or ED use [102], [116], fewer diabetes-related tests [116], those with longer duration of diabetes [100], [103], diabetes complications [112], [121] or hbA1c measurements of > 8% [113], [121] tend to be less compliant.

On the other hand, patients who experienced a recent critical medical event [115] or those with higher compliance to previous medications [104], [115] were more compliant. In terms of treatment burden, patients with higher co-pays [49, 60, 58, 45, 47, 62, 48, 65], greater complexity of medication regimen in terms of more daily number of tablets, number of co-medications, higher dosages (e.g. short-acting insulin requiring multiple injections vs. once daily injection of insulin glargine) [97]–[100], [103], [108], [109], [112], [115], [120], patients experiencing side effects from medications [96], [99], [101], [120], especially a history of a hypoglycemic event [98] were associated with lower medication compliance since patients might deliberately keep their blood glucose levels high to prevent further hypoglycemic events from occurring. Conversely, those using a mail order pharmacy as compared to retail pharmacy [99], [112], those using a pen device instead of conventional syringe and needles for insulin injections [95], [98], and those having prescription of medication for one other chronic condition [99] tend to have higher levels of compliance.

As for treatment-related beliefs, perceived treatment efficacy [96], [98]–[100], [120]–[122] as well as having trust and a good relationship with one's health care provider [97], [98], [100], [121] led to improved compliance. Although directional effects were not mentioned or there was no consensus on the directionality for the following variables, they were found to be significant predictors for medication compliance as well: gender, length of fill, number of available refills, number of phone calls made by patient, and having at least one missed appointment [95], [100], [101], [106], [112], [115], [124]. Lastly, while most of the studies were focused on the predictors of medication compliance, [112] stated that the factors resulting in better or worse persistence mirrored that of the factors identified by compliance.

The most common machine learning technique used to model medication compliance was Logistic Regression [103], [104], [112], [117], [120], [121], [123], [124] while other studies used ordinal regression [113] or boosting algorithms [106]. Studies modelling the time to discontinuation of the drug made use of Cox Proportional Hazard models [112]. Of the few studies which specified their model performance, medication compliance predictions had AUC values ranging from 0.695 – 0.881 when PDC was used.

Of note, [125] suggested a method to adjust for the number of days supplied for insulin to reflect a more accurate time between insulin prescriptions, thus addressing the challenges in using refill data to measure insulin use since patients are required to adaptively adjust the insulin dosage according to their blood glucose readings [110]. The authors found that patients receiving a 30 days' supply of insulin tend to fill their prescription after an average of 45 days from the previous fill. As such, they adjusted the days supplied by a factor of 45/30 to obtain a more appropriate measure of compliance.

Domain Problem Description

Motivation: Primary care providers (PCP) are burdened with numerous non-clinical tasks and laborious chronic disease management activities that do not require direct physician intervention. Patients with DM in particular require significant condition-specific management. To support PCPs, care managers manage the condition-specific care of patients with DM. Because of the large number of patients with DM, the patient panel size of each care manager is so large that they can only focus on the uncontrolled diabetic patients (those with A1C>7%), with the priority being to bring their diabetes back under control.

Scope: The goal of the intended use case solutions for T2DM is to use machine learning to assist care managers in caring for patients with DM. This will improve patient care, reduce the burden on PCPs, allow care managers to perform their job more efficiently, and improve overall staff satisfaction. With the assistance of ML predictions and optimizations, care managers may eventually expand their work into the proactive care of controlled or pre-diabetic patients (A1C <7%). Furthermore, we aim to improve quality of diabetes care for patients and reduce complications.

In particular, care managers want to identify risks of undesirable clinical events, such as disease progression, development of complications and non-compliance, in order to identify appropriate evidence-based interventions that may mitigate these risks. The needs of care managers may be classified as follows:

1. **Risk Stratification**: Who do I need to pay attention to?
2. **Care Plan Optimization**: What can I do for each patient?
3. **Outreach Optimization**: How do I get in touch with them?

Traditional care management is typically reactionary: cases appear in a work queue after a patient hits a threshold on utilization or clinical metrics or has an exacerbation event that necessitates high-touch engagement, such as an acute hospitalization or a recent avoidable ED encounter. Furthermore, recent hemoglobin A1c is the only quickly accessible measure care managers use to identify patients for interventions. This means that care managers have limited insight into patients without a recent A1c measurement (or who are just below the threshold of 7%) who may be nonetheless at risk for disease progression and complications.

Goals: The goal of predictive models for diabetes is to flag patients for engagement *before* a trigger event that requires a care manager's intervention occurs, allowing proactive correction. Additionally, predictions can help care managers prioritize activities by identifying *modifiable* risk factors (e.g., if the model identifies a patient to be at high risk due to smoking, smoking cessation could be recommended).

Machine Learning Problem Description

To address the needs of care managers, the following ML goals can be defined with respect to the three dimensions described above:

Need	Domain Goal	Modeling Goal
Risk Stratification	Enable care managers to identify the patients who are pre-diabetic and at risk of developing T2DM (A1C >=6.5%)	Predict risk and/or time to T2DM from pre-T2DM
	Enable care managers to identify the patients who are at risk of developing uncontrolled T2DM (A1C >=7%)	Predict risk and/or time to uncontrolled T2DM from T2DM
	Enable care managers to identify the patients who are at risk of developing microvascular complications associated with T2DM	Predict risk and/or time to event of developing microvascular complications associated with T2DM a. Neuropathy b. Nephropathy c. Retinopathy
	Enable care managers to identify the DM patients who are at risk of utilizing the ED for any reason	Predict all-cause ED utilization among DM patients
	Enable care managers to identify the patients who are not likely to show up for their scheduled appointments	Predict visit non-compliance (all patients)
	Enable care managers to identify the DM patients who are not likely to show up for their scheduled appointments	Predict visit non-compliance (DM patients)
	Enable care managers to identify the patients who are at risk of being non-adherent to medications	Predict medication non-adherence
Care Plan Optimization	Enable care managers to see the risk factors and the strength of their association with a predicted risk; show risk factors and actions in a ranked order based on strength of association with a predicted risk	Measure and rank features associated with each of the predicted risks (above), globally
	Enable care managers to see modifiable factors and the strength of their association with a predicted risk	Measure and rank features representing *modifiable risk factors* associated with each of the predicted risks (above), *per patient*
Outreach Optimization	Enable care managers to identify the optimal time of day to engage with patients via telephone visits, and whether patient reads email	Predict probability of response to a contact event, across different channels

Table 1. Care Manager optimization goals mapped to machine learning prediction problems

Machine Learning Design Constraints

The machine learning solution has the following design constraints for the use cases that we seek to address in this manuscript:

1. **Training and scoring on disparate populations**: The trained machine learning models will need to be deployed in an environment where the underlying population may be different from what is encountered in the training setting. Training, tuning and evaluation will be done centrally in a pre-deployment environment using a data set and population to be selected, but deployment and scoring will be done in a new environment on an unseen data set. It is therefore important to clearly state the assumptions about the underlying population that may affect scoring outcomes, characterize the cohorts on which the model was trained on, and measure model performance and biases on different cohorts.
2. **Minimal, readily available feature set with clear definitions (Bring Your Own Features)**: In the target deployment scenario, the deployment environment will compute the features required for the models to score the patients. Model tuning should be optimized to select the *minimal* set of features (say < 15) that give reasonable model performance, so as not to burden the end user with many features to compute and manage. Feature selection will be a critical part of the model training process. The selected features should be *easy* to compute based on *readily available* EHR data that all providers will have. The end user should be provided documentation on the required features with simple, unambiguous definitions so that the end user can compute the features to use the models.
3. **Modifiable vs unmodifiable risk factors**: Features used need to be clearly classified as modifiable (e.g., smoking) vs unmodifiable (e.g., gender). This distinction is important in the generation of interventions that can help to reduce risk. However, it is important to note that since we are not dealing with causal models, taking an action on a modifiable feature will not necessarily have an impact on the patient's risk. At best the modifiable factors can be used to inform the generation of risk for risk reduction. Additionally, we note that many of these types of features that are salient to this problem space (smoking, insurance, etc.) may be encoded differently across populations or health systems.
4. how do we make use of these features when the encoding of them differs across systems?
5. **Robust to missing features**: The trained models must be robust in the face of missing features. Not all required features may be available at different sites. The models should still be able to score the provided instances (albeit at a lower level of model performance) if some features are missing. The robustness of models to missing features should also be measured.
6. **Easily packaged and deployable in any environment**: Models should be able to be packaged and easily deployed in any environment, which could be as simple as a single virtual machine. There should not be any specialized technical requirements such as GPUs or clusters. There are a number of technical solutions that can be explored to enable easy and flexible deployment, such as packaging the models in containers with REST API interfaces exposed. Additionally, there is a need to understand the actions that end users are most likely to take upon these model outputs. This is important as there is the possibility for unfairness or bias (explicit or implicit) to creep in during delivery. Consequently, there is need to put guardrails upon use of these models before we package and deploy them.

7. **Explainable globally and locally**: The models and their underlying features should be easily explained at both the global and local levels, due to the business need for identifying modifiable risk factors.

The machine leaning models that we consider can be organized into the model prediction flow depicted in Figure 3.

1. Predict risk of pre-diabetes for normal (healthy) patients [10], [13], [15], [21].
2. Predict risk of diabetes [4], [7]–[13], [16]–[20], [22] for (a) normal [21], [24] (b) pre-diabetes [21] patients.
3. Predict risk of uncontrolled diabetes for (a) normal, (b) pre-diabetes and (c) diabetes patients.
4. Predict risk of specific diabetic complications for (a) diabetes and (b) uncontrolled diabetes patients.

We define the patient risk as follows:

a. *The likelihood of the risk event occurring in a specified time frame* [18]–[20], [27], [28], e.g., "30% probability of diabetic retinopathy in 6 months, 50% in 12 months". This can be predicted with probability scores from classification models. As an extension, this can also be presented as the likelihood of *early vs. late onset* of the risk event, where the relevant time frames (e.g., 6 vs. 12 months) can be defined for early or late onset.
b. *The time to the risk event occurring*, e.g., "onset of diabetic retinopathy is likely to happen in 6 months". This can be predicted using regression models that estimate the time of onset for the risk event.

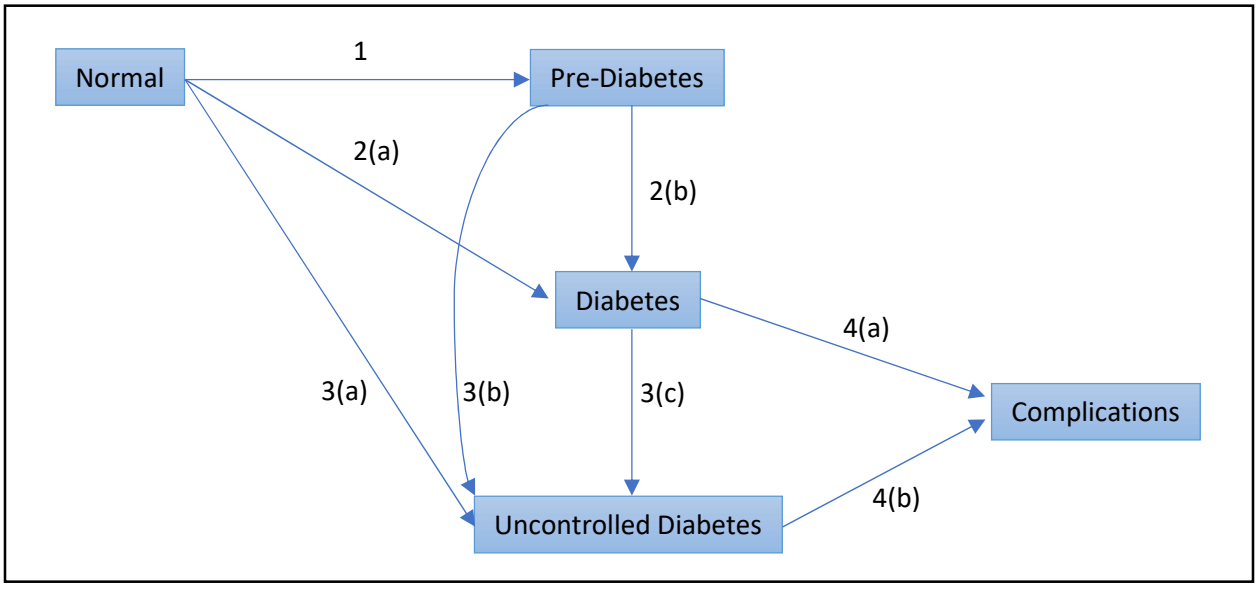


Figure 3. Machine Learning prediction flow set of problems

Data Requirements

The dataset that we consider contains patient encounters from January 2016 to June 2020. Temporal outliers are removed i.e., data with dates from the future and distant past relative to the majority of the encounters in the data set. Table 2 summarizes the features available for model training and testing. A full list can be found in Appendix F: Features for Model Training). Specific features used in each model will depend on the goals and usage setting of each model.

Category	Number of Features
Demographic	4
Diagnosis / Conditions	398
Lab	50
Lifestyle	1
Specialty	242
Utilization	12
Vitals	47

Table 2. Available features for model training.

DM Disease Prediction

The relevant conditions can be identified by ICD codes. ICD code corresponds to the International Statistical Classification of Diseases and Related Health Problems (ICD), a medical classification list by the World Health Organization (WHO). The set codes contain codes for diseases, symptoms, abnormal conditions, complaints, social circumstances, and external causes of injury or diseases. It is widely used in the encoding healthcare data including the data that we plan to use for model building described in this manuscript. ICD codes for T2DM and its complications are as follows:

Condition	ICD-10 (WHO)	ICD-10-CM (U.S.)
T2DM	E11	E11
Diabetic Neuropathy	E11.4 G73.0? G99.0? G59.0? G63.2?	E11.4
Diabetic Nephropathy	E11.2 N08.3	E11.21
Diabetic Retinopathy	E11.3 H36.0	E11.31 – E11.35

Table 3. Relevant ICD-10 codes

Diagnostic criteria as defined by the American Diabetes Association (except for Uncontrolled Diabetes) is described as any one of the three criteria need to be satisfied for a diagnosis [126] as given in Table 4.

Cohort	A1C	Fasting Plasma Glucose (FPG)	2-h Plasma Glucose (PG) during 75-g Oral Glucose Tolerance Test (OGTT)
Healthy	<= 5.6% (<= 38 mmol / mol)	<= 99 mg / dL (<= 5.5 mmol / L)	<= 139 mg / dL (<= 7.7 mmol / L)

Cohort	A1C	Fasting Plasma Glucose (FPG)	2-h Plasma Glucose (PG) during 75-g Oral Glucose Tolerance Test (OGTT)
Pre-T2DM	5.7% to 6.4% (39 to 47 mmol / mol)	100 to 125 mg / dL (5.6 to 6.9 mmol / L)	140 to 199 mg / dL (7.8 to 11.0 mmol / L)
T2DM	6.5% to 6.9% (48 to ? mmol / mol)	>= 126 mg / dL (>= 7.0 mmol / L)	>= 200 mg / dL (>= 11.1 mmol / L)
Uncontrolled T2DM	>= 7.0%		

Table 4. Diagnostic criteria for Type 2 Diabetes Mellitus

DM ED Utilization

For the ED utilization problems, the following sources of data need to be considered.

1. ED encounter data to would be used to define the target labels for each DM patient.
2. Diagnosis and problem list. Table 5 gives the relevant conditions which are required construct features on the type of historical ED visits that were made by a patient.

Condition	ICD-10
T2DM	E11
Hypoglycemia	E11.64
Hyperglycemia	E11.65, E11.0 (hyperosomolarity), E11.1 (ketoacidosis)

Table 5. ICD-10 Codes for T2DM, Hypoglycemia and Hyperglycemia

3. NYU ED Algorithm (EDA) [127], [128] to identify the types of ED visits to exclude. The EDA is a tool that can be used to classify ED visits based on ICD diagnosis codes into the following categories:
    a. Non-emergent: visits that do not require immediate medical care within 12 hours.
    b. Emergent – primary care treatable: visits that require treatment within 12 hours that could have been effectively treated in a primary care setting.
    c. Emergent – preventable / avoidable: visits that require emergency department care but could have been avoided with appropriate primary care management.
    d. Emergent – not preventable / avoidable: visits that require emergency department care and could not be prevented through ambulatory care treatment.

Due to the unique clinical needs of each patient, where patients sharing the same diagnosis code can have conditions with differing levels of severity (e.g., a diagnosis of “abdominal pain” might be given to patients complaining of stomach pain as well as those complaining of chest pain (possibly a heart attack)), the algorithm assigns a specific percentage to each of the categories above for each diagnosis code. The EDA also separately assigned each of the diagnosis codes to categories of mental health, alcohol, substance abuse and injury.

DM Visit Non-Compliance (All/DM patients)

1. The scheduled appointment data is used to:
    - Identify the appointments that will form the train and test data.
    - Create the target labels.
    - Create features using information from the current appointment.
    - Create features using past appointment information of each patient.

2. Calendar data is required to identify if appointment falls on / close to a holiday.

DM Medication Non-Adherence

The following data is needed to establish DM medication non-adherence.

1. A table of diabetic drug classes and drug classes related to the medical management of diabetes as well as the name of the medications within each drug class.
2. Medication order data of medications to be taken in the ambulatory setting.
3. Medication order dispensing data of medications to be taken in the ambulatory setting.

Records from 2 and 3 is used to calculate the 1-year PDC for each patient and drug class to form the target label.

Model Specifications

Risk Prediction Model Framework

Many of the risk prediction models in this solution described in this manuscript attempt to predict the incidence of a risk event, most commonly incidence of disease. As such, a common framework can be used to construct such models. In predicting risk events, one is often interested to know (a) the likelihood of the risk event occurring at some future time, or (b) when the risk event is most likely to occur. These problems can therefore be framed as either (a) a classification or survival problem or (b) a regression problem, respectively. In both instances, the prediction concerns a future event that has not happened. During model training, the training data set will contain examples for which the risk event has happened and others for which it has not happened. This does not mean that the event *will not* happen, just that it *has not* happened by the end of the study period in the data set. Such data is said to be *right-censored*, where the observed time-to-event is less than or equal to the true time-to-event [129]. Furthermore, the length of time for which data is collected per patient is usually variable in real-world medical data sets, with some patients having a significantly longer history of data than others. Supervised ML algorithms assume that the status of the risk event is known for all patients (positive or negative) [130]. One approach to apply supervised ML on censored data is to discard censored observations. However, this causes a loss of highly valuable information – the fact that those patients went a certain amount of time without experiencing the risk event is itself informative [131]. Another approach is to treat these censored observations as the negative class. This is not accurate, since some patients may experience the risk event shortly after the end of the study period; the resulting model will tend to underestimate the risks.

An alternative approach commonly used in healthcare is using survival analysis methods to model the likelihood and time-to-event of specific risks. [129] provides a useful taxonomy of statistical and machine learning methods for survival analysis. Of particular interest are the machine learning methods, which are able to model nonlinear relationships with overall higher quality of predictions. In a survival analysis problem, a binary indicator δ indicates whether the risk event has occurred for a given patient by the end of the study period. The time to the event of interest T is known only for patients where the risk event has occurred ($\delta = 1$) during the study period. For other patients ($\delta = 0$), only the censored time C is known, which typically represents the end of the observation period in the data set. Each patient therefore only has T or C but not both. Thus, the input to a ML survival model for patient i is the triplet (x_i, y_i, δ_i), where x_i is the feature vector and y_i is the observed time, which is equal to T_i for an

uncensored instance and C_i for a censored instance. The goal of survival analysis is to estimate the time to the risk event T_j (non-negative and continuous) for a new patient j with features x_j.

There following table summarizes three ways to formulate the ML problem for risk prediction:

Output	ML Problem	Label	Pros	Cons
Risk of event (%) in x months	Binary classification	Binary indicator δ of incidence of the risk event.	Can provide longitudinal predictions (e.g. risk in 3, 6, 12 months).	Treats censored data as negative class, introduces bias.
Risk of event (%) in x months and/or time to event (depending on model)	Survival	Binary indicator δ with observed time y, where: $y = \begin{cases} T, & \delta = 1 \\ C, & \delta = 0 \end{cases}$ T is the actual time-to-event C is the censored time.	Can provide longitudinal predictions. Works with censored data.	Evaluation metrics (e.g. C-index, Brier Score) are not widely understood.
Time to event (e.g. months)	Regression	T, the actual time-to-event for non-censored cases.		Ignores censored data, losing potentially valuable information. Cannot provide longitudinal predictions. Difficult to justify a single point-in-time prediction (e.g. "patient is likely to get T2DM in 4.5 months").

Table 6. Machine learning problem formulations for diabetes risk prediction

The recommended approach for risk predictions in this solution is to frame them as **survival analysis** problems based on the limitations of the other approaches described previously. In order to train ML models for survival analysis, model training data needs to be transformed into the appropriate format. For this solution, existing encounter-level features will be used. The data set comprises 33.2 million encounters for 755,000 patients, with a mean of 44 encounters per patient.

For each patient, the encounters are sorted by date. The date of first incidence of each type of risk (e.g., pre-T2DM, T2DM, diabetic neuropathy) are also identified and compared to the dates of each encounter. This may result in the following hypothetical timeline of three patients' encounters and risk events illustrated below, where:

- t_i is the ith time period
- E_j^p is the jth encounter for patient p

- R_r^p is the first occurrence of risk event r for patient p

Time	t_1	t_2	t_3	t_4	t_5	t_6	t_7	t_8
Patient 1	E_1^1		E_2^1		r_{T2DM}^1	E_3^1		E_4^1
Patient 2		E_1^2		E_2^2				
Patient 3			E_1^3	E_2^3		E_3^3		r_{T2DM}^3

In this example, there are a total of 9 encounters, each with a set of computed features such as diagnoses, labs and vitals. We can make the following observations:

- The time of the first and last encounter for each patient is not fixed. This is reflective of real-world clinical data, where different patients enter or leave the data set at different times.
- The total observation period (date of first to last encounter) is different for each patient.
- Data is right-censored for some patients (e.g. Patient 2), where the risk event is not observed during the observation period.
- For other patients, the risk event is observed, and the time-to-event from each encounter can be computed.

To form the training set for ML survival analysis models, the time to event (for observed risk event) or time to censoring (for no risk event observed) can be computed, provided the risk event has not happened before the encounter date. Encounters that occur after the risk event are not used, as the risk event has occurred and does not need to be predicted ($P(T > t) = 0$ for all future time t). The features and labels for each encounter can thus be computed as illustrated below:

Encounter Features	Binary Indicator δ	Time to Event T	Censored Time C	Observed Time y	Remarks
E_1^1	1	4	N.A.	4	
E_2^1	1	2	N.A.	2	
E_3^1	1	-1	N.A.	-1	Not used ($y \leq 0$)
E_4^1	1	-3	N.A.	-3	Not used ($y \leq 0$)
E_1^2	0	N.A.	2	2	
E_2^2	0	N.A.	0	0	
E_1^3	1	5	N.A.	5	
E_2^3	1	4	N.A.	4	
E_3^3	1	2	N.A.	2	

Thus, readily available encounter-level features can be transformed into the features and labels as illustrated above for ML survival models, as long as the encounter and event dates are known. Before describing the model specifications and data description for the various prediction problems we first give an overview of the various challenges and risks involved in deployment.

Challenges and Risks

Deployment

Model Training Pipeline

The following general model training pipeline can be applied to most, if not all, of the models in this document. A model training pipeline would facilitate code reuse, automate repetitive steps for greater productivity, and provide a consistent foundation on which a collection of models in this solution can be trained, deployed, retrained and maintained.

1. 70-30 train-test split
2. Feature pre-processing
    a. One-hot encoding of categorical features
    b. Normalization of continuous features
3. Missing value imputation – single value or distribution (see [28] for example)
4. Feature selection (recursive or univariate) to target <= 15 features per model
5. Model training with hyperparameter tuning in a 10-fold cross-validation – train multiple candidate models (depending on problem type) for comparison
    a. Candidate models for survival
        i. Cox Proportional Hazard (CoxPH) [132] with elastic net [133]
        ii. Accelerated Failure Time (AFT) [134]
        iii. Multi-Task Logistic Regression (MTLR) [135]
        iv. Random Survival Forests (RSF) [136]
        v. Survival Support Vector Machine (SSVM) [137]
    b. Candidate models for classification
        i. Naïve Bayes (NB)
        ii. Logistic Regression (LR)
        iii. Generalized Additive Model with Interactions (GA2M)
        iv. SVM with Linear Kernel (SVM-Linear)
        v. SVM with RBF Kernel (SVM-RBF)
        vi. Decision Tree (DT)
        vii. Random Forest (RF)
        viii. xgBoost (XGB)
    c. Candidate models for regression
        i. Linear Regression (LinR)
        ii. SVR with Linear Kernel (SVR-Linear)
        iii. SVR with RBF Kernel (SVR-RBF)
        iv. Decision Tree (DT)
        v. Random Forest (RF)
        vi. xgBoost (XGB)
6. Model evaluation (on test set)
    a. Metrics for survival
        i. Concordance Index [138]
        ii. Unbiased Concordance Index [139]
        iii. Brier Score / Integrated Brier Score [140]

    b. Metrics for classification
        i. AUC
        ii. Accuracy
        iii. Balanced Accuracy
        iv. Precision
        v. Recall
        vi. F1
    c. Metrics for regression
        i. RMSE
        ii. MAE
        iii. R2
7. Model selection
8. Model explanation
    a. Global: Top global risk factors for each model, and a measure of the strength of association between the risk factor and the target risk
    b. Local: A means to compute the top risk factors for each individual (instance) as they are scored by the model

The whole pipeline, from feature pre-processing and including the final selected model, should then be serialized into a deployable format (e.g., pickle file containing a full scikit-learn pipeline).

Modelling Pipeline

We consider six prediction tasks which are framed as survival analysis tasks, with different target events. Predictions were made for each encounter, so that when the models are deployed at a provider, patient risk profiles can be updated after every encounter with the latest patient data. Since these models are designed to be used in an outpatient setting, we assumed that prediction happens *after* each inpatient or outpatient encounter, and complete information of each encounter is available. The following pipeline was used to train and test models for all tasks. The pipeline is configuration-driven, and therefore is able to support different survival analysis tasks by specifying different data sets and labels as input. For details, refer to the following sections in the rest of this document.

1. **Label and feature preparation**: Selected features were used for modelling which were curated to ensure repeatability across providers, so that the Diabetes models can be widely deployed at multiple customers (see Appendix A). Labels were also constructed for the five prediction tasks using the underlying Epic data on encounters, labs and diagnoses.
2. **Cohort selection**: Filtering criteria were applied to select appropriate cohorts for each prediction task (see the cohort criteria used for each task in the following sections).
3. **Feature pre-processing**: Patient Flow features were already partially processed (e.g., one-hot encoded). Outliers with numeric features greater than 3 standard deviations above the mean were removed. Missing values were imputed using different strategies depending on the type of feature:
    a. “daysSince” features were imputed using the maximum value among all instances.
    b. Labs and vitals were imputed using the mean values among other instances with the same age bucket and sex.

c. All remaining features were imputed with zeros, as they are binary or counts of events.

4. **Model signature generation**: A backward feature elimination loop was used to select the best subset of up to 30 features per prediction task, including the mandatory features. This was conducted in two stages. Starting with the full set of about 1,200 features (excluding mandatory features), Stage 1 eliminated 5 percent (about 60 features) per iteration, to efficiently narrow down the search to the top 30 features. In stage 2, one feature was eliminated per iteration, to fine-tune the search for the best subset of features. Mandatory features were protected from elimination, thereby guaranteeing that they remain in the final set of selected features. At each iteration of the loop, a Cox proportional hazards [4], [5] model was trained on the subset of features, and its performance measured by Concordance Index [6]. The smallest set of features that achieved a cross-validation score within 0.01 of the maximum score was selected for the model signature. This margin allowed fewer features to be selected when there is a plateau in the performance
5. curve, without sacrificing much performance. The selected features (including mandatory features) became the "model signature" of each task.
6. **Training and test data preparation**: The data for each task was randomly divided into a 70% training set and 30% test set.
7. **Parameter optimization on 70% training set**: Available open-source implementations of survival ML algorithms from the PySurvival [7] package were used. The following list of candidate models were explored and optimized for each task:
    a. Cox proportional hazards (CoxPH) [8]
    b. DeepSurv Cox proportional hazards deep neural network (DeepSurv) [9]
    c. Random survival forest (RSF) [10]
    d. Conditional survival forest (CSF) [11]
    e. Extra survival trees (EST)

    Distributed parameter search was performed on a Spark cluster using Hyperopt [12], which optimizes the search using Tree-structured Parzen Estimators [4]. For each task and candidate model, the search was performed for up to 200 parameter combinations and 12 hours of maximum run time. Each trained model was evaluated using Concordance Index in a 5-fold cross-validation set up, and the cross-validation scores were reported.

8. **Model training on 70% training set:** Each candidate model was re-trained on the full training set using the best set of model parameters found, i.e. the one resulting in the highest cross-validated Concordance Index during parameter search.
9. **Model evaluation on 30% test set**: The trained models were evaluated on the test set using the following metrics:
    a. Concordance Index (C-Index) [5], which measures the probability that the predicted risks for any given pair of test examples are in the correct rank order, adjusted for censoring times to achieve unbiased and consistent estimates [13]. CIdx produces real values in [0, 1], with 1 being the best score and 0.5 being the expected score for random predictions.
    b. Integrated Brier Score (IBS) [10]. The Brier Score (BS) measures the average squared distance between the observed survival status and predicted survival probability at any given time t, adjusted for censoring. The Integrated Brier Score gives an overall measure by computing the integral of BS over all available times. Both BS and IBS produce real values in [0, 1], with 0 being the best score 0.25 being the expected score for random predictions.
    c. Similarity of the average survival function curve to the Kaplan Meier (KM) survival curve.
    d. Brier Score over time.

10. **Selection of best model**: One best model with the highest CIdx score on the test set was selected. Detailed evaluation metrics were further computed for the selected model, including model performance by different sub-cohorts such as demographic groups.
11. **Model explanation**: Global and local model explanations were generated for each of the five selected models. The **global explanations** were generated using permutation importance where each feature is randomly shuffled and the change in concordance index is measured – a greater change would mean that the feature is more important. As for **local explanations (individual patient level explanations)**, because available explanation packages only work for regression and classification tasks, the predicted survival functions were converted into classification probabilities at different future times – 3, 6, 9, 12, 18 and 24 months – and local surrogate models (LIME) [14] were trained to explain the predictions for each future time and example. 3 examples were selected for local explanations by sampling the risk scores of the test examples in the first quartile ("low risk"), second to third quartiles ("medium risk") and fourth quartile ("high risk"). Additional notes:
    a. Explanations of up to a maximum of 20 global and 10 local features are shown
    b. Probabilities were generated using 1 – S(t), where S(t) is the survival function, which translates to the probability of having the disease or complication at time t.
    c. Risk scores of examples are not comparable across models as they do not have a fixed scale; they only indicate *relative* predicted risk between encounters.
12. **Model calibration (experimental)**: After the trained models are deployed in a customer environment, they may need to be calibrated as the characteristics of the target patient population may be different from that used to train the models. The goal of calibration is to optimize model performance with respect to a target population, in an efficient way that does not involve re-training the underlying pre-trained model. In Appendix D, we experiment with a calibration method proposed by [15] for survival models under a proportional hazards assumption.

Inclusion and Exclusion Criteria for Assigning Class Labels

The following criteria were used to detect the first occurrence of each of the following events, per patient. The dates of the events for each patient (or lack thereof indicating censoring) were then used to construct the training labels (binary and time to event or censoring) for the survival models, as follows:

- Binary indicator $\delta = \begin{cases} 1, & Event \\ 0, & No\ Event \end{cases}$
- Time to event (or censoring) $y = \begin{cases} T, & \delta = 1 \\ C, & \delta = 0 \end{cases}$

See the respective sections in the rest of this document for the "Table 1" statistics for each label / task.

Pre-DM

Pre-DM events were detected based on diagnostic criteria published in [14], i.e. any one test meeting the following criteria:

- From Labs: 100 mg/dL ≤ Fasting Plasma Glucose (FPG) ≤ 125 mg/dL (outpatient only) OR
- From Labs: 140 mg/dL ≤ 2-h Plasma Glucose (2hPG) ≤ 199 mg/dL during Oral Glucose Tolerance Test (OGTT) (outpatient only) OR
- From Labs: 140 mg/dL ≤ Random Plasma Glucose (RPG) ≤ 199 mg/dL (outpatient only) OR
- From Labs: 5.7% ≤ A1C ≤ 6.4%

DM

DM events were detected based on diagnostic criteria published in [14], i.e. two abnormal test results from the same sample or separate test samples, in the last 4 weeks (0 to 27 days, inclusive):

- Fasting Plasma Glucose (FPG) ≥ 126 mg/dL (outpatient only)
- 2-h Plasma Glucose (2hPG) ≥ 200 mg/dL during Oral Glucose Tolerance Test (OGTT) (outpatient only)
- Random Glucose (RG) ≥ 200 mg/dL (outpatient only)
- A1C ≥ 6.5%

Uncontrolled DM

Uncontrolled DM events were detected based on A1C ≥ 9.0%.

Diabetic Nephropathy

Diabetic nephropathy events were detected based on ICD-10 codes:

- E11.2: Type 2 diabetes mellitus with kidney complications
- E11.21: Type 2 diabetes mellitus with diabetic nephropathy
- E11.22: Type 2 diabetes mellitus with chronic kidney disease
- E11.29: Type 2 diabetes mellitus with other diabetic kidney complication

Diabetic Neuropathy

Diabetic neuropathy events were detected based on ICD-10 codes:

- E11.4: Type 2 diabetes mellitus with neurological complications
- E11.40: Type 2 diabetes mellitus with diabetic neuropathy, unspecified
- E11.41: Type 2 diabetes mellitus with diabetic mononeuropathy
- E11.42: Type 2 diabetes mellitus with diabetic polyneuropathy
- E11.43: Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy
- E11.44: Type 2 diabetes mellitus with diabetic amyotrophy
- E11.49: Type 2 diabetes mellitus with other diabetic neurological complication

Diabetic Retinopathy

Diabetic retinopathy events were detected based on ICD-10 codes:

- E11.3: Type 2 diabetes mellitus with ophthalmic complications
- E11.31*: Type 2 diabetes mellitus with unspecified diabetic retinopathy
- E11.32*: Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy
- E11.33*: Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy
- E11.34*: Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy
- E11.35*: Type 2 diabetes mellitus with proliferative diabetic retinopathy
- E11.36*: Type 2 diabetes mellitus with diabetic cataract
- E11.37*: Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment
- E11.39: Type 2 diabetes mellitus with other diabetic ophthalmic complication

T1DM

T1DM events were detected based on ICD-10 codes:

- E10*: Type 1 diabetes mellitus

This label was used to exclude T1DM patients from the cohorts.

Model Descriptions and Results

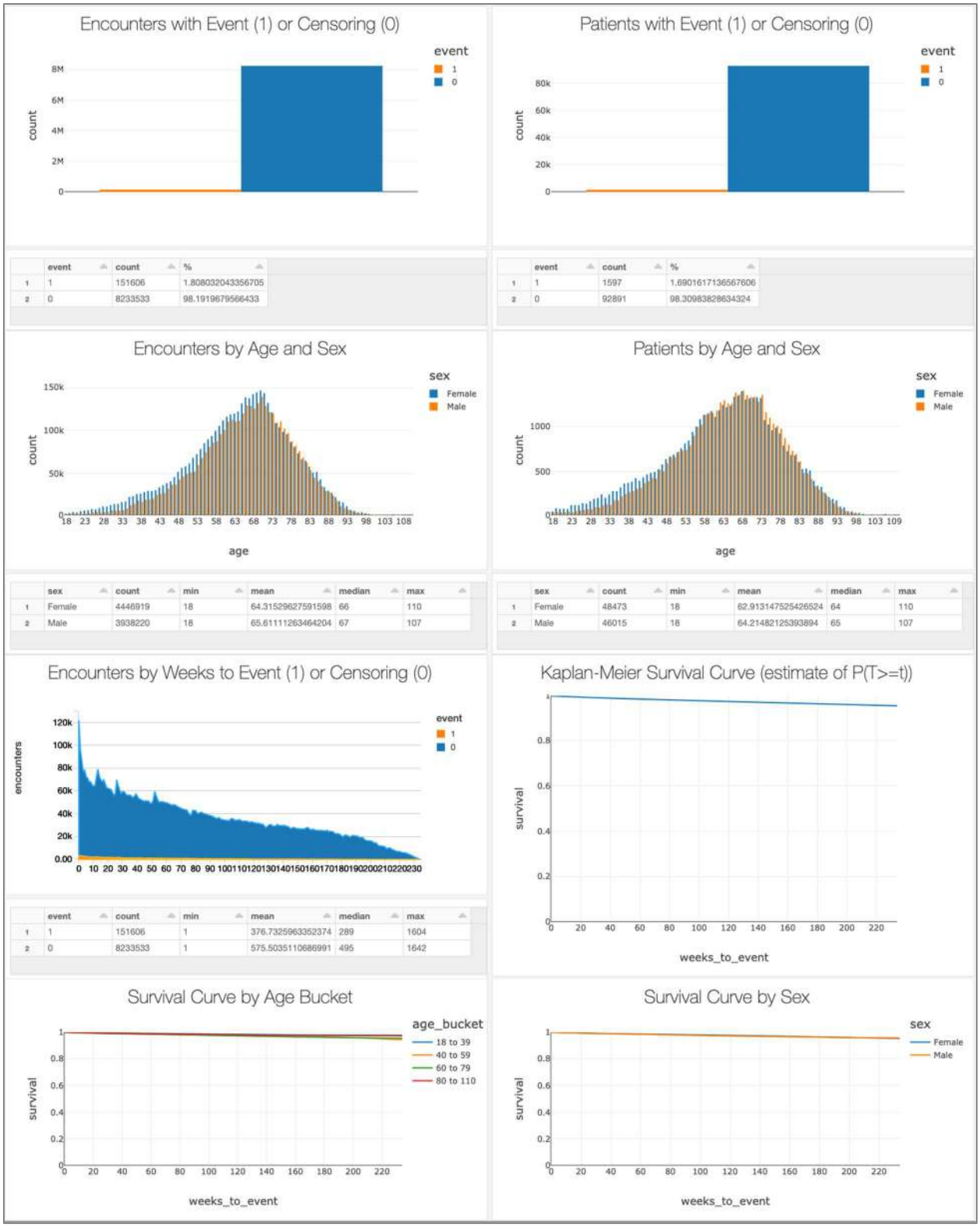
In the next few sections, we describe the data requirements, model signatures, model evaluation and model explanations for a series of models related to prediction of Type 2 Diabetes and its complications

T2DM to Microvascular Complications Prediction

The following apply to each of the complications of interest, namely diabetic nephropathy, diabetic neuropathy and diabetic retinopathy.

Item	Specification
ML Class	Survival
Usage Setting	Outpatient
Instances for Prediction	Encounter
Labels for Instances	• Binary indicator $\delta = \begin{cases} 1, & Complication \\ 0, & No\ Complication \end{cases}$ • Time to event (or censoring) $y = \begin{cases} T, & \delta = 1 \\ C, & \delta = 0 \end{cases}$
Cohort Criteria	• $18 \leq age \leq 110$ (adults without outliers) • Met T2DM diagnostic criteria before encounter date • Never diagnosed with the target complication before encounter date
Input Features	• Demographic • Diagnoses EXCEPT the target complication • Labs EXCEPT those used to diagnose the target complication • Vitals
Optimization Metric	Concordance Index
Evaluation Metrics	• Concordance Index • Integrated Brier Score

Preliminary data exploration of encounters meeting the cohort criteria for **T2DM to diabetic nephropathy prediction**:



	event	count	%
1	1	151606	1.808032043356705
2	0	8233533	98.1919679566433

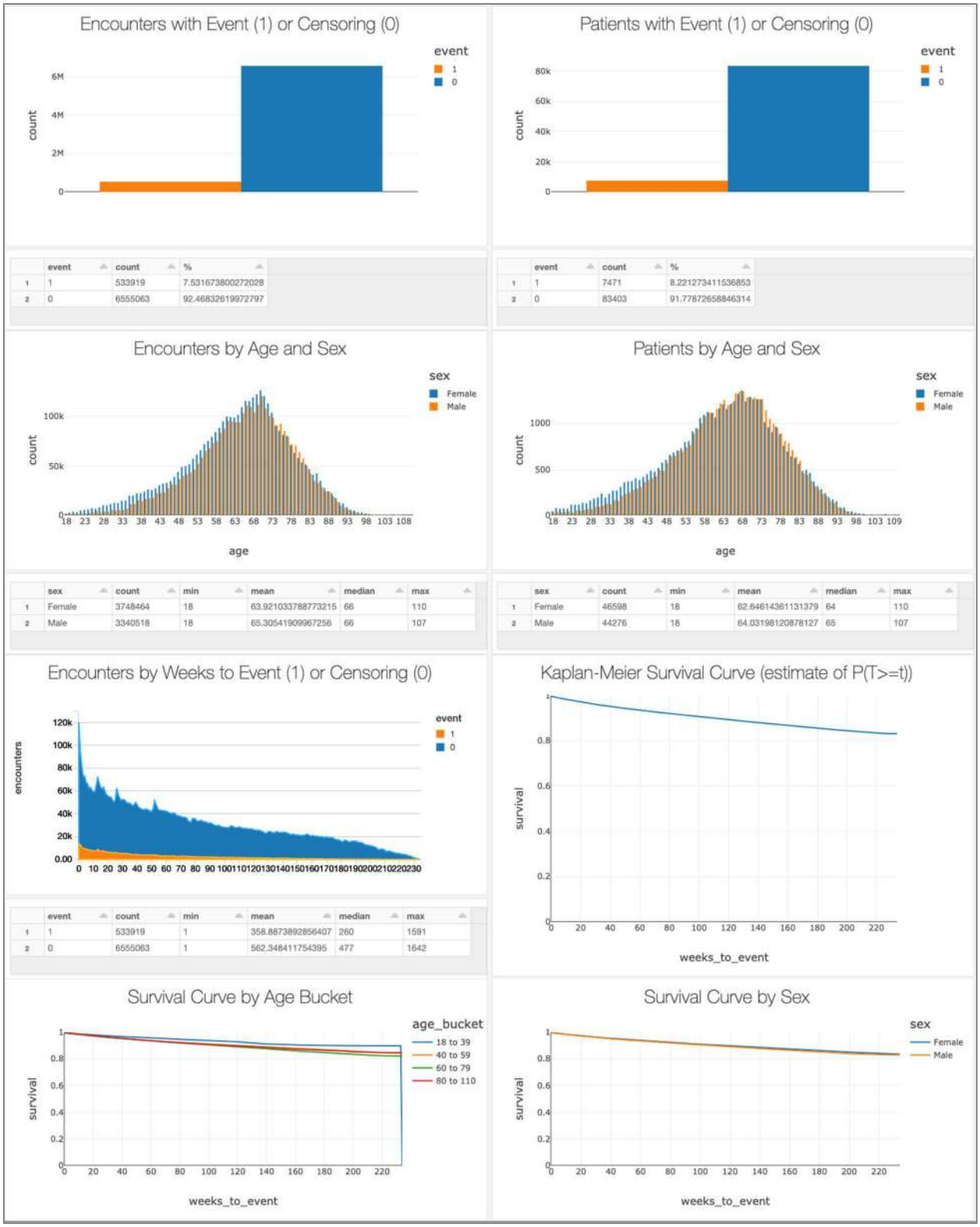
	event	count	%
1	1	1597	1.6901617136567606
2	0	92891	98.30983828634324

	sex	count	min	mean	median	max
1	Female	4446919	18	64.31529627591598	66	110
2	Male	3938220	18	65.61111263464204	67	107

	sex	count	min	mean	median	max
1	Female	48473	18	62.913147525426524	64	110
2	Male	46015	18	64.21482125393894	65	107

	event	count	min	mean	median	max
1	1	151606	1	376.7325963352374	289	1604
2	0	8233533	1	575.5035110686991	495	1642

Preliminary data exploration of encounters meeting the cohort criteria for **T2DM to diabetic neuropathy prediction**:



	event	count	%
1	1	533919	7.531673800272028
2	0	6555063	92.46832619972797

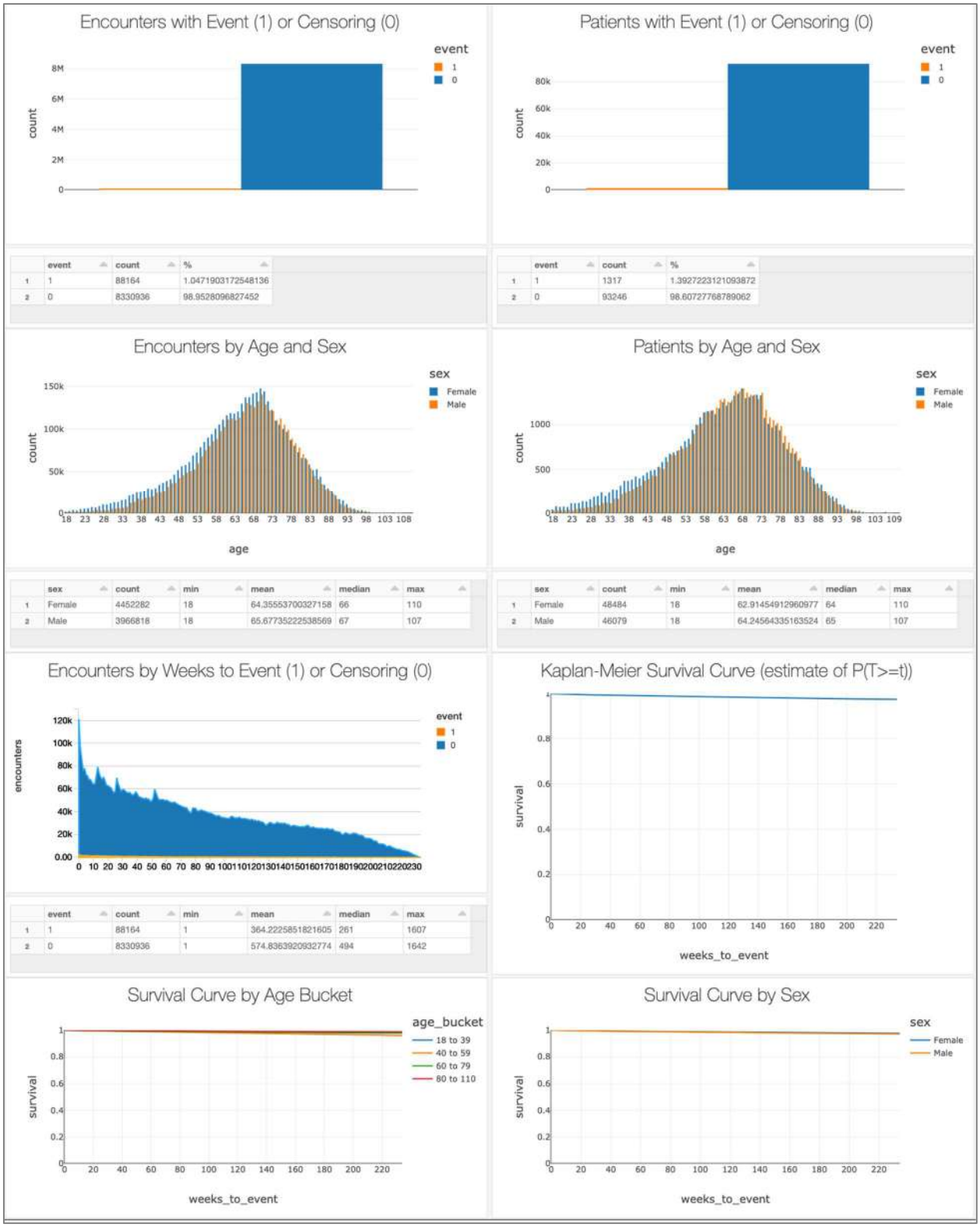
	event	count	%
1	1	7471	8.221273411536853
2	0	83403	91.77872658846314

	sex	count	min	mean	median	max
1	Female	3748464	18	63.921033788773215	66	110
2	Male	3340518	18	65.30541909967256	66	107

	sex	count	min	mean	median	max
1	Female	46598	18	62.64614361131379	64	110
2	Male	44276	18	64.03198120878127	65	107

	event	count	min	mean	median	max
1	1	533919	1	358.8873892856407	260	1591
2	0	6555063	1	562.348411754395	477	1642

Preliminary data exploration of encounters meeting the cohort criteria for **T2DM to diabetic retinopathy prediction**:



	event	count	%
1	1	88164	1.0471903172548136
2	0	8330936	98.9528096827452

	event	count	%
1	1	1317	1.3927223121093872
2	0	93246	98.60727768789062

	sex	count	min	mean	median	max
1	Female	4452282	18	64.35553700327158	66	110
2	Male	3966818	18	65.67735222538569	67	107

	sex	count	min	mean	median	max
1	Female	48484	18	62.91454912960977	64	110
2	Male	46079	18	64.24564335163524	65	107

	event	count	min	mean	median	max
1	1	88164	1	364.2225851821605	261	1607
2	0	8330936	1	574.8363920932774	494	1642

T2DM ED Utilization Prediction

Item	Specification
ML Class	Classification
Usage Setting	Outpatient
Instances for Prediction	Patient

Labels for Instances	• Binary indicator
	$y = \begin{cases} 1, & \geq 3 \; all \; cause \; ED \; visits \; in \; next \; 12 \; months \\ 0, & otherwise \end{cases}$
	• Remove ED visits occurring within 3 days after a previous ED visit to avoid double counting
	• Exclude ED visits relating to injury
	• Construct 2 models:
	  ○ Include all remaining ED visits ("Non-emergent", "Emergent – primary care treatable", "Emergent – preventable / avoidable", "Emergent – not preventable / avoidable")
	  ○ From the remaining ED visits, exclude the "Emergent – not preventable / avoidable" ED visits

Cohort Criteria	• $18 \leq age \leq 110$ (adults without outliers) • Met the diagnostic criteria of DM, Uncontrolled DM or any of the DM Complications before the prediction • Include pregnant women and those with gestational diabetes
Input Features	• Demographic • Diabetes treatment type and medications • Diabetes duration and complications • Healthcare utilization • Diagnoses, labs, vitals See Appendix E for details
Optimization Metric	AUC
Evaluation Metrics	• AUC • Accuracy • Balanced Accuracy • Precision • Recall

Visit Non-Compliance Prediction (All patients)

Item	Specification
ML Class	Classification
Usage Setting	Outpatient
Instances for Prediction	Appointment
Labels for Instances	• Binary indicator $y = \begin{cases} 1, & No \; Show \; or \; Late \; Cancellation \\ 0, & Completed \; Appointment \end{cases}$ Late Cancellation is defined as within 24 hours prior to appointment time

Item	Specification

	• $y = 1,\ No\ Show\ or\ Late\ Cancellation$
	  ○ Status == "No Show", or
	  ○ Status == "Canceled" & Cancel initiator == "Patient" & Cancel reason != "Deceased" & cancellation was late
	• $y = 0,\ Completed\ Appointment$
	  ○ Status == "Completed" & Cancel reason == "No Reason"

Cohort Criteria	• $18 \leq age \leq 110$ (adults without outliers) • Exclude visits without any prior appointment (walk_in_yn == "Y") • Exclude appointments made within 48 hours of actual appointment
Input Features	• Demographic • Medication adherence • Patient appointment history • Current appointment characteristics • Diagnoses, labs, vitals See Appendix E for details
Optimization Metric	AUC
Evaluation Metrics	• AUC • Accuracy • Balanced Accuracy • Precision • Recall

T2DM Visit Non-Compliance Prediction (DM patients)

Item	Specification
ML Class	Classification
Usage Setting	Outpatient
Instances for Prediction	Appointment

Labels for Instances	• Binary indicator
	y= $\begin{cases} 1,\ No\ Show\ or\ Late\ Cancellation \\ 0,\ Completed\ Appointment \end{cases}$
	Late Cancellation is defined as within 24 hours prior to appointment time
	• $y = 1,\ No\ Show\ or\ Late\ Cancellation$
	  ○ Status == "No Show", or
	  ○ Status == "Canceled" & Cancel initiator == "Patient" & Cancel reason != "Deceased" & cancellation was late
	• $y = 0,\ Completed\ Appointment$
	  ○ Status == "Completed" & Cancel reason == "No Reason"

Cohort Criteria	• $18 \leq age \leq 110$ (adults without outliers) • Met the diagnostic criteria of DM, Uncontrolled DM or any of the DM Complications before the appointment date

Item	Specification
	• Exclude visits without any prior appointment (walk_in_yn == "Y") • Exclude appointments made within 48 hours of appointment time
Input Features	• Demographic • Diabetes treatment type • Medication adherence • Patient appointment history • Current appointment characteristics • Diagnoses, labs, vitals See Appendix E for details
Optimization Metric	AUC
Evaluation Metrics	• AUC • Accuracy • Balanced Accuracy • Precision • Recall

Additional Notes

Usage Settings: x days before appointment date / at time of scheduling / any time between appointment schedule and appointment time

Instance for prediction: Appointment vs. patient level prediction

Pros for predicting on appointments:

- It will be easier to model appointment specific characteristics.
- Definition of the response variable is more straightforward whereas patient level prediction requires setting arbitrary cut-offs for the percentage of missed appointments as well as the time period over which the percentage will be computed.

Cons for predicting on appointments:

- In some cases, the care manager might want to understand the patient's visit compliance in general rather than with respect to a specific appointment.

T2DM Medication Non-Adherence Prediction

Item	Specification
ML Class	Classification
Usage Setting	Outpatient
Instances for Prediction	Patient
Labels for Instances	• Binary indicator $y = \begin{cases} 1, & PDC\ over\ 1\ year \geq 80\% \\ 0, & otherwise \end{cases}$

Item	Specification
	$$PDC = \frac{No.of\ days\ in\ period^{*}\ covered}{No.of\ days\ in\ period^{*}} \times 100\%$$ A day is considered to be covered only when the patient has access to all the antidiabetic medications specified. *Exclude PDC calculation for days which the patient is hospitalized
Cohort Criteria	• $18 \leq age \leq 110$ (adults without outliers) • Met the diagnostic criteria of DM, Uncontrolled DM or any of the DM Complications before the prediction • Include patients with at least 1 prescription of an OAD or insulin • Exclude patients using Metformin for polycystic ovary syndrome only
Input Features	• Demographic • Diabetes treatment type and medications • Diabetes duration and complications • Healthcare utilization • Diagnoses, labs, vitals See Appendix E for details
Optimization Metric	AUC
Evaluation Metrics	• AUC • Accuracy • Balanced Accuracy • Precision • Recall

Additional Notes

Usage Settings

What are the specific use cases for medication adherence prediction? Will we be scoring daily using a rolling window?

Labels for Instances

1. How should we handle multiple medications?
2. What would be a meaningful time interval for compliance with diabetic medications? Is 90 days too long / short?
3. Do we want to focus only on adherence relating diabetic medications only or all medications that are prescribed / medications typically taken by diabetic patients to control blood pressure for example?
4. The 80% threshold for PDC is arbitrary, should we come up with certain heuristics to determine the threshold?

Cohort Criteria

1. Do we want to include prediction for primary non-adherence (patients that never filled their first prescription)? (e.g., Exclude patients with less than 2 prescription fills for a medication)
2. Do we want to exclude patients receiving their medication by mail?
3. Are we able to find out patients with prolonged institution and exclude them?

Pre-DM to DM Prediction

Item	Specification
Business Goal	Enable care managers to identify the patients who are pre-diabetic and at risk of developing DM
Usage Setting	Outpatient
ML Task	Predict risk and/or time from pre-DM to DM
ML Class	Survival
Instances for Prediction	Encounters
Labels for Instances	Binary indicator and time to event or censoring for DM • Binary indicator $\delta = \begin{cases} 1, & T2DM \\ 0, & No\ T2DM \end{cases}$ • Time to event (or censoring) $y = \begin{cases} T, & \delta = 1 \\ C, & \delta = 0 \end{cases}$
Cohort Criteria	• 2016-01-01 $\leq$ encounter date $\leq$ 2020-06-30 (available Epic data, excluding outliers) • Encounter date is not within the first 90 days of when the patient entered the data set, to adjust for left-censoring • 18 $\leq$ age $\leq$ 110 (adults without outliers) • No T1DM diagnosis • Not pregnant • No "Do Not Resuscitate" diagnosis • Pre-DM event before encounter date • No DM or uncontrolled DM event before encounter date • No DM or uncontrolled DM event up to 6 days after encounter date (encounters where lab results confirm event within the week)

Item	Specification

Input Features	• Demographic
	• Diagnosis, except:
	  ○ hasDiabetes*
	  ○ has_END002* (Diabetes mellitus without complication)
	  ○ has_END003* (Diabetes mellitus with complication)
	  ○ has_END004* (Diabetes mellitus, Type 1)
	  ○ has_END005* (Diabetes mellitus, Type 2)
	  ○ has_END006* (Diabetes mellitus, due to underlying condition, drug or chemical induced, or other specified type)
	• Labs
	• Utilization
	• Vitals
	
	See Appendix E for details.

Evaluation Metrics	• Concordance Index • Integrated Brier Score

Data

The following charts summarize the key characteristics of the data after applying the cohort criteria stated above, along with selected features (see Model Signature below).

Category	summary Variable	count	mean	stddev	min	25%	50%	75%	max
Demographic	AgeBucket_18_to_39	258142.0	0.069903	0.254985	0.00	0.000	0.000	0.000	1.00
	AgeBucket_40_to_59	258142.0	0.248332	0.432046	0.00	0.000	0.000	0.000	1.00
	AgeBucket_60_to_79	258142.0	0.543267	0.498125	0.00	0.000	1.000	1.000	1.00
	AgeBucket_80_to_109	258142.0	0.138497	0.345422	0.00	0.000	0.000	0.000	1.00
	Sex_Female	258142.0	0.627515	0.483467	0.00	0.000	1.000	1.000	1.00
	Sex_Male	258142.0	0.372485	0.483467	0.00	0.000	0.000	1.000	1.00
	Ethnicity_Hispanic_or_Latino	258142.0	0.054687	0.227369	0.00	0.000	0.000	0.000	1.00
	Ethnicity_Not_Hispanic_or_Latino	258142.0	0.945313	0.227369	0.00	1.000	1.000	1.000	1.00
Encounter	EncounterType_Emergency	258142.0	0.183232	0.386858	0.00	0.000	0.000	0.000	1.00
	EncounterType_Inpatient	258142.0	0.079848	0.271058	0.00	0.000	0.000	0.000	1.00
	EncounterType_Outpatient	258142.0	0.736920	0.440306	0.00	0.000	1.000	1.000	1.00
Label	Time	258142.0	15.740631	11.314076	0.00	6.000	14.000	24.000	50.00
	Event	258142.0	0.064608	0.245833	0.00	0.000	0.000	0.000	1.00
Feature	age	258142.0	64.481131	14.647176	18.00	56.000	66.000	75.000	107.00
	Male_sex	258142.0	0.372485	0.483467	0.00	0.000	0.000	1.000	1.00
	Hispanic_or_Latino_ethnicity	258142.0	0.054687	0.227369	0.00	0.000	0.000	0.000	1.00
	maxhbA1ClnPast365Days	258142.0	6.144908	0.536921	3.00	5.900	6.121	6.228	9.80
	lasthbA1ClnPast365Days	258142.0	6.034896	0.491028	2.20	5.800	6.022	6.103	8.90
	meandiastolicinPast365Days	258142.0	74.510641	7.465089	43.63	71.000	74.678	77.830	107.67
	meansystolicinPast365Days	258142.0	130.507721	11.237634	81.00	125.900	130.162	134.500	180.00
	BMI	258142.0	32.052144	6.993803	2.71	28.009	31.894	35.243	326.11
	meantriglyceroidsInPast365Days	258142.0	141.515197	48.161881	11.00	119.839	142.732	147.721	468.50
	meanldlcholesterolInPast365Days	258142.0	95.182333	23.631750	2.80	84.968	97.608	107.000	201.00
	meanhdlcholesterolInPast365Days	258142.0	47.882752	10.369947	6.00	42.348	47.000	52.436	98.00
	has_BLD005_Past12Months	258142.0	0.001189	0.034465	0.00	0.000	0.000	0.000	1.00
	has_CIR007_Past12Months	258142.0	0.165409	0.371550	0.00	0.000	0.000	0.000	1.00
	has_CIR008_Past12Months	258142.0	0.009239	0.095675	0.00	0.000	0.000	0.000	1.00
	has_NEO016_Past12Months	258142.0	0.003146	0.055997	0.00	0.000	0.000	0.000	1.00
	has_PRG029	258142.0	0.015968	0.125352	0.00	0.000	0.000	0.000	1.00
	has_FAC006	258142.0	0.040509	0.197149	0.00	0.000	0.000	0.000	1.00
	has_DIG018	258142.0	0.022488	0.148263	0.00	0.000	0.000	0.000	1.00
	has_SKN003	258142.0	0.052475	0.222983	0.00	0.000	0.000	0.000	1.00
	has_RSP015	258142.0	0.002750	0.052372	0.00	0.000	0.000	0.000	1.00
	has_NEO017	258142.0	0.011966	0.108734	0.00	0.000	0.000	0.000	1.00
	has_INJ057	258142.0	0.001708	0.041297	0.00	0.000	0.000	0.000	1.00

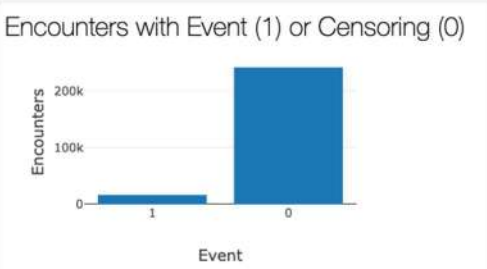
(Percentages for binary variables can be read from the “mean” column.)

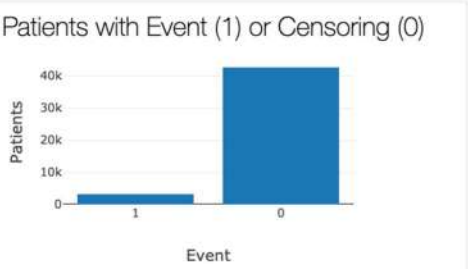
Encounters and Patients

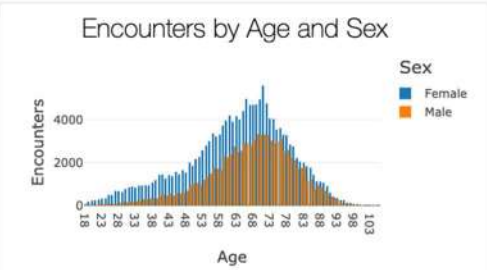
	Examples	Encounters	Patients
1	258142	258142	45851

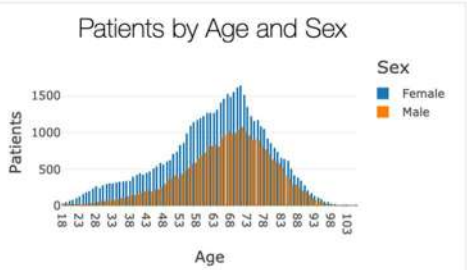
Train and Test Sets

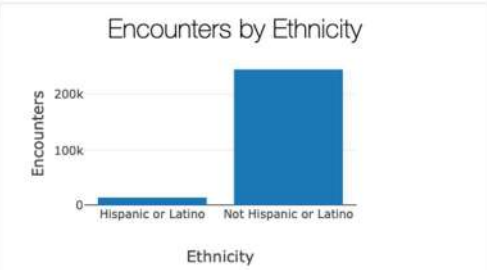
	Set	No Event	No Event %	Event	Event %	Total	Total %
1	Test	72364	30	4958	29.7	77322	30
2	Train	169100	70	11720	70.3	180820	70
3	Total	241464	100	16678	100	258142	100

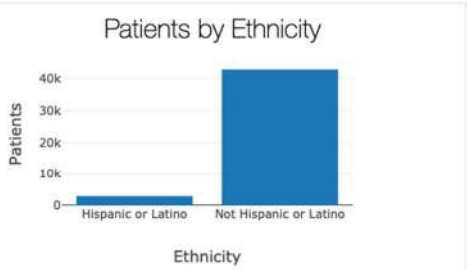


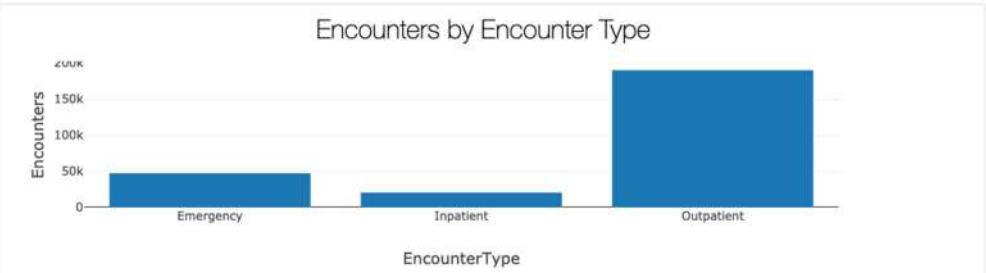


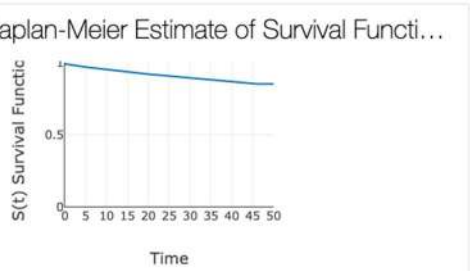








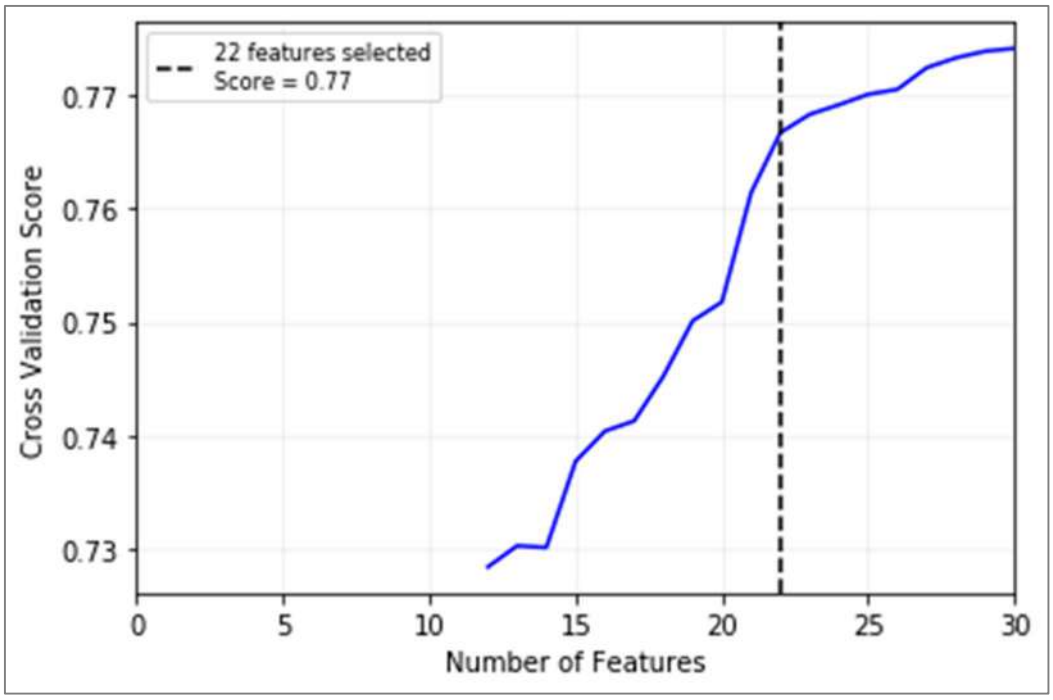




Model Signature

The model signature has 22 features, comprising of 12 mandatory features and 10 other selected features. These are the selected features, in rank order (the last feature to be eliminated is ranked 1):

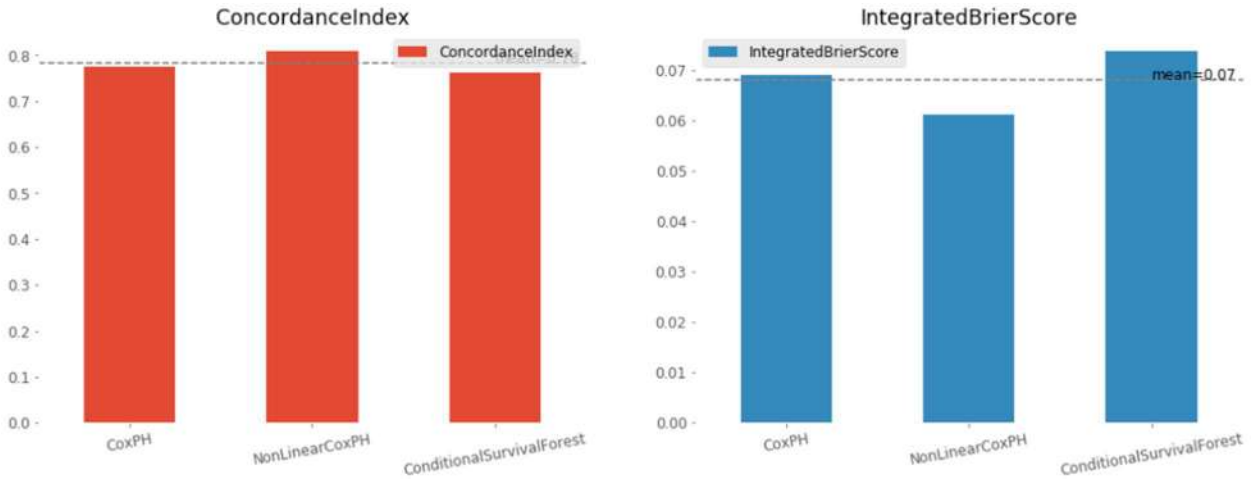
1. has_BLD005_Past12Months (Sickle cell trait/anemia)
2. has_PRG029 (Uncomplicated pregnancy, delivery or puerperium)
3. has_NEO016_Past12Months (Gastrointestinal cancers - anus)
4. has_INJ057 (Effect of foreign body entering opening, subsequent encounter)
5. has_DIG018 (Hepatic failure)
6. maxhbA1CInPast365Days
7. has_RSP015 (Mediastinal disorders)
8. has_NEO017 (Gastrointestinal cancers - liver)
9. has_SKN003 (Pressure ulcer of skin)
10. has_FAC006 (Encounter for antineoplastic therapies)
11. Male_sex
12. lasthbA1CInPast365Days
13. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)
14. Hispanic_or_Latino_ethnicity
15. has_CIR007_Past12Months (Essential hypertension)
16. meanhdlcholesterolInPast365Days
17. meansystolicinPast365Days
18. BMI
19. meandiastolicinPast365Days
20. age
21. meanldlcholesterolInPast365Days
22. meantriglyceroidsInPast365Days



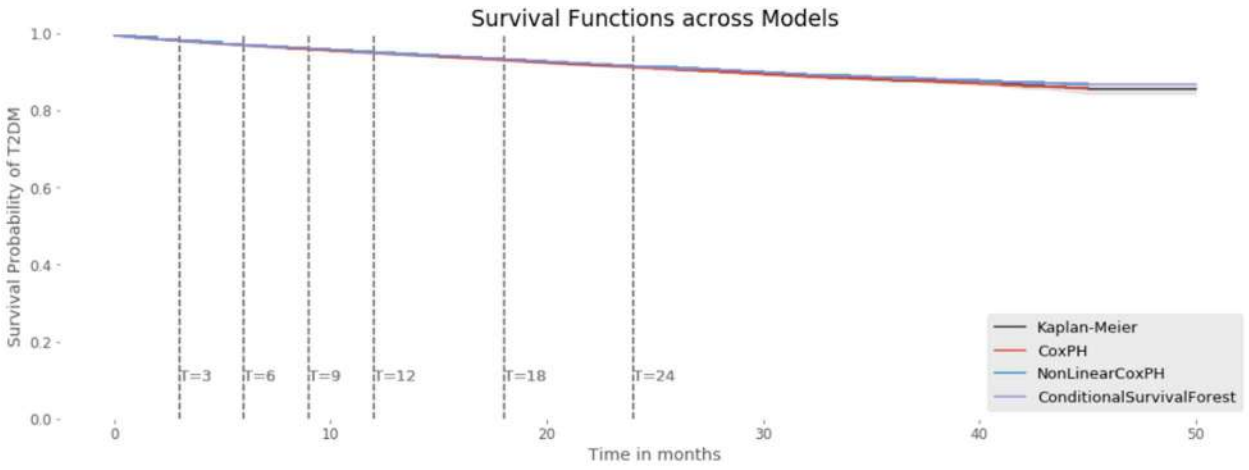
Model Performance

The following table and chart summarize the performance of all candidate models on the test set for this prediction task in terms of the Concordance Index and the Integrated Brier Score.

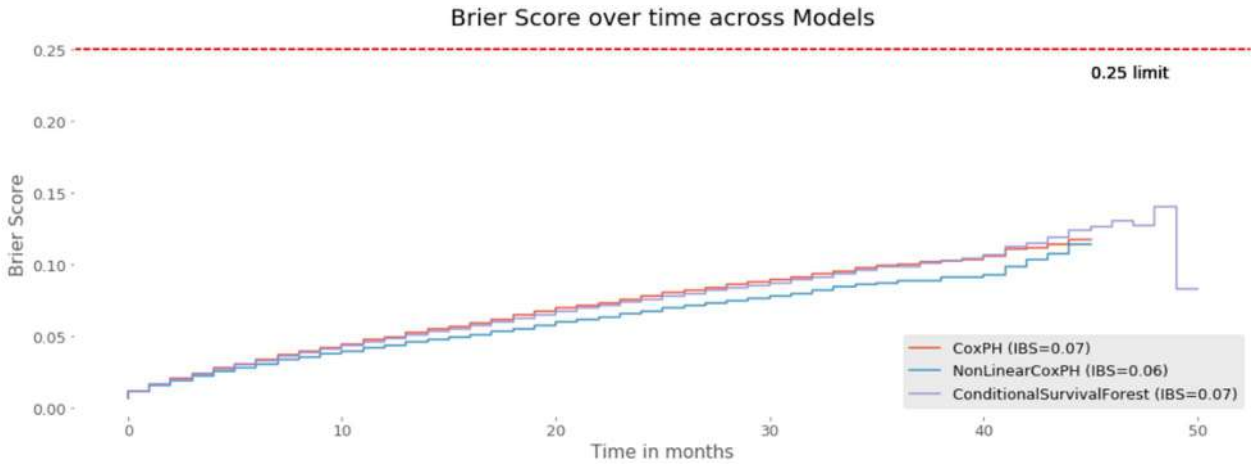
Model	No. of Parameter Combinations Successfully Tested	Concordance Index	Integrated Brier Score
CoxPH	89	0.78	0.07
DeepSurv	60	**0.81**	**0.06**
RSF	Timeout	-	-
CSF	7	0.76	0.07
EST	Timeout	-	-



The following chart shows how the average survival function curves of the candidate models compare to the KM survival curve, the more similar their curves are to the KM survival curve the better.



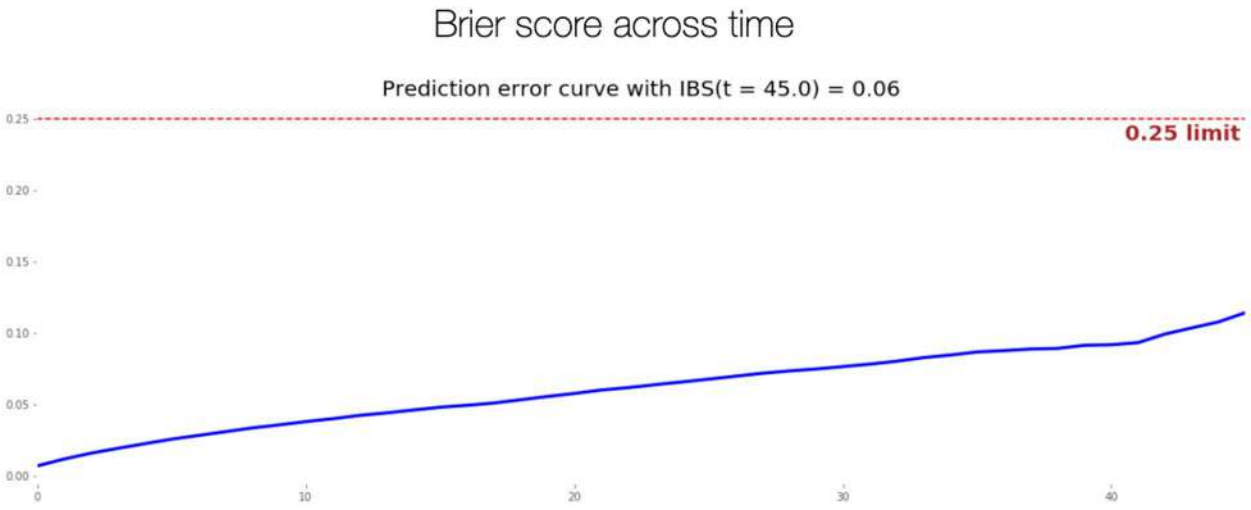
This chart shows the change in the Brier Score over time for all candidate models, the closer the scores are to 0 the better.



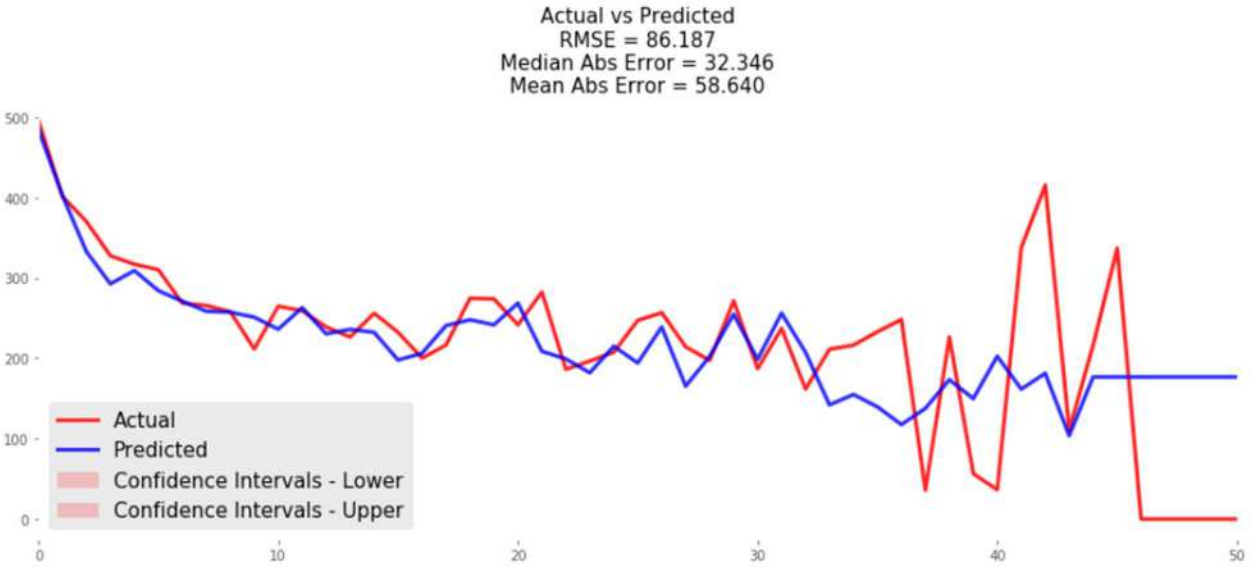
Model Evaluation of Selected Model (DeepSurv)

Overall

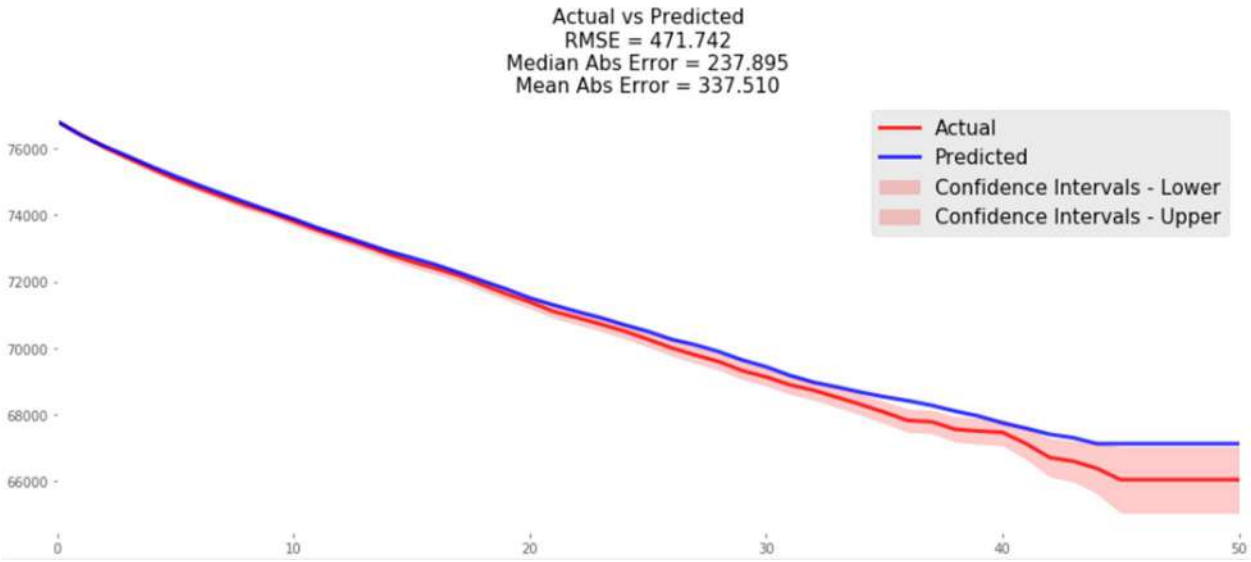
This chart shows the change in the Brier Score over time for the selected model, the closer the scores are to 0 the better.



The following chart shows the actual vs. predicted density functions, i.e. number of instances that get the disease / complication at each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



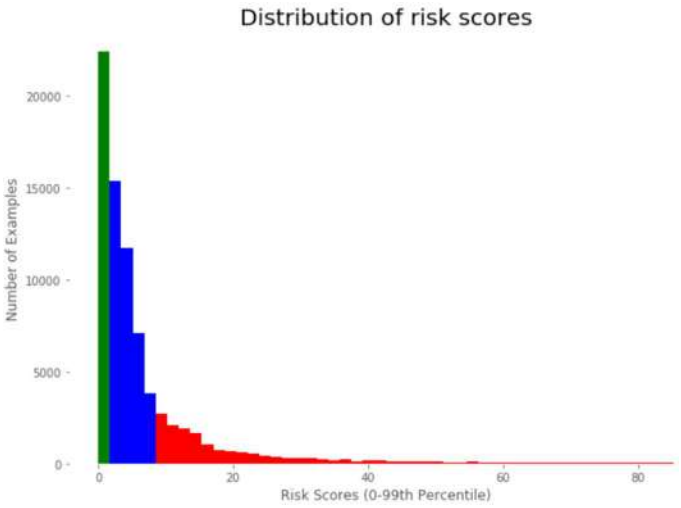
The following chart shows the actual vs. predicted survival functions, i.e. the number of instances that have not had the disease / complication by each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.


Actual vs Predicted
RMSE = 471.742
Median Abs Error = 237.895
Mean Abs Error = 337.510
Actual
Predicted
Confidence Intervals - Lower
Confidence Intervals - Upper
76000
74000
72000
70000
68000
66000
0
10
20
30
40
50

Risk Stratification

The low, medium and high risk groups are defined as examples with predicted risk scores belonging to the first quartile, second to third quartiles, and fourth quartile respectively.

	Percentile	Risk Scores
Low Risk	0-25th	[0.0,1.419]
Medium Risk	26th-75th	[1.419,7.388]
High Risk	75th-100th	[7.388,1738.43798828125]



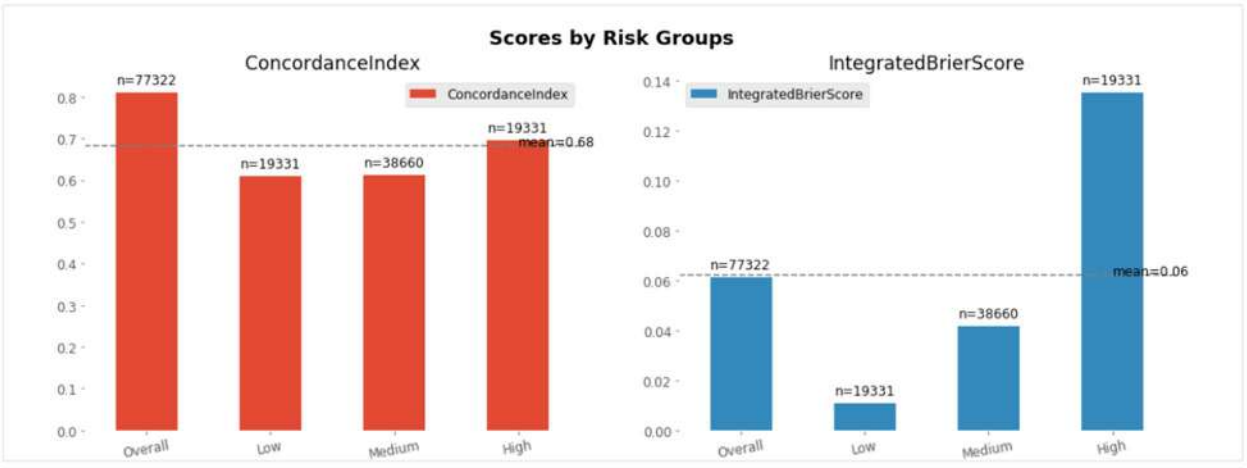
Summary Metrics across Subgroups

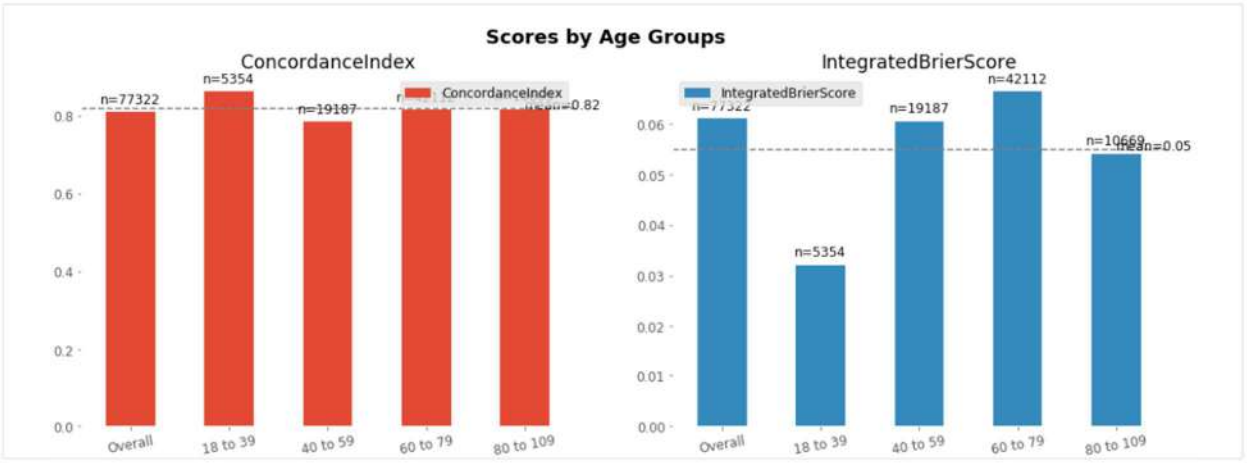
The table below displays the summary metrics across subgroups of risk, age, sex, ethnicity and patient history.

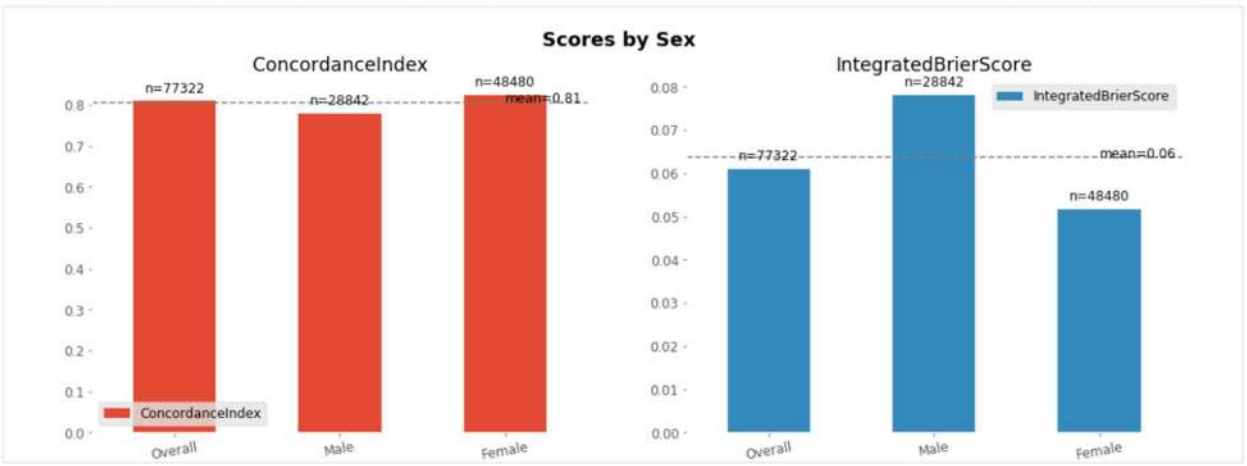
Category	Subgroup	Cohort Size	Concordance Index	Brier Score	Mean AUC	Mean Specificity	Mean Sensitivity	S(t), t=3	S(t), t=6	S(t), t=9	S(t), t=12	S(t), t=18	S(t), t=24
NaN	Overall	77322.00	0.81	0.06	0.82	0.79	0.69	0.98	0.97	0.96	0.95	0.93	0.91
Risk	Low	19331.00	0.61	0.01	0.61	1.00	0.00	1.00	1.00	1.00	1.00	0.99	0.99
Risk	Medium	38660.00	0.61	0.04	0.62	1.00	0.01	0.99	0.98	0.98	0.97	0.96	0.95
Risk	High	19331.00	0.70	0.14	0.72	0.12	0.97	0.94	0.91	0.88	0.85	0.81	0.76
Age Bucket	18 to 39	5354.00	0.86	0.03	0.87	0.93	0.53	0.99	0.98	0.98	0.98	0.97	0.96
Age Bucket	40 to 59	19187.00	0.78	0.06	0.80	0.82	0.63	0.98	0.97	0.96	0.95	0.93	0.92
Age Bucket	60 to 79	42112.00	0.82	0.07	0.82	0.75	0.74	0.98	0.96	0.95	0.94	0.92	0.90
Age Bucket	80 to 109	10669.00	0.82	0.05	0.81	0.87	0.58	0.98	0.98	0.97	0.96	0.95	0.93
Sex	Male	28842.00	0.78	0.08	0.80	0.70	0.75	0.97	0.96	0.95	0.93	0.91	0.89
Sex	Female	48480.00	0.83	0.05	0.83	0.84	0.63	0.98	0.97	0.97	0.96	0.94	0.93
Ethnicity	Hispanic or Latino	4197.00	0.87	0.06	0.87	0.83	0.70	0.98	0.97	0.96	0.95	0.93	0.92
Ethnicity	Not Hispanic or Latino	73125.00	0.81	0.06	0.82	0.79	0.69	0.98	0.97	0.96	0.95	0.93	0.91
History Bucket	<= 6	2528.00	0.80	0.07	0.80	0.74	0.71	0.98	0.96	0.95	0.94	0.92	0.90
History Bucket	7 to 12	6661.00	0.83	0.07	0.82	0.76	0.74	0.97	0.96	0.95	0.94	0.92	0.90
History Bucket	13 to 24	21015.00	0.81	0.06	0.82	0.79	0.69	0.98	0.97	0.96	0.95	0.93	0.91
History Bucket	25 to 36	22240.00	0.81	0.04	0.82	0.82	0.66	0.98	0.97	0.96	0.95	0.94	0.92
History Bucket	37 to 60	24878.00	0.83	0.03	nan	nan	0.70	0.98	0.97	0.96	0.95	0.94	0.92

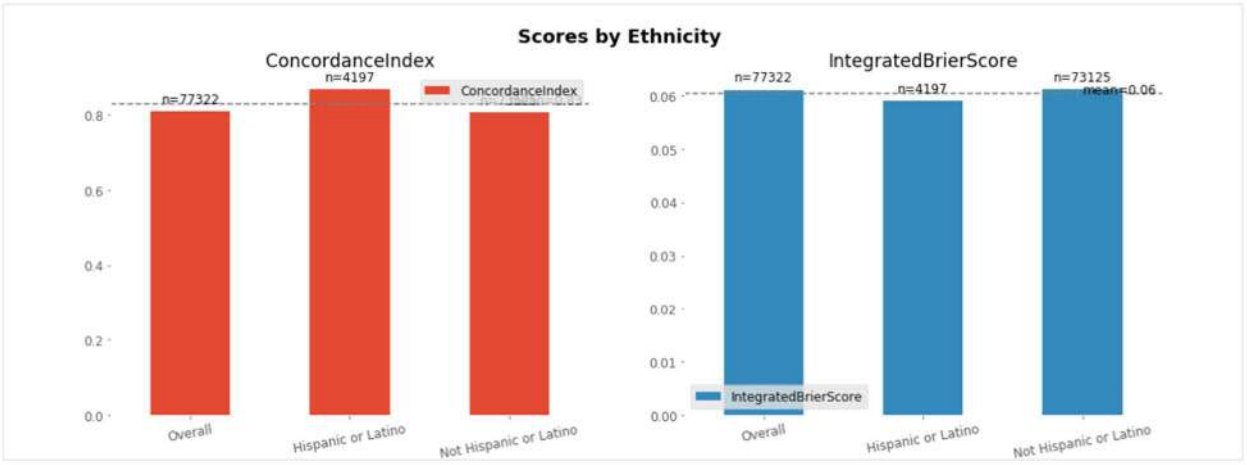
Concordance Index & Integrated Brier Score

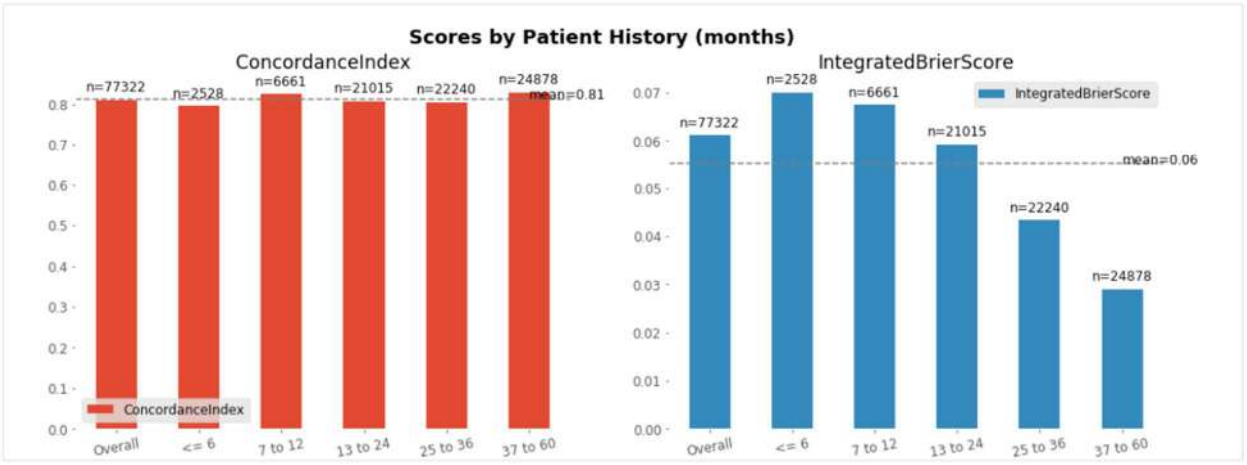
The following charts show how the Concordance Index and Integrated Brier Score varies among subgroups of risk, age, sex, ethnicity and patient history.





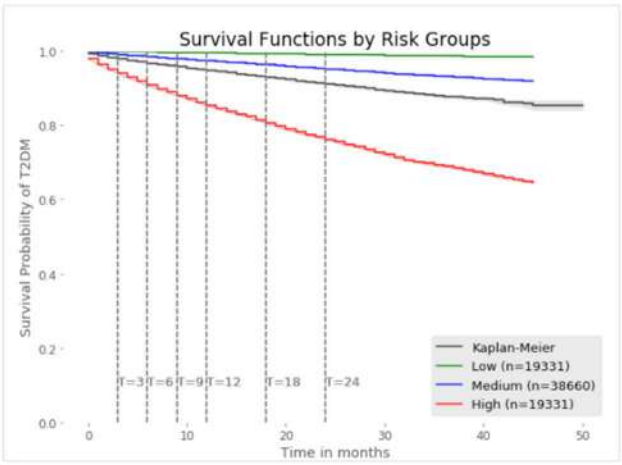


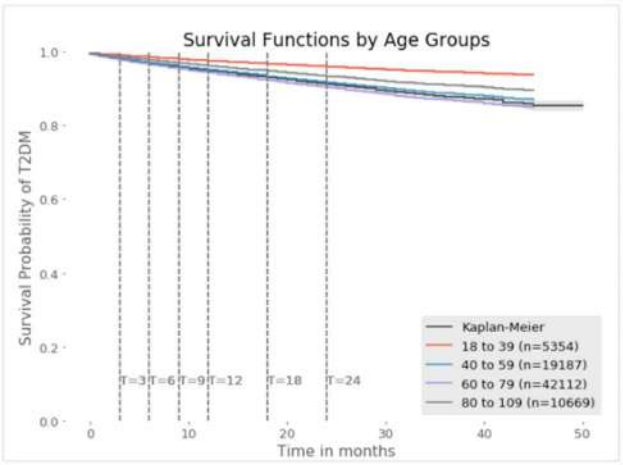

Scores by Ethnicity
ConcordanceIndex
n=77322
n=4197
ConcordanceIndex
0.8
0.6
0.4
0.2
0.0
Overall
Hispanic or Latino
Not Hispanic or Latino
IntegratedBrierScore
n=77322
n=4197
n=73125
mean=0.06
0.06
0.05
0.04
0.03
0.02
0.01
0.00
IntegratedBrierScore
Overall
Hispanic or Latino
Not Hispanic or Latino

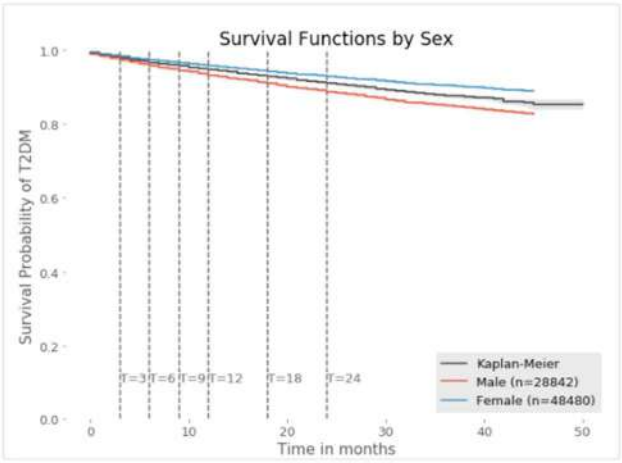

Scores by Patient History (months)
ConcordanceIndex
n=77322
n=2528
n=6661
n=21015
n=22240
n=24878
mean=0.81
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
ConcordanceIndex
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60
IntegratedBrierScore
n=77322
n=2528
n=6661
n=21015
n=22240
n=24878
mean=0.06
IntegratedBrierScore
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60

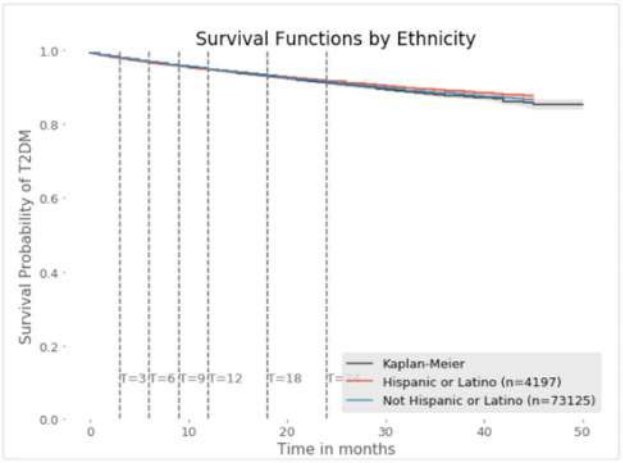
Average Survival Function Curves

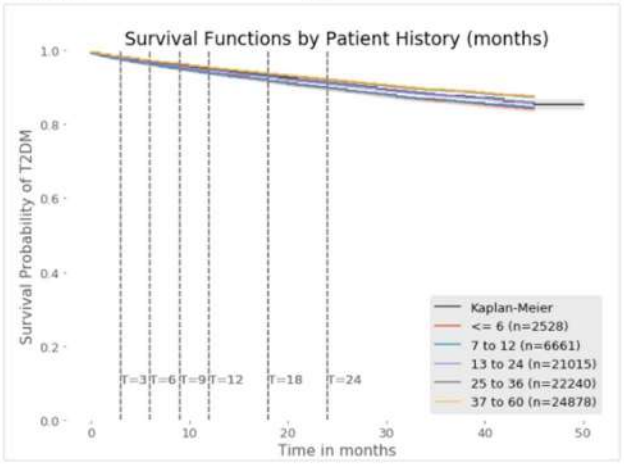
The following charts show how the average survival function curve varies among subgroups of risk, age, sex, ethnicity and patient history.





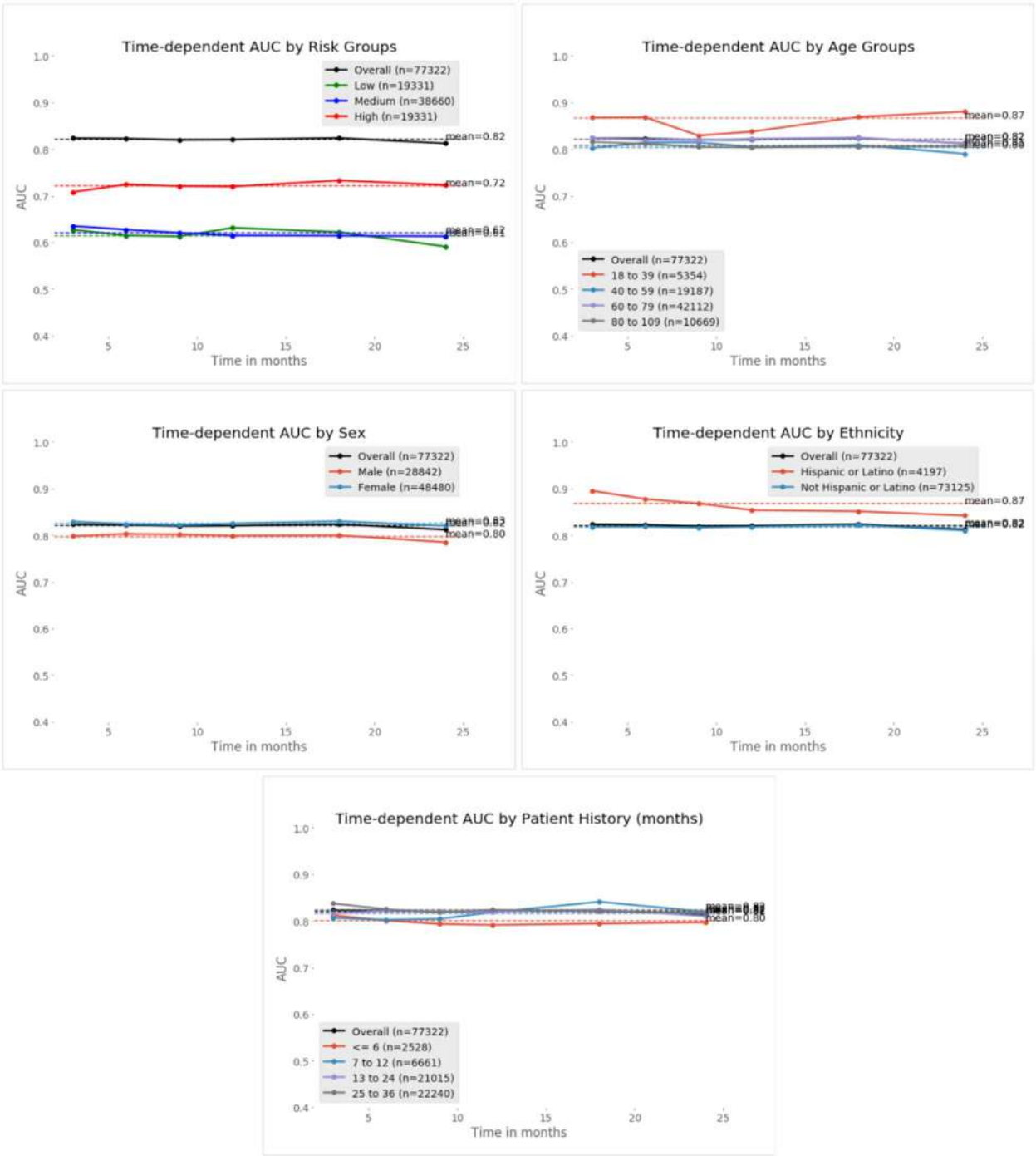






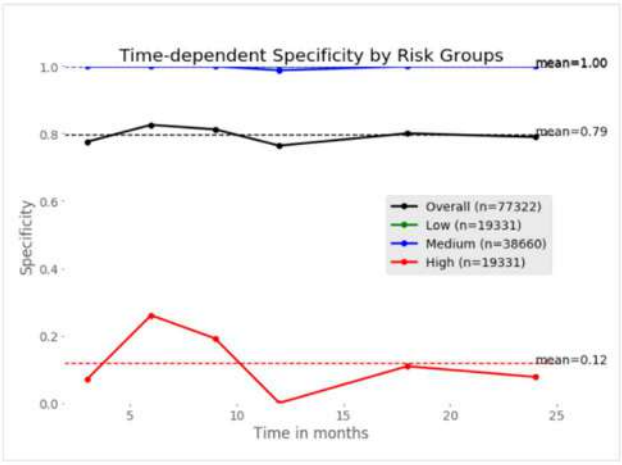
Time-dependent AUC

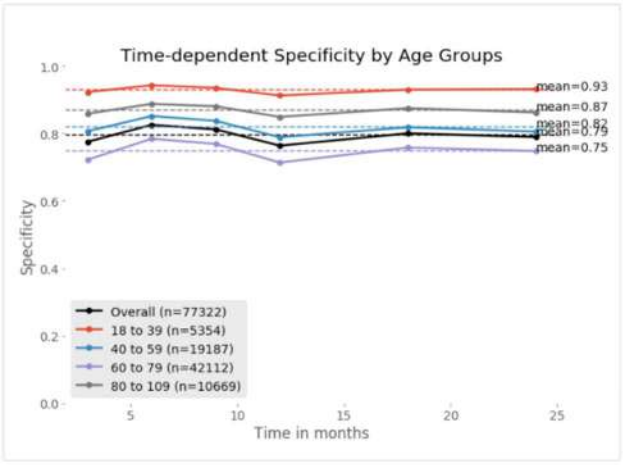
The following charts show how the AUC across time varies among subgroups of risk, age, sex, ethnicity and patient history.

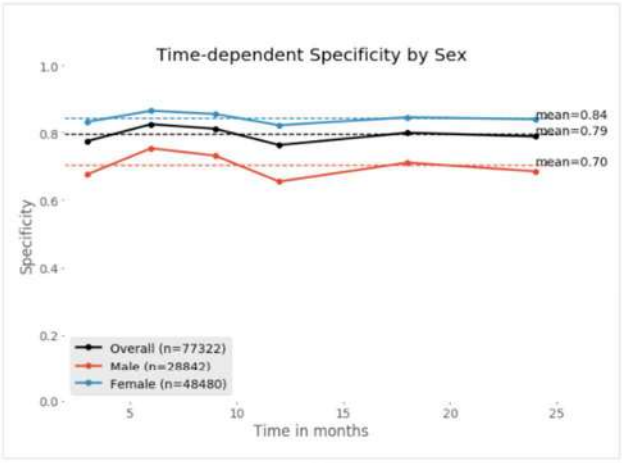


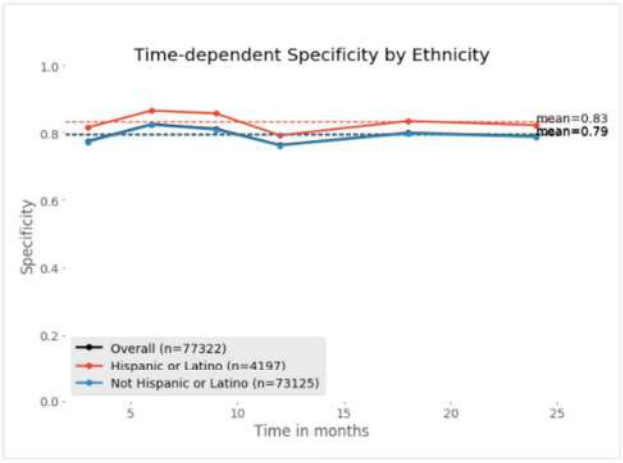
Time-dependent Specificity

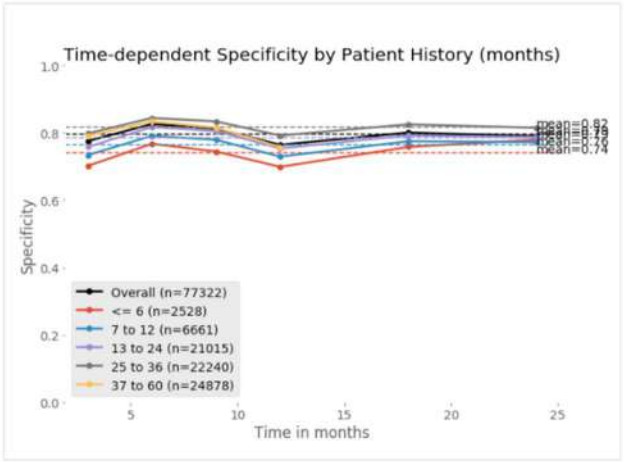
The following charts show how the specificity across time varies among subgroups of risk, age, sex, ethnicity and patient history.





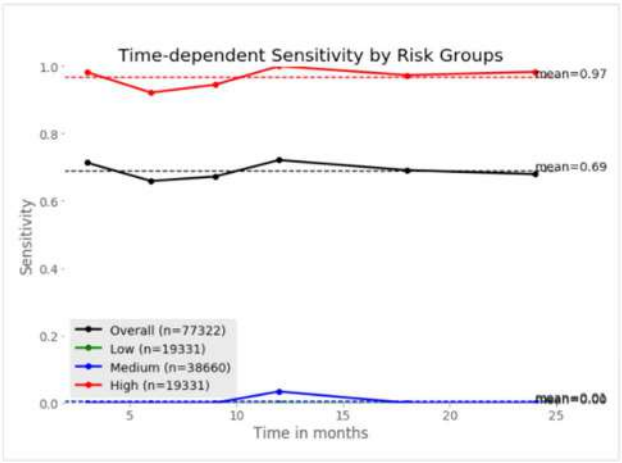


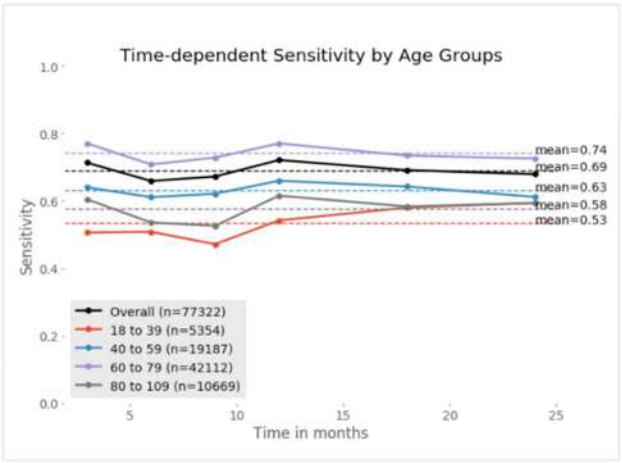


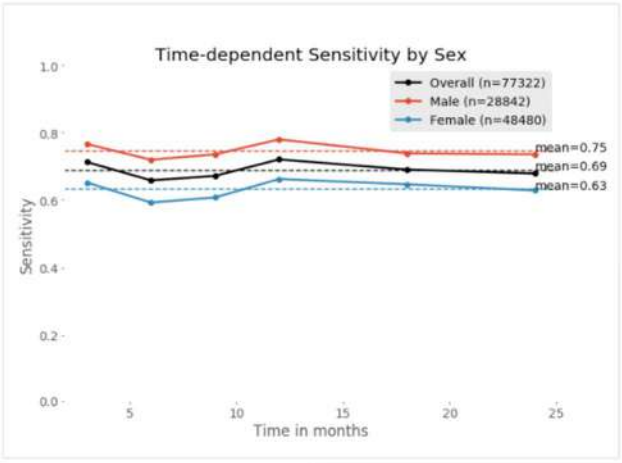


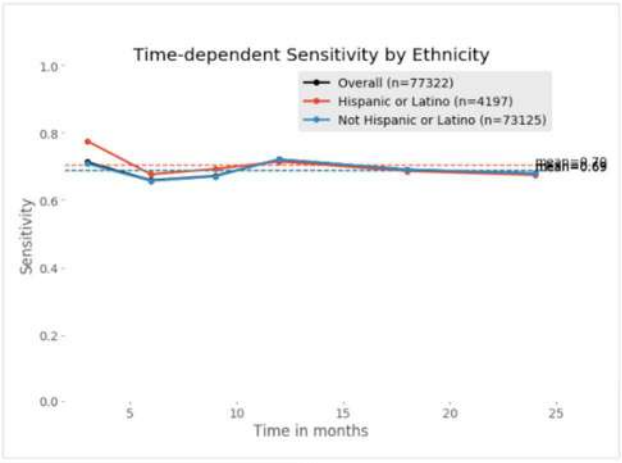
Time-dependent Sensitivity

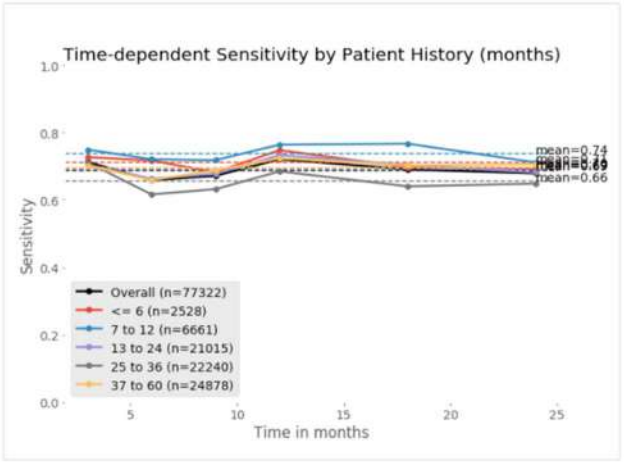
The following charts show how the sensitivity across time varies among subgroups of risk, age, sex, ethnicity and patient history.







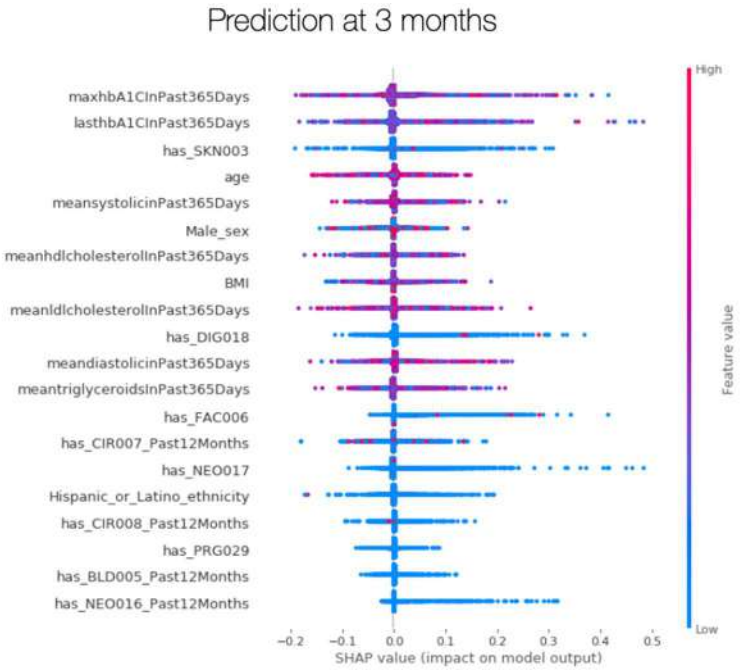


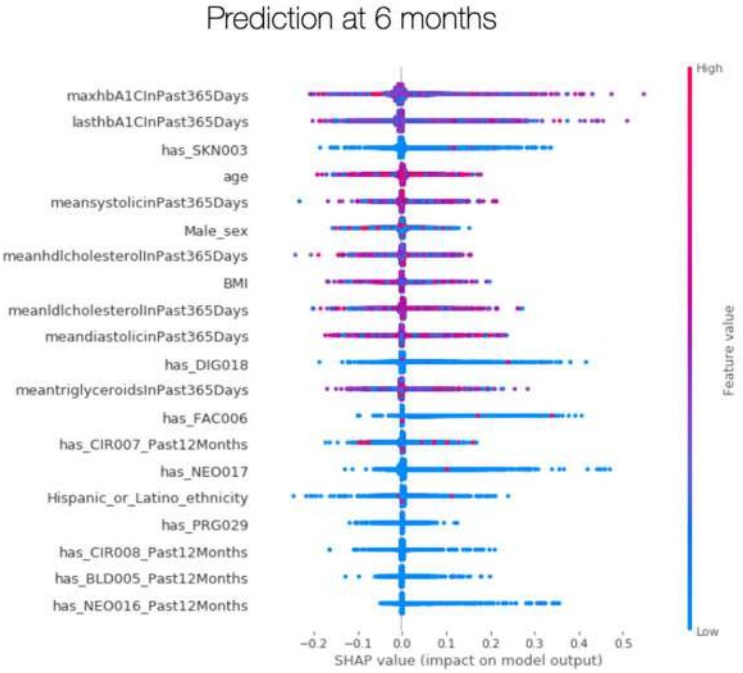


Model Explanation (DeepSurv)

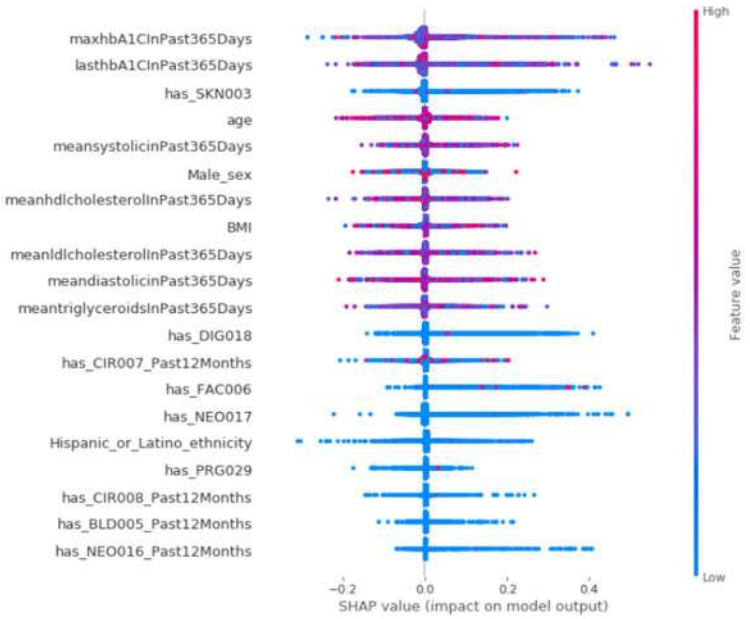
Global

The following plots show the SHAP values of each instance in the training set for each future time (3, 6, 9, 12, 18 and 24 months). The features are sorted by the total magnitude of the SHAP values over all instances and the distribution of the effect that each feature has on the model's output can be observed.

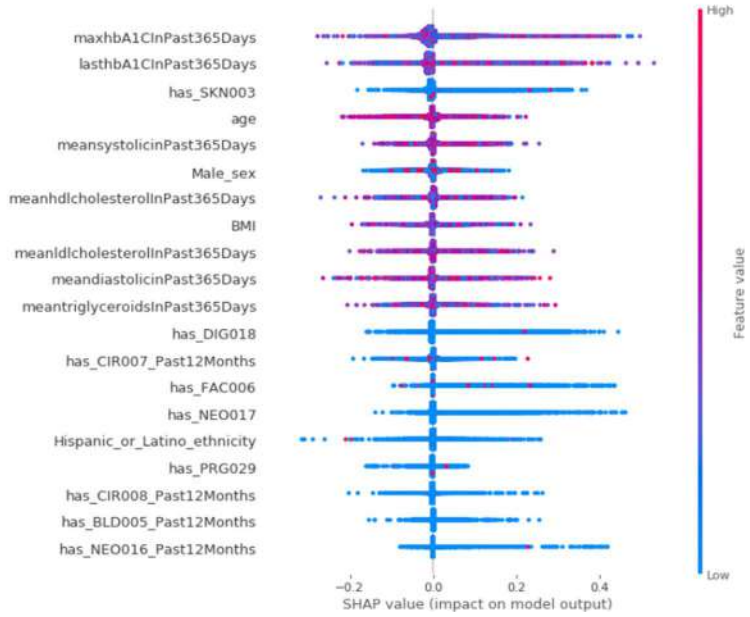




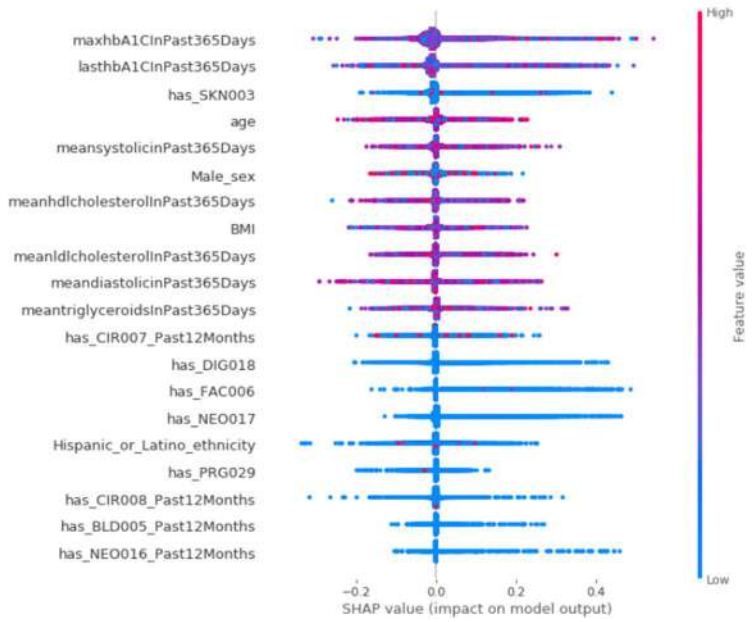
Prediction at 9 months



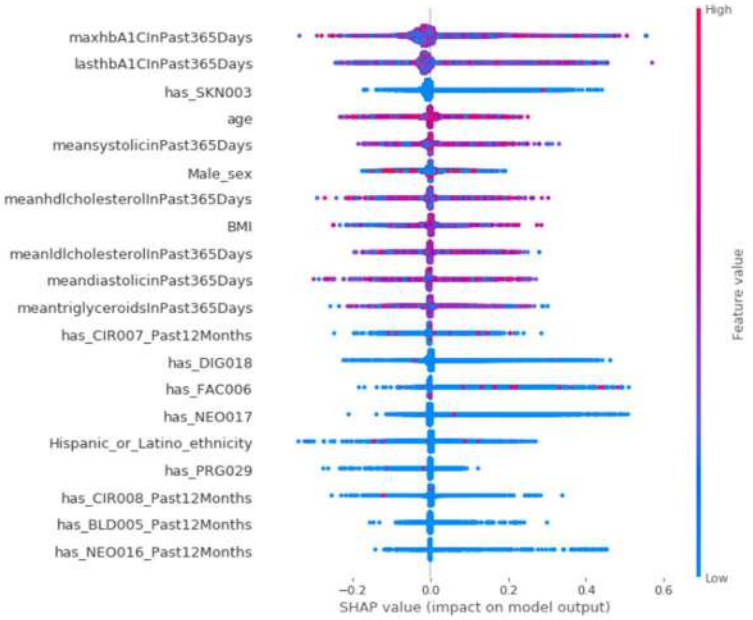
Prediction at 12 months



Prediction at 18 months

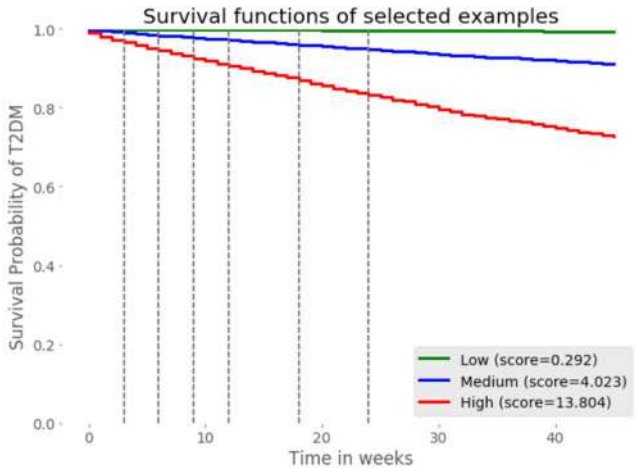


Prediction at 24 months

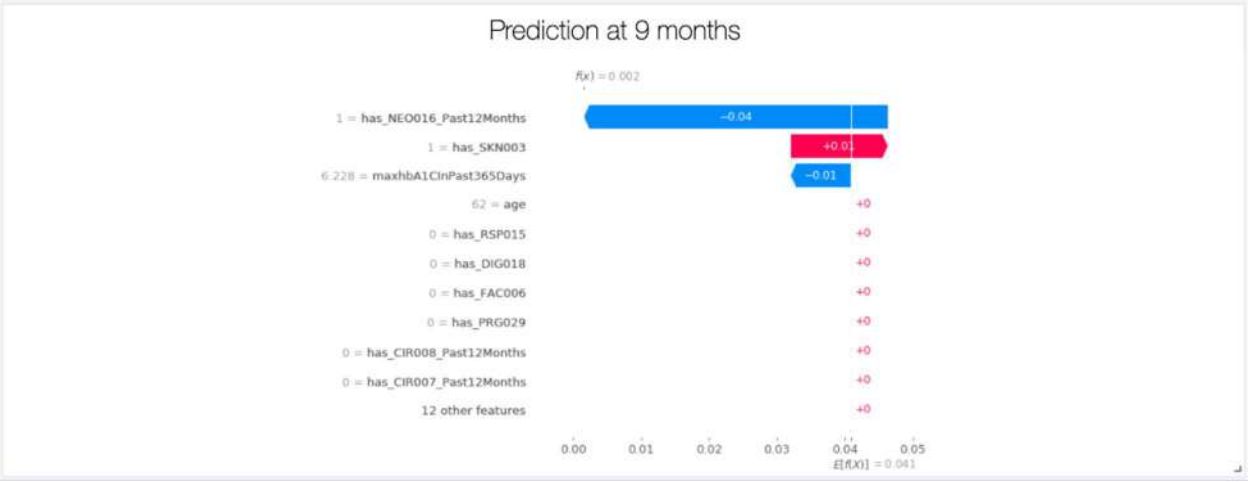


Local

SHAP values were also generated to explain the predictions of individual examples for each future time (3, 6, 9, 12, 18 and 24 months). A total of 3 examples were selected by sampling of risk scores at the 5th, 50th and 95th percentile to represent instances at low, medium and high risks respectively.

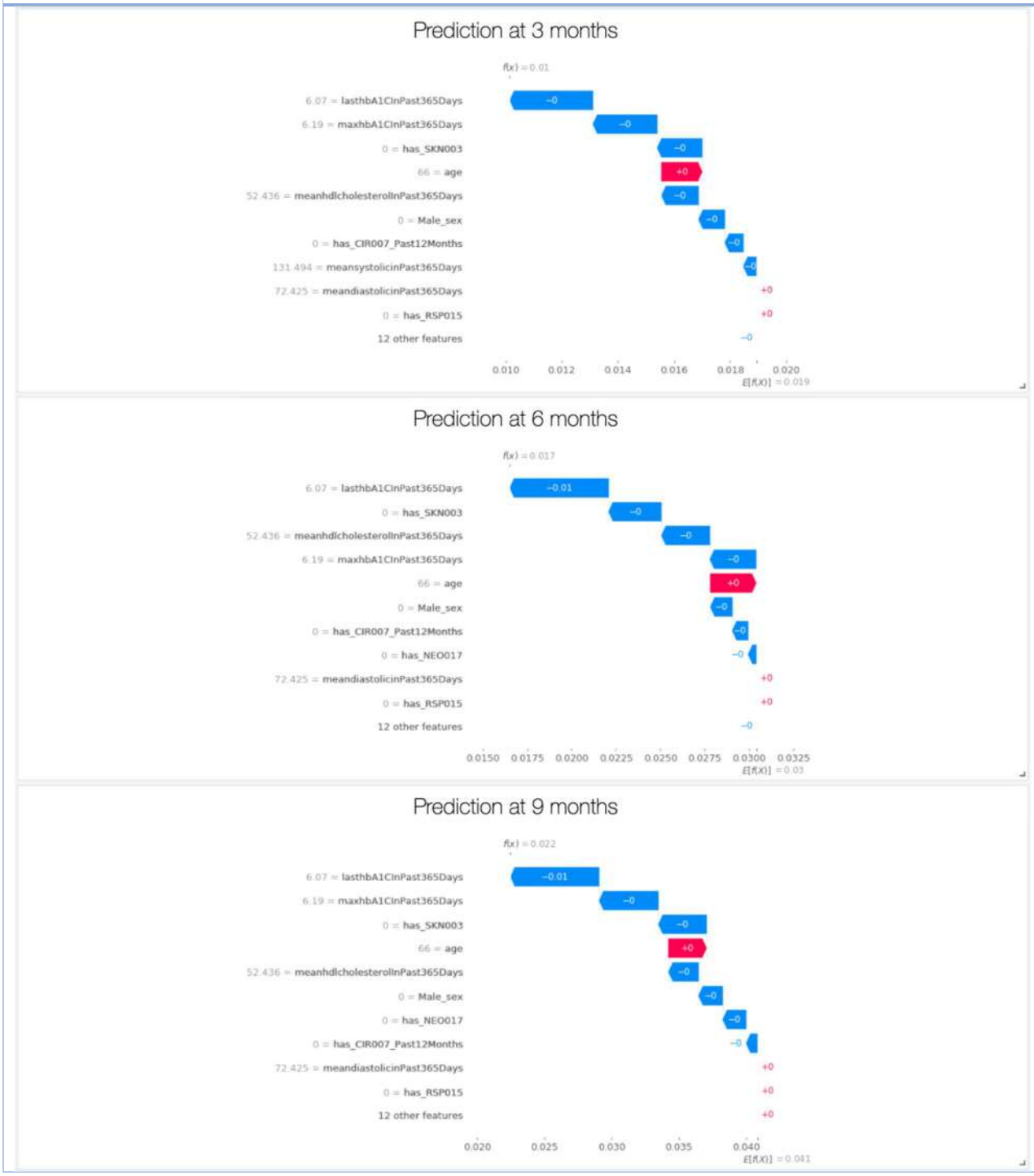


Low Risk
Risk Score: 0.292



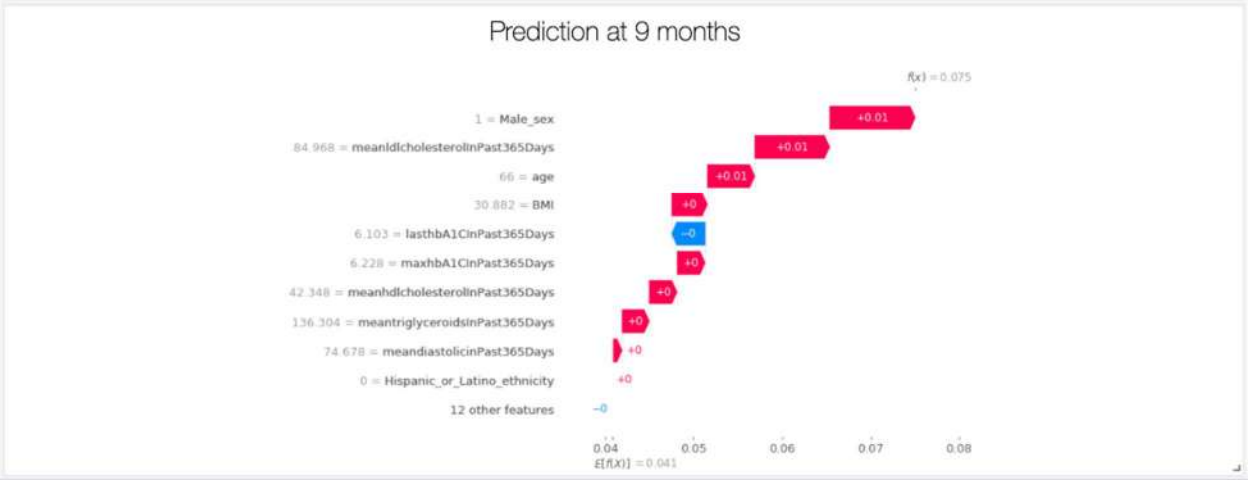
Low Risk
Risk Score: 0.292

Medium Risk
Risk Score: 4.023

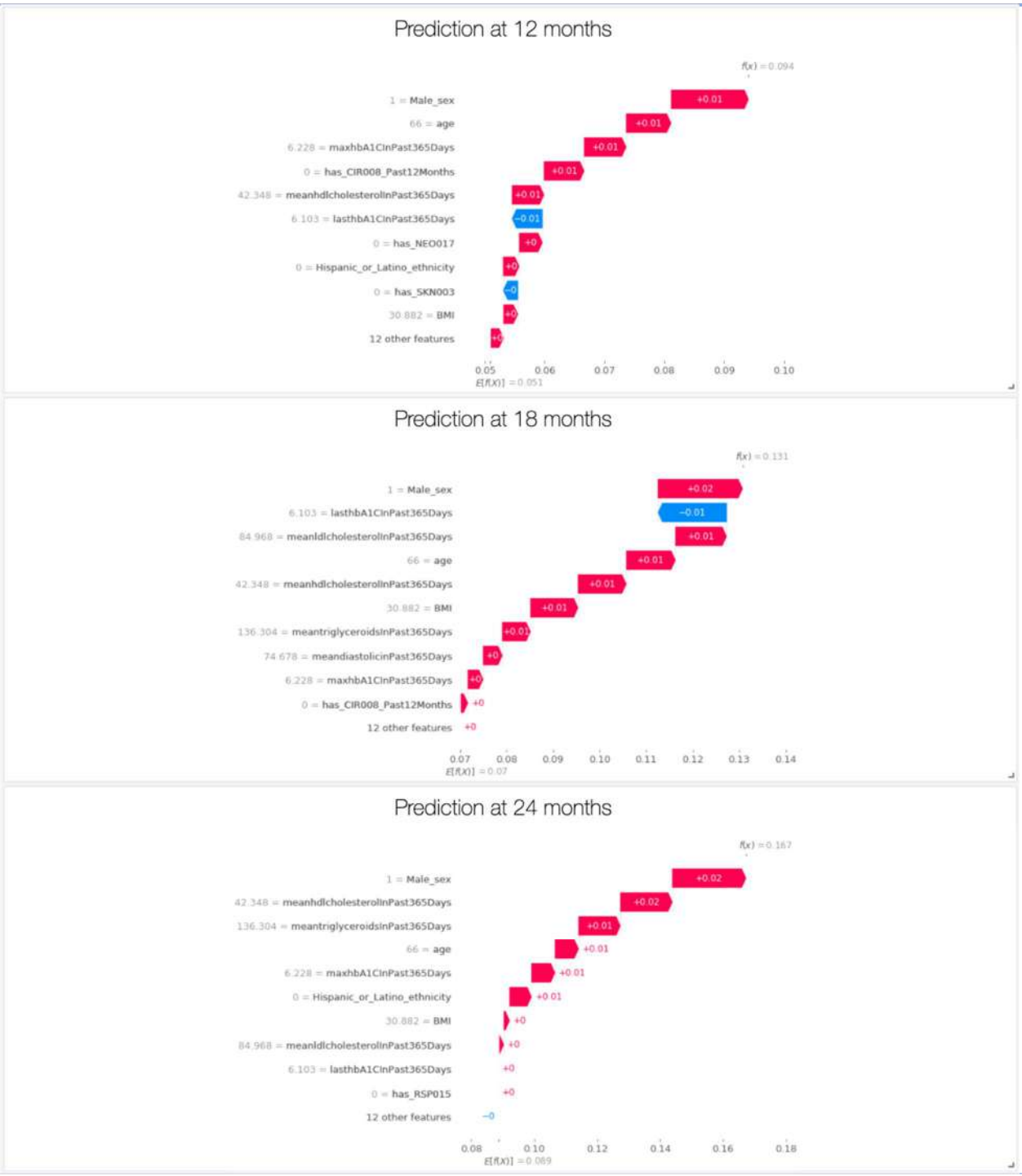


Medium Risk
Risk Score: 4.023

High Risk
Risk Score: 13.804



High Risk
Risk Score: 13.804



DM to Uncontrolled DM Prediction

Item	Specification
Business Goal	Enable care managers to identify the patients who are at risk of developing uncontrolled DM
Usage Setting	Outpatient
ML Task	Predict risk and/or time from DM to uncontrolled DM
ML Class	Survival
Instances for Prediction	Encounters
Labels for Instances	Binary indicator and time to event or censoring for uncontrolled DM • Binary indicator $\delta = \begin{cases} 1, & Uncontrolled\ T2DM \\ 0, & No\ Uncontrolled\ T2DM \end{cases}$ • Time to event (or censoring) $y = \begin{cases} T, & \delta = 1 \\ C, & \delta = 0 \end{cases}$
Cohort Criteria	• 2016-01-01 $\leq$ encounter date $\leq$ 2020-06-30 (available Epic data, excluding outliers) • Encounter date is not within the first 90 days of when the patient entered the data set, to adjust for left-censoring • 18 $\leq$ age $\leq$ 110 (adults without outliers) • No T1DM diagnosis • Not pregnant • No "Do Not Resuscitate" diagnosis • DM event before encounter date • No uncontrolled DM event before encounter date • No uncontrolled DM event up to 6 days after encounter date (encounters where lab results confirm event within the week)

Input Features	• Demographic
	• Diagnosis, except:
	  ○ hasDiabetes*
	  ○ has_END002* (Diabetes mellitus without complication)
	  ○ has_END003* (Diabetes mellitus with complication)
	  ○ has_END004* (Diabetes mellitus, Type 1)
	  ○ has_END005* (Diabetes mellitus, Type 2)
	  ○ has_END006* (iabetes mellitus, due to underlying condition, drug or chemical induced, or other specified type)
	• Labs
	• Utilization
	• Vitals
	
	See Appendix E for details.

Evaluation Metrics	• Concordance Index • Integrated Brier Score

Data

The following charts summarize the key characteristics of the data after applying the cohort criteria stated above, along with selected features (see Model Signature below).

Category	summary / Variable	count	mean	stddev	min	25%	50%	75%	max
Demographic	AgeBucket_18_to_39	49849.0	0.038035	0.191282	0.00	0.000	0.000	0.000	1.00
	AgeBucket_40_to_59	49849.0	0.226785	0.418757	0.00	0.000	0.000	0.000	1.00
	AgeBucket_60_to_79	49849.0	0.584325	0.492843	0.00	0.000	1.000	1.000	1.00
	AgeBucket_80_to_109	49849.0	0.150856	0.357912	0.00	0.000	0.000	0.000	1.00
	Sex_Female	49849.0	0.549780	0.497521	0.00	0.000	1.000	1.000	1.00
	Sex_Male	49849.0	0.450220	0.497521	0.00	0.000	0.000	1.000	1.00
	Ethnicity_Hispanic_or_Latino	49849.0	0.062288	0.241681	0.00	0.000	0.000	0.000	1.00
	Ethnicity_Not_Hispanic_or_Latino	49849.0	0.937712	0.241681	0.00	1.000	1.000	1.000	1.00
Encounter	EncounterType_Emergency	49849.0	0.212341	0.408969	0.00	0.000	0.000	0.000	1.00
	EncounterType_Inpatient	49849.0	0.113864	0.317649	0.00	0.000	0.000	0.000	1.00
	EncounterType_Outpatient	49849.0	0.673795	0.468828	0.00	0.000	1.000	1.000	1.00
Label	Time	49849.0	15.095669	11.302945	0.00	5.000	13.000	23.000	49.00
	Event	49849.0	0.106682	0.308712	0.00	0.000	0.000	0.000	1.00
Feature	age	49849.0	66.416297	13.014329	18.00	59.000	68.000	75.000	102.00
	Male_sex	49849.0	0.450220	0.497521	0.00	0.000	0.000	1.000	1.00
	Hispanic_or_Latino_ethnicity	49849.0	0.062288	0.241681	0.00	0.000	0.000	0.000	1.00
	lasthbA1ClnPast365Days	49849.0	6.871925	0.766836	3.60	6.600	6.866	7.200	8.90
	meandiastolicinPast365Days	49849.0	72.694129	7.925292	43.62	68.888	73.000	76.790	107.56
	meansystolicinPast365Days	49849.0	131.636895	11.790046	81.00	127.316	131.065	136.050	180.00
	BMI	49849.0	32.705948	6.495782	10.37	29.190	32.440	35.570	80.03
	meantriglyceroidsInPast365Days	49849.0	161.155430	52.310612	19.00	138.000	163.096	170.874	458.00
	meanldlcholesterolInPast365Days	49849.0	85.611683	21.682910	8.00	80.720	85.917	95.500	200.00
	meanhdlcholesterolInPast365Days	49849.0	43.558758	9.079637	5.00	39.813	43.000	47.864	97.00
	has_MAL004_Past12Months	49849.0	0.000622	0.024930	0.00	0.000	0.000	0.000	1.00
	has_CIR007_Past12Months	49849.0	0.196774	0.397564	0.00	0.000	0.000	0.000	1.00
	has_NEO061_Past12Months	49849.0	0.001063	0.032590	0.00	0.000	0.000	0.000	1.00
	has_CIR008_Past12Months	49849.0	0.011134	0.104928	0.00	0.000	0.000	0.000	1.00
	has_EXT030	49849.0	0.001324	0.036363	0.00	0.000	0.000	0.000	1.00
	has_NEO029	49849.0	0.004674	0.068208	0.00	0.000	0.000	0.000	1.00
	has_END013	49849.0	0.005055	0.070921	0.00	0.000	0.000	0.000	1.00
	has_CIR038	49849.0	0.006038	0.077472	0.00	0.000	0.000	0.000	1.00
	has_MUS029	49849.0	0.007182	0.084441	0.00	0.000	0.000	0.000	1.00

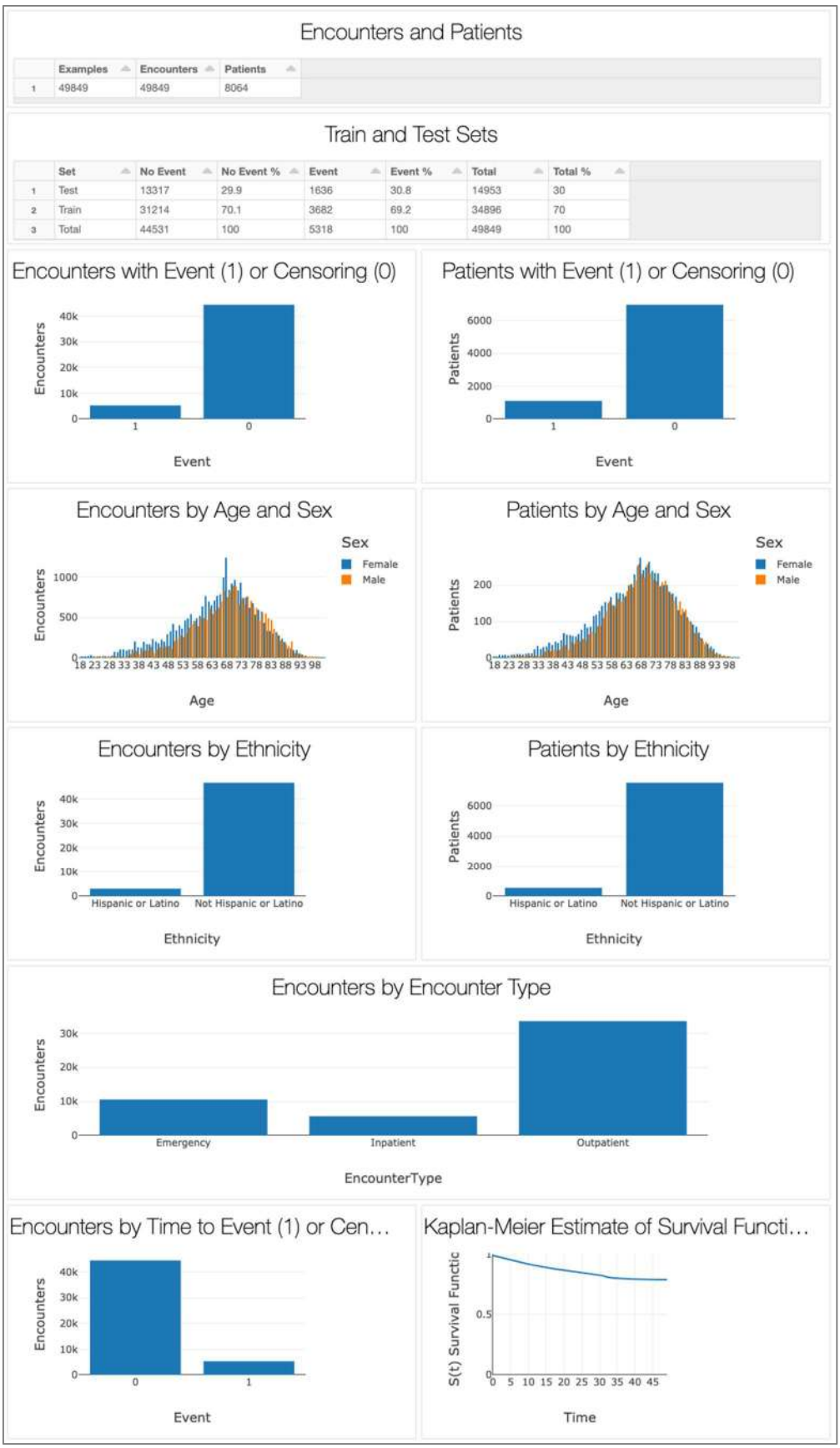
(Percentages for binary variables can be read from the “mean” column.)

Encounters and Patients

	Examples	Encounters	Patients
1	49849	49849	8064

Train and Test Sets

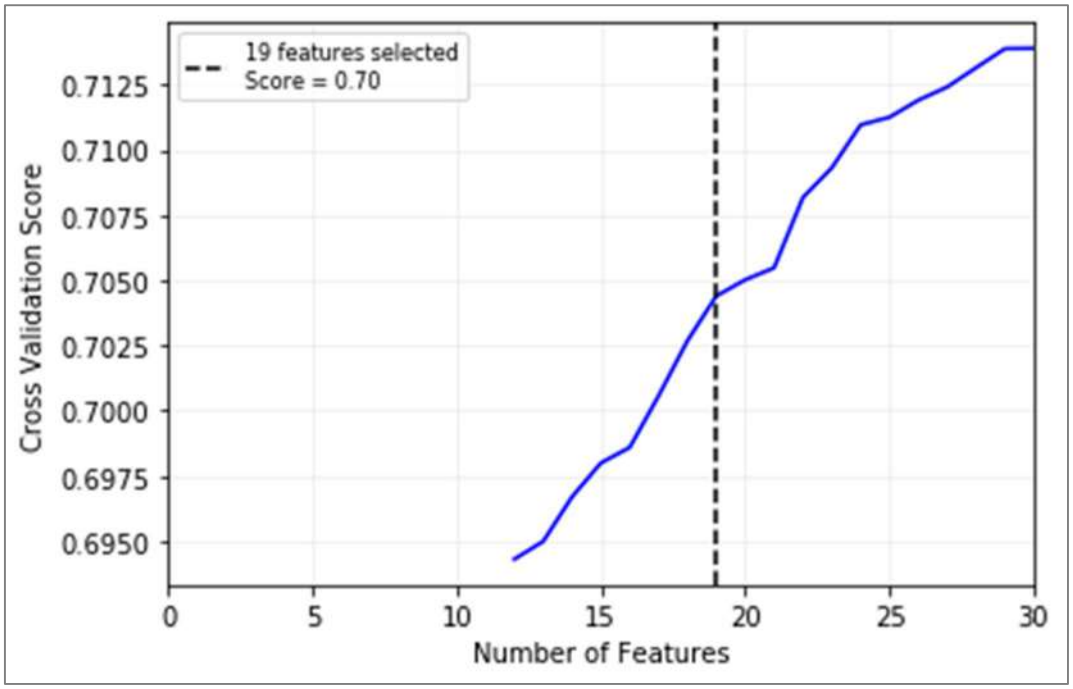
	Set	No Event	No Event %	Event	Event %	Total	Total %
1	Test	13317	29.9	1636	30.8	14953	30
2	Train	31214	70.1	3682	69.2	34896	70
3	Total	44531	100	5318	100	49849	100



Model Signature

The model signature has 19 features, comprising of 12 mandatory features and 7 other selected features. These are the selected features, in rank order (the last feature to be eliminated is ranked 1):

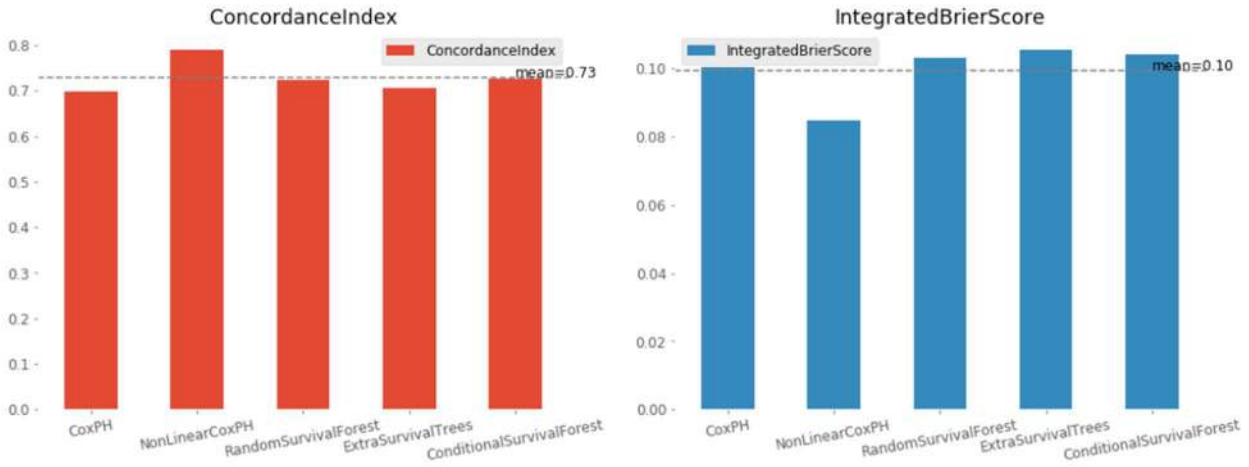
1. has_CIR038 (Postprocedural or postoperative circulatory system complication)
2. has_END013 (Pituitary disorders)
3. has_MAL004_Past12Months (Nervous system congenital anomalies)
4. has_EXT030 (External cause codes: sequela)
5. has_NEO061_Past12Months (Leukemia - chronic lymphocytic leukemia (CLL))
6. has_MUS029 (Disorders of jaw)
7. has_NEO029 (Breast cancer - ductal carcinoma in situ (DCIS))
8. lasthbA1CInPast365Days
9. Hispanic_or_Latino_ethnicity
10. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)
11. has_CIR007_Past12Months (Essential hypertension)
12. BMI
13. Male_sex
14. age
15. meansystolicinPast365Days
16. meanhdlcholesterolInPast365Days
17. meandiastolicinPast365Days
18. meanldlcholesterolInPast365Days
19. meantriglyceroidsInPast365Days



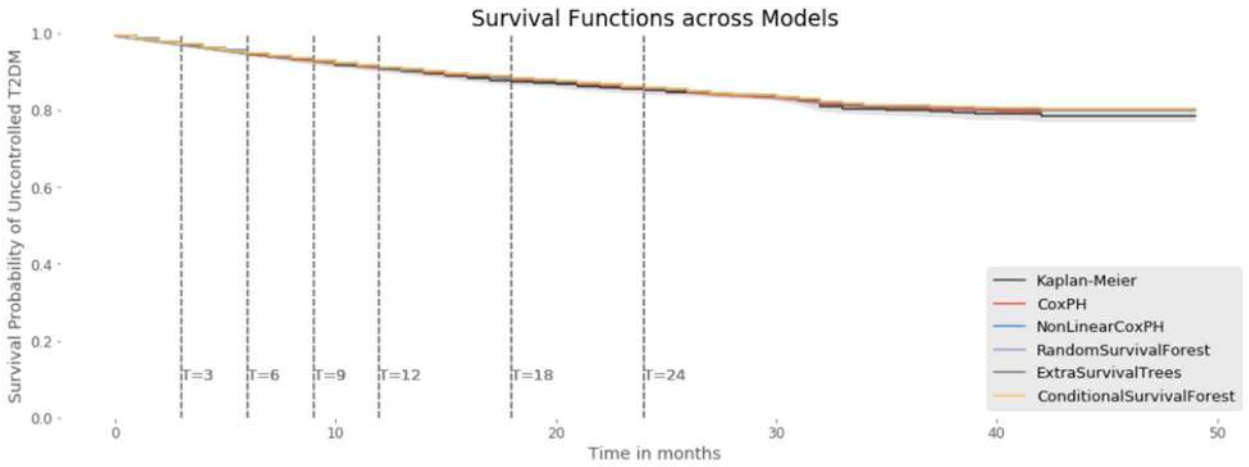
Model Performance

The following table and chart summarize the performance of all candidate models on the test set for this prediction task in terms of the Concordance Index and the Integrated Brier Score.

Model	No. of Parameter Combinations Successfully Tested	Concordance Index	Integrated Brier Score
CoxPH	94	0.70	0.10
DeepSurv	161	**0.79**	**0.08**
RSF	143	0.72	0.10
CSF	82	0.71	0.11
EST	71	0.73	0.10



The following chart shows how the average survival function curves of the candidate models compare to the KM survival curve, the more similar their curves are to the KM survival curve the better.

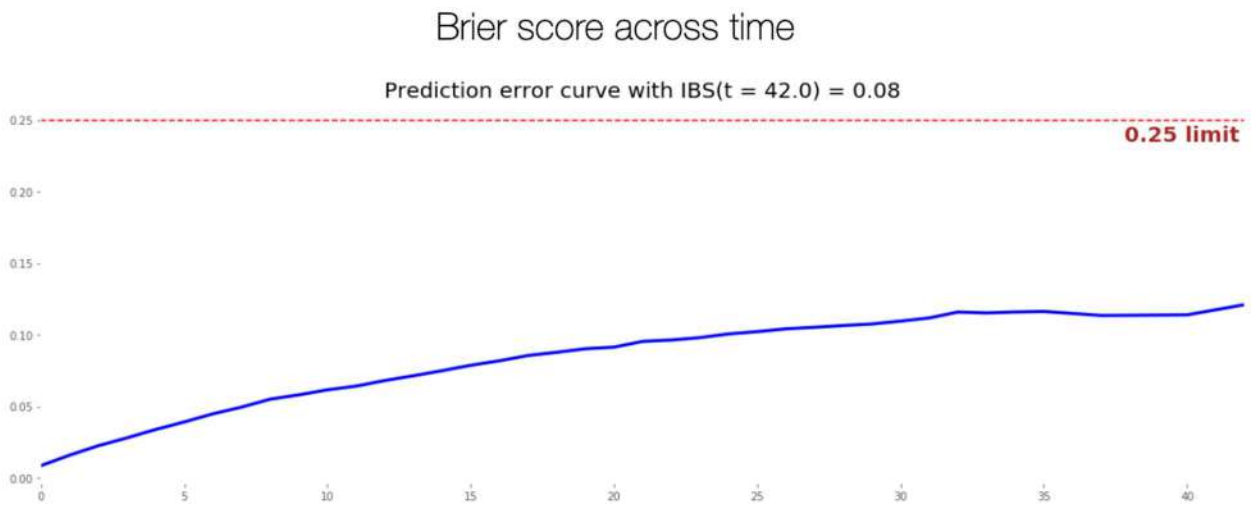


This chart shows the change in the Brier Score over time for all candidate models, the closer the scores are to 0 the better.

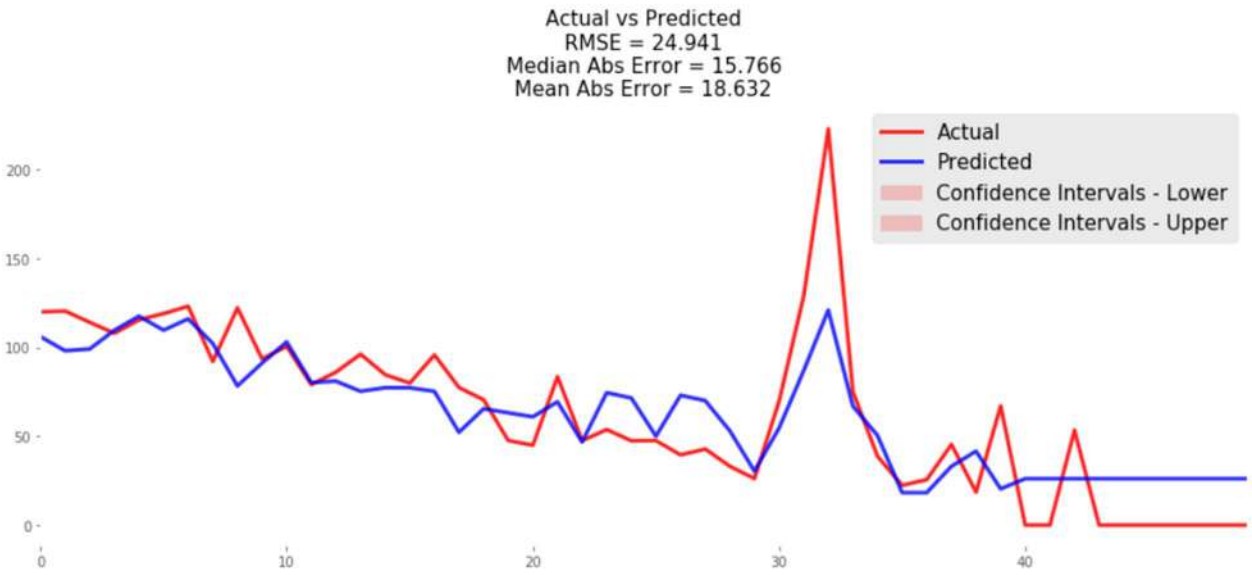
Model Evaluation of Selected Model (DeepSurv)

Overall

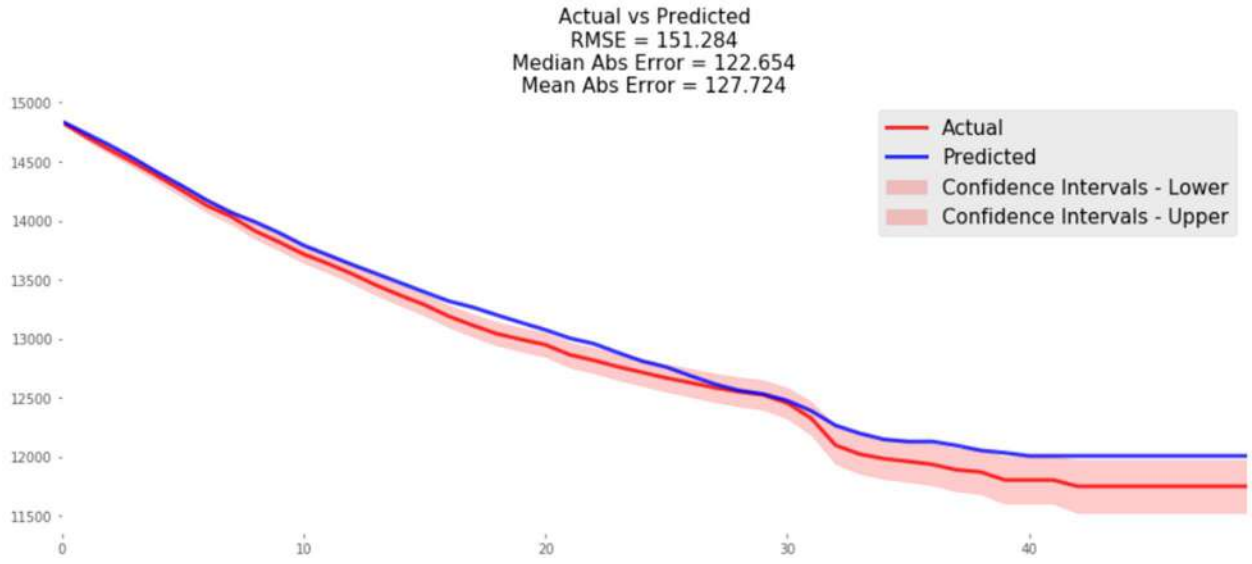
This chart shows the change in the Brier Score over time for the selected model, the closer the scores are to 0 the better.



The following chart shows the actual vs. predicted density functions, i.e. number of instances that get the disease / complication at each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



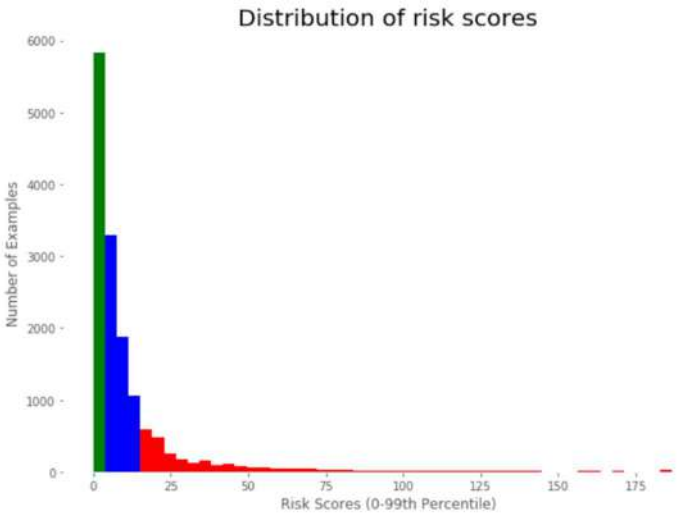
The following chart shows the actual vs. predicted survival functions, i.e. the number of instances that have not had the disease / complication by each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



Risk Stratification

The low, medium and high risk groups are defined as examples with predicted risk scores belonging to the first quartile, second to third quartiles, and fourth quartile respectively.

	Percentile	Risk Scores
Low Risk	0-25th	[0.0,2.044]
Medium Risk	26th-75th	[2.044,12.049]
High Risk	75th-100th	[12.049,65906.4140625]



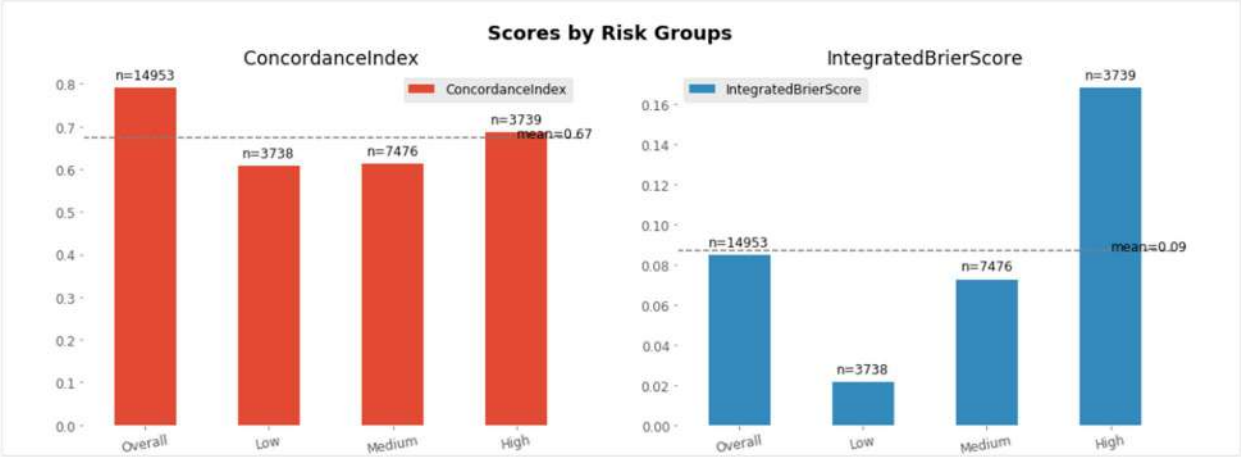
Summary Metrics across Subgroups

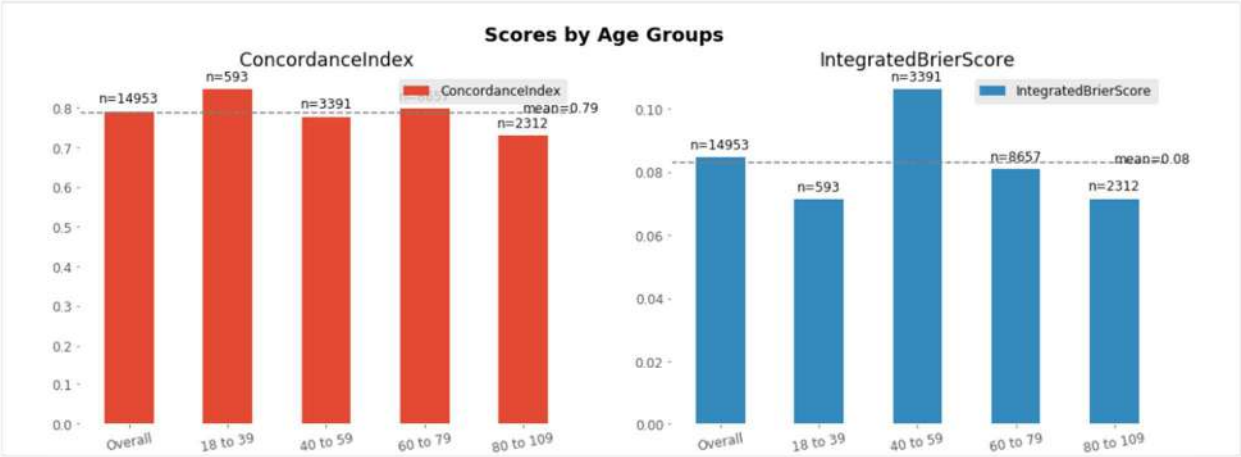
The table below displays the summary metrics across subgroups of risk, age, sex, ethnicity and patient history.

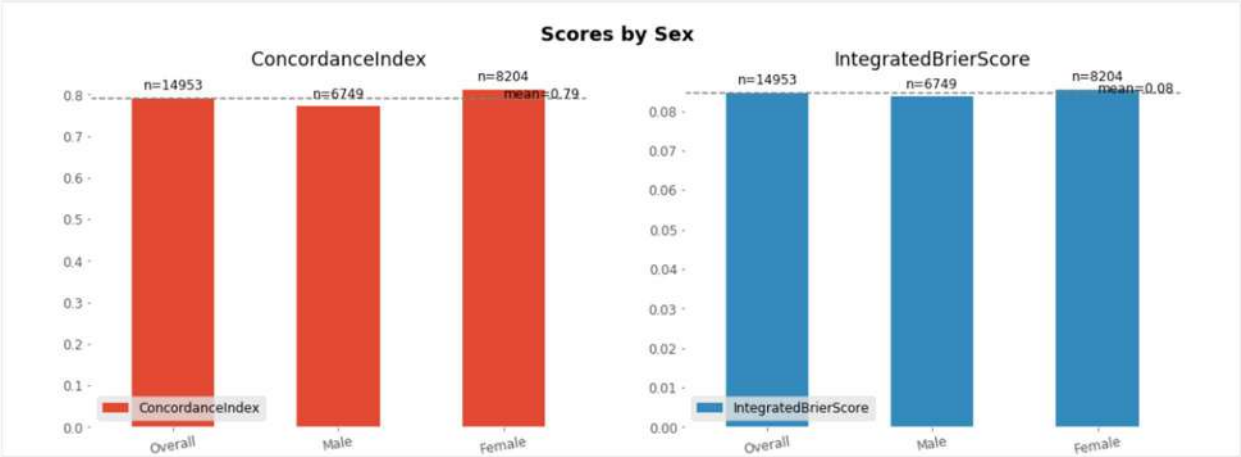
Category	Subgroup	Cohort Size	Concordance Index	Brier Score	Mean AUC	Mean Specificity	Mean Sensitivity	S(t), t=3	S(t), t=6	S(t), t=9	S(t), t=12	S(t), t=18	S(t), t=24
NaN	Overall	14953.00	0.79	0.08	0.80	0.73	0.73	0.97	0.94	0.92	0.91	0.87	0.85
Risk	Low	3738.00	0.61	0.02	0.61	1.00	0.00	1.00	1.00	1.00	0.99	0.99	0.99
Risk	Medium	7476.00	0.61	0.07	0.63	0.89	0.25	0.99	0.98	0.96	0.95	0.93	0.91
Risk	High	3739.00	0.69	0.17	0.72	0.00	1.00	0.91	0.84	0.79	0.74	0.67	0.61
Age Bucket	18 to 39	593.00	0.85	0.07	0.86	0.65	0.88	0.96	0.93	0.91	0.89	0.86	0.83
Age Bucket	40 to 59	3391.00	0.78	0.11	0.78	0.63	0.80	0.96	0.93	0.91	0.89	0.85	0.82
Age Bucket	60 to 79	8657.00	0.80	0.08	0.81	0.75	0.71	0.97	0.95	0.93	0.92	0.89	0.86
Age Bucket	80 to 109	2312.00	0.73	0.07	0.76	0.82	0.57	0.98	0.96	0.95	0.94	0.91	0.89
Sex	Male	6749.00	0.77	0.08	0.79	0.73	0.70	0.97	0.95	0.93	0.91	0.89	0.86
Sex	Female	8204.00	0.81	0.09	0.81	0.72	0.76	0.97	0.95	0.93	0.91	0.88	0.85
Ethnicity	Hispanic or Latino	952.00	0.84	0.08	0.83	0.74	0.73	0.96	0.92	0.90	0.88	0.85	0.82
Ethnicity	Not Hispanic or Latino	14001.00	0.79	0.08	0.80	0.73	0.73	0.97	0.95	0.93	0.91	0.89	0.86
History Bucket	<= 6	405.00	0.72	0.09	0.65	0.67	0.62	0.96	0.94	0.92	0.90	0.86	0.83
History Bucket	7 to 12	1524.00	0.81	0.07	0.81	0.74	0.74	0.97	0.95	0.93	0.91	0.88	0.85
History Bucket	13 to 24	4374.00	0.80	0.09	0.80	0.71	0.73	0.97	0.94	0.92	0.90	0.87	0.85
History Bucket	25 to 36	4229.00	0.78	0.07	0.79	0.74	0.70	0.97	0.95	0.94	0.92	0.89	0.87
History Bucket	37 to 60	4421.00	0.83	0.05	nan	nan	0.79	0.97	0.95	0.93	0.91	0.88	0.86

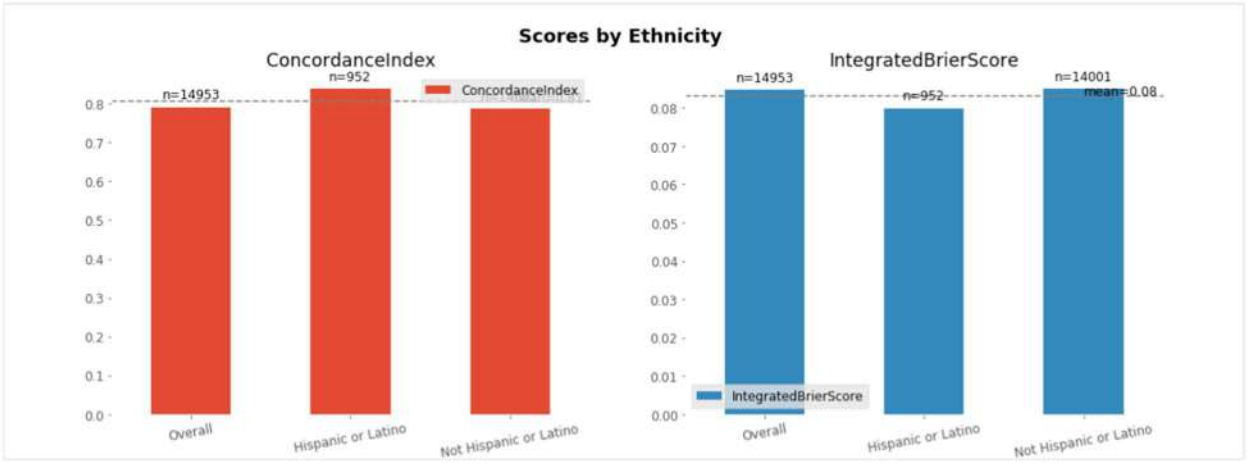
Concordance Index & Integrated Brier Score

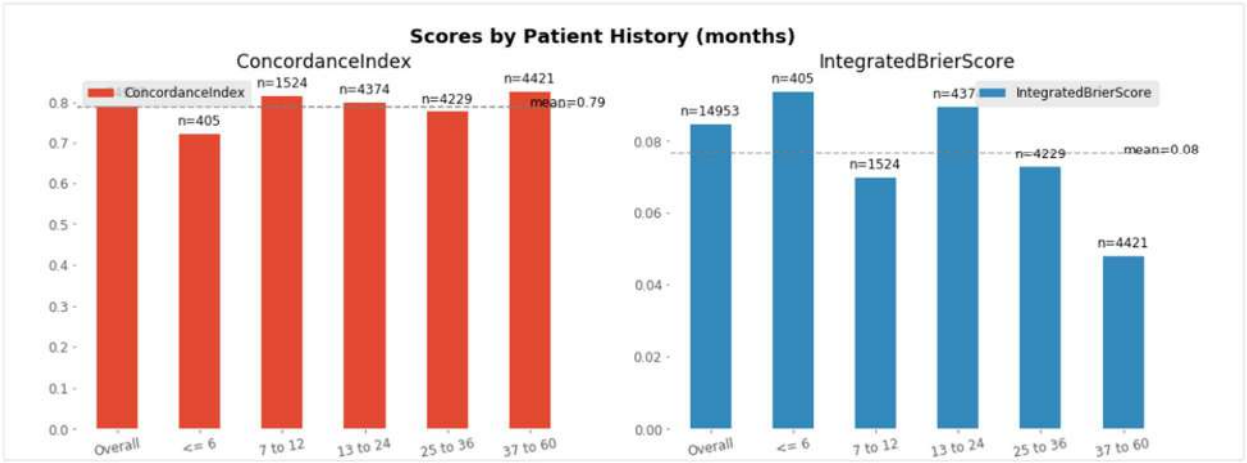
The following charts show how the Concordance Index and Integrated Brier Score varies among subgroups of risk, age, sex, ethnicity and patient history.





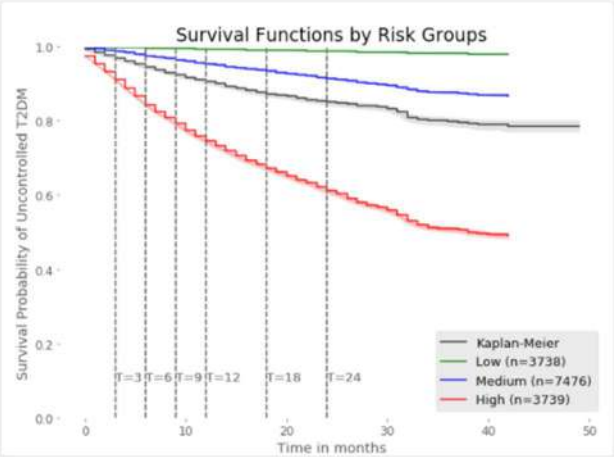


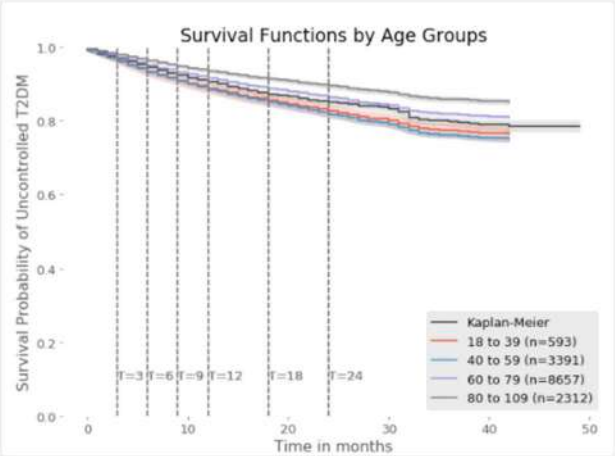

Scores by Ethnicity
ConcordanceIndex
IntegratedBrierScore
n=14953
n=952
n=14001
mean=0.08
Overall
Hispanic or Latino
Not Hispanic or Latino

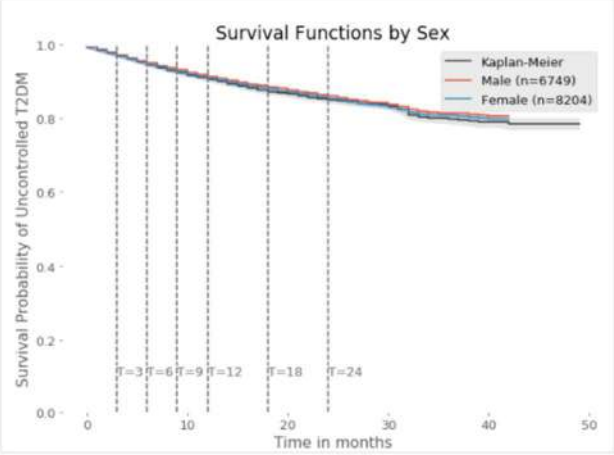

Scores by Patient History (months)
ConcordanceIndex
IntegratedBrierScore
n=14953
n=405
n=1524
n=4374
n=4229
n=4421
mean=0.79
n=437
mean=0.08
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60

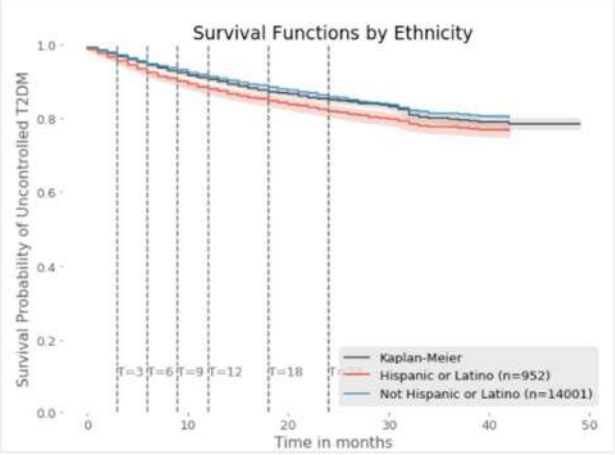
Average Survival Function Curves

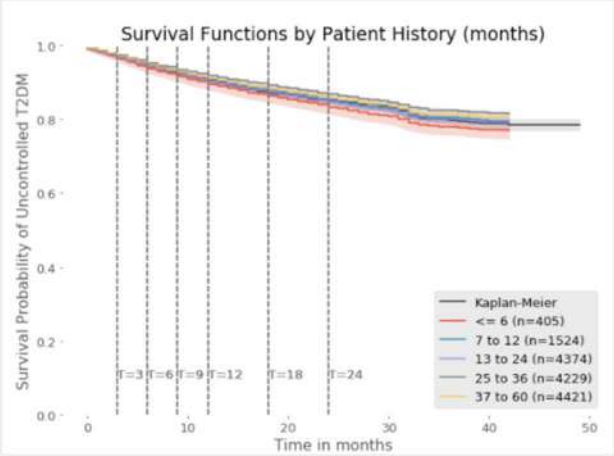
The following charts show how the average survival function curve varies among subgroups of risk, age, sex, ethnicity and patient history.





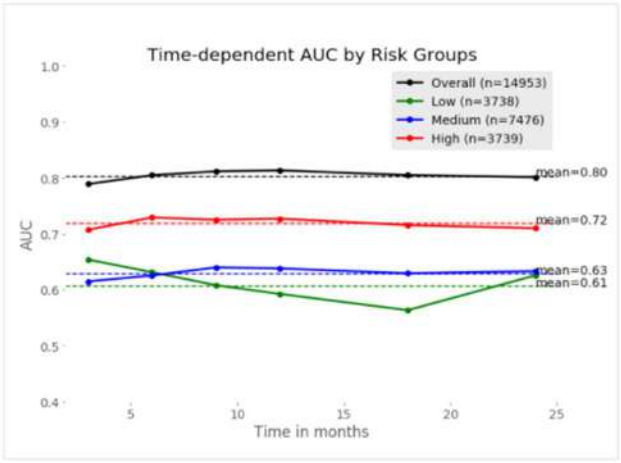


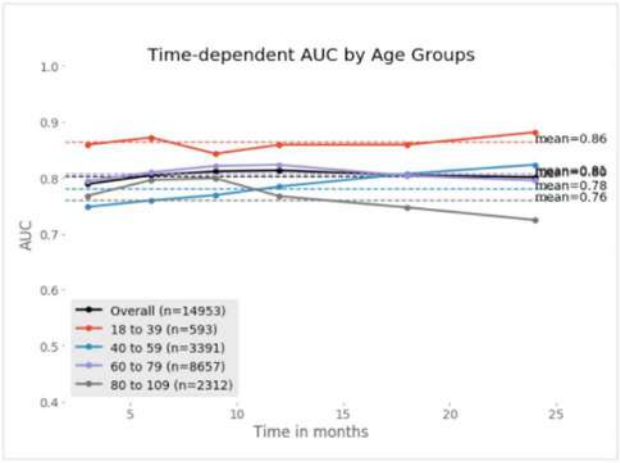


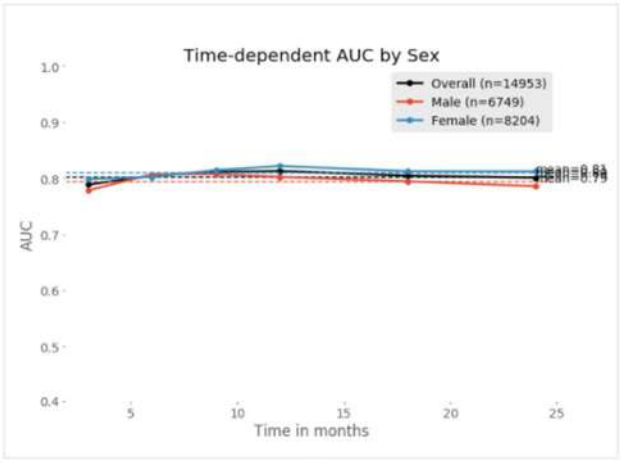


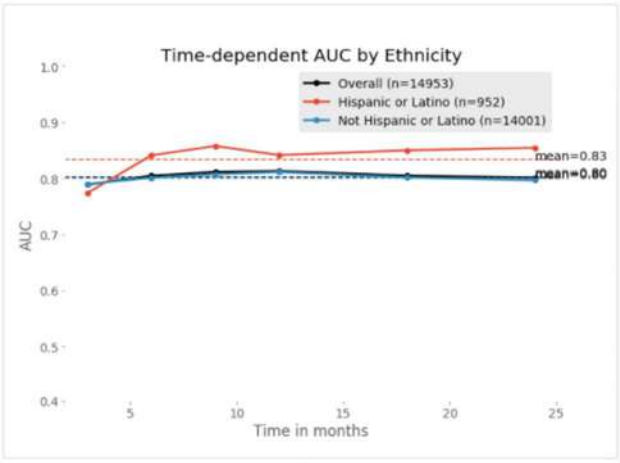
Time-dependent AUC

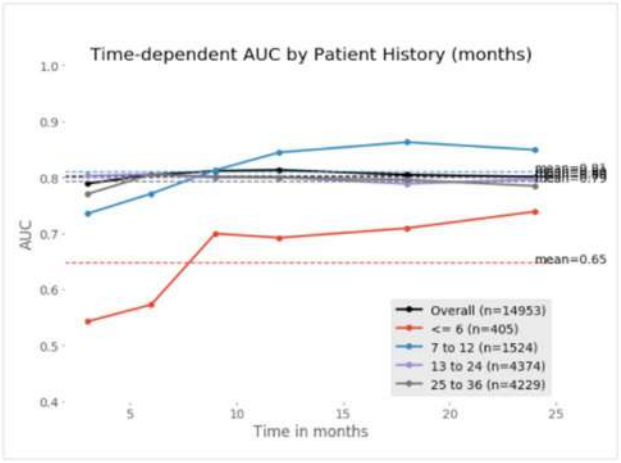
The following charts show how the AUC across time varies among subgroups of risk, age, sex, ethnicity and patient history.





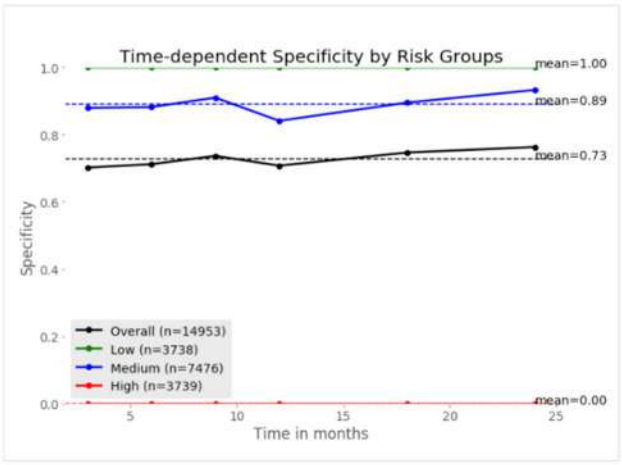


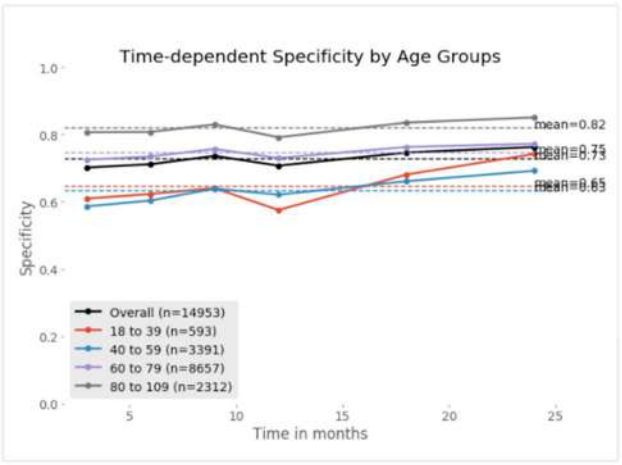


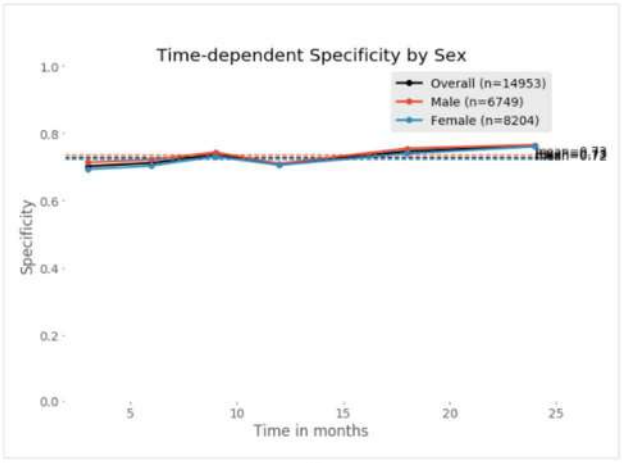


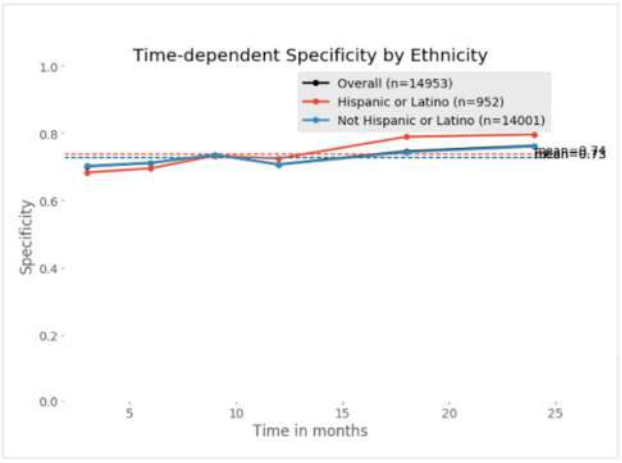
Time-dependent Specificity

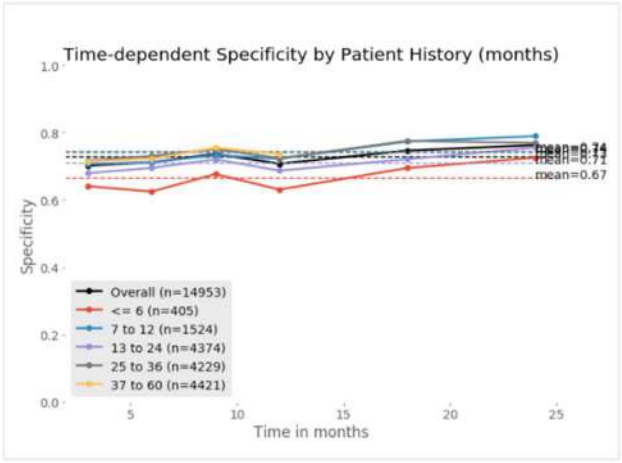
The following charts show how the specificity across time varies among subgroups of risk, age, sex, ethnicity and patient history.





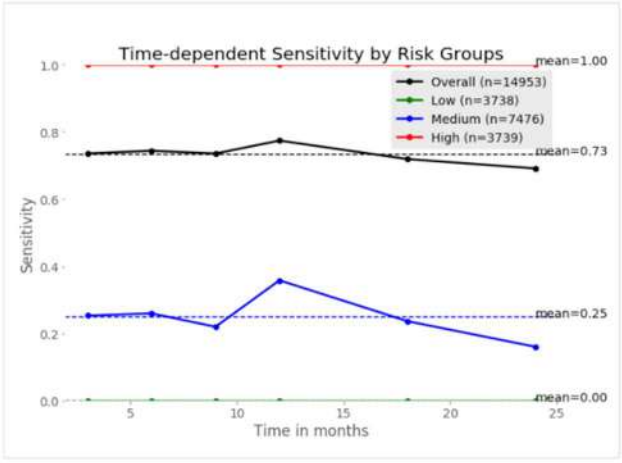


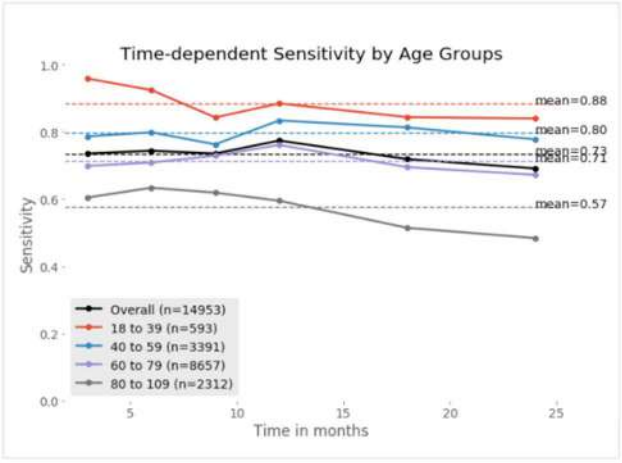


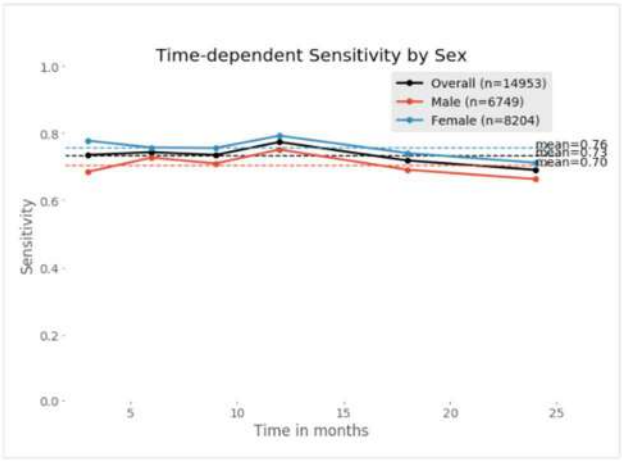


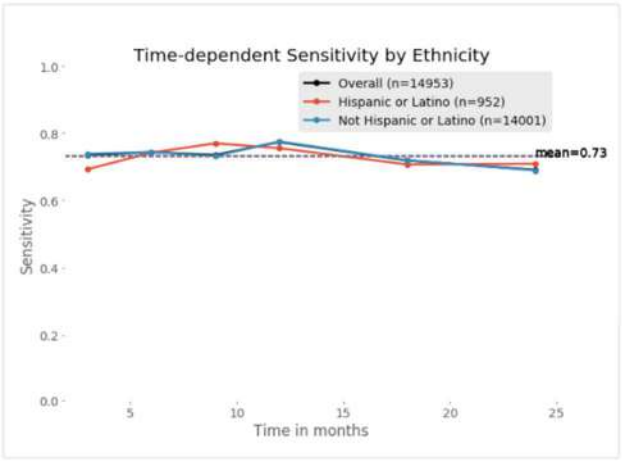
Time-dependent Sensitivity

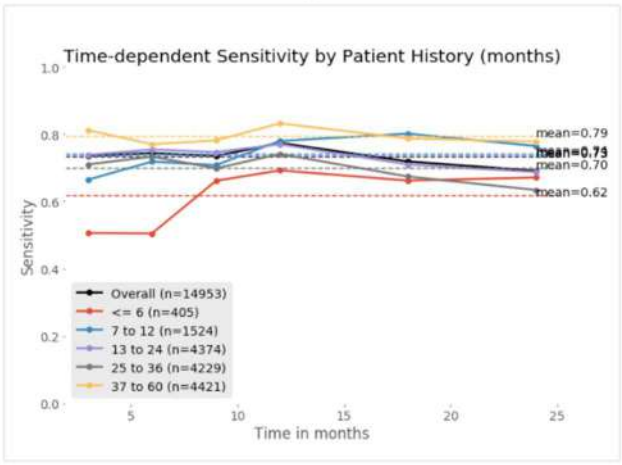
The following charts show how the sensitivity across time varies among subgroups of risk, age, sex, ethnicity and patient history.







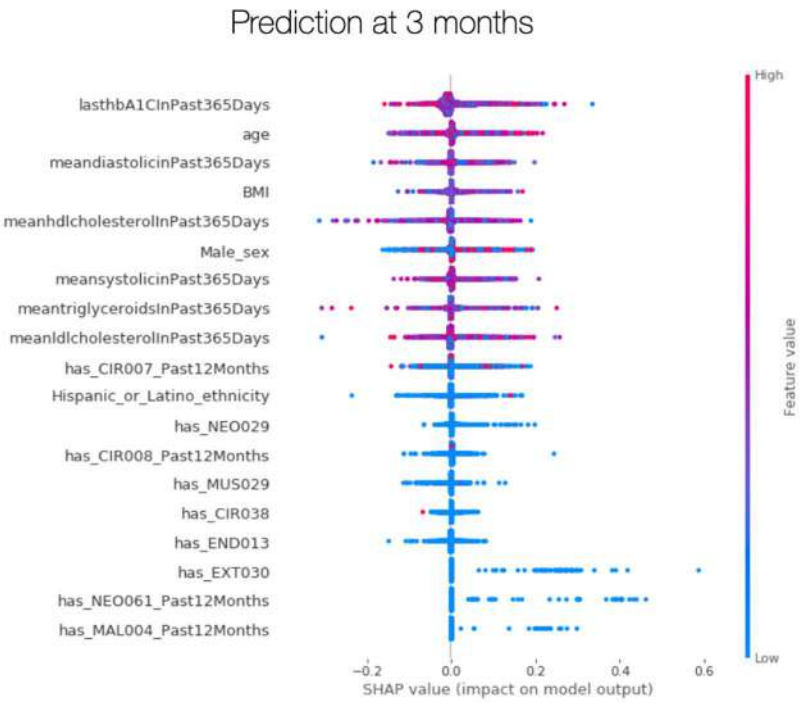


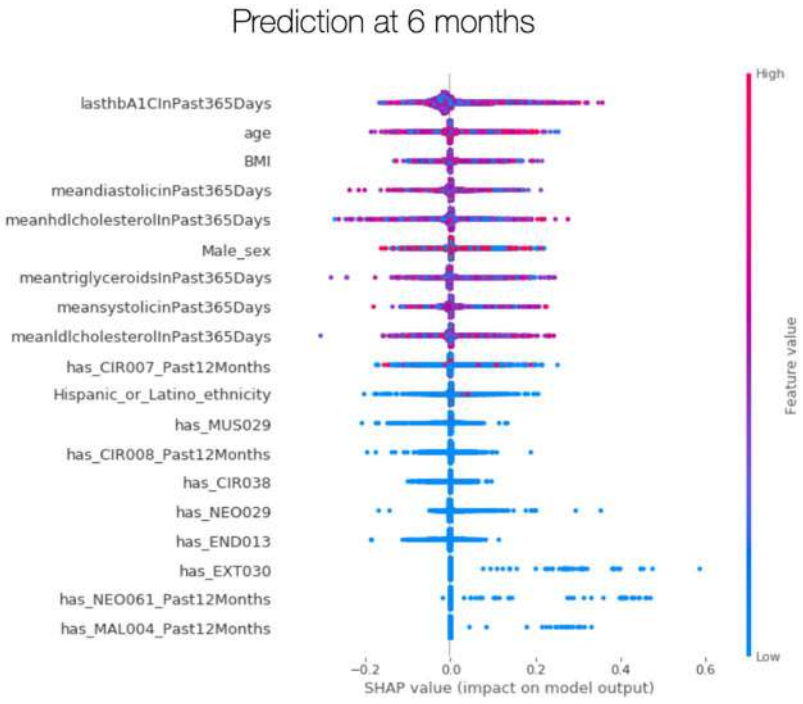


Model Explanation (DeepSurv)

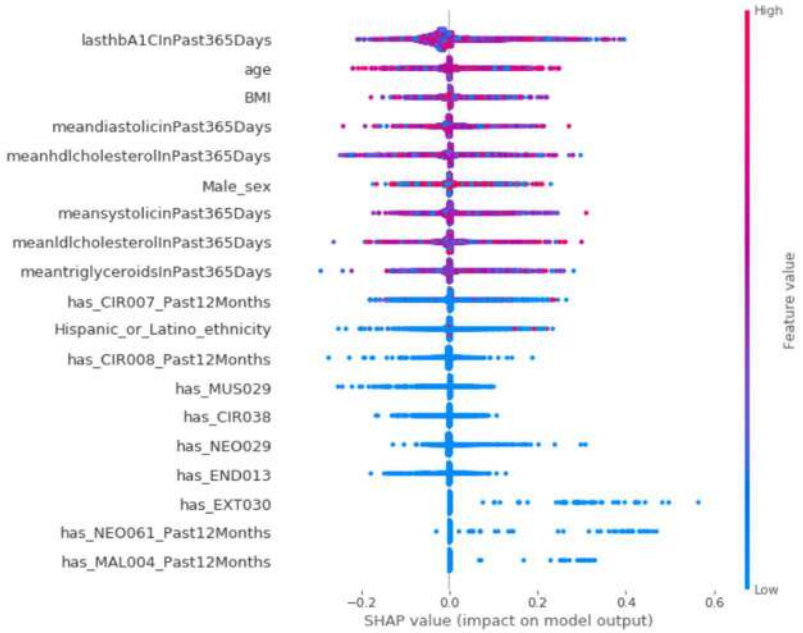
Global

The following plots show the SHAP values of each instance in the training set for each future time (3, 6, 9, 12, 18 and 24 months). The features are sorted by the total magnitude of the SHAP values over all instances and the distribution of the effect that each feature has on the model's output can be observed.

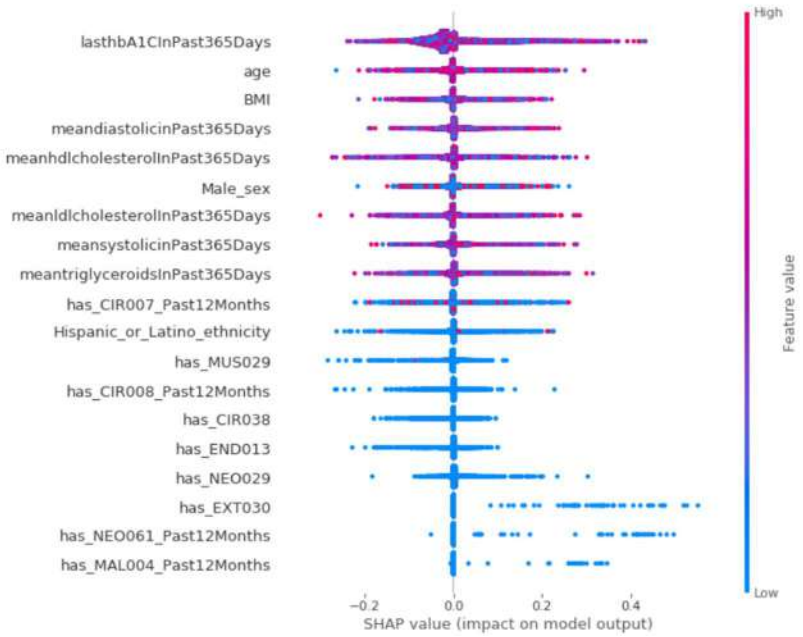




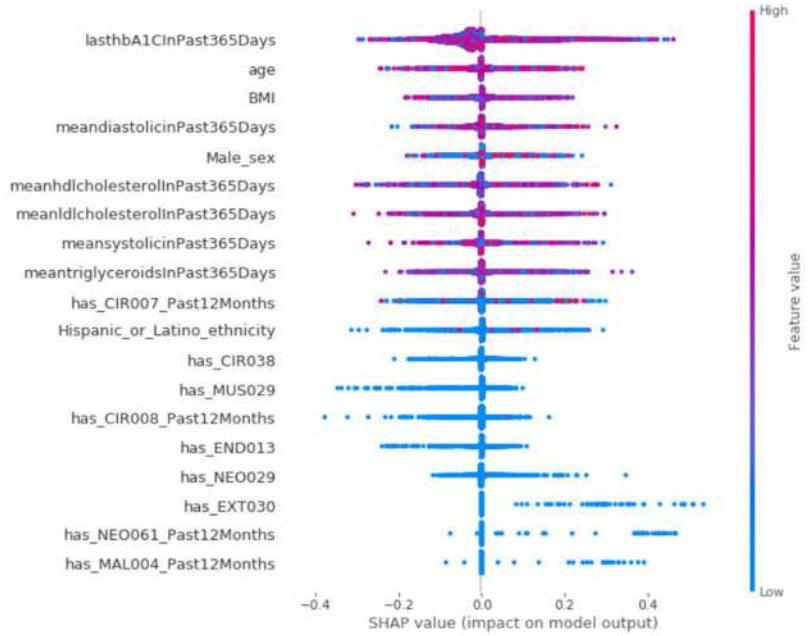
Prediction at 9 months



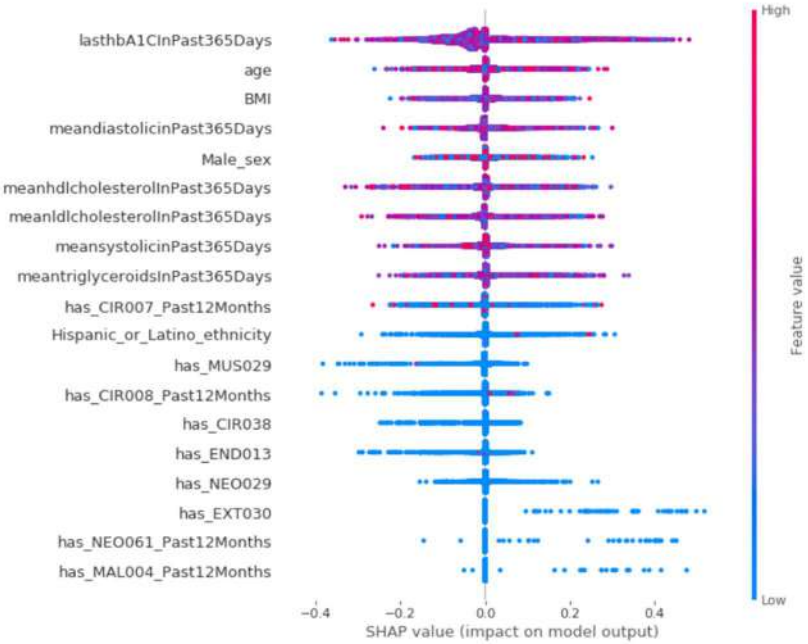
Prediction at 12 months



Prediction at 18 months

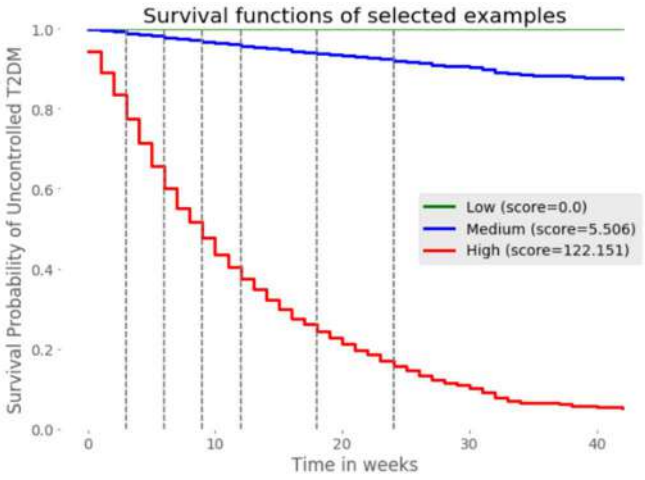


Prediction at 24 months



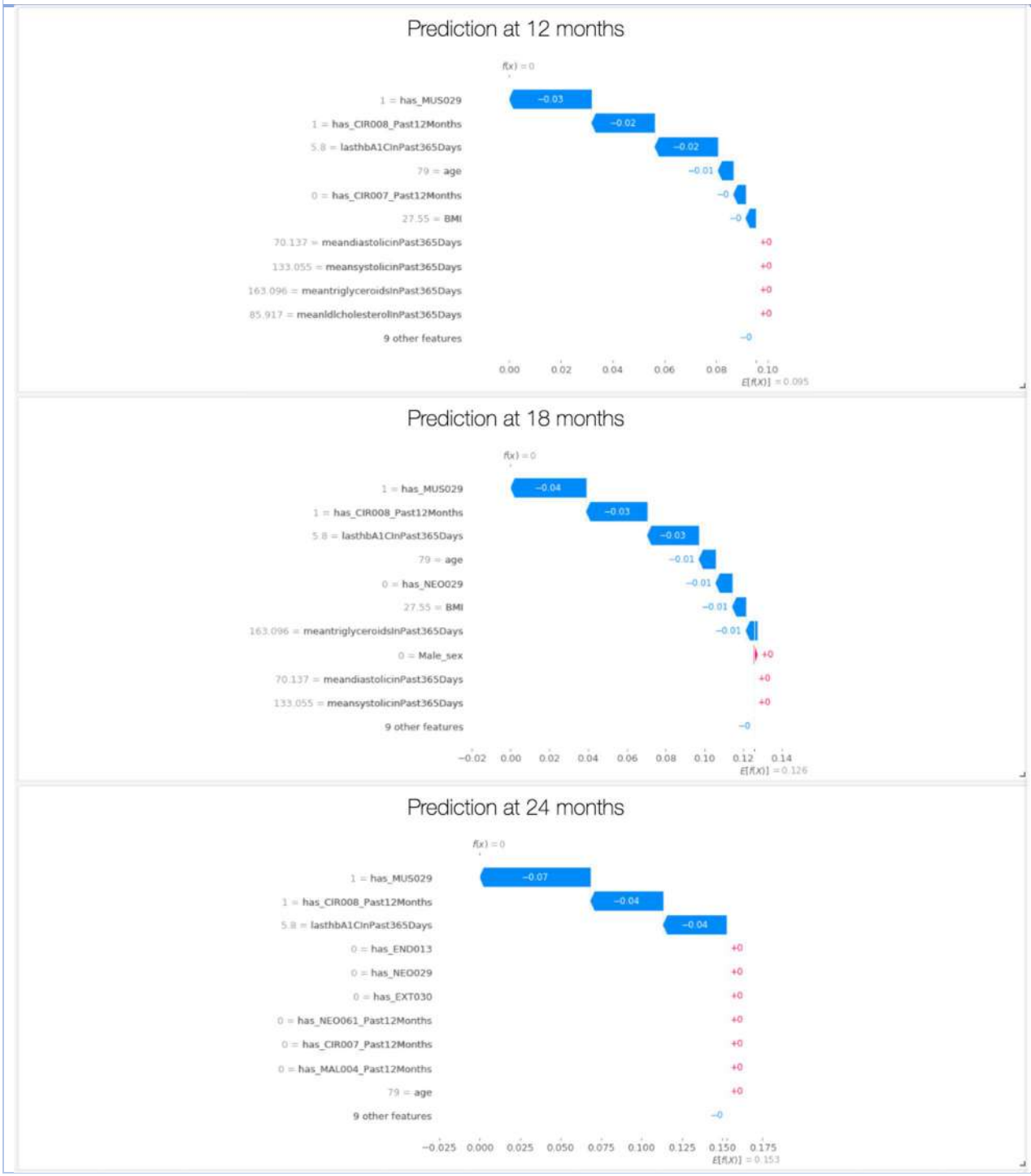
Local

SHAP values were also generated to explain the predictions of individual examples for each future time (3, 6, 9, 12, 18 and 24 months). A total of 3 examples were selected by sampling of risk scores at the 5th, 50th and 95th percentile to represent instances at low, medium and high risks respectively.

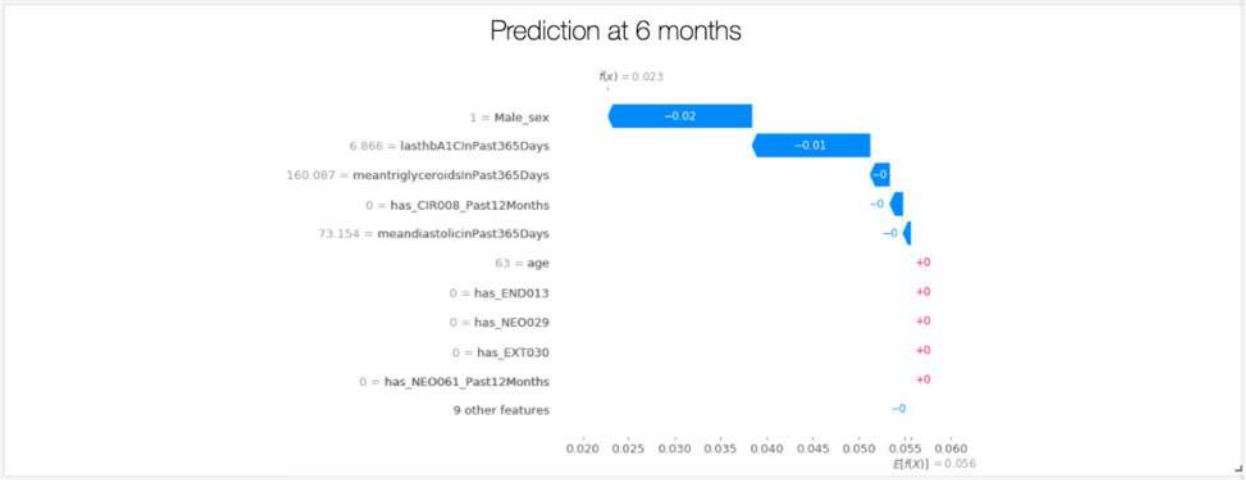


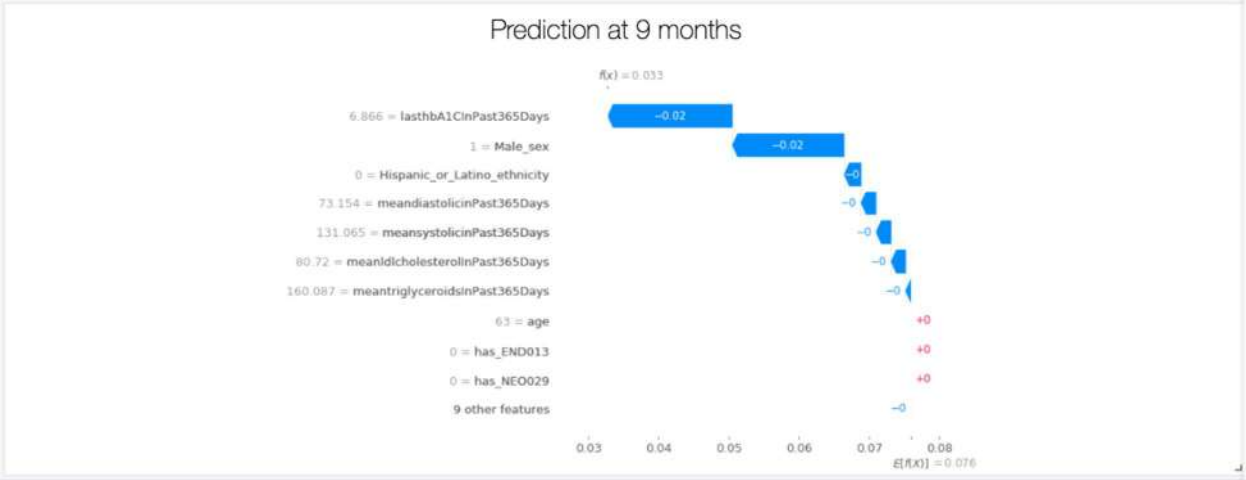
Low Risk
Risk Score: 0.0

Low Risk
Risk Score: 0.0



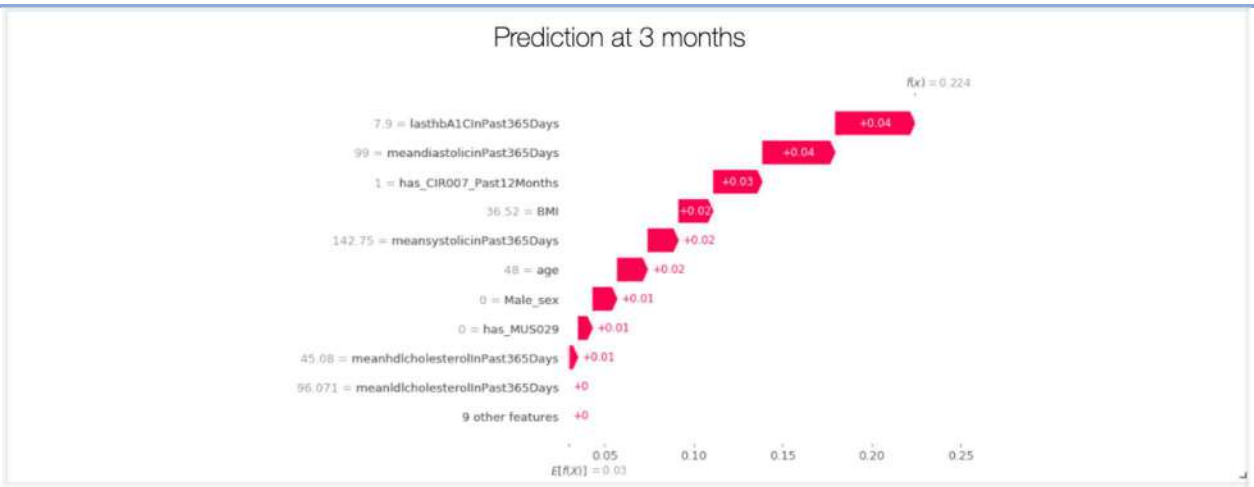
Medium Risk
Risk Score: 5.506

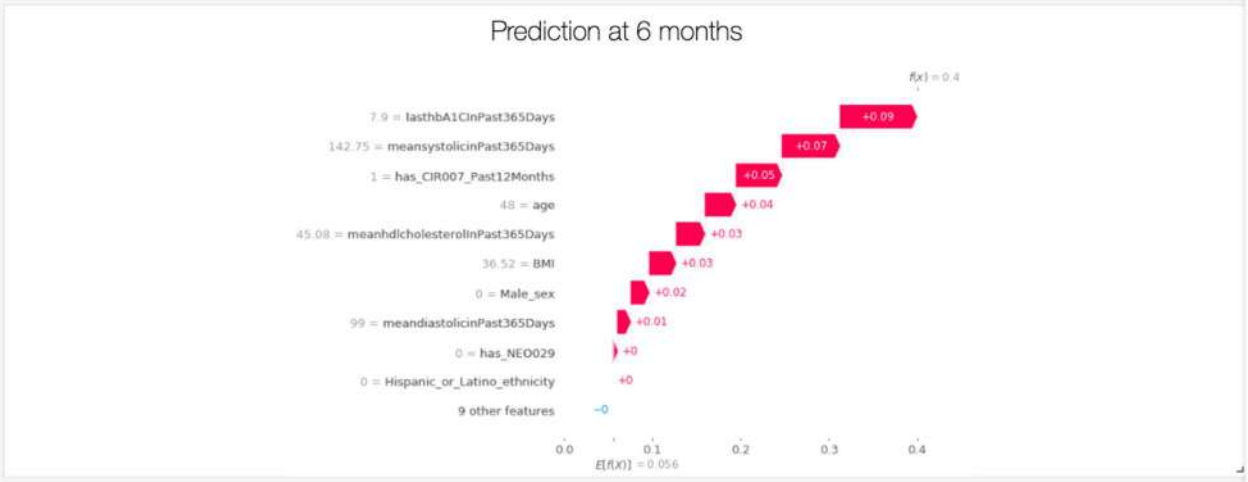


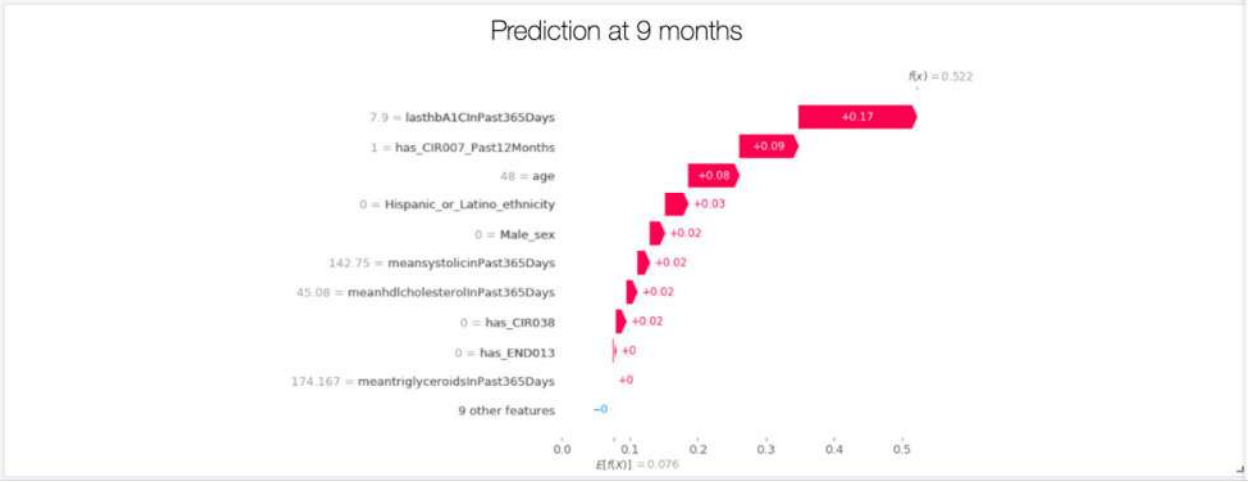


Medium Risk
Risk Score: 5.506

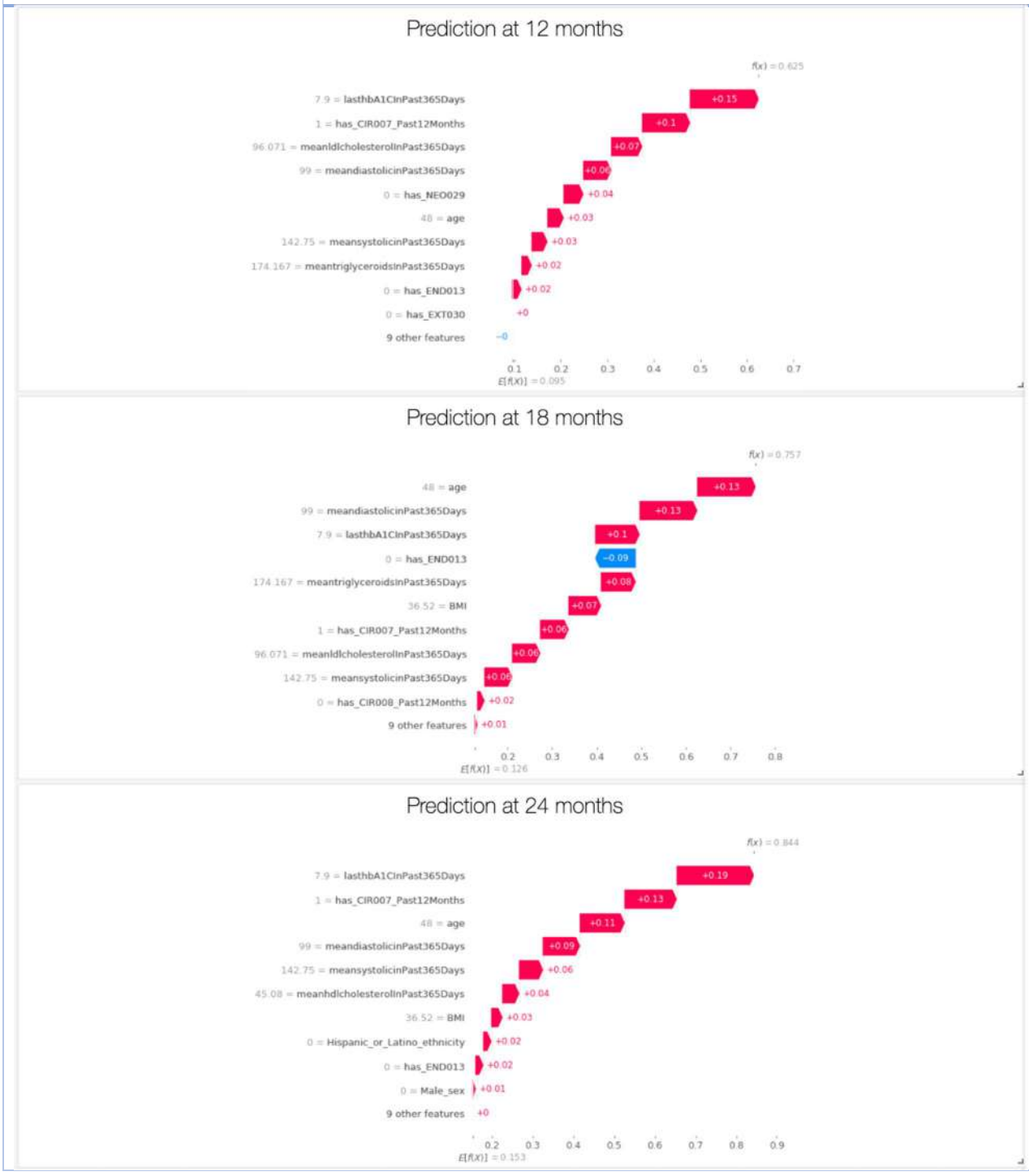
High Risk
Risk Score: 122.151







High Risk
Risk Score: 122.151



Pre-DM to Uncontrolled DM Prediction

Item	Specification
Business Goal	Enable care managers to identify the patients who are at risk of developing uncontrolled DM
Usage Setting	Outpatient
ML Task	Predict risk and/or time from DM to uncontrolled DM
ML Class	Survival
Instances for Prediction	Encounters
Labels for Instances	Binary indicator and time to event or censoring for uncontrolled DM
Cohort Criteria	• 2016-01-01 $\leq$ encounter date $\leq$ 2020-06-30 (available Epic data, excluding outliers) • Encounter date is not within the first 90 days of when the patient entered the data set, to adjust for left-censoring • 18 $\leq$ age $\leq$ 110 (adults without outliers) • No T1DM diagnosis • Not pregnant • No "Do Not Resuscitate" diagnosis • Pre-DM event before encounter date • No DM event before encounter date • No DM event up to 6 days after encounter date • No uncontrolled DM event before encounter date • No uncontrolled DM event up to 6 days after encounter date (encounters where lab results confirm event within the week)

Input Features	• Demographic
	• Diagnosis, except:
	  ○ hasDiabetes*
	  ○ has_END002* (Diabetes mellitus without complication)
	  ○ has_END003* (Diabetes mellitus with complication)
	  ○ has_END004* (Diabetes mellitus, Type 1)
	  ○ has_END005* (Diabetes mellitus, Type 2)
	  ○ has_END006* (Diabetes mellitus, due to underlying condition, drug or chemical induced, or other specified type)
	• Labs
	• Utilization
	• Vitals
	
	See Appendix E for details.

Evaluation Metrics	• Concordance Index • Integrated Brier Score

Data

The following charts summarize the key characteristics of the data after applying the cohort criteria stated above, along with selected features (see Model Signature below).

Category	summary Variable	count	mean	stddev	min	25%	50%	75%	max
Demographic	AgeBucket_18_to_39	258142.0	0.069903	0.254985	0.00	0.000	0.000	0.000	1.00
	AgeBucket_40_to_59	258142.0	0.248332	0.432046	0.00	0.000	0.000	0.000	1.00
	AgeBucket_60_to_79	258142.0	0.543267	0.498125	0.00	0.000	1.000	1.000	1.00
	AgeBucket_80_to_109	258142.0	0.138497	0.345422	0.00	0.000	0.000	0.000	1.00
	Sex_Female	258142.0	0.627515	0.483467	0.00	0.000	1.000	1.000	1.00
	Sex_Male	258142.0	0.372485	0.483467	0.00	0.000	0.000	1.000	1.00
	Ethnicity_Hispanic_or_Latino	258142.0	0.054687	0.227369	0.00	0.000	0.000	0.000	1.00
	Ethnicity_Not_Hispanic_or_Latino	258142.0	0.945313	0.227369	0.00	1.000	1.000	1.000	1.00
Encounter	EncounterType_Emergency	258142.0	0.183232	0.386858	0.00	0.000	0.000	0.000	1.00
	EncounterType_Inpatient	258142.0	0.079848	0.271058	0.00	0.000	0.000	0.000	1.00
	EncounterType_Outpatient	258142.0	0.736920	0.440306	0.00	0.000	1.000	1.000	1.00
Label	Time	258142.0	16.275395	11.351408	0.00	7.000	14.000	25.000	50.00
	Event	258142.0	0.023673	0.152029	0.00	0.000	0.000	0.000	1.00
Feature	age	258142.0	64.481131	14.647176	18.00	56.000	66.000	75.000	107.00
	Male_sex	258142.0	0.372485	0.483467	0.00	0.000	0.000	1.000	1.00
	Hispanic_or_Latino_ethnicity	258142.0	0.054687	0.227369	0.00	0.000	0.000	0.000	1.00
	lasthbA1CInPast365Days	258142.0	6.034896	0.491028	2.20	5.800	6.022	6.103	8.90
	meandiastolicinPast365Days	258142.0	74.510641	7.465089	43.63	71.000	74.678	77.830	107.67
	meansystolicinPast365Days	258142.0	130.507721	11.237634	81.00	125.910	130.162	134.500	180.00
	BMI	258142.0	32.052144	6.993803	2.71	28.009	31.894	35.243	326.11
	meantriglyceroidsInPast365Days	258142.0	141.515197	48.161881	11.00	119.839	142.732	147.721	468.50
	meanldlcholesterolInPast365Days	258142.0	95.182333	23.631750	2.80	84.968	97.608	107.000	201.00
	meanhdlcholesterolInPast365Days	258142.0	47.882752	10.369947	6.00	42.348	47.000	52.436	98.00
	has_BLD005_Past12Months	258142.0	0.001189	0.034465	0.00	0.000	0.000	0.000	1.00
	has_SKN005_Past12Months	258142.0	0.004970	0.070324	0.00	0.000	0.000	0.000	1.00
	has_INJ014_Past12Months	258142.0	0.000686	0.026176	0.00	0.000	0.000	0.000	1.00
	has_CIR007_Past12Months	258142.0	0.165409	0.371550	0.00	0.000	0.000	0.000	1.00
	has_NEO022_Past12Months	258142.0	0.026927	0.161871	0.00	0.000	0.000	0.000	1.00
	has_CIR008_Past12Months	258142.0	0.009239	0.095675	0.00	0.000	0.000	0.000	1.00
	has_NEO029_Past12Months	258142.0	0.004269	0.065198	0.00	0.000	0.000	0.000	1.00
	has_BLD005	258142.0	0.002119	0.045984	0.00	0.000	0.000	0.000	1.00
	has_INJ007	258142.0	0.004846	0.069446	0.00	0.000	0.000	0.000	1.00
	has_INJ054	258142.0	0.001522	0.038989	0.00	0.000	0.000	0.000	1.00
	has_GEN018	258142.0	0.014829	0.120869	0.00	0.000	0.000	0.000	1.00
	has_NEO044	258142.0	0.001120	0.033441	0.00	0.000	0.000	0.000	1.00
	has_INJ035	258142.0	0.007031	0.083556	0.00	0.000	0.000	0.000	1.00
	has_INJ049	258142.0	0.001941	0.044012	0.00	0.000	0.000	0.000	1.00
	has_NEO012	258142.0	0.005745	0.075577	0.00	0.000	0.000	0.000	1.00

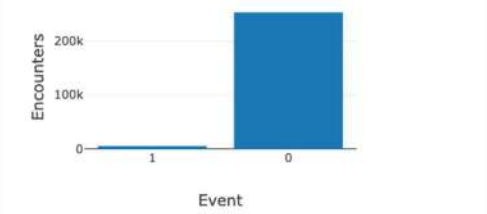
(Percentages for binary variables can be read from the “mean” column.)

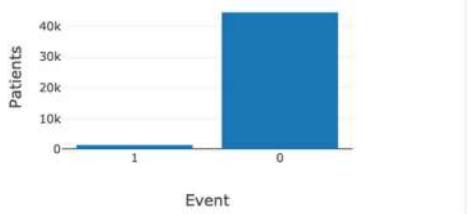
Encounters and Patients

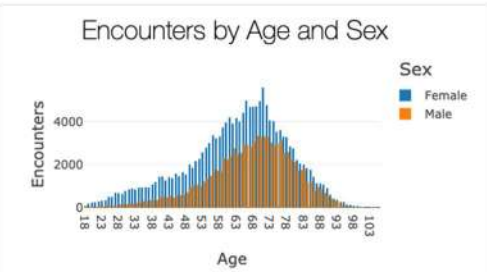
	Examples	Encounters	Patients
1	258142	258142	45851

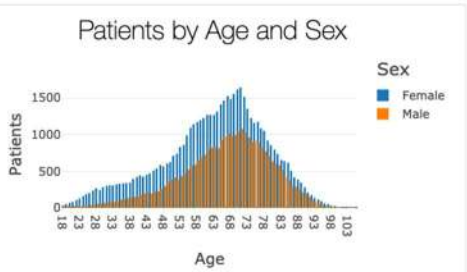
Train and Test Sets

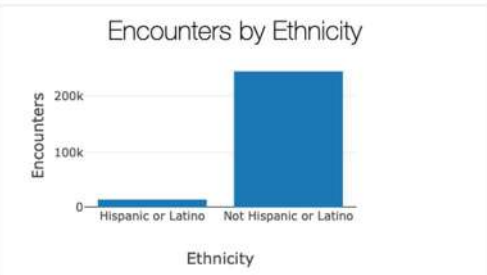
	Set	No Event	No Event %	Event	Event %	Total	Total %
1	Train	176915	70.2	4282	70.1	181197	70.2
2	Test	75116	29.8	1829	29.9	76945	29.8
3	Total	252031	100	6111	100	258142	100

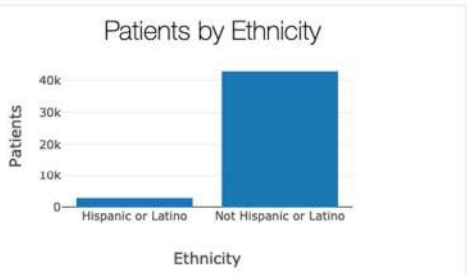


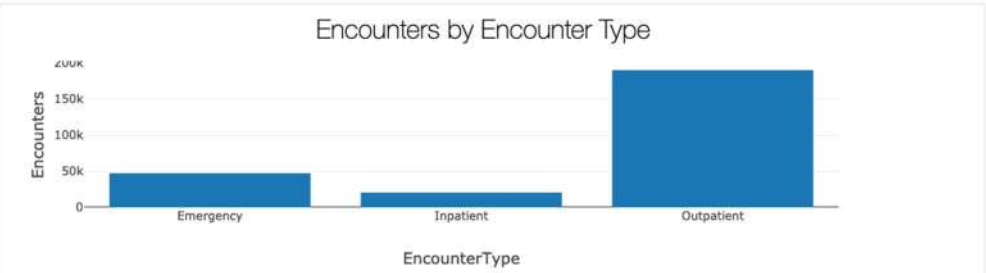


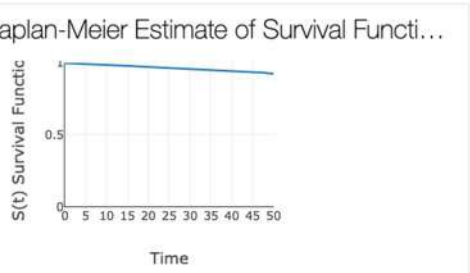








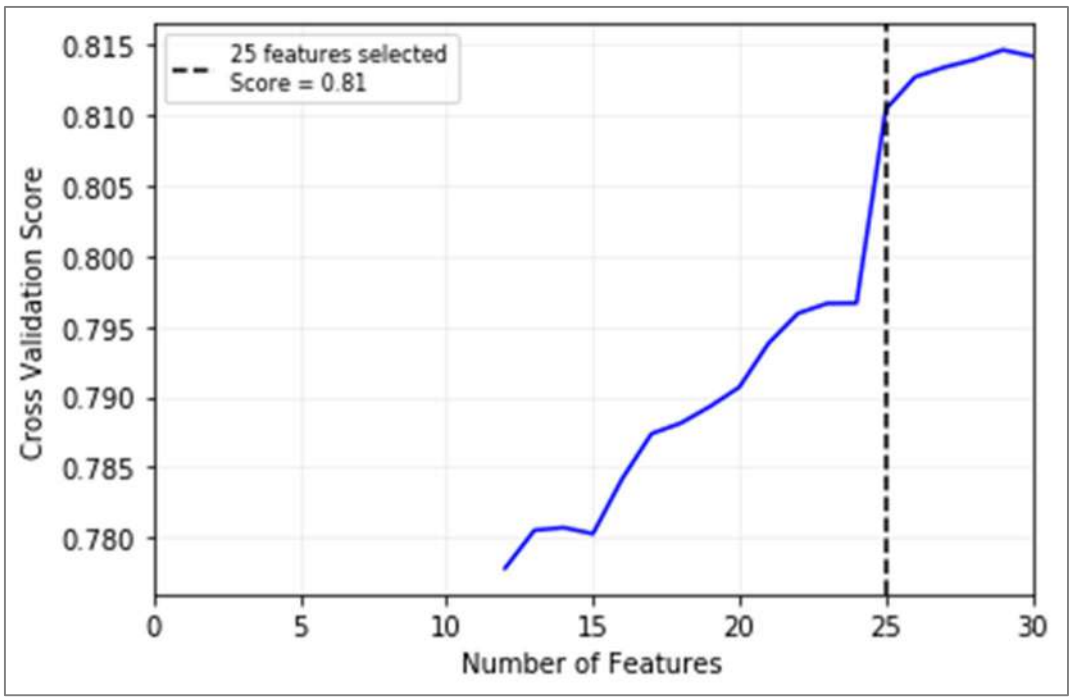




Model Signature

The model signature has 25 features, comprising of 12 mandatory features and 13 other selected features. These are the selected features, in rank order (the last feature to be eliminated is ranked 1):

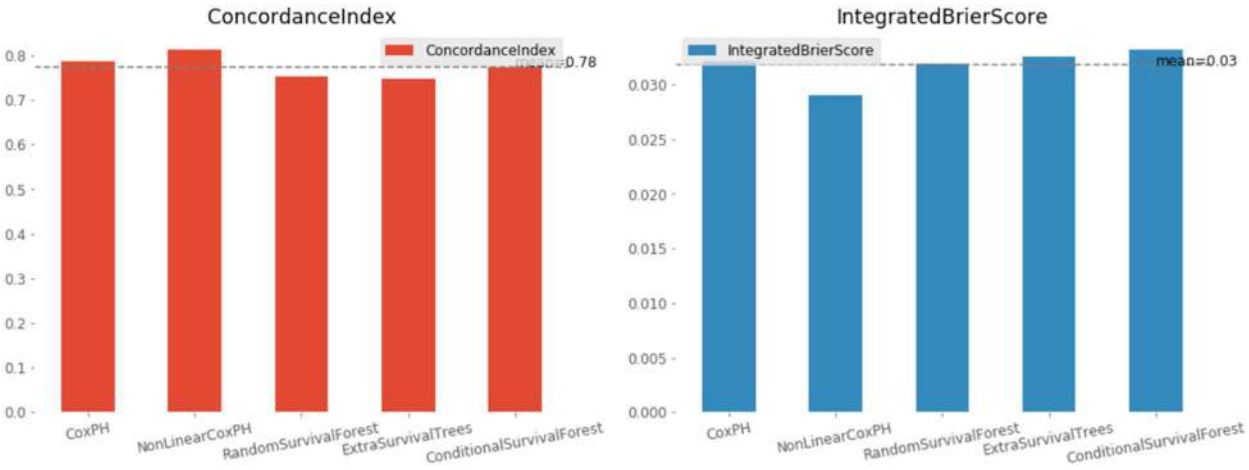
1. has_BLD005_Past12Months (Sickle cell trait/anemia)
2. has_INJ035 (Complication of internal orthopedic device or implant, initial encounter)
3. has_INJ014_Past12Months (Amputation of a limb, initial encounter)
4. has_INJ049 (Open wounds to limbs, subsequent encounter)
5. has_NEO022_Past12Months (Respiratory cancers)
6. has_INJ054 (Superficial injury; contusion, subsequent encounter)
7. has_NEO044 (Urinary system cancers - ureter and renal pelvis)
8. lasthbA1CInPast365Days
9. has_SKN005_Past12Months (Contact dermatitis)
10. has_NEO029_Past12Months (Breast cancer - ductal carcinoma in situ (DCIS))
11. has_BLD005 (Sickle cell trait/anemia)
12. has_NEO012 (Gastrointestinal cancers - esophagus)
13. has_INJ007 (Dislocations, initial encounter)
14. has_GEN018 (Inflammatory diseases of female pelvic organs)
15. Male_sex
16. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)
17. Hispanic_or_Latino_ethnicity
18. age
19. BMI
20. meanhdlcholesterolInPast365Days
21. has_CIR007_Past12Months (Essential hypertension)
22. meansystolicinPast365Days
23. meantriglyceroidsInPast365Days
24. meandiastolicinPast365Days
25. meanldlcholesterolInPast365Days



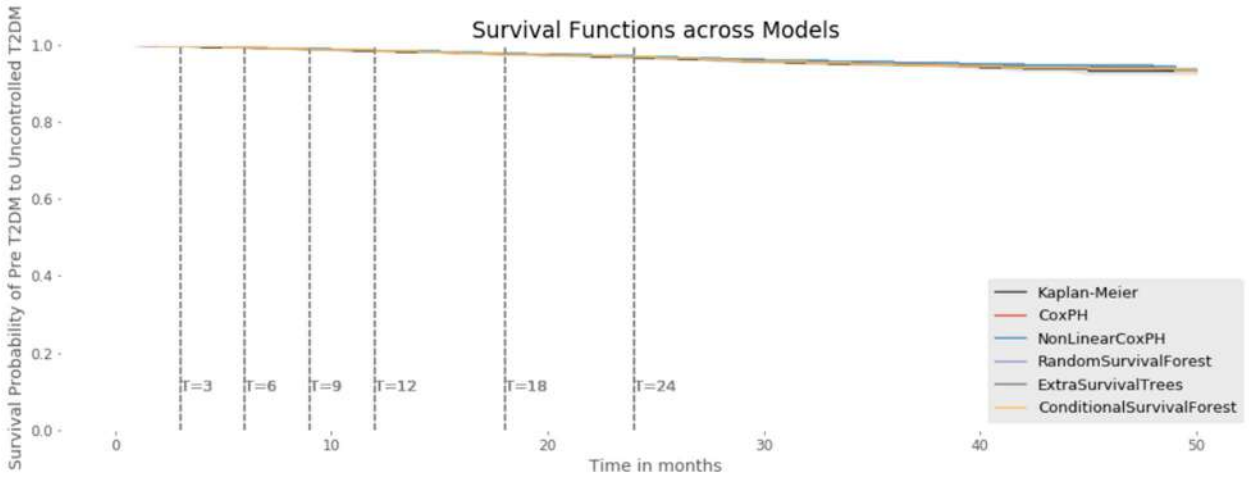
Model Performance

The following table and chart summarize the performance of all candidate models on the test set for this prediction task in terms of the Concordance Index and the Integrated Brier Score.

Model	No. of Parameter Combinations Successfully Tested	Concordance Index	Integrated Brier Score
CoxPH	83	0.79	**0.03**
DeepSurv	81	**0.81**	**0.03**
RSF	1	0.75	**0.03**
CSF	5	0.75	**0.03**
EST	1	0.77	**0.03**



The following chart shows how the average survival function curves of the candidate models compare to the KM survival curve, the more similar their curves are to the KM survival curve the better.

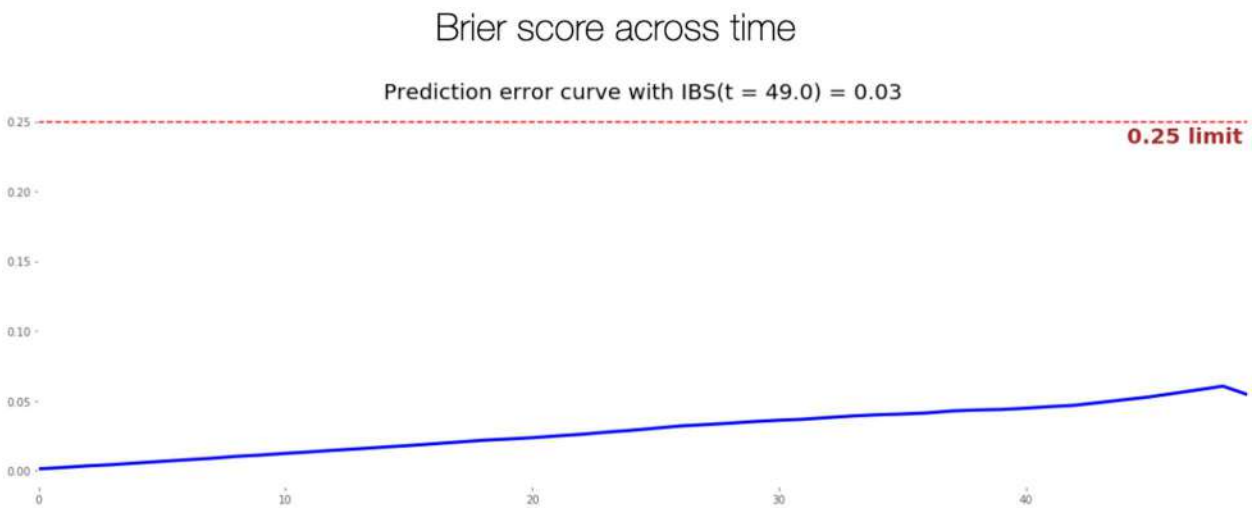


This chart shows the change in the Brier Score over time for all candidate models, the closer the scores are to 0 the better.

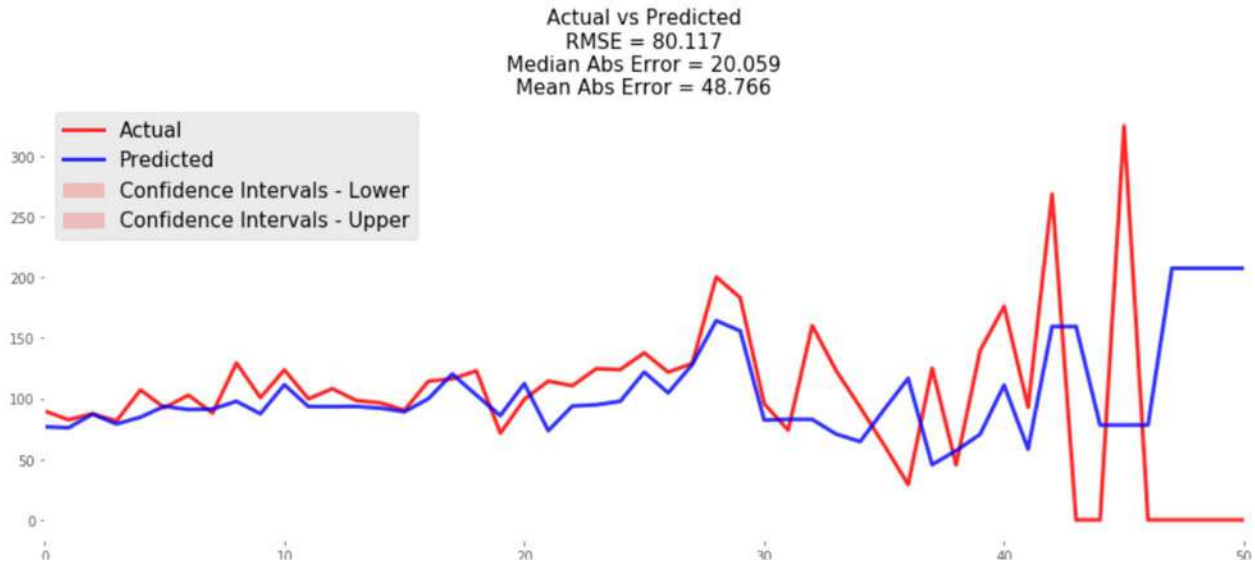
Model Evaluation of Selected Model (DeepSurv)

Overall

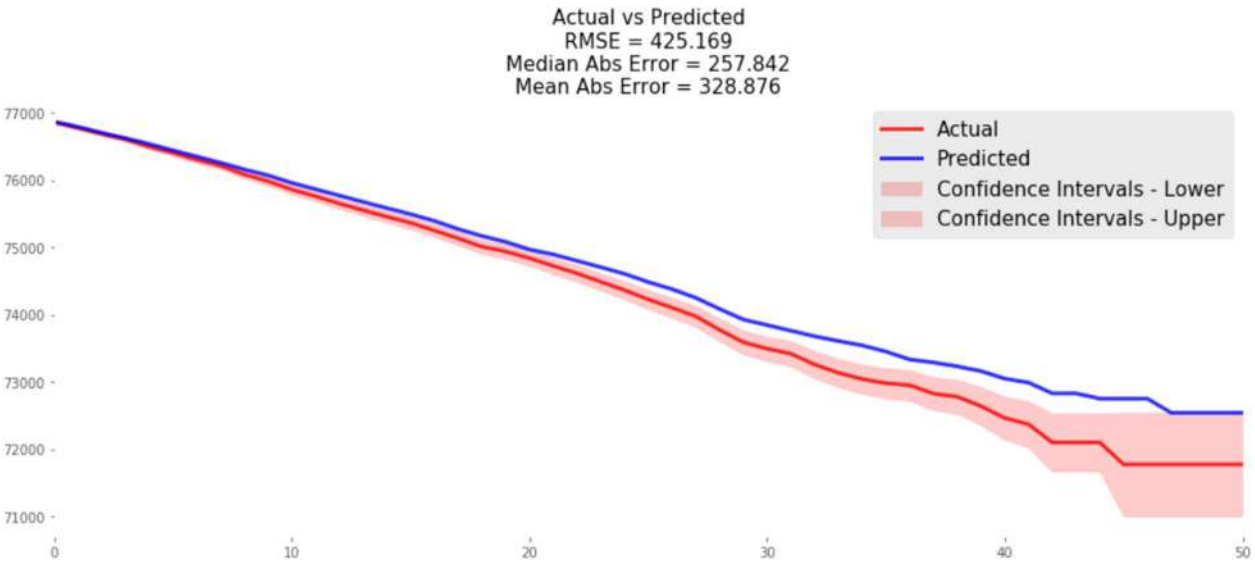
This chart shows the change in the Brier Score over time for the selected model, the closer the scores are to 0 the better.



The following chart shows the actual vs. predicted density functions, i.e. number of instances that get the disease / complication at each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



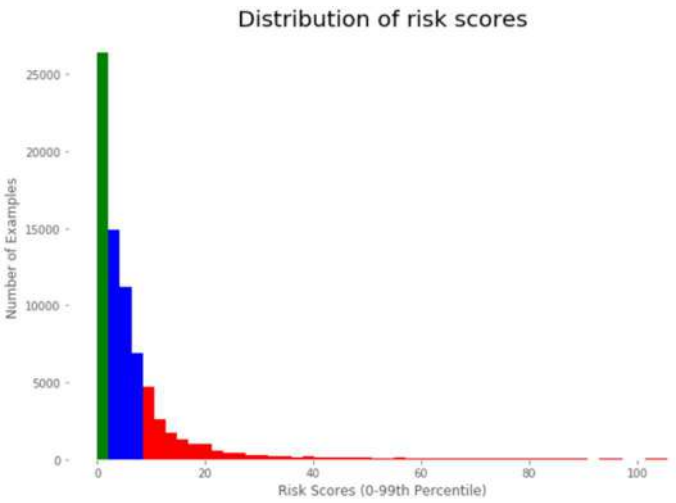
The following chart shows the actual vs. predicted survival functions, i.e. the number of instances that have not had the disease / complication by each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



Risk Stratification

The low, medium and high risk groups are defined as examples with predicted risk scores belonging to the first quartile, second to third quartiles, and fourth quartile respectively.

	Percentile	Risk Scores
Low Risk	0-25th	[0.0,1.303]
Medium Risk	26th-75th	[1.303,7.826]
High Risk	75th-100th	[7.826,9292.021484375]



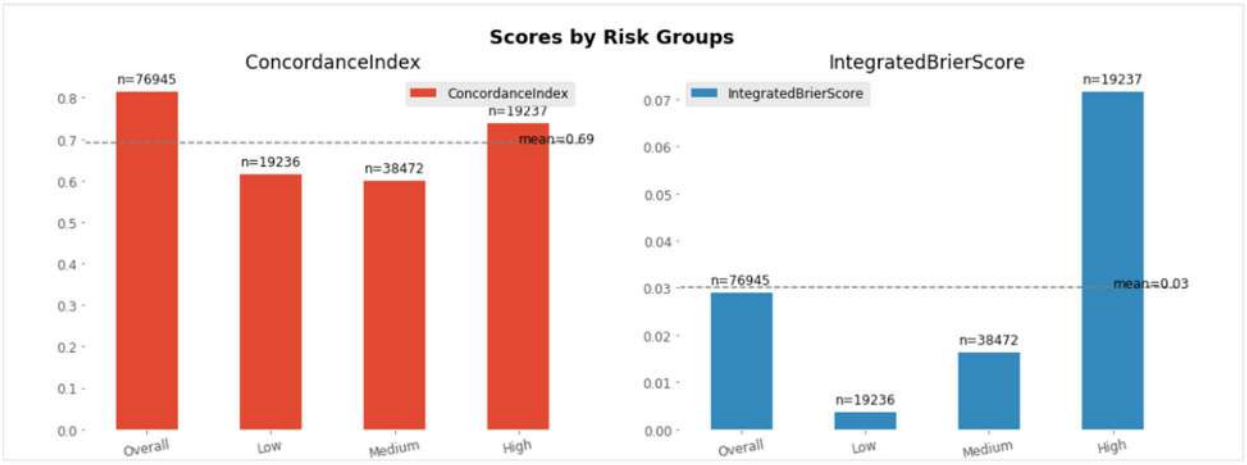
Summary Metrics across Subgroups

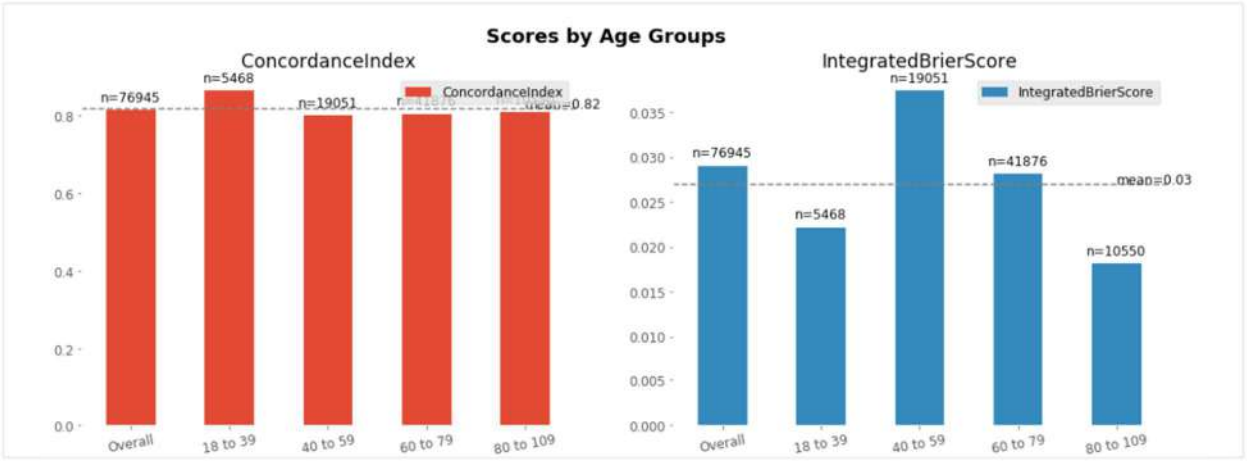
The table below displays the summary metrics across subgroups of risk, age, sex, ethnicity and patient history.

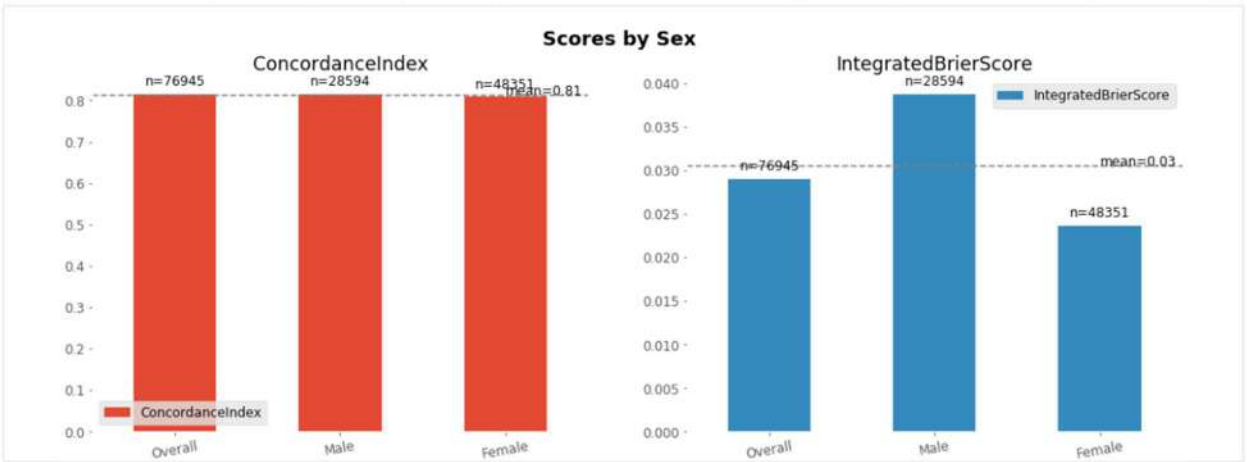
Category	Subgroup	Cohort Size	Concordance Index	Brier Score	Mean AUC	Mean Specificity	Mean Sensitivity	S(t), t=3	S(t), t=6	S(t), t=9	S(t), t=12	S(t), t=18	S(t), t=24
NaN	Overall	76945.00	0.81	0.03	0.84	0.83	0.68	1.00	0.99	0.99	0.98	0.97	0.97
Risk	Low	19236.00	0.61	0.00	0.62	1.00	0.00	1.00	1.00	1.00	1.00	1.00	1.00
Risk	Medium	38472.00	0.60	0.02	0.64	1.00	0.00	1.00	1.00	0.99	0.99	0.99	0.98
Risk	High	19237.00	0.74	0.07	0.76	0.33	0.88	0.99	0.98	0.97	0.95	0.93	0.91
Age Bucket	18 to 39	5468.00	0.86	0.02	0.83	0.90	0.62	1.00	0.99	0.99	0.99	0.98	0.98
Age Bucket	40 to 59	19051.00	0.80	0.04	0.84	0.80	0.71	0.99	0.99	0.99	0.98	0.97	0.96
Age Bucket	60 to 79	41876.00	0.80	0.03	0.84	0.82	0.68	1.00	0.99	0.99	0.98	0.98	0.97
Age Bucket	80 to 109	10550.00	0.81	0.02	0.83	0.92	0.54	1.00	1.00	0.99	0.99	0.99	0.98
Sex	Male	28594.00	0.81	0.04	0.81	0.72	0.72	0.99	0.99	0.98	0.98	0.97	0.96
Sex	Female	48351.00	0.81	0.02	0.86	0.89	0.64	1.00	0.99	0.99	0.99	0.98	0.98
Ethnicity	Hispanic or Latino	4192.00	0.86	0.03	0.87	0.85	0.71	0.99	0.99	0.98	0.98	0.97	0.96
Ethnicity	Not Hispanic or Latino	72753.00	0.81	0.03	0.84	0.83	0.67	1.00	0.99	0.99	0.99	0.98	0.97
History Bucket	<= 6	2437.00	0.90	0.02	0.88	0.81	0.77	1.00	0.99	0.99	0.98	0.98	0.97
History Bucket	7 to 12	6688.00	0.81	0.03	0.83	0.81	0.67	1.00	0.99	0.99	0.98	0.97	0.96
History Bucket	13 to 24	20985.00	0.81	0.03	0.83	0.83	0.65	1.00	0.99	0.99	0.98	0.97	0.97
History Bucket	25 to 36	22329.00	0.82	0.02	0.86	0.85	0.68	1.00	0.99	0.99	0.99	0.98	0.97
History Bucket	37 to 60	24506.00	0.85	0.01	nan	nan	0.70	1.00	0.99	0.99	0.99	0.98	0.97

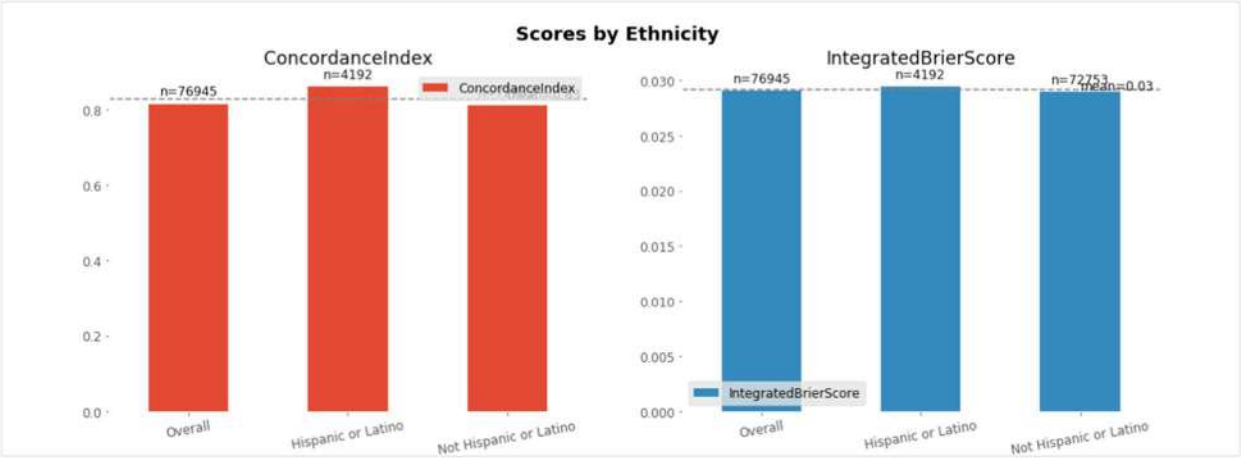
Concordance Index & Integrated Brier Score

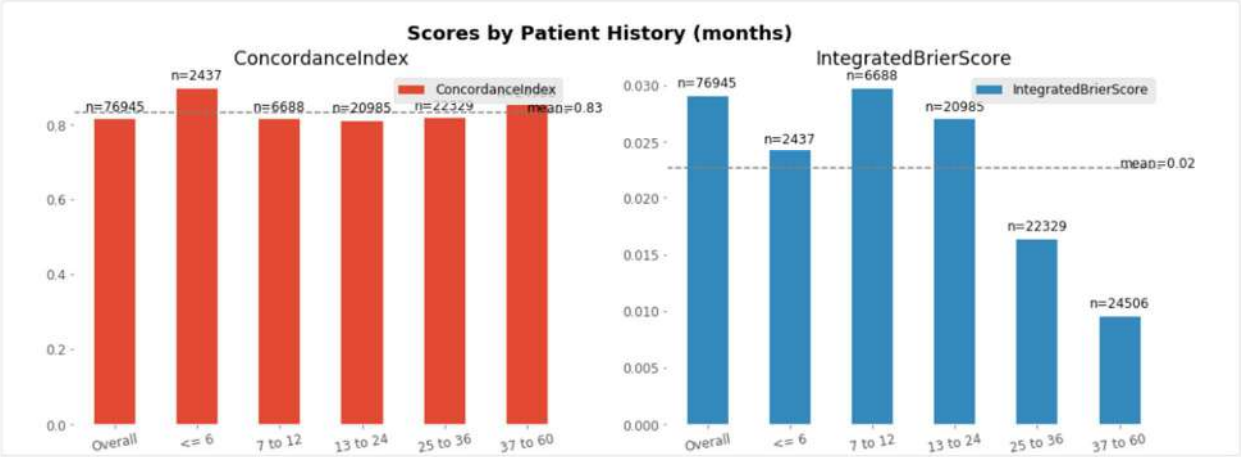
The following charts show how the Concordance Index and Integrated Brier Score varies among subgroups of risk, age, sex, ethnicity and patient history.





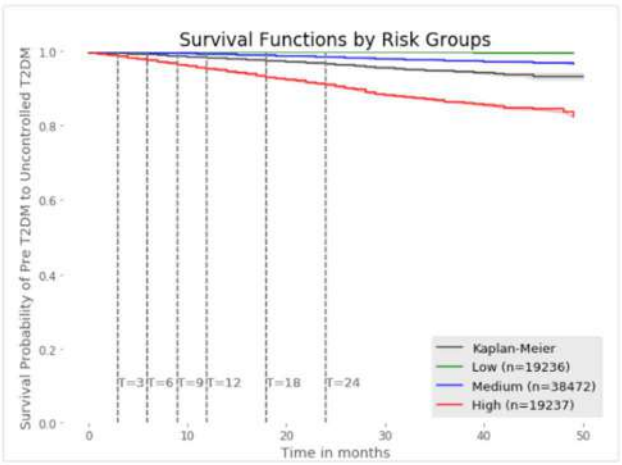


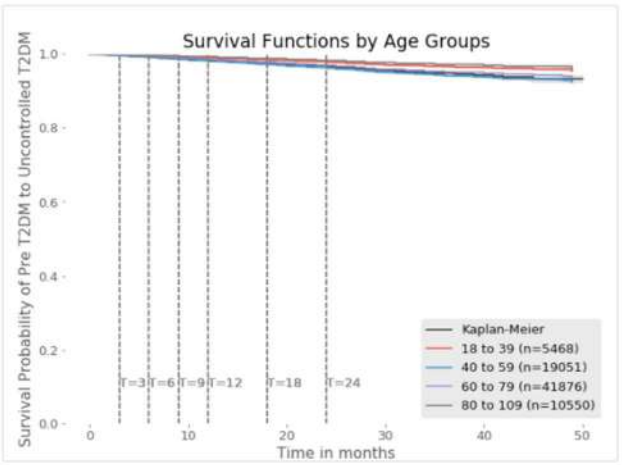

Scores by Ethnicity
ConcordanceIndex
n=4192
n=76945
ConcordanceIndex
0.8
0.6
0.4
0.2
0.0
Overall
Hispanic or Latino
Not Hispanic or Latino
IntegratedBrierScore
n=76945
n=4192
n=72753
mean=0.03
0.030
0.025
0.020
0.015
0.010
0.005
0.000
IntegratedBrierScore
Overall
Hispanic or Latino
Not Hispanic or Latino

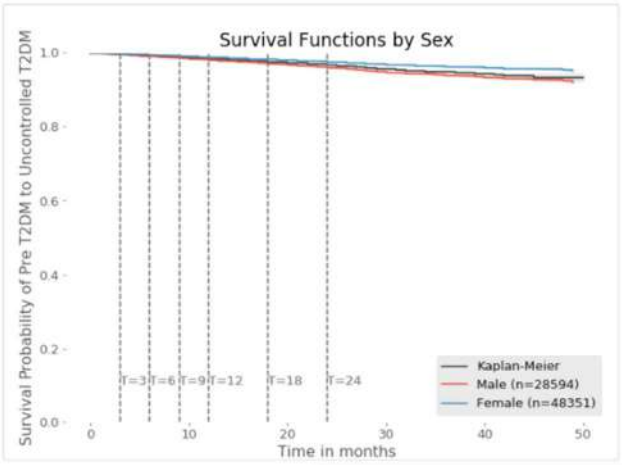

Scores by Patient History (months)
ConcordanceIndex
n=2437
n=76945
n=6688
n=20985
n=22329
mean=0.83
ConcordanceIndex
0.8
0.6
0.4
0.2
0.0
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60
IntegratedBrierScore
n=76945
n=6688
n=2437
n=20985
mean=0.02
n=22329
n=24506
IntegratedBrierScore
0.030
0.025
0.020
0.015
0.010
0.005
0.000
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60

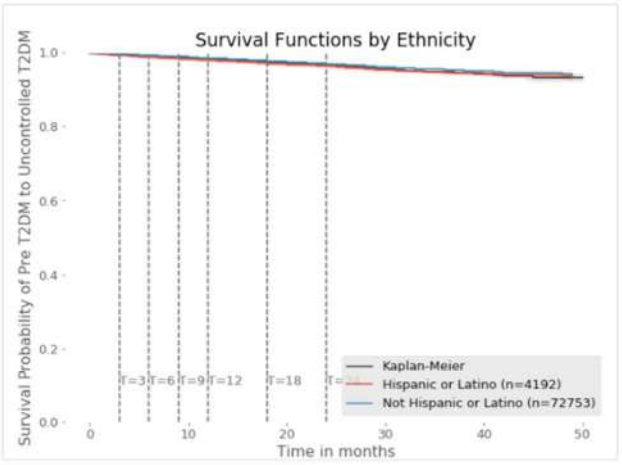
Average Survival Function Curves

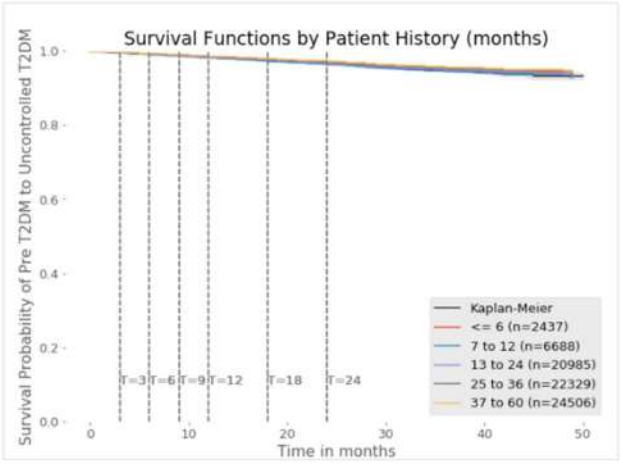
The following charts show how the average survival function curve varies among subgroups of risk, age, sex, ethnicity and patient history.





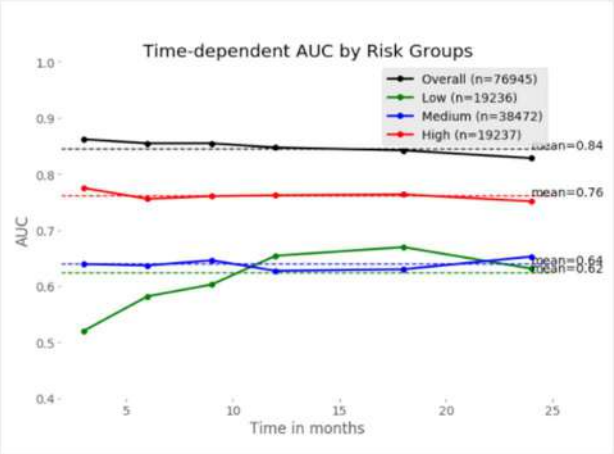


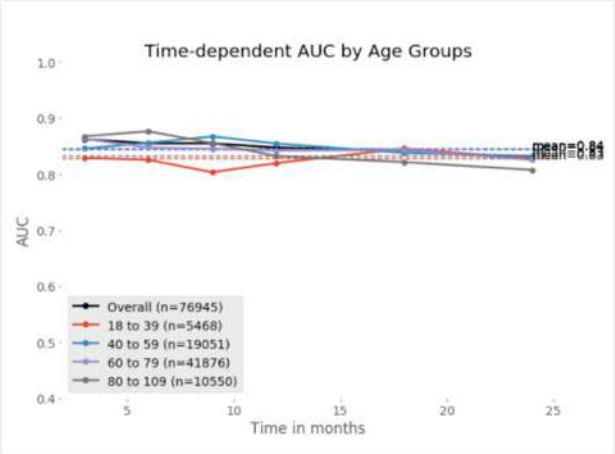


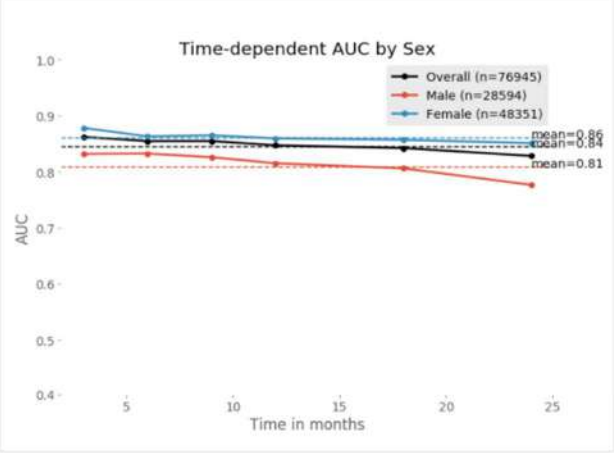


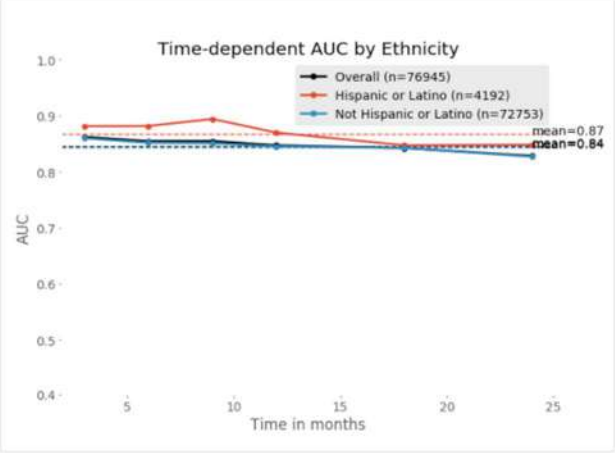
Time-dependent AUC

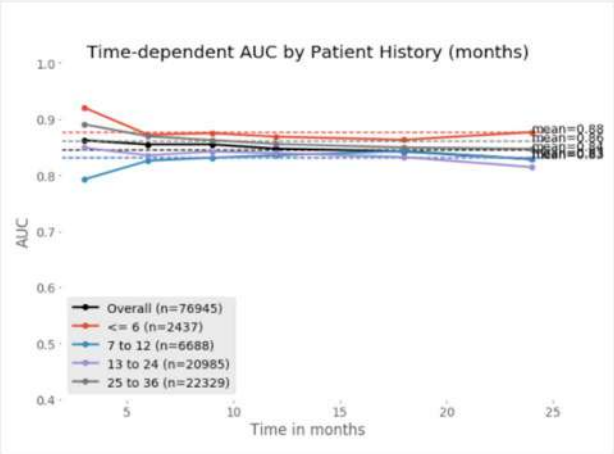
The following charts show how the AUC across time varies among subgroups of risk, age, sex, ethnicity and patient history.





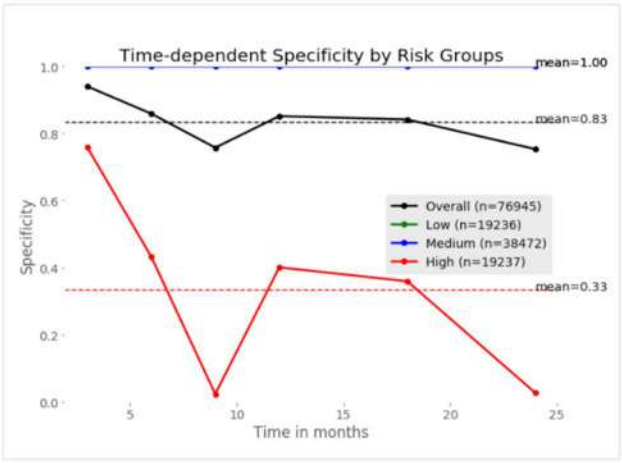


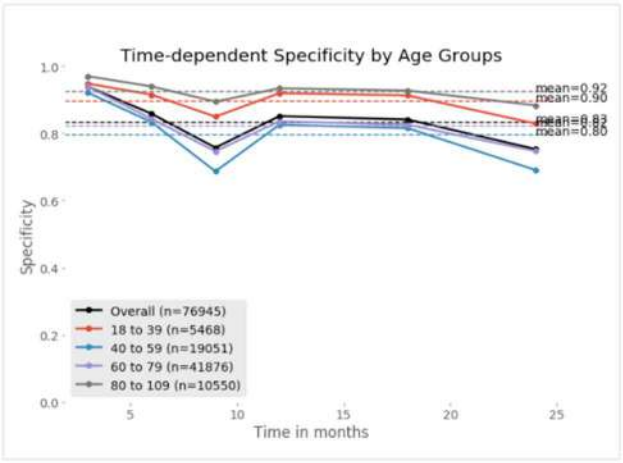


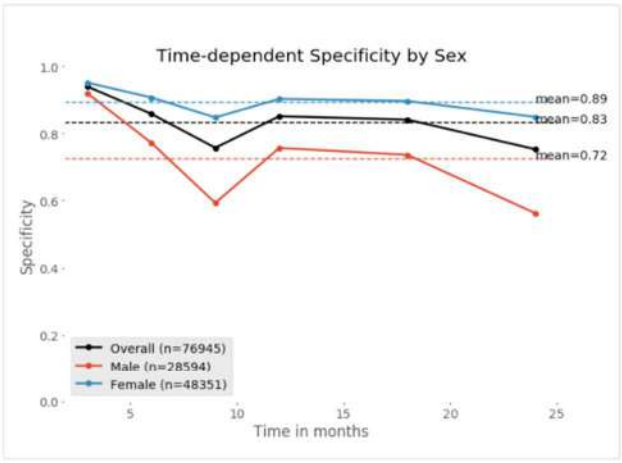


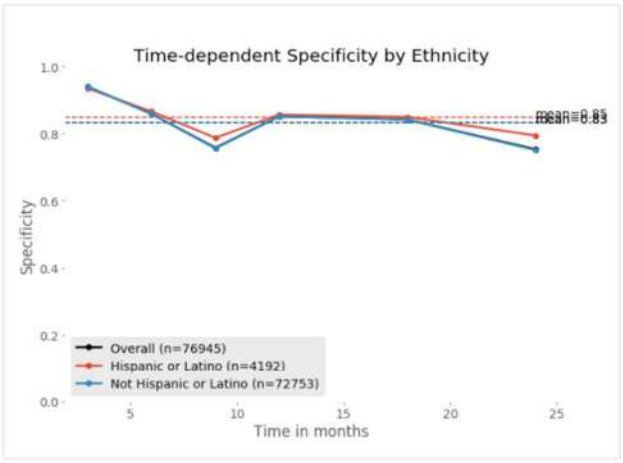
Time-dependent Specificity

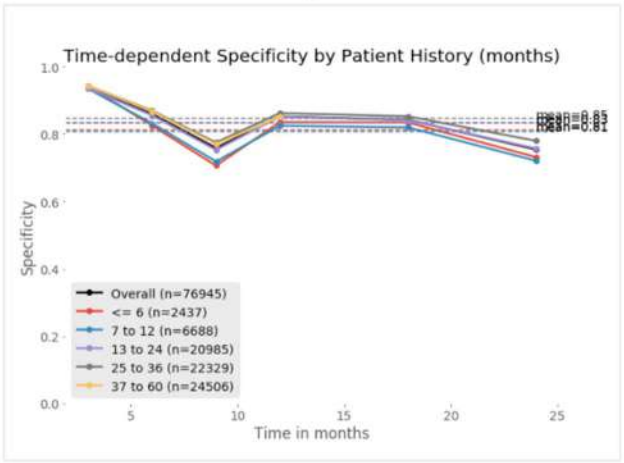
The following charts show how the specificity across time varies among subgroups of risk, age, sex, ethnicity and patient history.





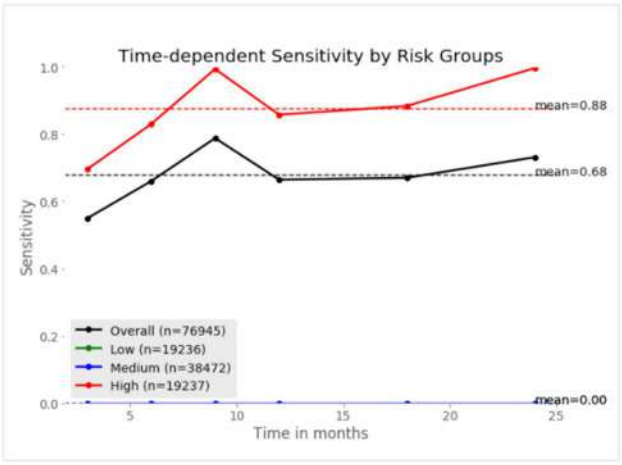


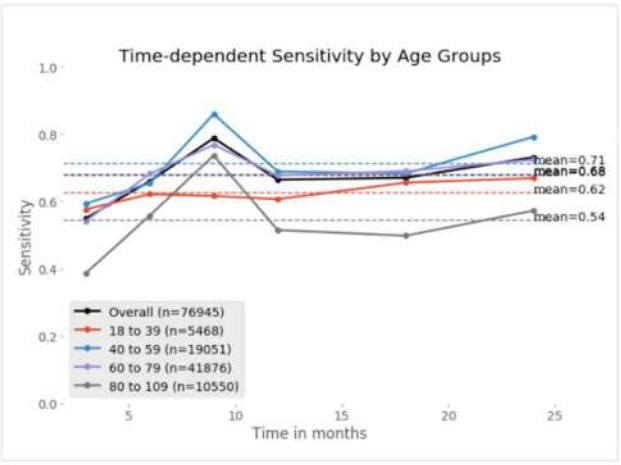


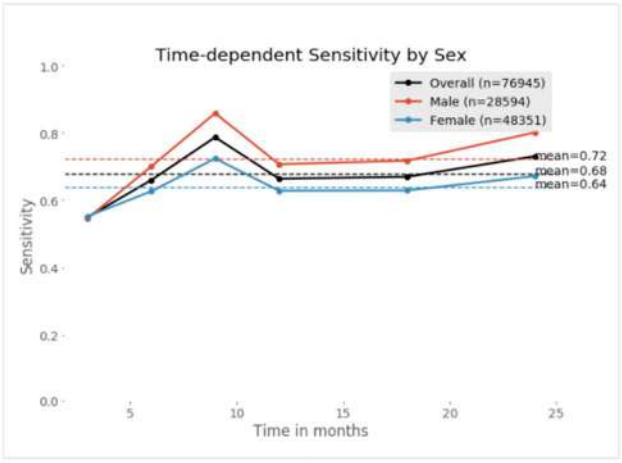


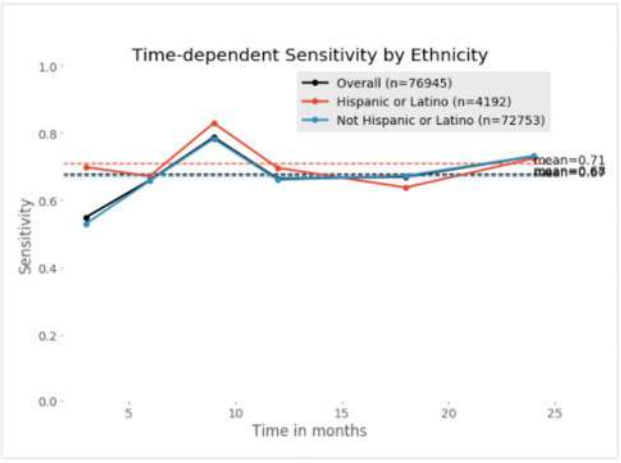
Time-dependent Sensitivity

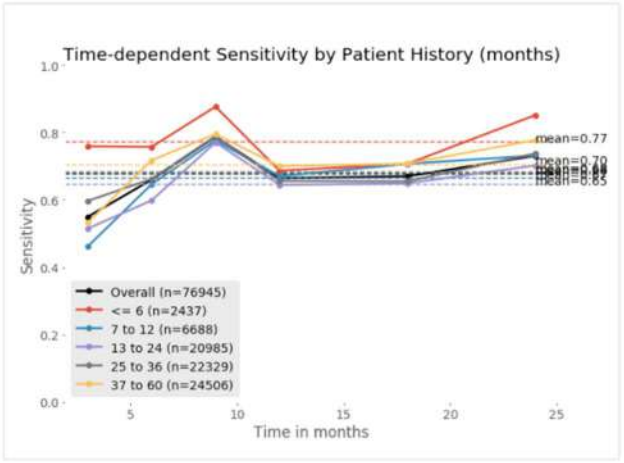
The following charts show how the sensitivity across time varies among subgroups of risk, age, sex, ethnicity and patient history.







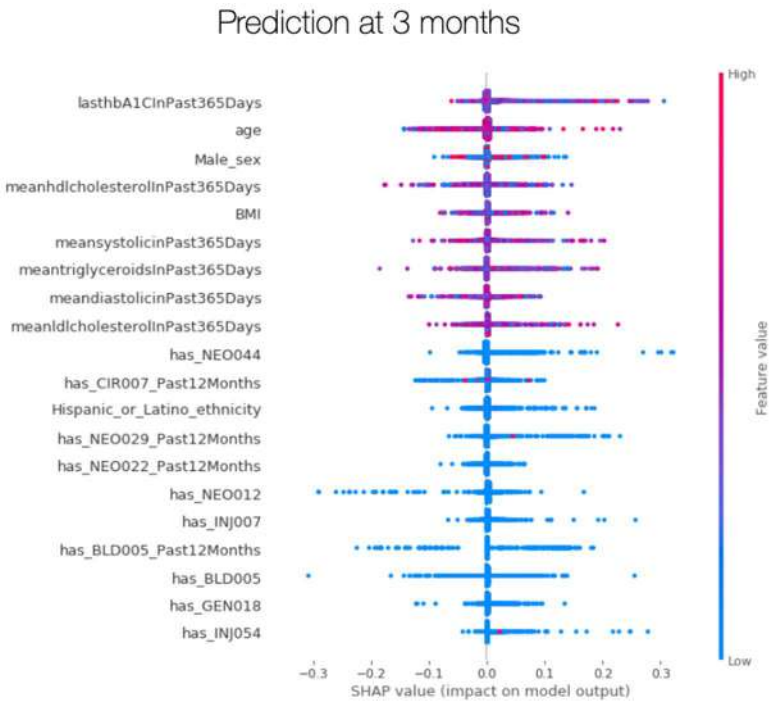


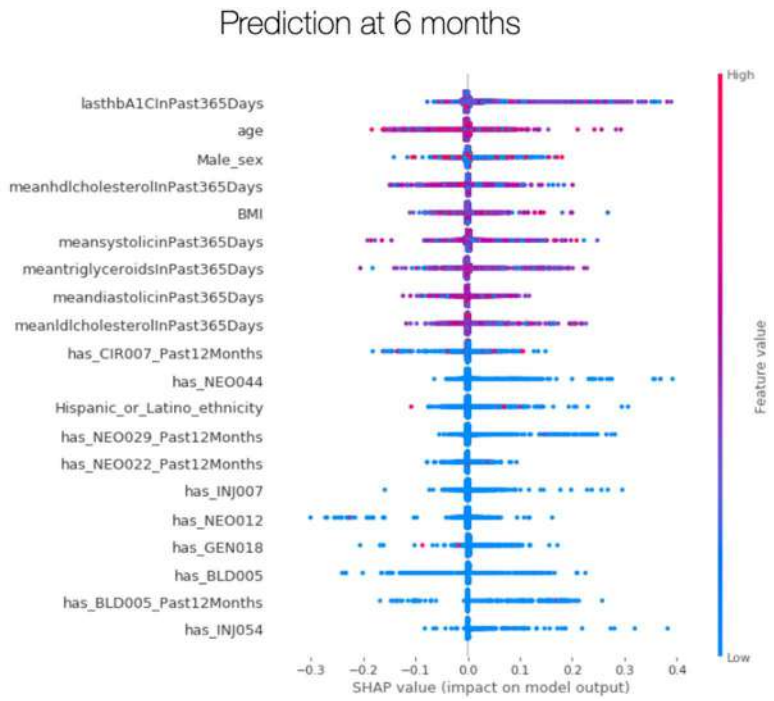


Model Explanation (DeepSurv)

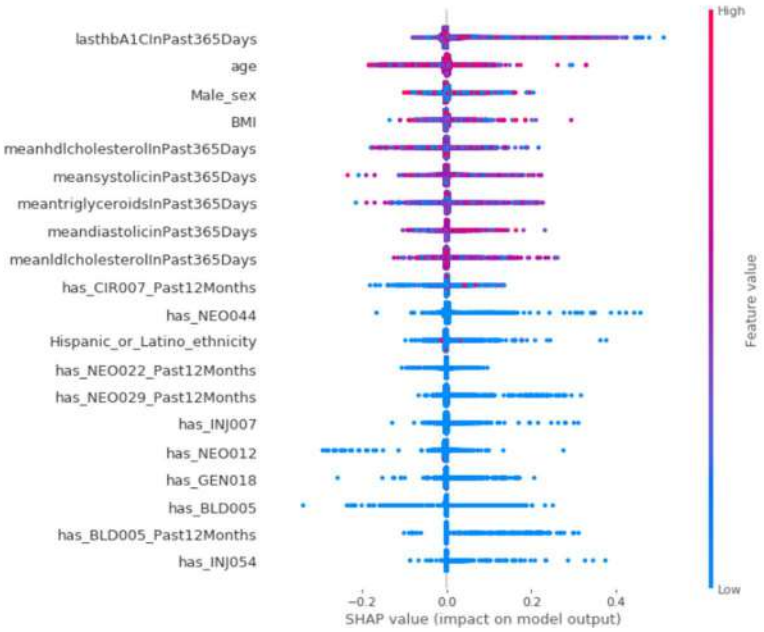
Global

The following plots show the SHAP values of each instance in the training set for each future time (3, 6, 9, 12, 18 and 24 months). The features are sorted by the total magnitude of the SHAP values over all instances and the distribution of the effect that each feature has on the model's output can be observed.

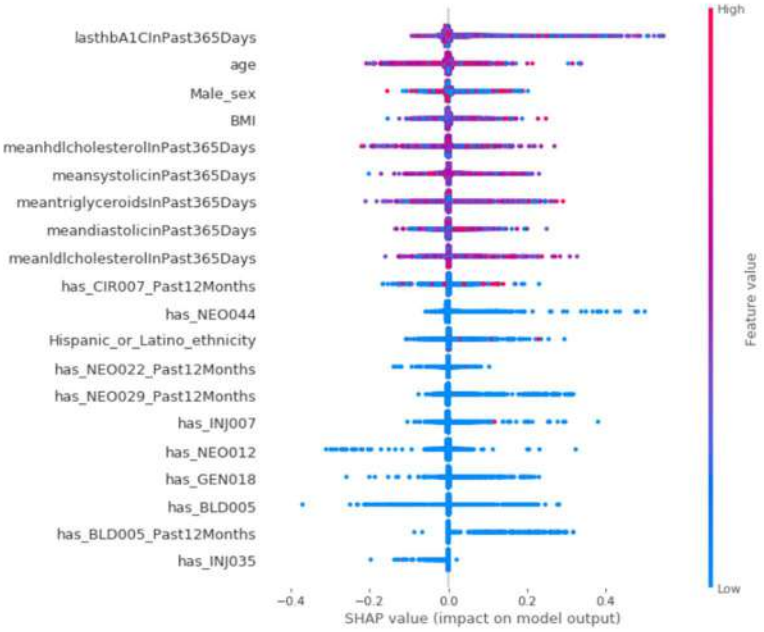




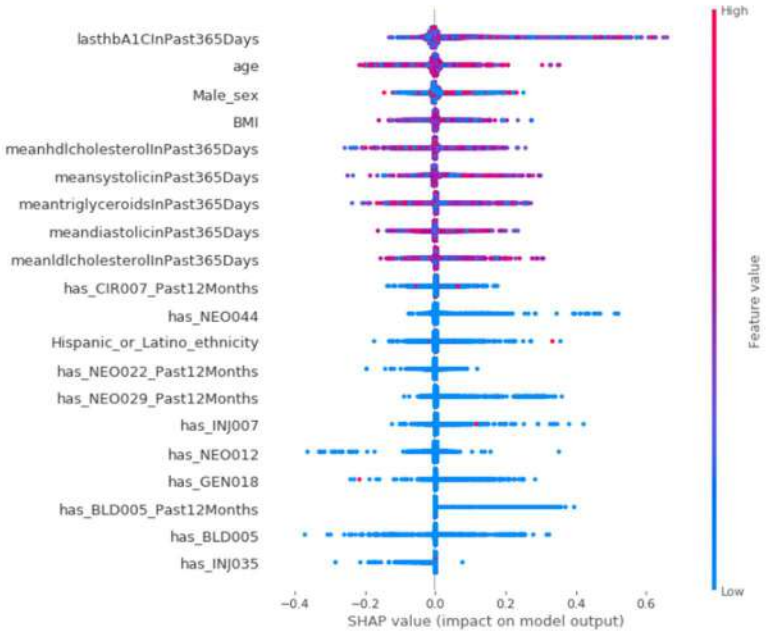
Prediction at 9 months



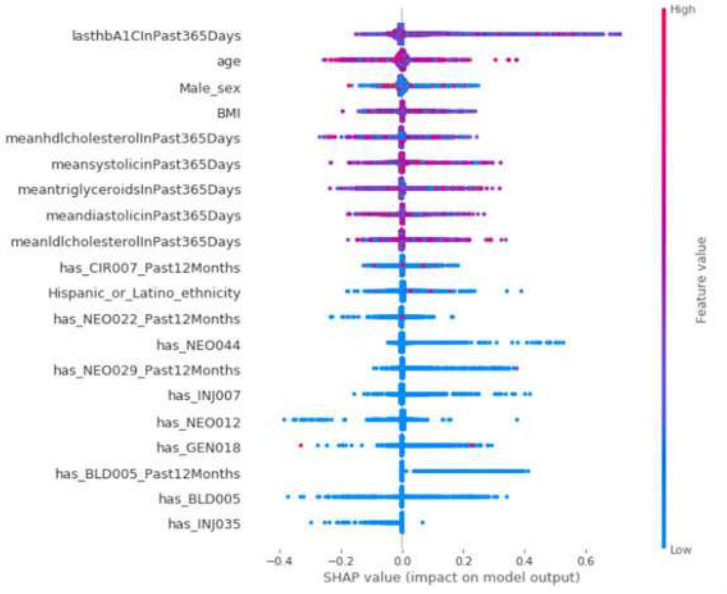
Prediction at 12 months



Prediction at 18 months

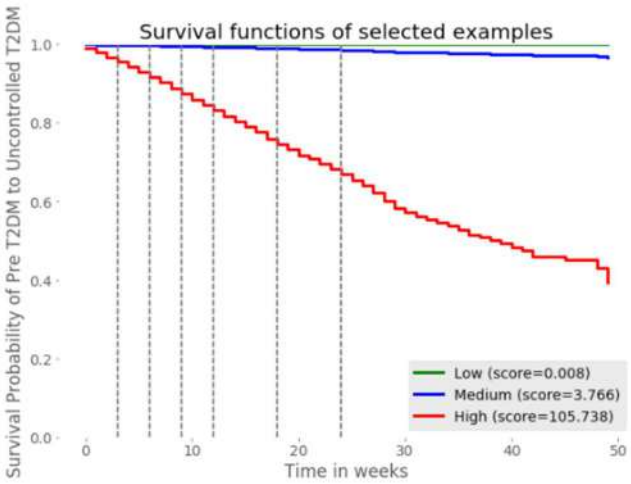


Prediction at 24 months

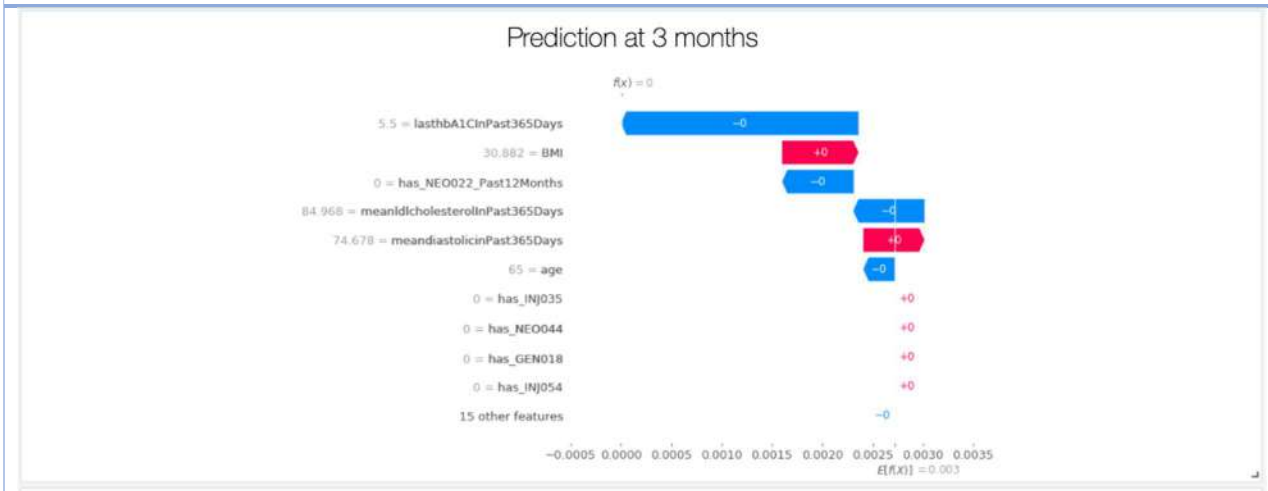


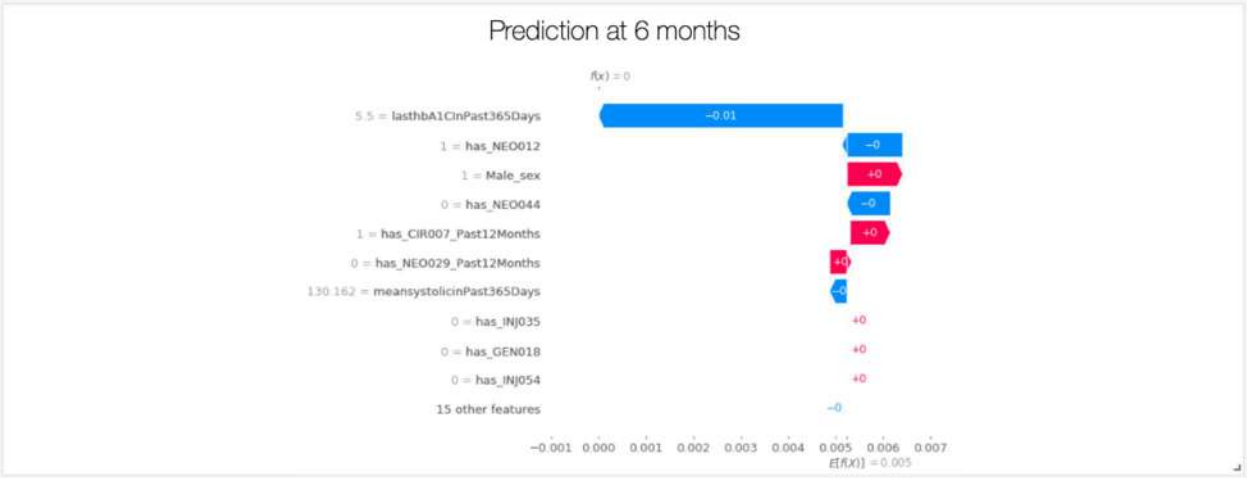
Local

SHAP values were also generated to explain the predictions of individual examples for each future time (3, 6, 9, 12, 18 and 24 months). A total of 3 examples were selected by sampling of risk scores at the 5th, 50th and 95th percentile to represent instances at low, medium and high risks respectively.



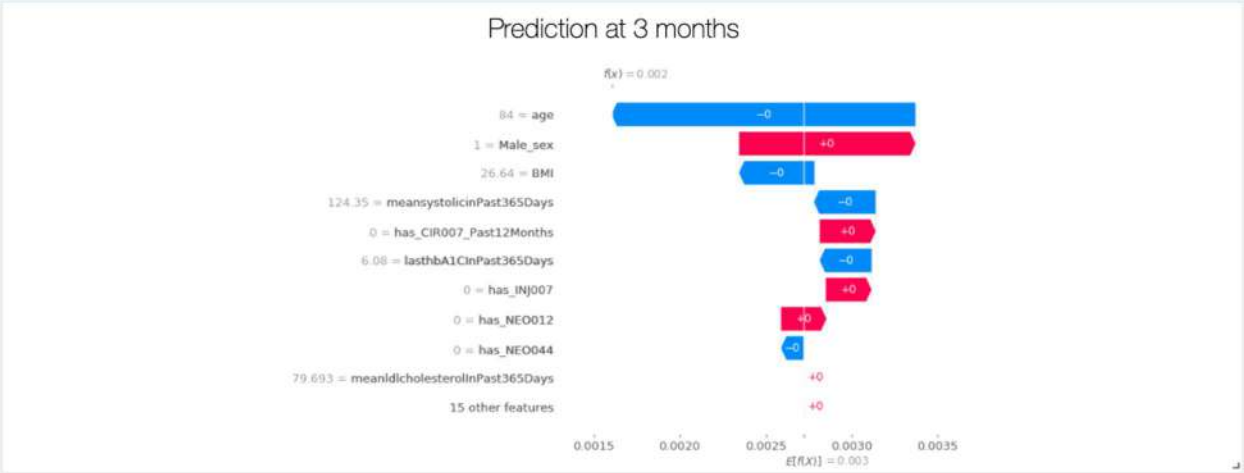
Low Risk
Risk Score: 0.008

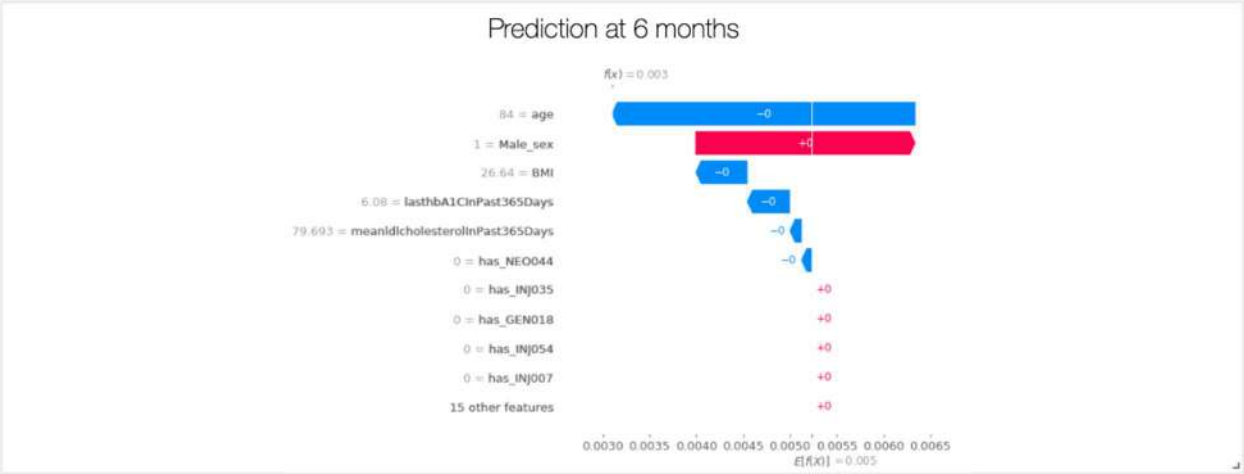


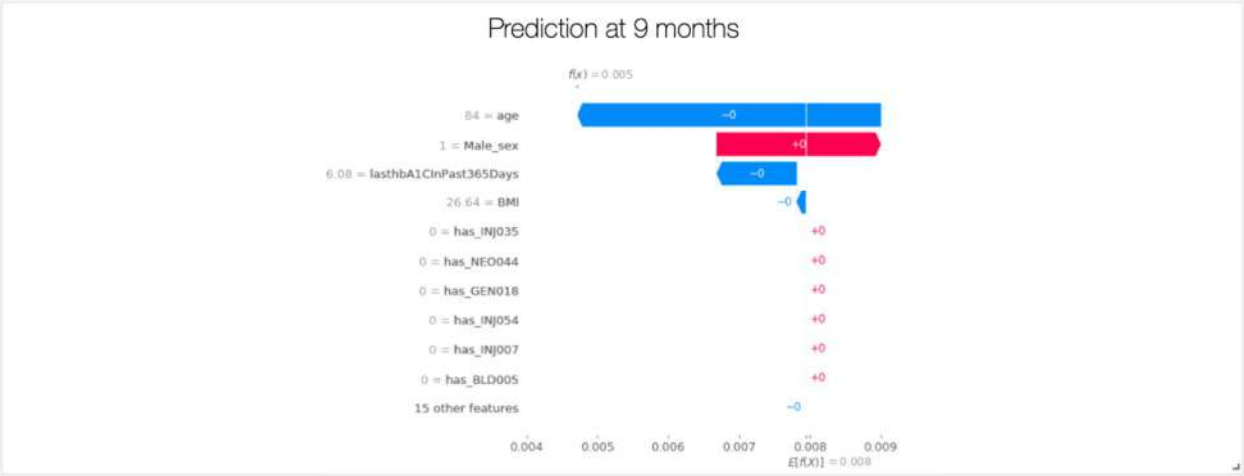


Low Risk
Risk Score: 0.008

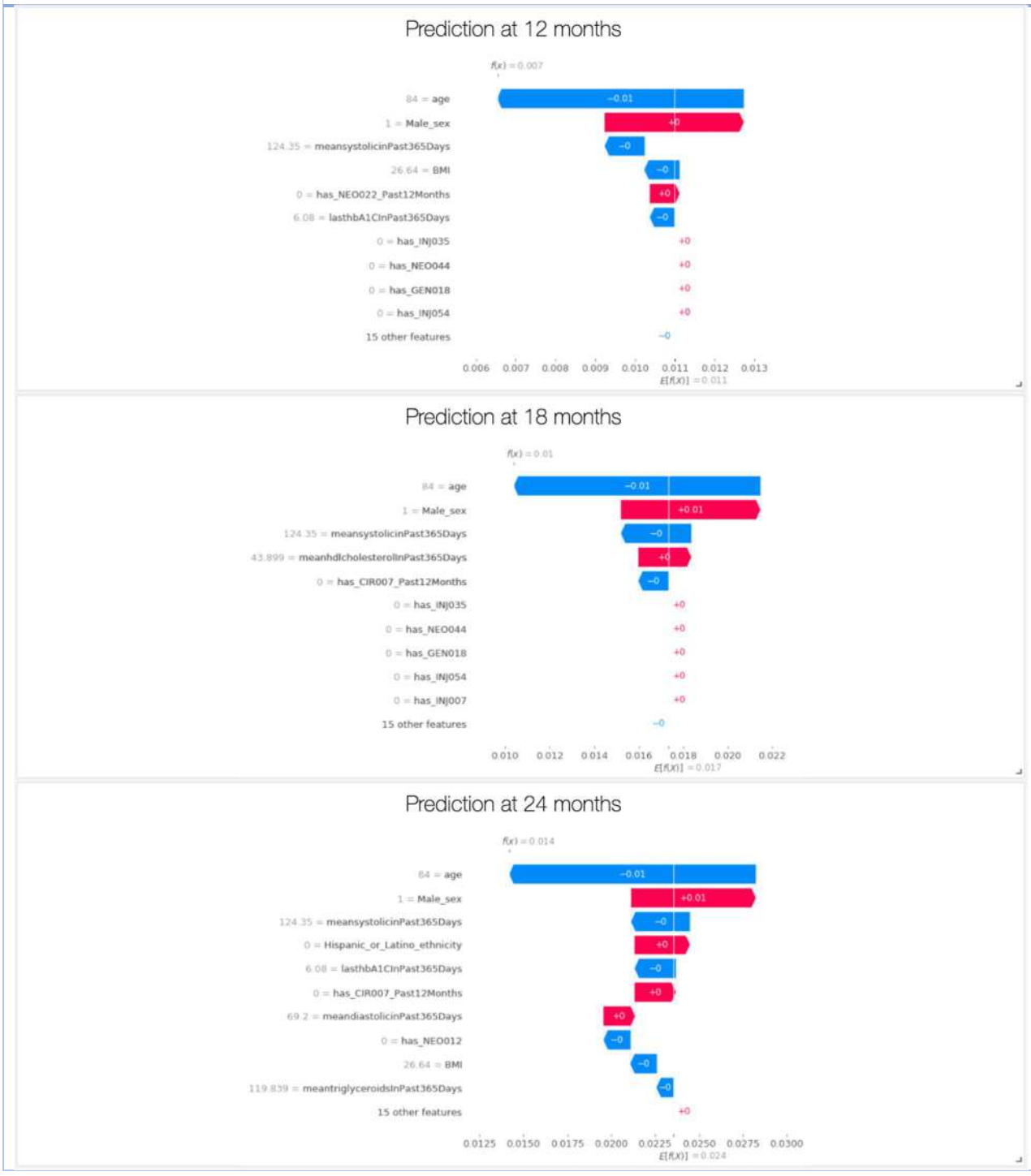
Medium Risk
Risk Score: 3.766



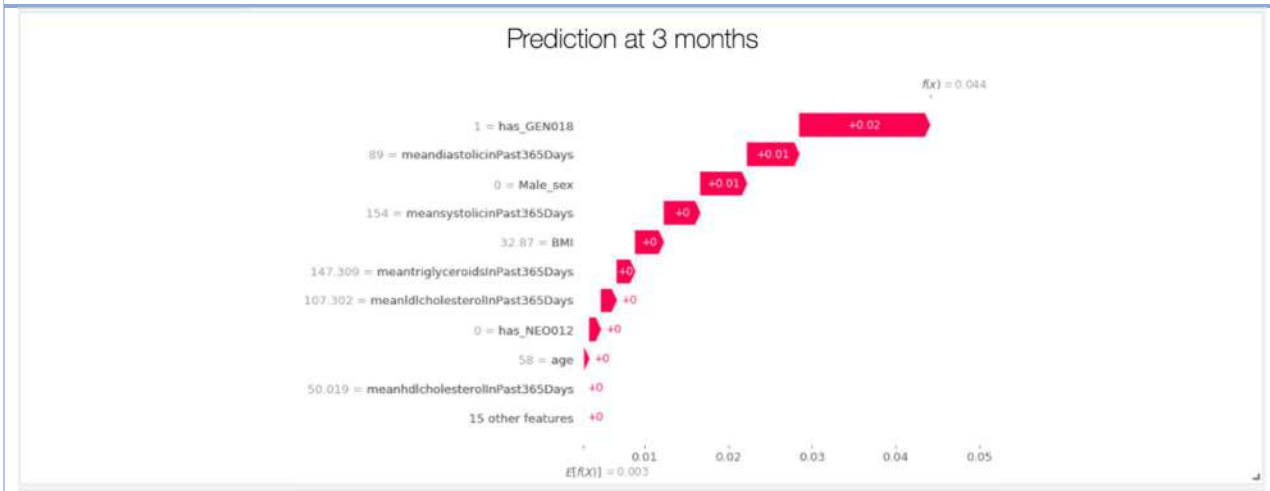


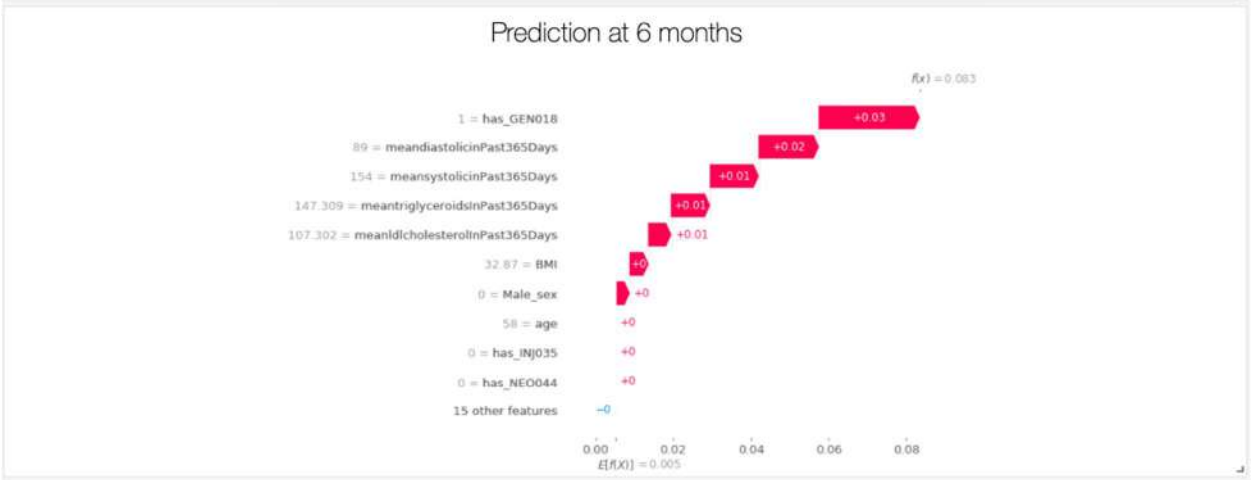


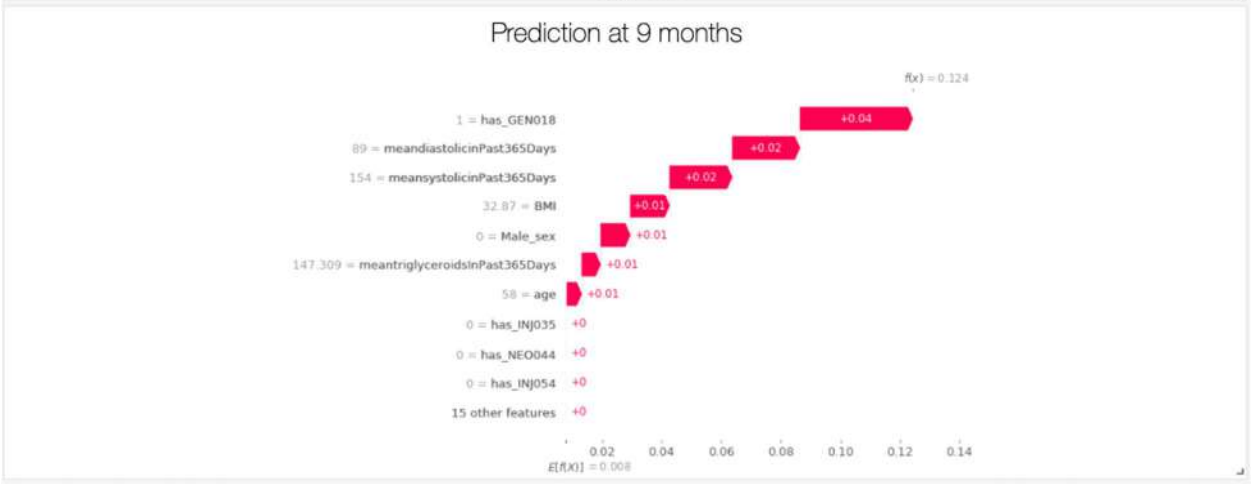
Medium Risk
Risk Score: 3.766



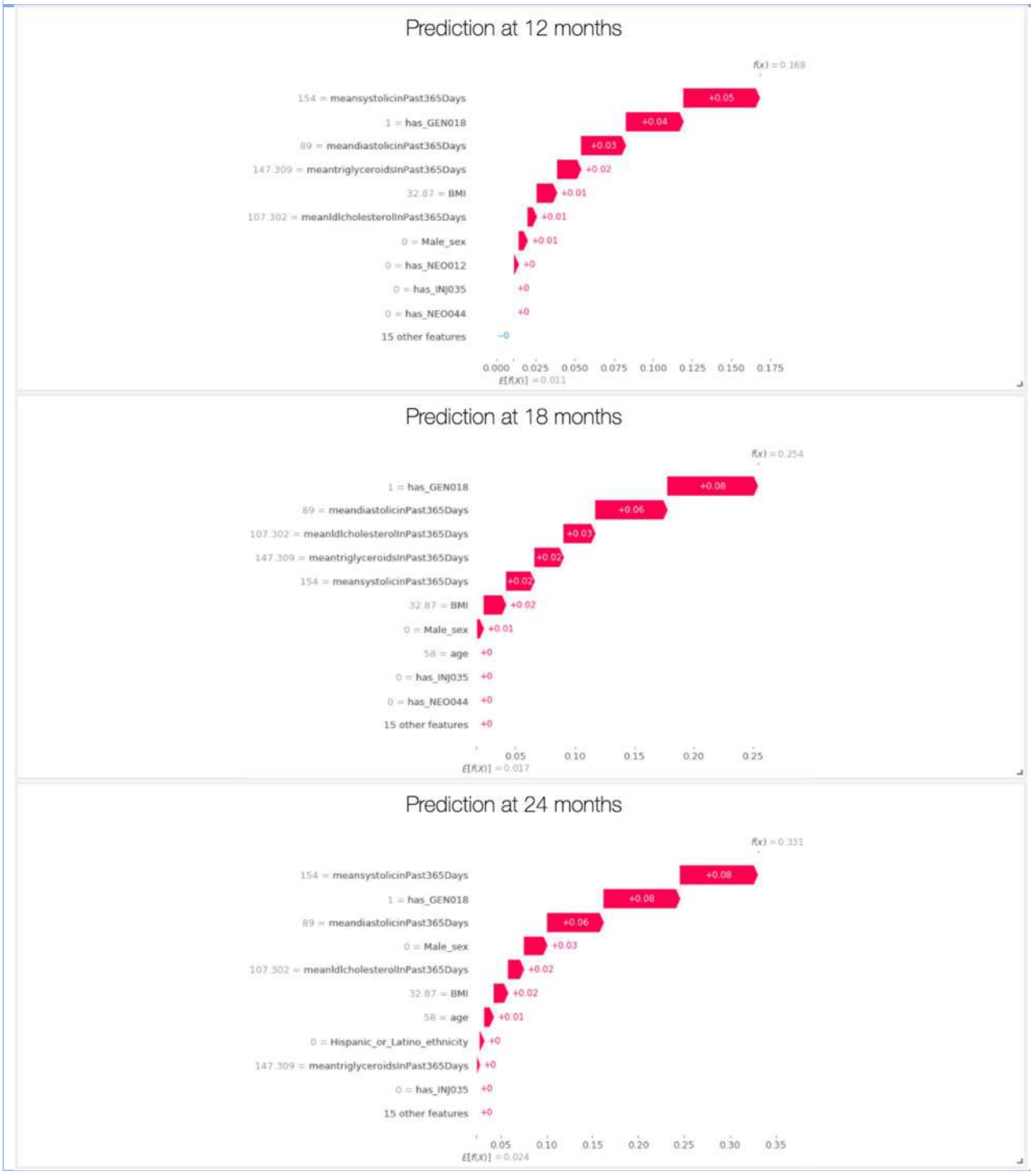
High Risk
Risk Score: 105.738







High Risk
Risk Score: 105.738



DM to Diabetic Nephropathy Prediction

Item	Specification
Business Goal	Enable care managers to identify the patients who are at risk of developing diabetic nephropathy
Usage Setting	Outpatient
ML Task	Predict risk and/or time from DM or uncontrolled DM to diabetic nephropathy
ML Class	Survival
Instances for Prediction	Encounters
Labels for Instances	Binary indicator and time to event or censoring for diabetic nephropathy
Cohort Criteria	• 2016-01-01 $\leq$ encounter date $\leq$ 2020-06-30 (available Epic data, excluding outliers) • Encounter date is not within the first 90 days of when the patient entered the data set, to adjust for left-censoring • 18 $\leq$ age $\leq$ 110 (adults without outliers) • No T1DM diagnosis • Not pregnant • No "Do Not Resuscitate" diagnosis • DM or uncontrolled DM event before encounter date • No diabetic nephropathy event before encounter date • No diabetic nephropathy event up to 6 days after encounter date (encounters where diagnoses confirm event within the week)

Input Features	• Demographic
	• Diagnosis, except:
	  ○ hasDiabetesNephropathy*
	  ○ has_GEN001* (Nephritis; nephrosis; renal sclerosis)
	  ○ has_GEN002* (Acute and unspecified renal failure)
	  ○ has_GEN003* (Chronic kidney disease)
	  ○ has_GEN006* (Other specified and unspecified diseases of kidney and ureters)
	• Labs
	• Utilization
	• Vitals
	
	See Appendix E for details.

Evaluation Metrics	• Concordance Index • Integrated Brier Score

Data

The following charts summarize the key characteristics of the data after applying the cohort criteria stated above, along with selected features (see Model Signature below).

Category	summary Variable	count	mean	stddev	min	25%	50%	75%	max
Demographic	AgeBucket_18_to_39	63765.0	0.049400	0.216704	0.00	0.000	0.000	0.000	1.00
	AgeBucket_40_to_59	63765.0	0.299976	0.458251	0.00	0.000	0.000	1.000	1.00
	AgeBucket_60_to_79	63765.0	0.552309	0.497260	0.00	0.000	1.000	1.000	1.00
	AgeBucket_80_to_109	63765.0	0.098314	0.297741	0.00	0.000	0.000	0.000	1.00
	Sex_Female	63765.0	0.572367	0.494739	0.00	0.000	1.000	1.000	1.00
	Sex_Male	63765.0	0.427633	0.494739	0.00	0.000	0.000	1.000	1.00
	Ethnicity_Hispanic_or_Latino	63765.0	0.073332	0.260682	0.00	0.000	0.000	0.000	1.00
	Ethnicity_Not_Hispanic_or_Latino	63765.0	0.926668	0.260682	0.00	1.000	1.000	1.000	1.00
Encounter	EncounterType_Emergency	63765.0	0.224731	0.417409	0.00	0.000	0.000	0.000	1.00
	EncounterType_Inpatient	63765.0	0.091759	0.288687	0.00	0.000	0.000	0.000	1.00
	EncounterType_Outpatient	63765.0	0.683510	0.465110	0.00	0.000	1.000	1.000	1.00
Label	Time	63765.0	15.200580	11.223469	0.00	6.000	13.000	23.000	50.00
	Event	63765.0	0.116365	0.320664	0.00	0.000	0.000	0.000	1.00
Feature	age	63765.0	63.402556	13.069697	18.00	55.000	65.000	72.000	100.00
	Male_sex	63765.0	0.427633	0.494739	0.00	0.000	0.000	1.000	1.00
	Hispanic_or_Latino_ethnicity	63765.0	0.073332	0.260682	0.00	0.000	0.000	0.000	1.00
	lasthbA1ClnPast365Days	63765.0	7.600242	1.215191	3.50	6.900	7.529	8.000	12.70
	meandiastolicinPast365Days	63765.0	74.097812	7.814768	44.00	70.050	74.041	79.110	107.56
	meansystolicinPast365Days	63765.0	131.832214	11.574736	82.00	127.597	131.574	135.440	180.00
	BMI	63765.0	33.819156	6.815868	13.43	29.840	33.718	37.340	85.68
	meantriglyceroidsInPast365Days	63765.0	169.037094	57.815160	19.00	141.000	167.131	182.483	460.50
	meanldlcholesterolInPast365Days	63765.0	89.617346	23.508239	8.00	81.282	89.776	97.772	201.00
	meanhdlcholesterolInPast365Days	63765.0	43.042894	9.097396	5.00	37.685	42.780	47.646	98.00
	has_NEO024_Past12Months	63765.0	0.001600	0.039964	0.00	0.000	0.000	0.000	1.00
	has_RSP010_Past12Months	63765.0	0.005003	0.070553	0.00	0.000	0.000	0.000	1.00
	has_CIR007_Past12Months	63765.0	0.191578	0.393546	0.00	0.000	0.000	0.000	1.00
	has_CIR008_Past12Months	63765.0	0.008829	0.093549	0.00	0.000	0.000	0.000	1.00
	has_NVS018	63765.0	0.008970	0.094287	0.00	0.000	0.000	0.000	1.00
	has_NEO050	63765.0	0.003936	0.062617	0.00	0.000	0.000	0.000	1.00
	has_INJ026	63765.0	0.003607	0.059950	0.00	0.000	0.000	0.000	1.00
	has_EXT017	63765.0	0.004077	0.063725	0.00	0.000	0.000	0.000	1.00
	has_CIR034	63765.0	0.004768	0.068883	0.00	0.000	0.000	0.000	1.00
	has_EYE012	63765.0	0.005018	0.070663	0.00	0.000	0.000	0.000	1.00
	has_FAC023	63765.0	0.043770	0.204585	0.00	0.000	0.000	0.000	1.00
	has_NEO008	63765.0	0.002729	0.052167	0.00	0.000	0.000	0.000	1.00
	has_NVS005	63765.0	0.004642	0.067975	0.00	0.000	0.000	0.000	1.00
	has_GEN010	63765.0	0.015306	0.122769	0.00	0.000	0.000	0.000	1.00
	has_END011	63765.0	0.238767	0.426334	0.00	0.000	0.000	0.000	1.00
	has_CIR008	63765.0	0.031459	0.174557	0.00	0.000	0.000	0.000	1.00

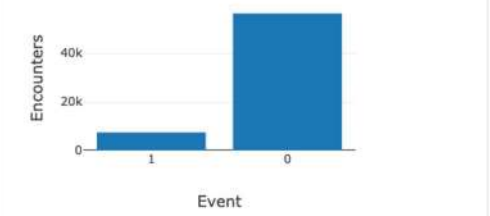
(Percentages for binary variables can be read from the “mean” column.)

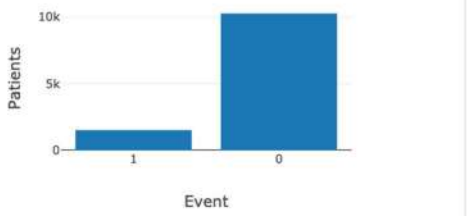
Encounters and Patients

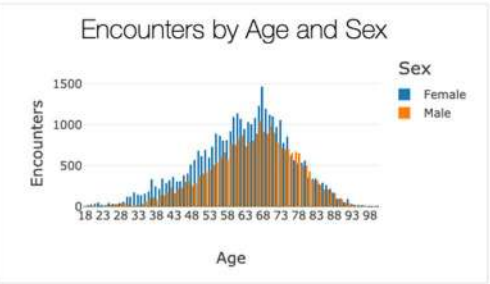
	Examples	Encounters	Patients
1	63765	63765	11801

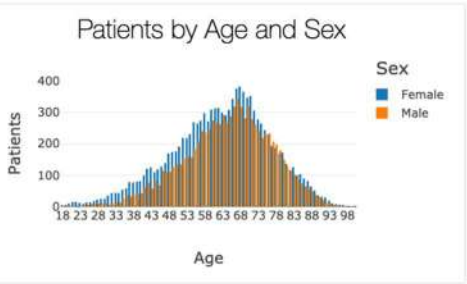
Train and Test Sets

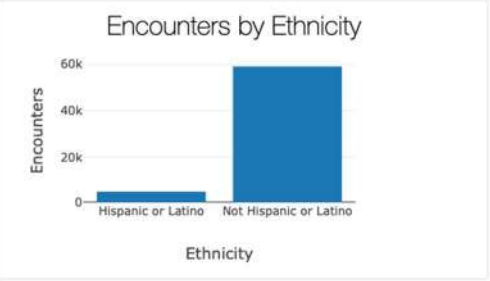
	Set	No Event	No Event %	Event	Event %	Total	Total %
1	Train	39492	70.1	5214	70.3	44706	70.1
2	Test	16853	29.9	2206	29.7	19059	29.9
3	Total	56345	100	7420	100	63765	100

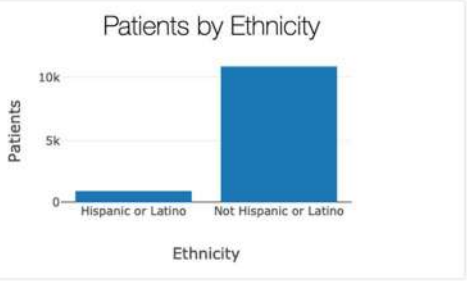


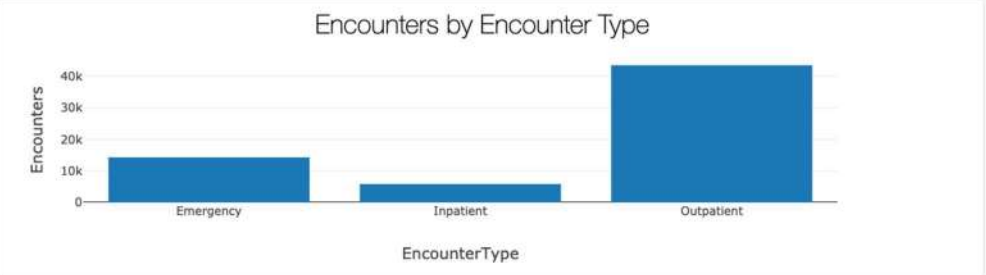


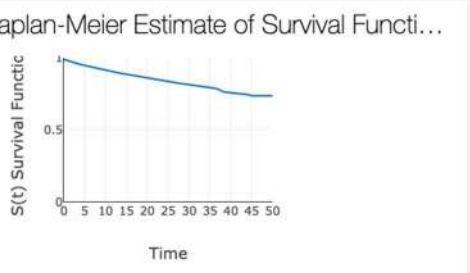








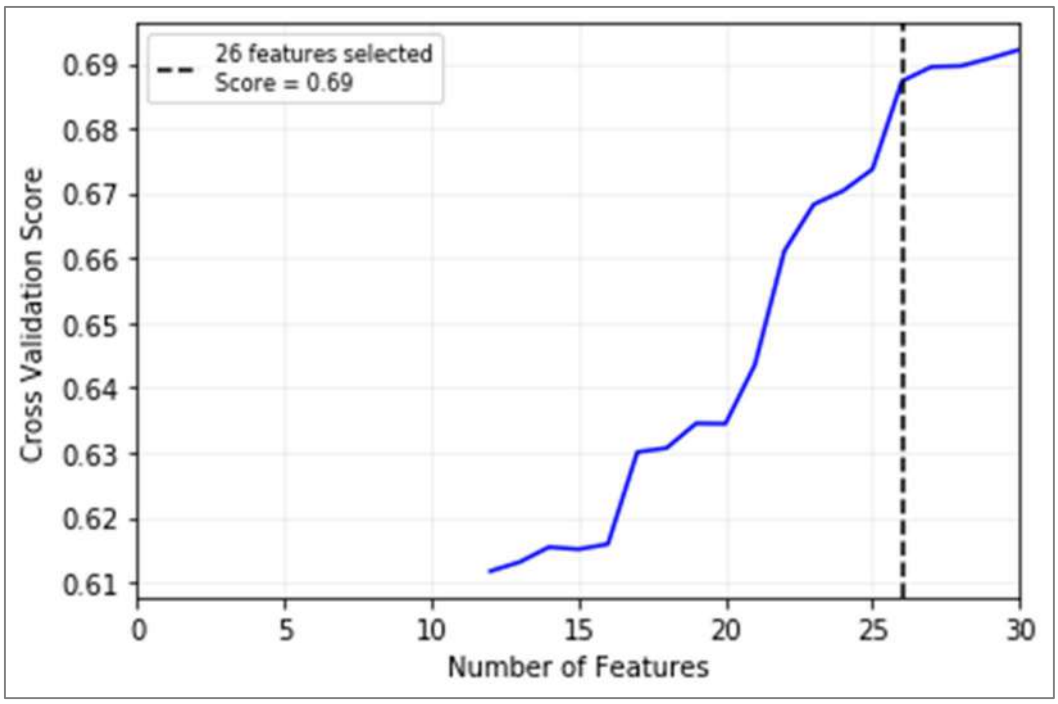




Model Signature

The model signature has 26 features, comprising of 12 mandatory features and 14 other selected features. These are the selected features, in rank order (the last feature to be eliminated is ranked 1):

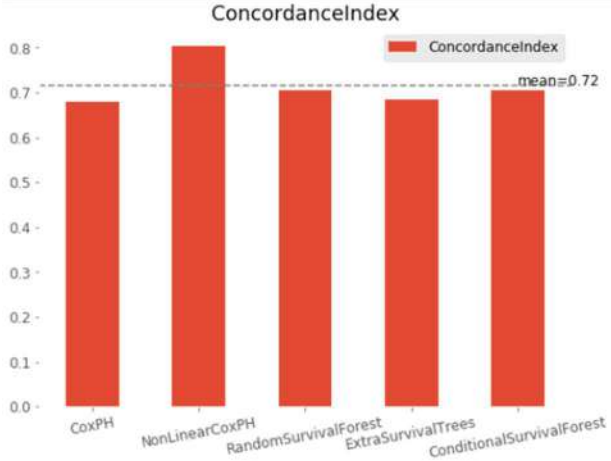
1. has_NEO008 (Head and neck cancers - laryngeal)
2. has_EXT017 (External cause codes: suffocation/inhalation; initial encounter)
3. has_NEO024_Past12Months (Sarcoma)
4. has_EYE012 (Other specified eye disorders)
5. has_CIR034 (Chronic phlebitis; thrombophlebitis and thromboembolism)
6. has_NVS005 (Multiple sclerosis)
7. has_INJ026 (Other specified injury)
8. has_CIR008 (Hypertension with complications and secondary hypertension)
9. has_RSP010_Past12Months (Aspiration pneumonitis)
10. has_GEN010 (Proteinuria)
11. has_END011 (Fluid and electrolyte disorders)
12. has_NVS018 (Myopathies)
13. has_NEO050 (Endocrine system cancers - thyroid)
14. has_FAC023 (Organ transplant status)
15. Hispanic_or_Latino_ethnicity
16. Male_sex
17. has_CIR007_Past12Months (Essential hypertension)
18. lasthbA1CInPast365Days
19. age
20. BMI
21. meandiastolicinPast365Days
22. meansystolicinPast365Days
23. meanhdlcholesterolInPast365Days
24. meanldlcholesterolInPast365Days
25. meantriglyceroidsInPast365Days
26. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)

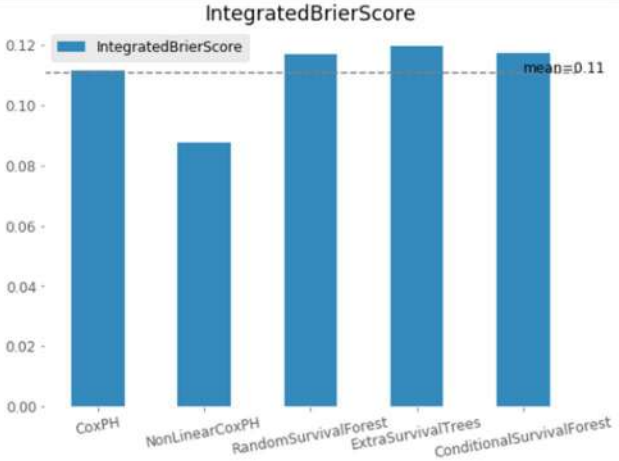


Model Performance

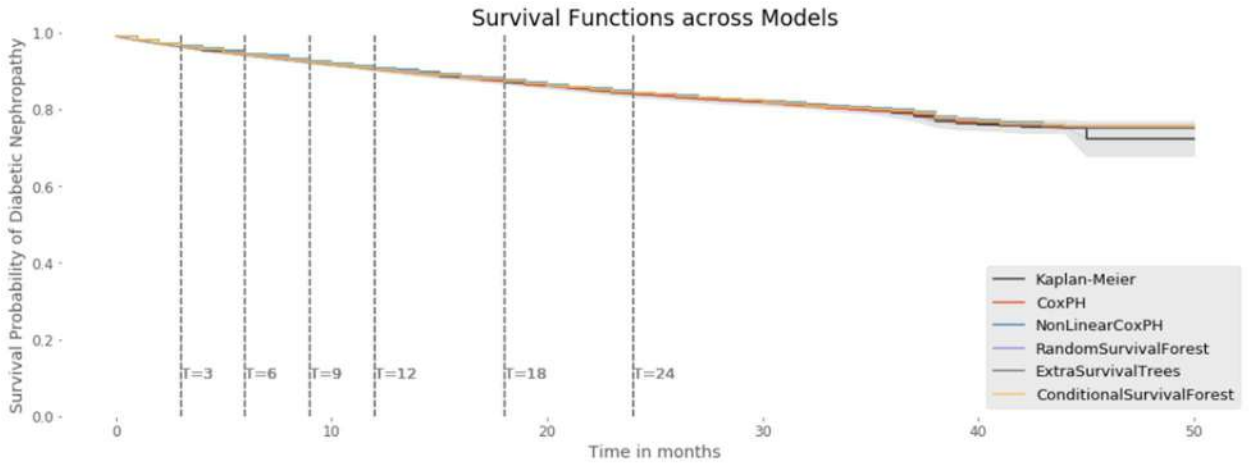
The following table and chart summarize the performance of all candidate models on the test set for this prediction task in terms of the Concordance Index and the Integrated Brier Score.

Model	No. of Parameter Combinations Successfully Tested	Concordance Index	Integrated Brier Score
CoxPH	117	0.68	0.11
DeepSurv	175	**0.80**	**0.09**
RSF	35	0.71	0.12
CSF	35	0.69	0.12
EST	27	0.71	0.12

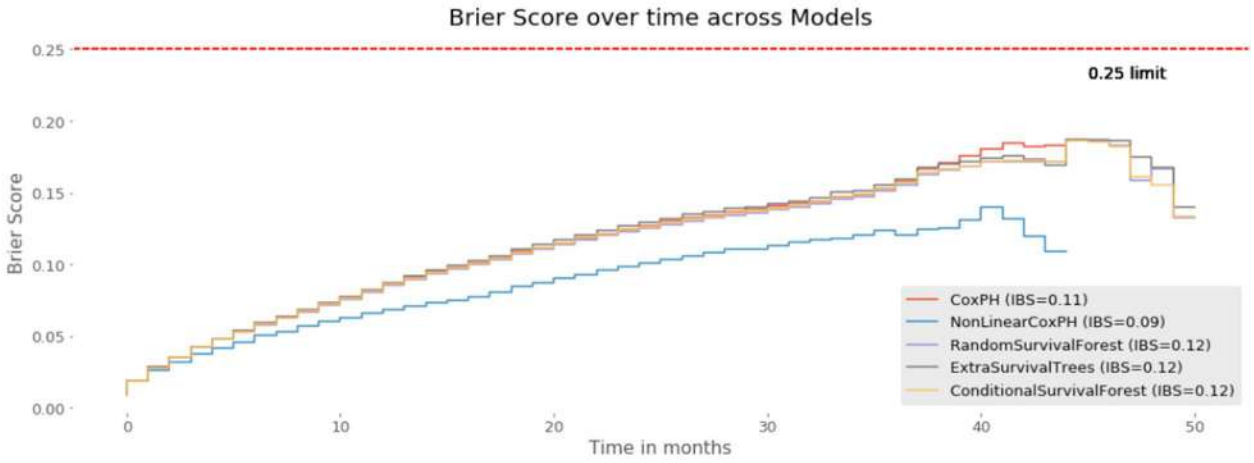




The following chart shows how the average survival function curves of the candidate models compare to the KM survival curve, the more similar their curves are to the KM survival curve the better.



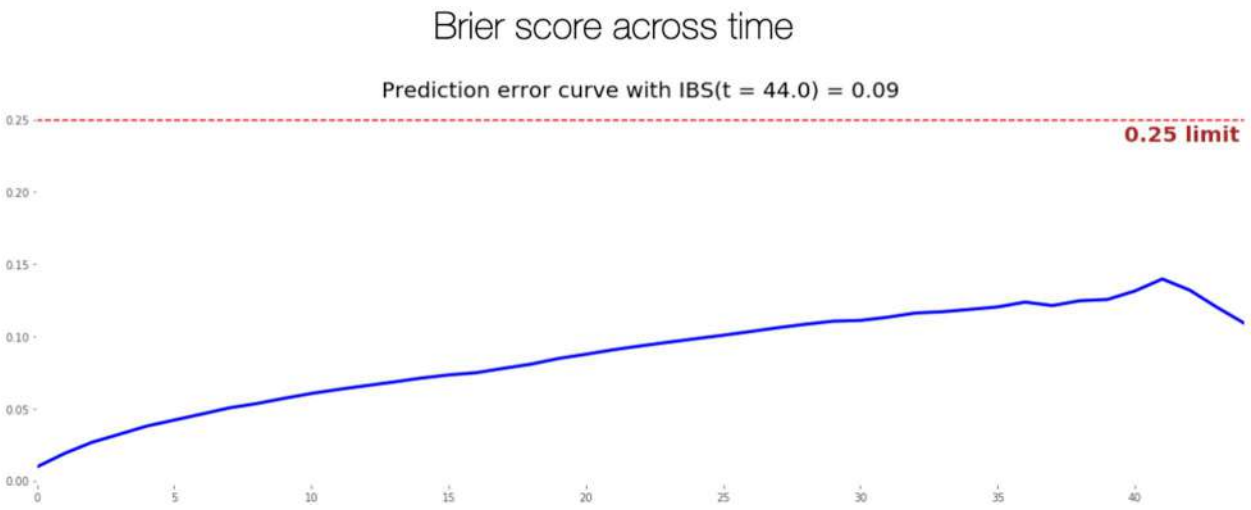
This chart shows the change in the Brier Score over time for all candidate models, the closer the scores are to 0 the better.



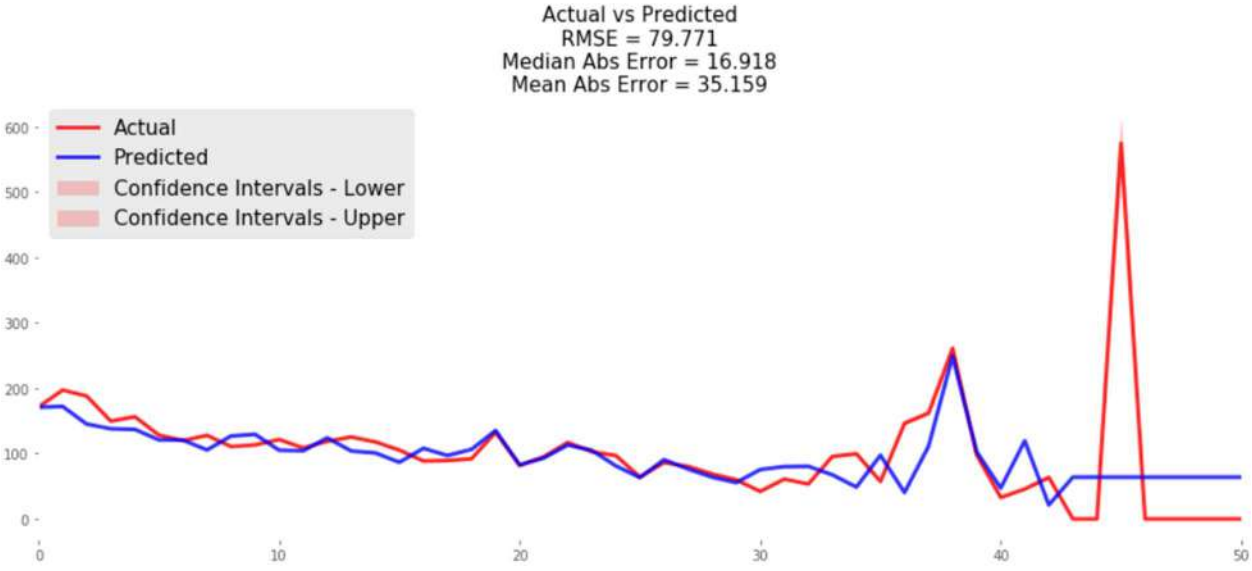
Model Evaluation of Selected Model (DeepSurv)

Overall

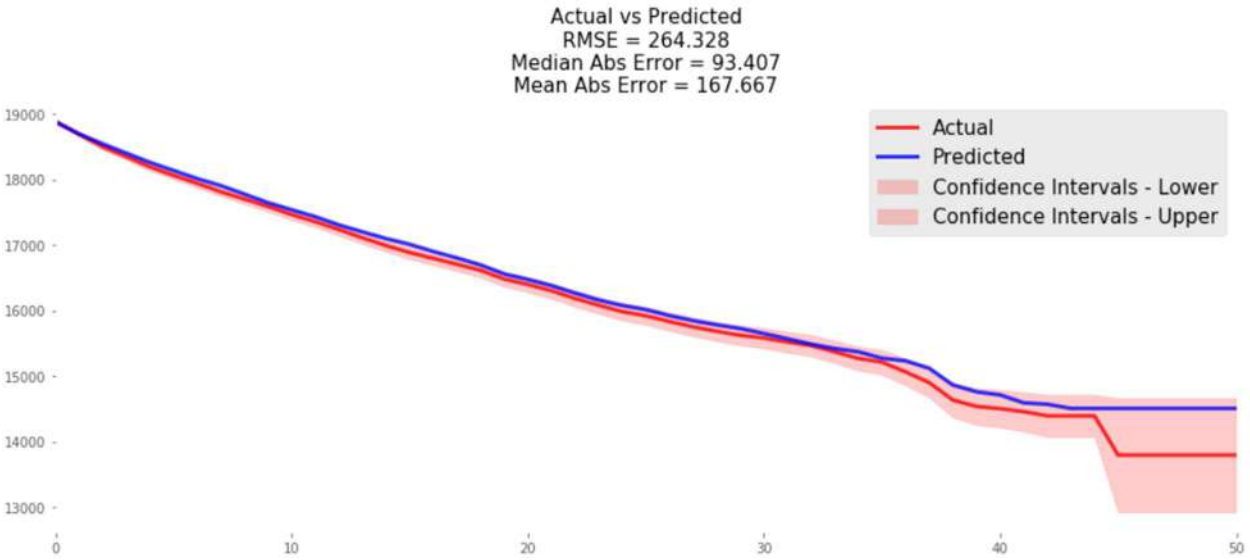
This chart shows the change in the Brier Score over time for the selected model, the closer the scores are to 0 the better.



The following chart shows the actual vs. predicted density functions, i.e. number of instances that get the disease / complication at each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



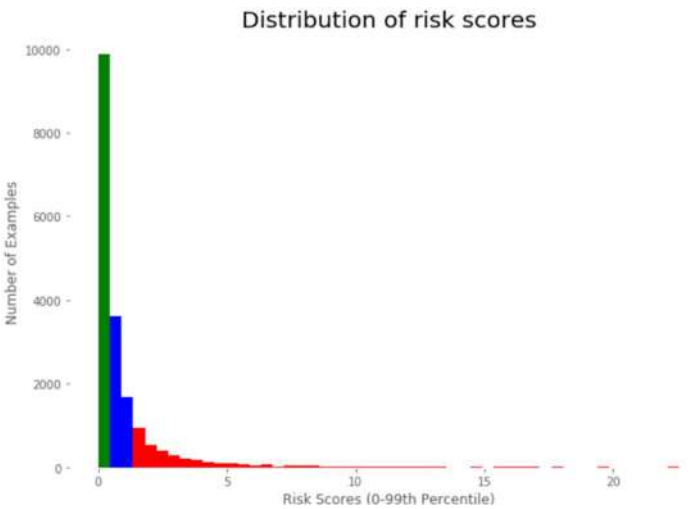
The following chart shows the actual vs. predicted survival functions, i.e. the number of instances that have not had the disease / complication by each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



Risk Stratification

The low, medium and high risk groups are defined as examples with predicted risk scores belonging to the first quartile, second to third quartiles, and fourth quartile respectively.

	Percentile	Risk Scores
Low Risk	0-25th	[0.0,0.143]
Medium Risk	26th-75th	[0.143,1.095]
High Risk	75th-100th	[1.095,13426.0400390625]



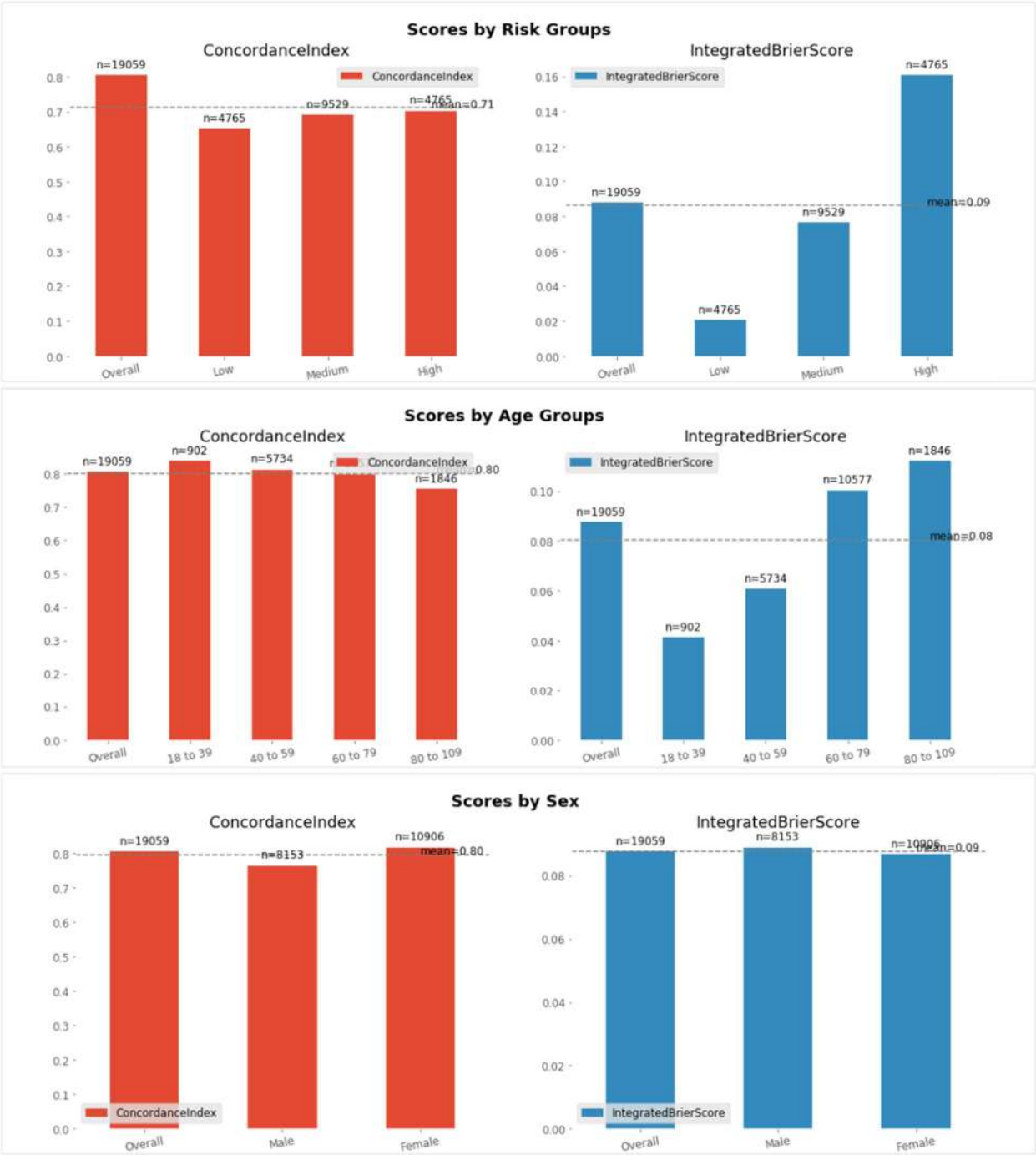
Summary Metrics across Subgroups

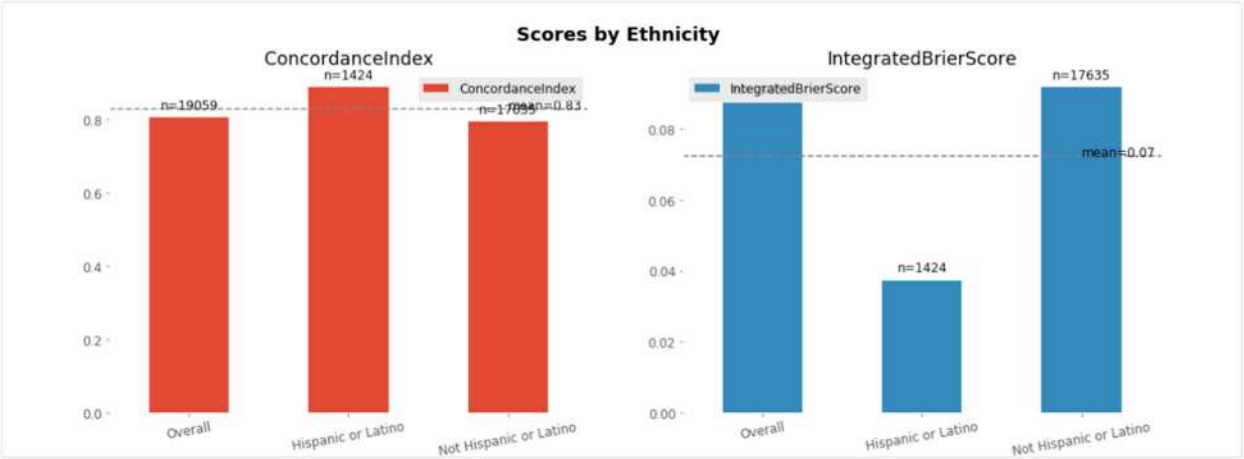
The table below displays the summary metrics across subgroups of risk, age, sex, ethnicity and patient history.

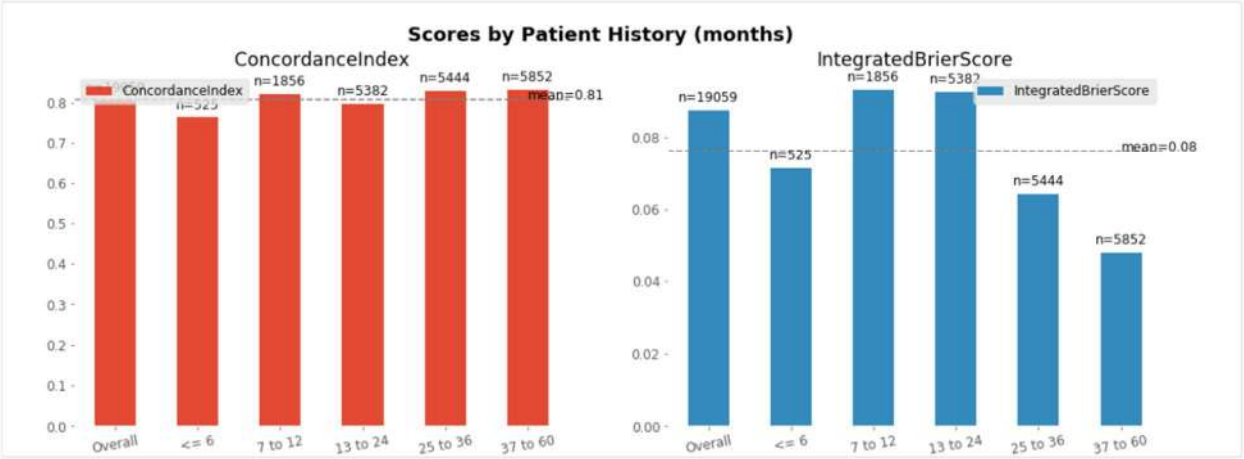
Category	Subgroup	Cohort Size	Concordance Index	Brier Score	Mean AUC	Mean Specificity	Mean Sensitivity	S(t), t=3	S(t), t=6	S(t), t=9	S(t), t=12	S(t), t=18	S(t), t=24
NaN	Overall	19059.00	0.80	0.09	0.83	0.76	0.73	0.96	0.94	0.92	0.90	0.87	0.84
Risk	Low	4765.00	0.65	0.02	0.66	1.00	0.00	1.00	1.00	1.00	1.00	0.99	0.99
Risk	Medium	9529.00	0.69	0.08	0.63	0.94	0.13	0.99	0.98	0.97	0.96	0.94	0.91
Risk	High	4765.00	0.70	0.16	0.75	0.00	1.00	0.89	0.83	0.77	0.72	0.64	0.56
Age Bucket	18 to 39	902.00	0.84	0.04	0.85	0.95	0.50	0.99	0.98	0.97	0.97	0.96	0.95
Age Bucket	40 to 59	5734.00	0.81	0.06	0.87	0.88	0.68	0.98	0.96	0.95	0.94	0.92	0.90
Age Bucket	60 to 79	10577.00	0.80	0.10	0.80	0.70	0.73	0.96	0.94	0.91	0.89	0.86	0.82
Age Bucket	80 to 109	1846.00	0.75	0.11	0.79	0.60	0.80	0.95	0.92	0.89	0.86	0.82	0.77
Sex	Male	8153.00	0.77	0.09	0.82	0.73	0.75	0.96	0.94	0.92	0.90	0.86	0.83
Sex	Female	10906.00	0.82	0.09	0.83	0.78	0.71	0.97	0.95	0.93	0.92	0.89	0.86
Ethnicity	Hispanic or Latino	1424.00	0.89	0.04	0.92	0.89	0.84	0.97	0.95	0.94	0.93	0.91	0.88
Ethnicity	Not Hispanic or Latino	17635.00	0.79	0.09	0.82	0.75	0.72	0.97	0.94	0.92	0.91	0.87	0.84
History Bucket	<= 6	525.00	0.76	0.07	0.76	0.74	0.66	0.97	0.95	0.94	0.92	0.89	0.85
History Bucket	7 to 12	1856.00	0.82	0.09	0.86	0.76	0.81	0.96	0.94	0.92	0.90	0.87	0.84
History Bucket	13 to 24	5382.00	0.80	0.09	0.82	0.74	0.74	0.96	0.94	0.92	0.90	0.86	0.83
History Bucket	25 to 36	5444.00	0.83	0.06	0.84	0.78	0.72	0.96	0.94	0.92	0.91	0.88	0.84
History Bucket	37 to 60	5852.00	0.83	0.05	nan	nan	0.67	0.97	0.95	0.94	0.92	0.89	0.86

Concordance Index & Integrated Brier Score

The following charts show how the Concordance Index and Integrated Brier Score varies among subgroups of risk, age, sex, ethnicity and patient history.

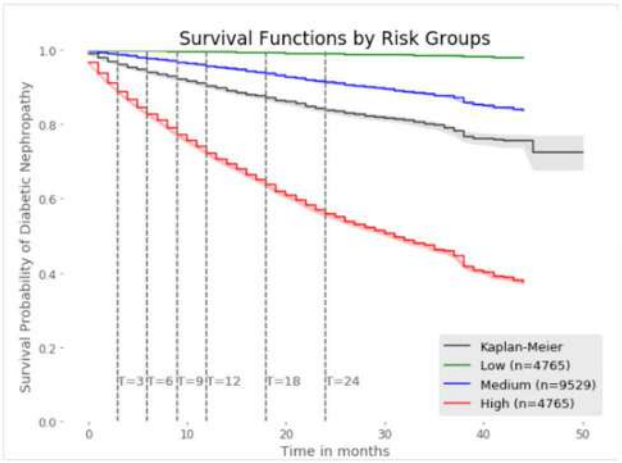


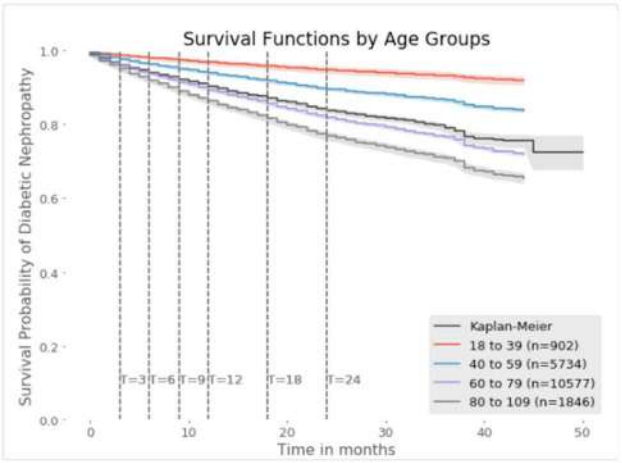

Scores by Ethnicity
ConcordanceIndex
IntegratedBrierScore
n=19059
n=1424
n=17635
mean=0.83
mean=0.07
Overall
Hispanic or Latino
Not Hispanic or Latino

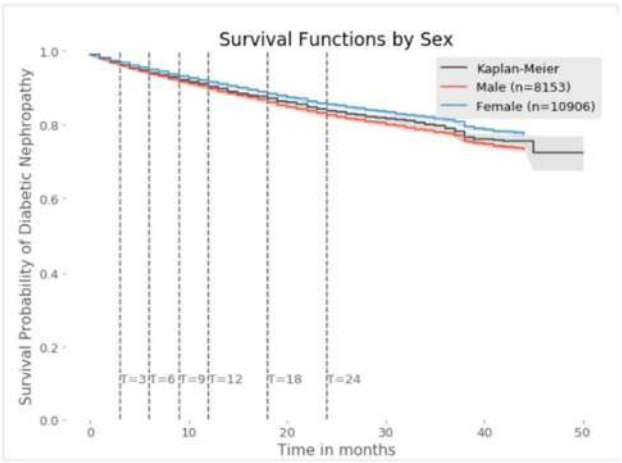

Scores by Patient History (months)
ConcordanceIndex
IntegratedBrierScore
n=19059
n=525
n=1856
n=5382
n=5444
n=5852
mean=0.81
mean=0.08
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60

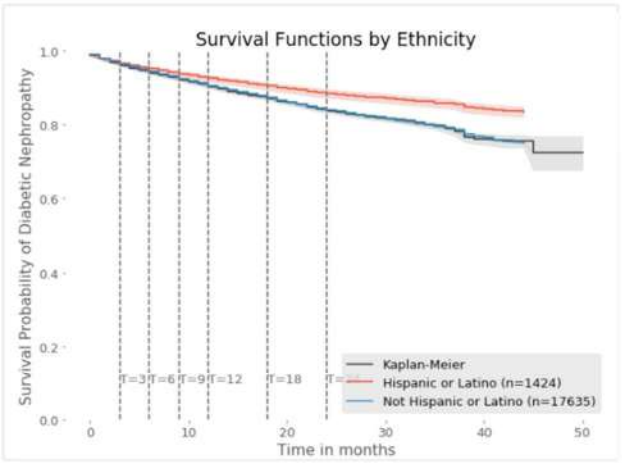
Average Survival Function Curves

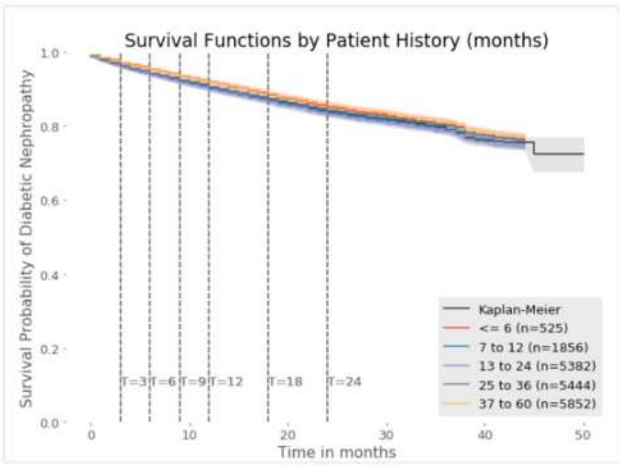
The following charts show how the average survival function curve varies among subgroups of risk, age, sex, ethnicity and patient history.





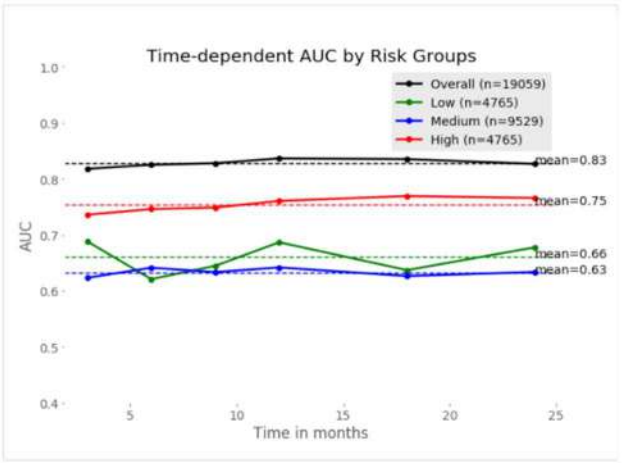


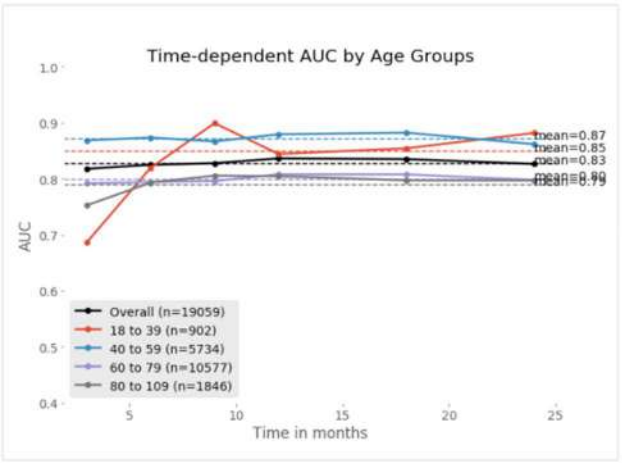


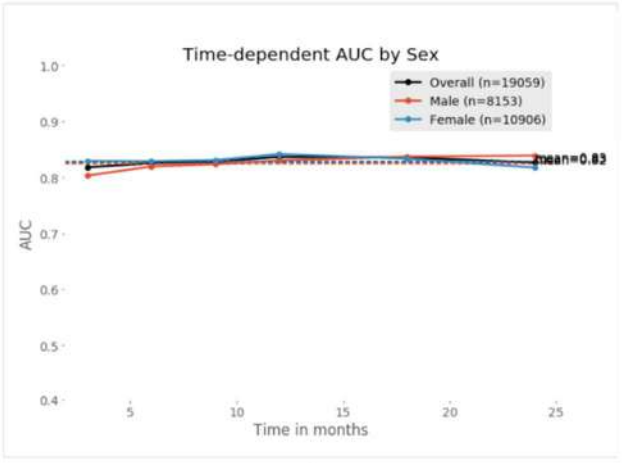


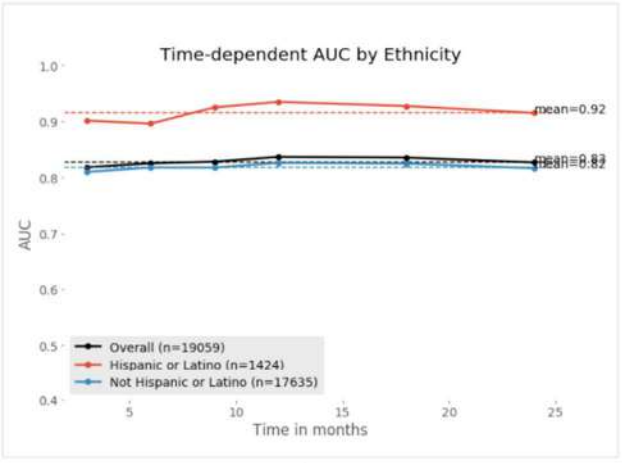
Time-dependent AUC

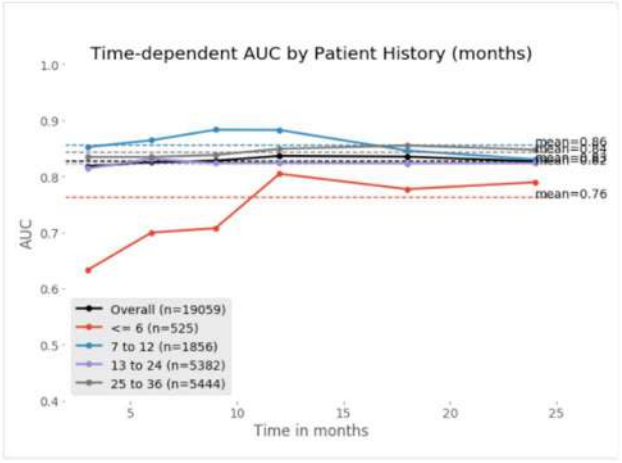
The following charts show how the AUC across time varies among subgroups of risk, age, sex, ethnicity and patient history.





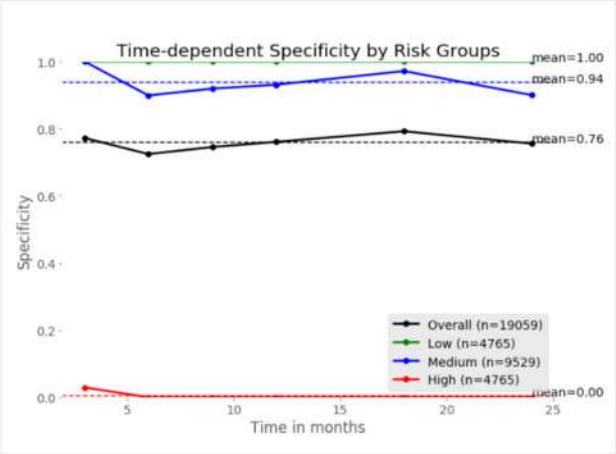


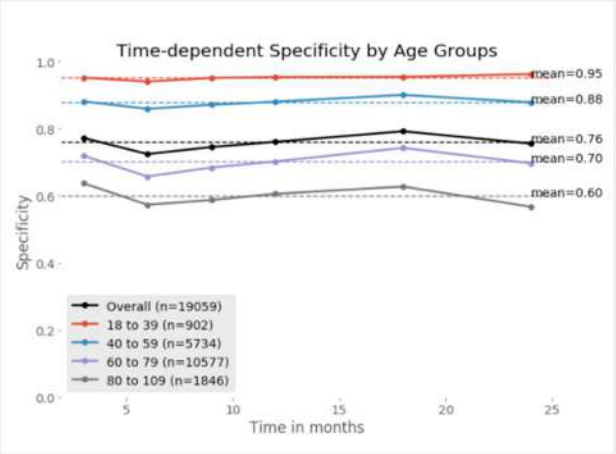


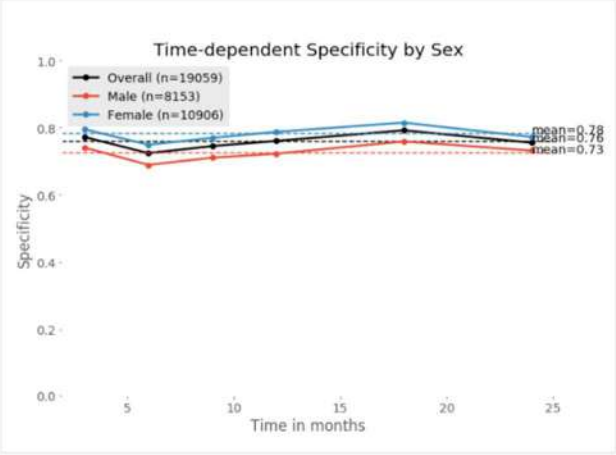


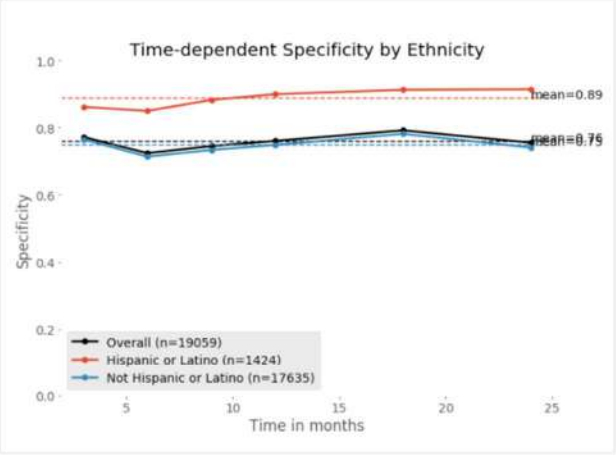
Time-dependent Specificity

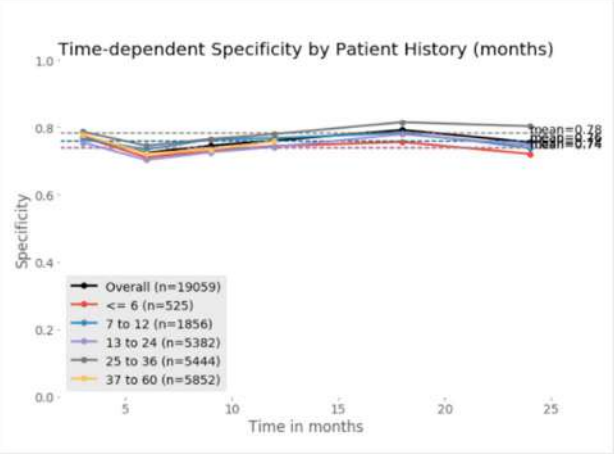
The following charts show how the specificity across time varies among subgroups of risk, age, sex, ethnicity and patient history.





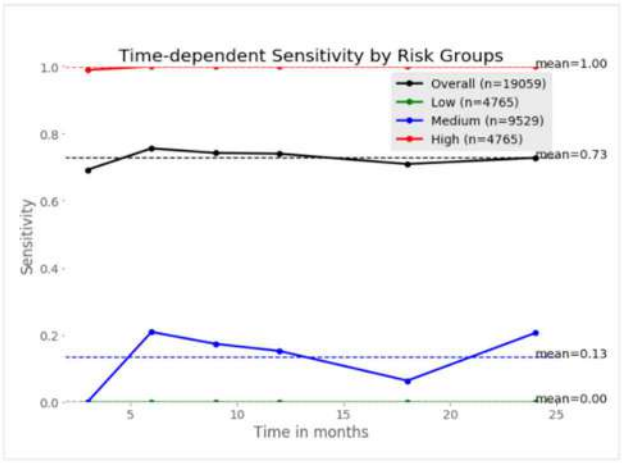


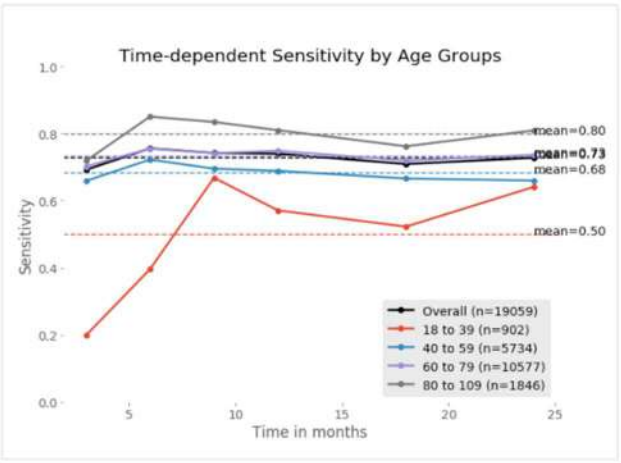


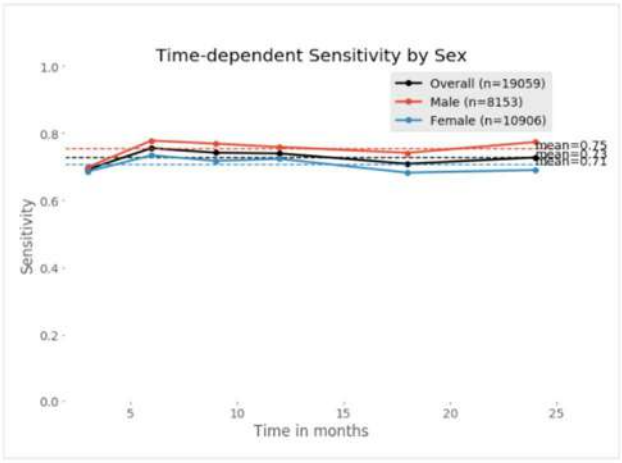


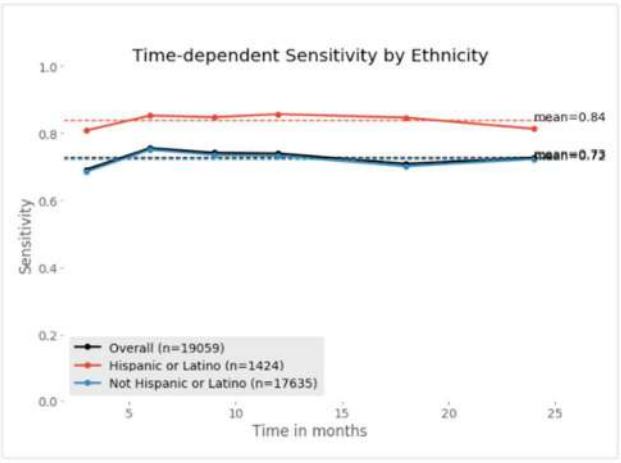
Time-dependent Sensitivity

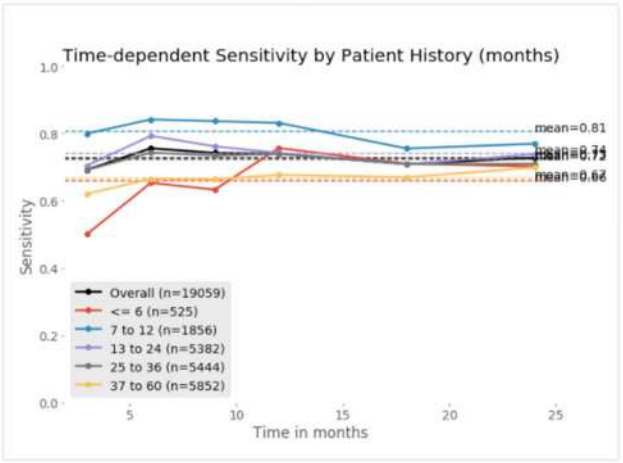
The following charts show how the sensitivity across time varies among subgroups of risk, age, sex, ethnicity and patient history.







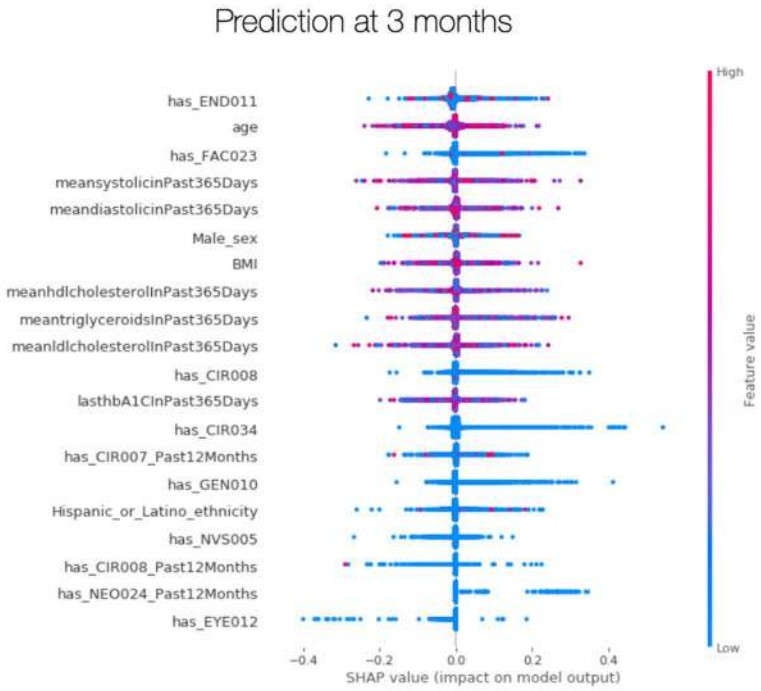


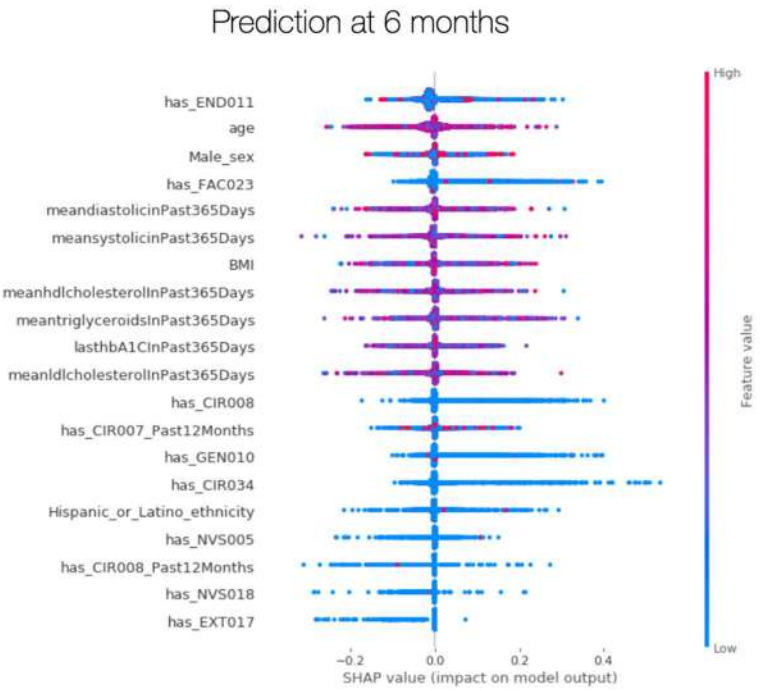


Model Explanation (DeepSurv)

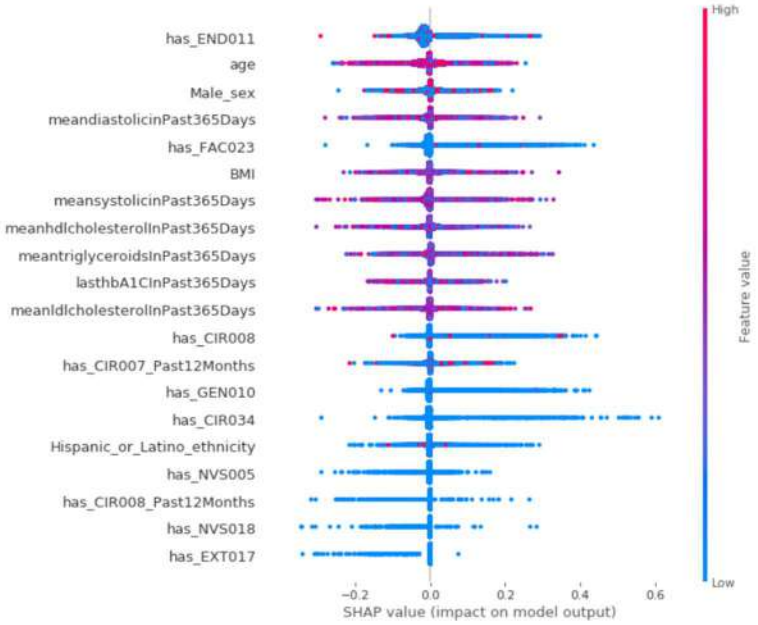
Global

The following plots show the SHAP values of each instance in the training set for each future time (3, 6, 9, 12, 18 and 24 months). The features are sorted by the total magnitude of the SHAP values over all instances and the distribution of the effect that each feature has on the model's output can be observed.

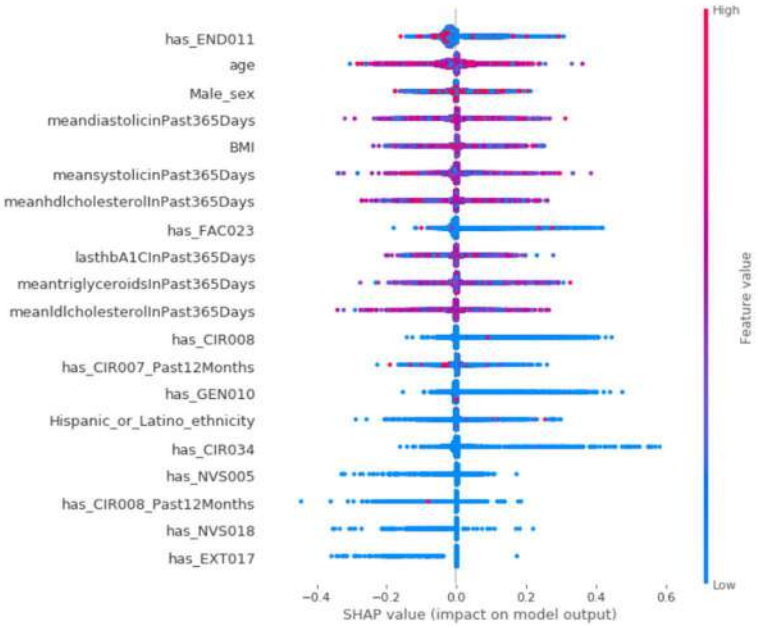




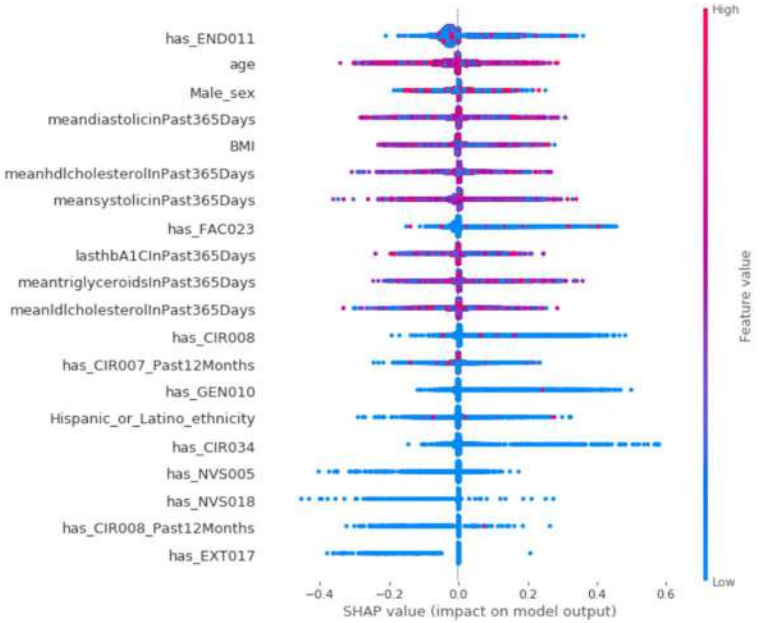
Prediction at 9 months



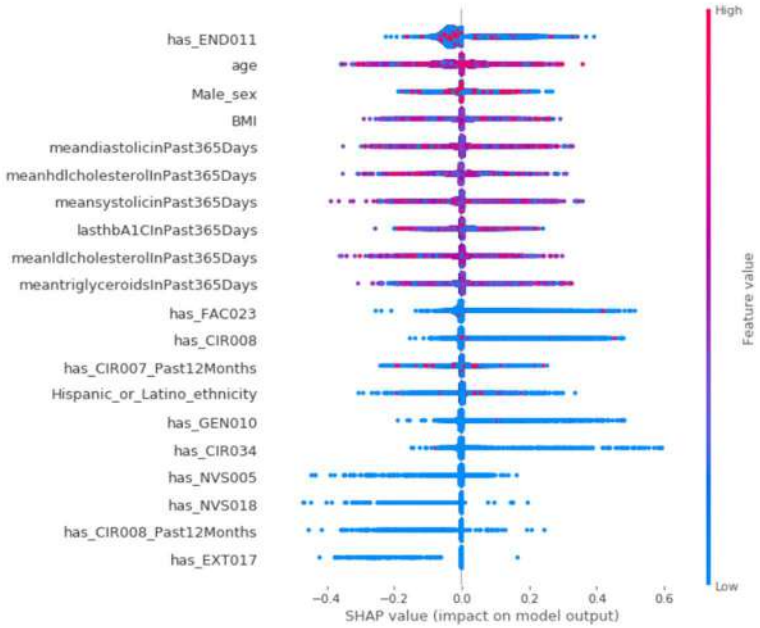
Prediction at 12 months



Prediction at 18 months

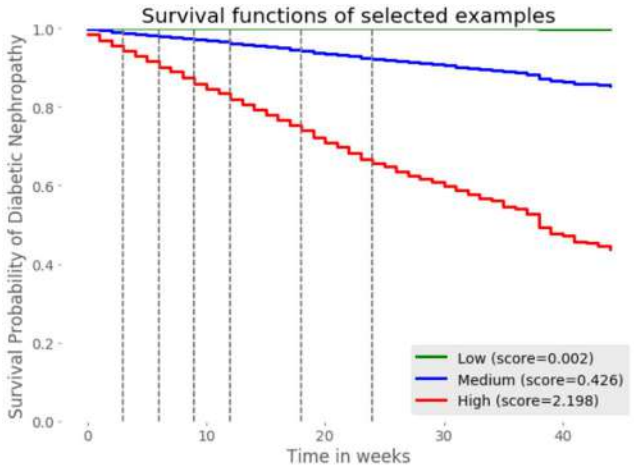


Prediction at 24 months

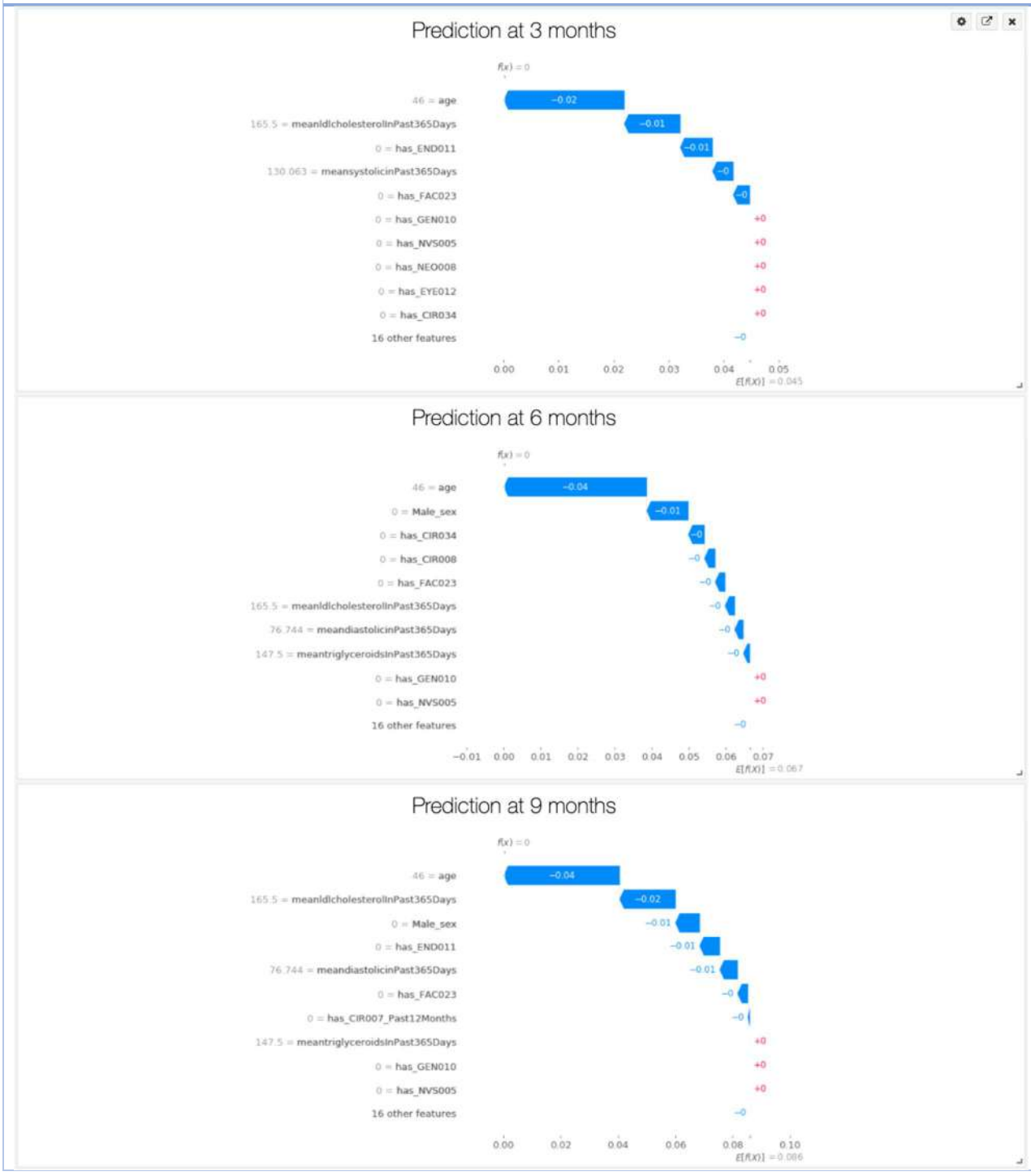


Local

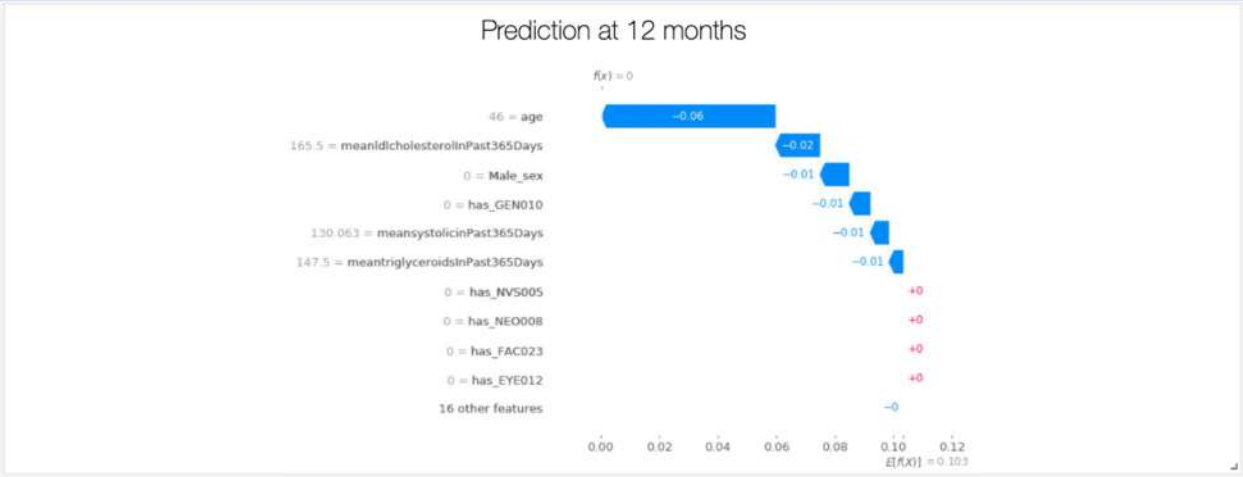
SHAP values were also generated to explain the predictions of individual examples for each future time (3, 6, 9, 12, 18 and 24 months). A total of 3 examples were selected by sampling of risk scores at the 5th, 50th and 95th percentile to represent instances at low, medium and high risks respectively.



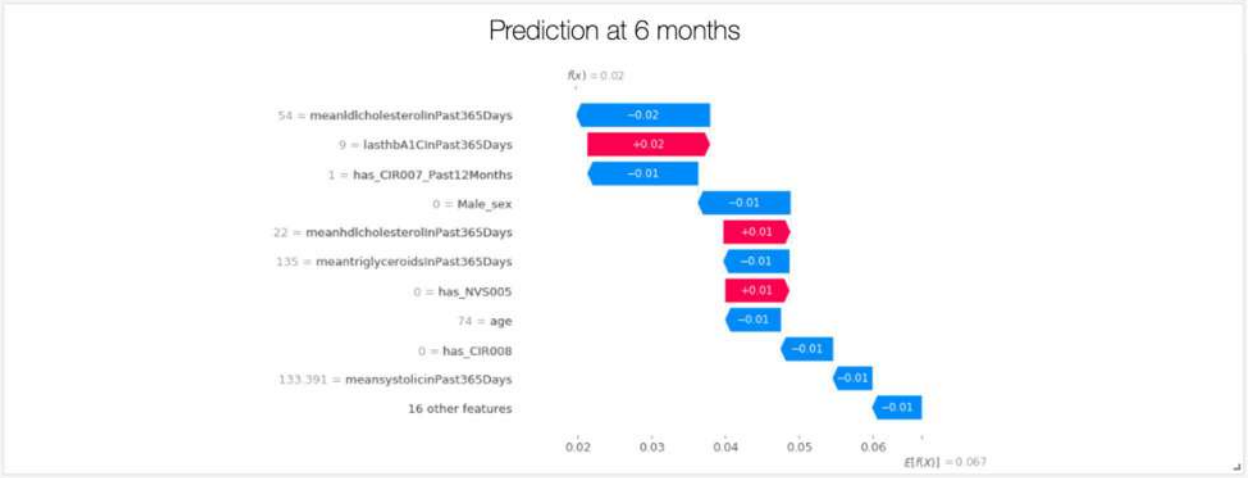
Low Risk
Risk Score: 0.002

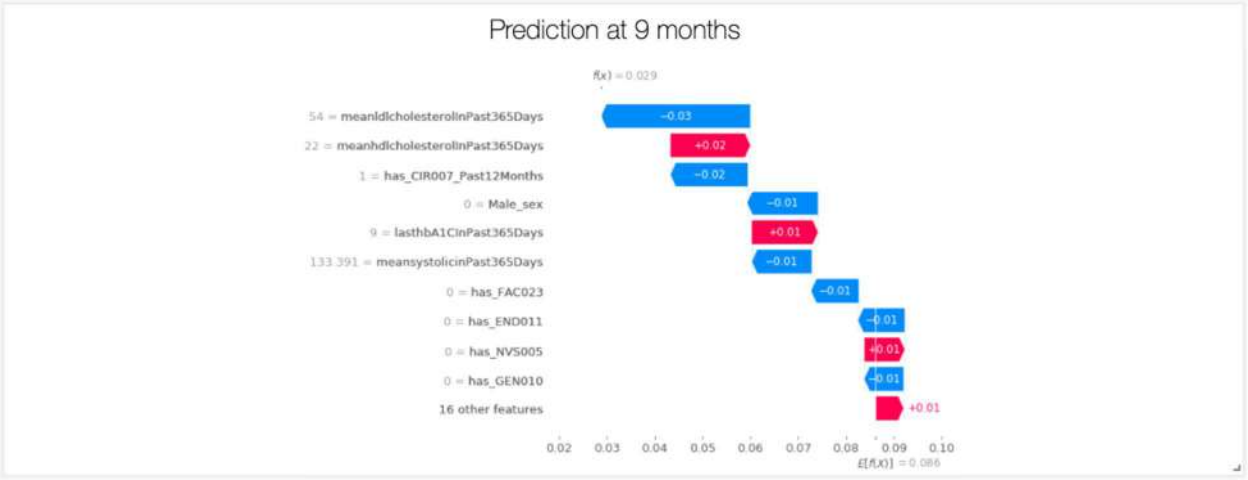


Low Risk
Risk Score: 0.002

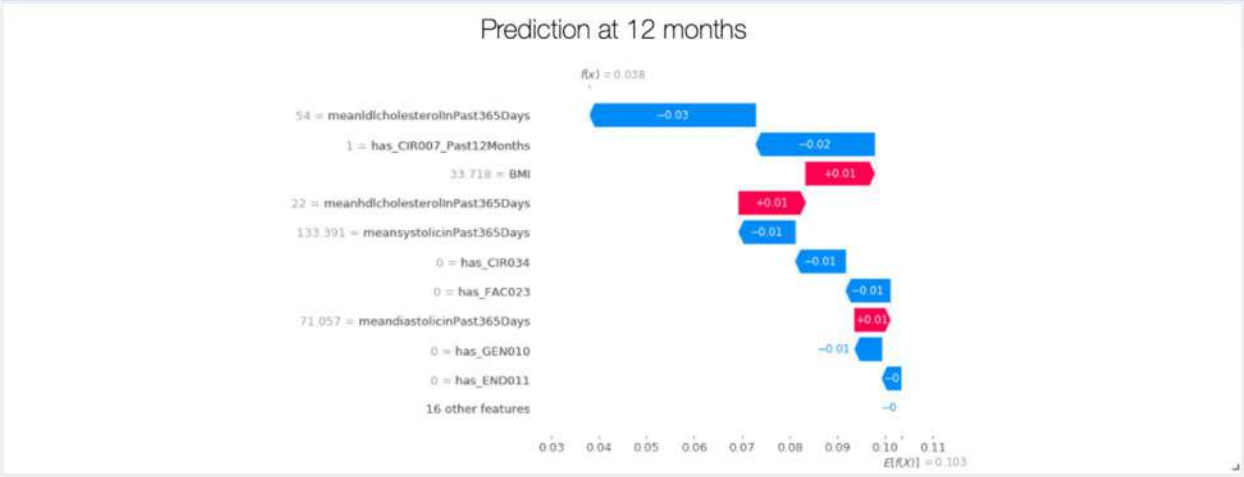


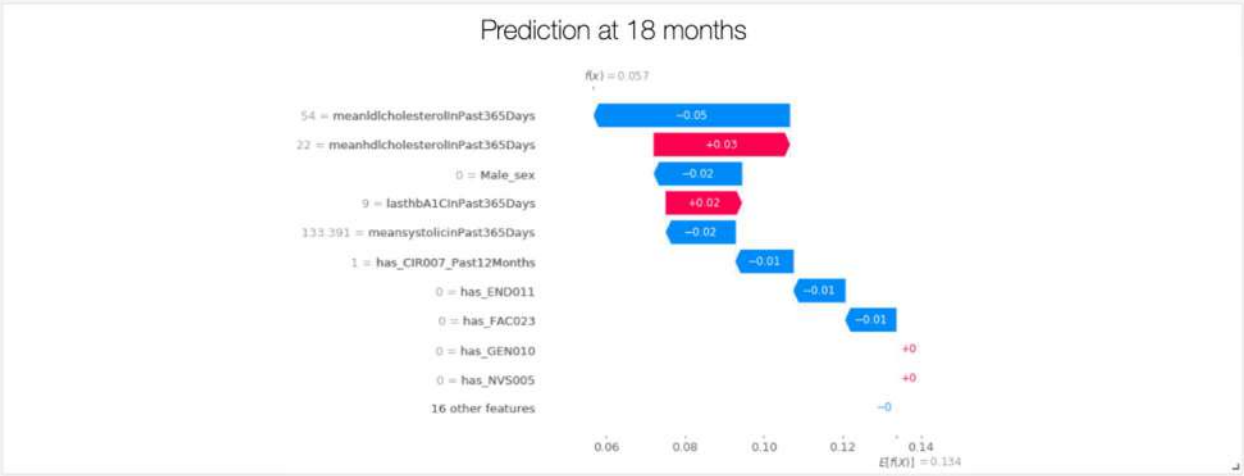
Medium Risk
Risk Score: 0.426

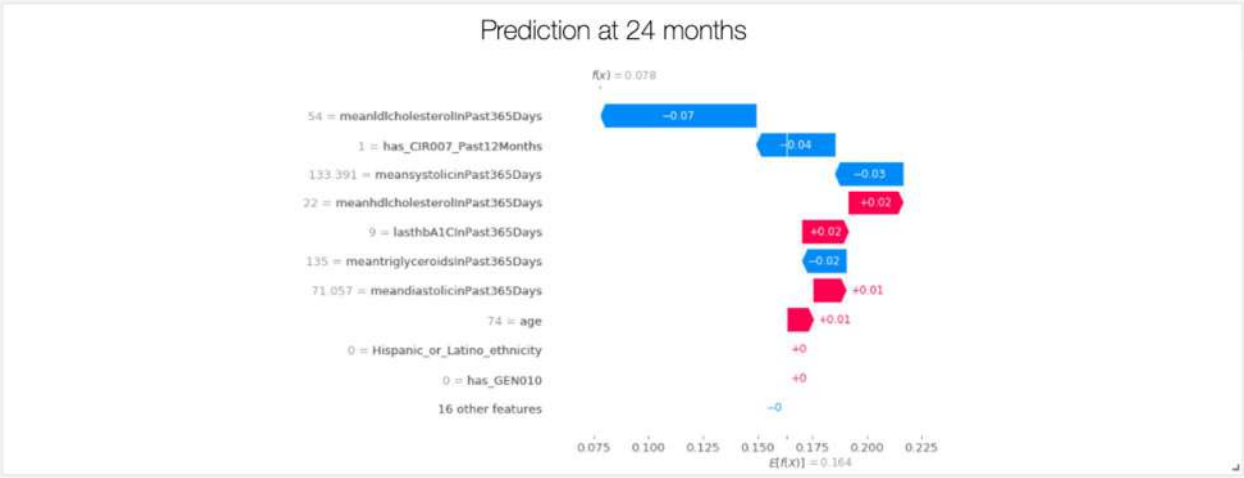




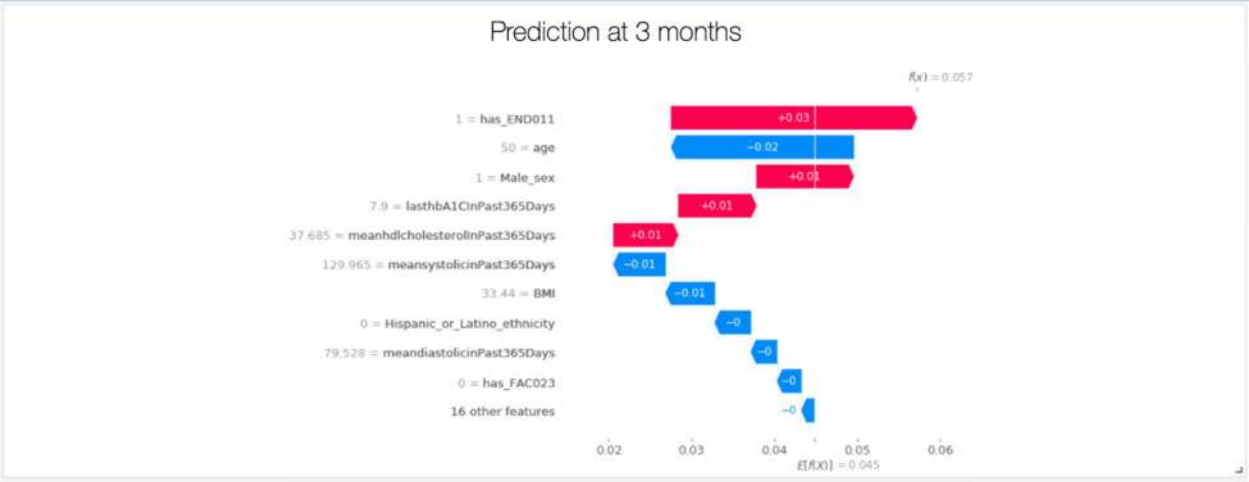
Medium Risk
Risk Score: 0.426

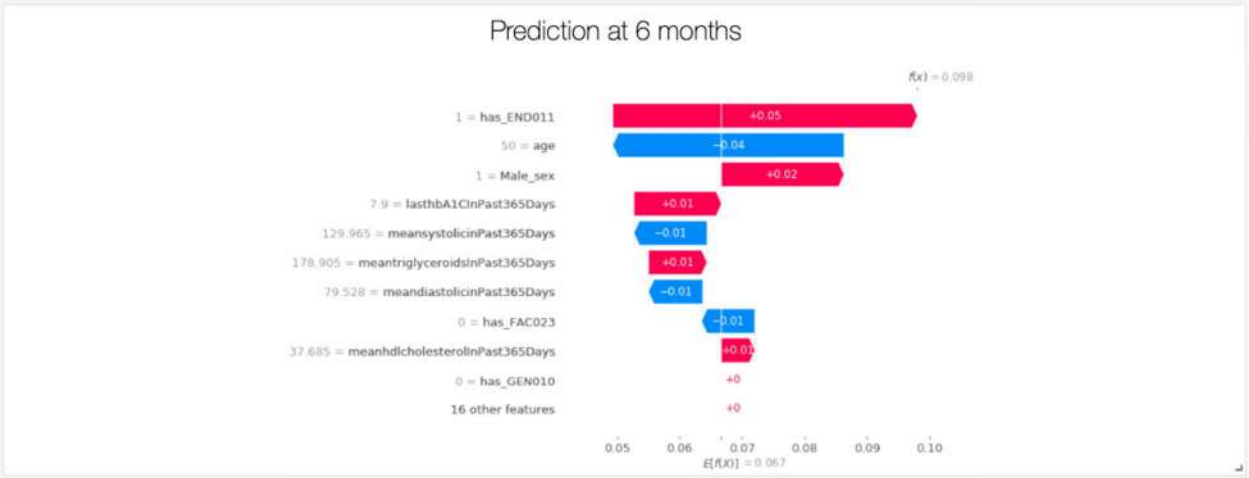


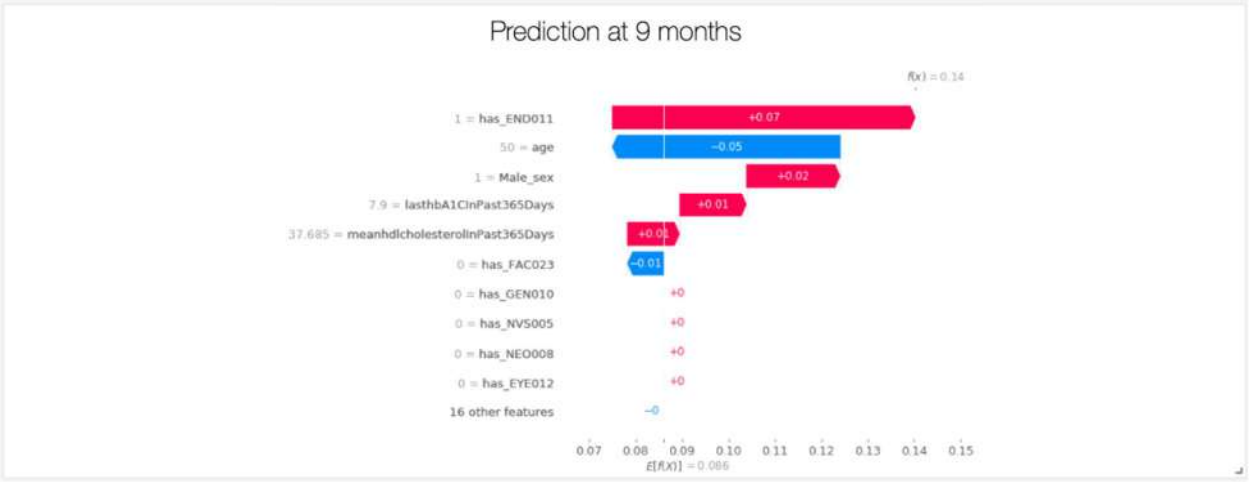




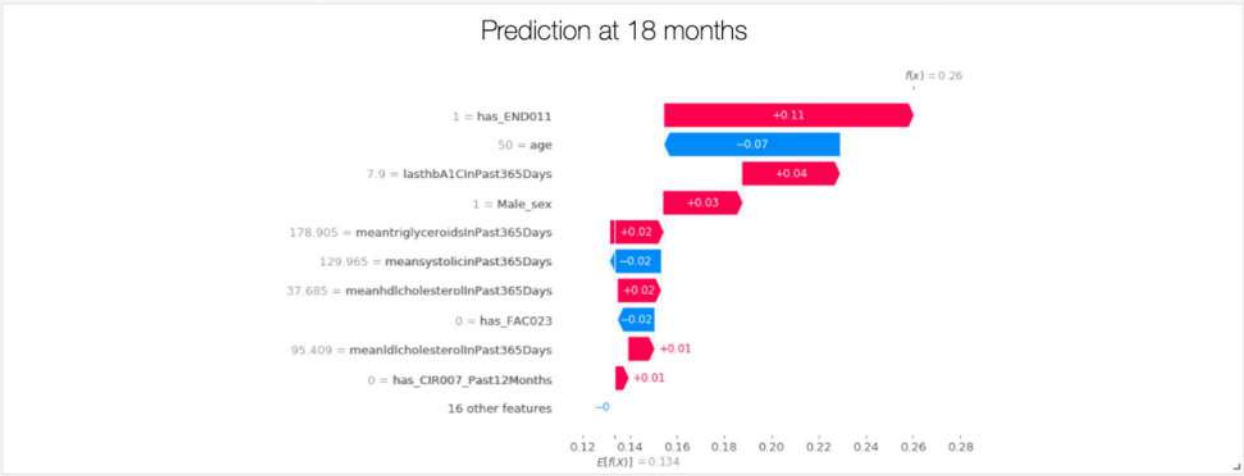
High Risk
Risk Score: 2.198

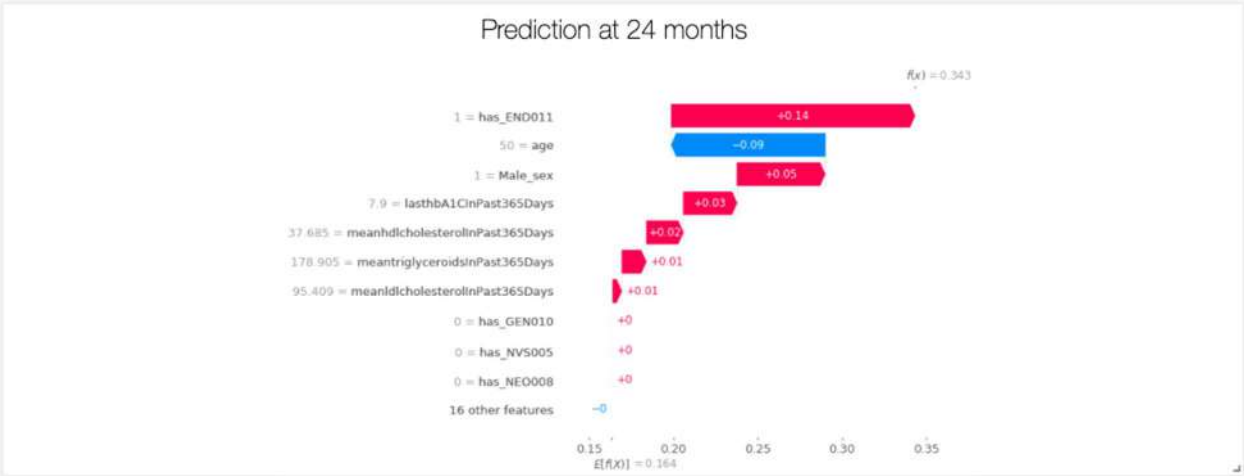






High Risk
Risk Score: 2.198





DM to Diabetic Neuropathy Prediction

Item	Specification
Business Goal	Enable care managers to identify the patients who are at risk of developing diabetic neuropathy
Usage Setting	Outpatient
ML Task	Predict risk and/or time from DM or uncontrolled DM to diabetic neuropathy
ML Class	Survival
Instances for Prediction	Encounters
Labels for Instances	Binary indicator and time to event or censoring for diabetic neuropathy
Cohort Criteria	• 2016-01-01 $\leq$ encounter date $\leq$ 2020-06-30 (available Epic data, excluding outliers) • Encounter date is not within the first 90 days of when the patient entered the data set, to adjust for left-censoring • 18 $\leq$ age $\leq$ 110 (adults without outliers) • No T1DM diagnosis • Not pregnant • No "Do Not Resuscitate" diagnosis • DM or uncontrolled DM event before encounter date • No diabetic neuropathy event before encounter date • No diabetic neuropathy event up to 6 days after encounter date (encounters where diagnoses confirm event within the week)

Input Features	• Demographic
	• Diagnosis, except:
	  ○ hasDiabetesNeuropathy*
	  ○ has_NVS015* (Polyneuropathies)
	  ○ has_NVS017* (Nerve and nerve root disorders)
	  ○ has_NVS020* (Other specified nervous system disorders)
	• Labs
	• Utilization
	• Vitals
	
	See Appendix E for details.

Evaluation Metrics	• Concordance Index • Integrated Brier Score

Data

The following charts summarize the key characteristics of the data after applying the cohort criteria stated above, along with selected features (see Model Signature below).

Category	summary Variable	count	mean	stddev	min	25%	50%	75%	max
Demographic	AgeBucket_18_to_39	62735.0	0.046704	0.211007	0.00	0.000	0.000	0.000	1.00
	AgeBucket_40_to_59	62735.0	0.277246	0.447642	0.00	0.000	0.000	1.000	1.00
	AgeBucket_60_to_79	62735.0	0.561266	0.496236	0.00	0.000	1.000	1.000	1.00
	AgeBucket_80_to_109	62735.0	0.114784	0.318764	0.00	0.000	0.000	0.000	1.00
	Sex_Female	62735.0	0.557201	0.496721	0.00	0.000	1.000	1.000	1.00
	Sex_Male	62735.0	0.442799	0.496721	0.00	0.000	0.000	1.000	1.00
	Ethnicity_Hispanic_or_Latino	62735.0	0.072113	0.258677	0.00	0.000	0.000	0.000	1.00
	Ethnicity_Not_Hispanic_or_Latino	62735.0	0.927887	0.258677	0.00	1.000	1.000	1.000	1.00
Encounter	EncounterType_Emergency	62735.0	0.217327	0.412430	0.00	0.000	0.000	0.000	1.00
	EncounterType_Inpatient	62735.0	0.105220	0.306840	0.00	0.000	0.000	0.000	1.00
	EncounterType_Outpatient	62735.0	0.677453	0.467455	0.00	0.000	1.000	1.000	1.00
Label	Time	62735.0	15.240121	11.253042	0.00	6.000	13.000	23.000	50.00
	Event	62735.0	0.083207	0.276197	0.00	0.000	0.000	0.000	1.00
Feature	age	62735.0	64.341325	13.274743	18.00	56.000	66.000	73.000	102.00
	Male_sex	62735.0	0.442799	0.496721	0.00	0.000	0.000	1.000	1.00
	Hispanic_or_Latino_ethnicity	62735.0	0.072113	0.258677	0.00	0.000	0.000	0.000	1.00
	lasthbA1ClnPast365Days	62735.0	7.497466	1.188137	3.60	6.800	7.437	7.900	12.70
	meandiastolicinPast365Days	62735.0	73.863716	7.822996	43.62	69.760	73.991	78.750	107.56
	meansystolicinPast365Days	62735.0	132.057551	11.677764	82.00	127.478	131.921	135.900	180.00
	BMI	62735.0	33.435473	6.698827	10.37	29.360	33.670	37.040	157.25
	meantriglyceroidsInPast365Days	62735.0	165.787573	56.316318	19.00	138.750	164.470	180.836	460.50
	meanldlcholesterolInPast365Days	62735.0	88.837422	23.230243	8.00	81.915	89.011	98.902	201.00
	meanhdlcholesterolInPast365Days	62735.0	43.294861	9.027876	5.00	38.000	42.145	47.634	98.00
	has_INJ004_Past12Months	62735.0	0.006647	0.081258	0.00	0.000	0.000	0.000	1.00
	has_NEO043_Past12Months	62735.0	0.005149	0.071570	0.00	0.000	0.000	0.000	1.00
	has_NEO012_Past12Months	62735.0	0.003459	0.058712	0.00	0.000	0.000	0.000	1.00
	has_NEO030_Past12Months	62735.0	0.034670	0.182943	0.00	0.000	0.000	0.000	1.00
	has_CIR007_Past12Months	62735.0	0.192205	0.394037	0.00	0.000	0.000	0.000	1.00
	has_MBD003_Past12Months	62735.0	0.006344	0.079398	0.00	0.000	0.000	0.000	1.00
	has_CIR008_Past12Months	62735.0	0.009421	0.096602	0.00	0.000	0.000	0.000	1.00
	has_FAC013	62735.0	0.008321	0.090838	0.00	0.000	0.000	0.000	1.00
	has_DIG006	62735.0	0.006934	0.082982	0.00	0.000	0.000	0.000	1.00
	has_NEO065	62735.0	0.004702	0.068413	0.00	0.000	0.000	0.000	1.00
	has_FAC004	62735.0	0.001435	0.037849	0.00	0.000	0.000	0.000	1.00
	has_GEN025	62735.0	0.041859	0.200268	0.00	0.000	0.000	0.000	1.00
	has_RSP017	62735.0	0.011015	0.104372	0.00	0.000	0.000	0.000	1.00
	has_NVS004	62735.0	0.009022	0.094556	0.00	0.000	0.000	0.000	1.00
	has_MUS037	62735.0	0.011923	0.108541	0.00	0.000	0.000	0.000	1.00
	has_CIR035	62735.0	0.009644	0.097729	0.00	0.000	0.000	0.000	1.00

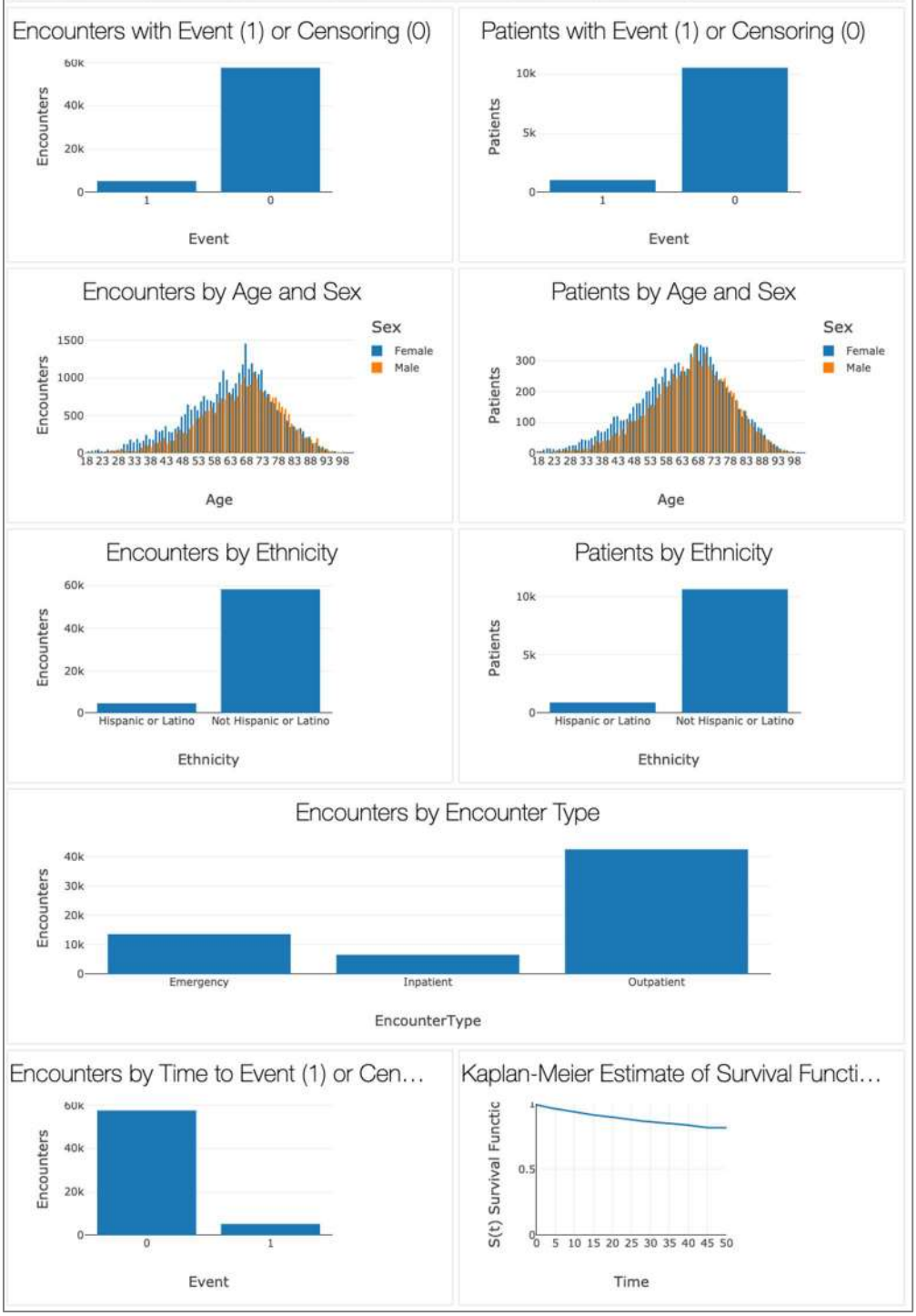
(Percentages for binary variables can be read from the “mean” column.)

Encounters and Patients

	Examples	Encounters	Patients
1	62735	62735	11539

Train and Test Sets

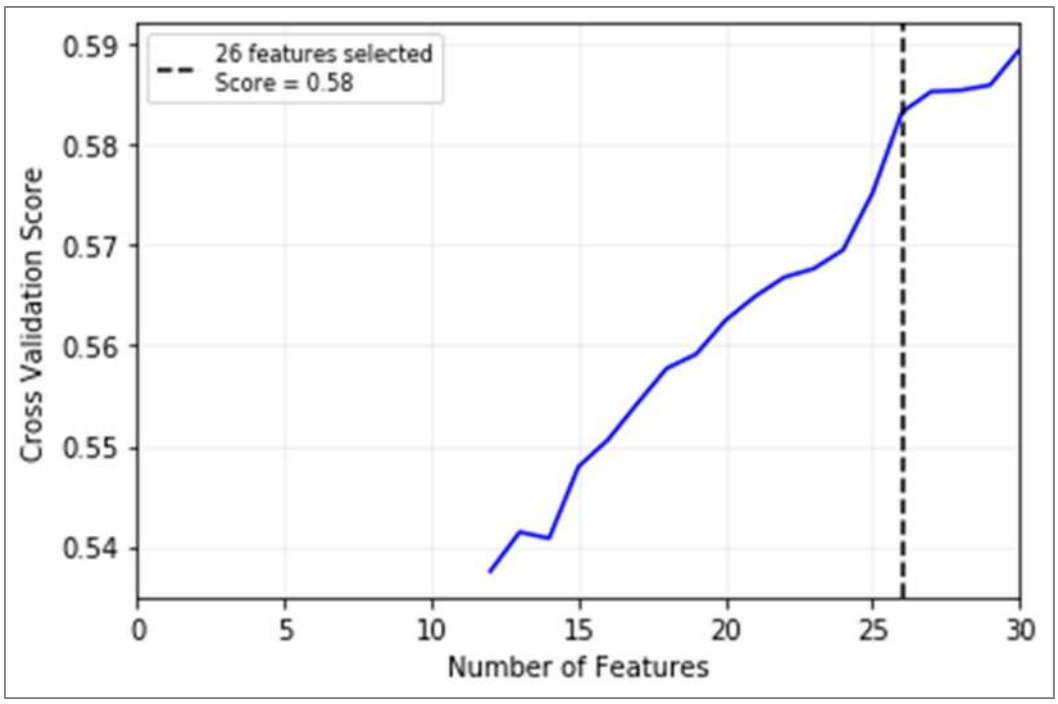
	Set	No Event	No Event %	Event	Event %	Total	Total %
1	Test	17003	29.6	1540	29.5	18543	29.6
2	Train	40512	70.4	3680	70.5	44192	70.4
3	Total	57515	100	5220	100	62735	100



Model Signature

The model signature has 26 features, comprising of 12 mandatory features and 14 other selected features. These are the selected features, in rank order (the last feature to be eliminated is ranked 1):

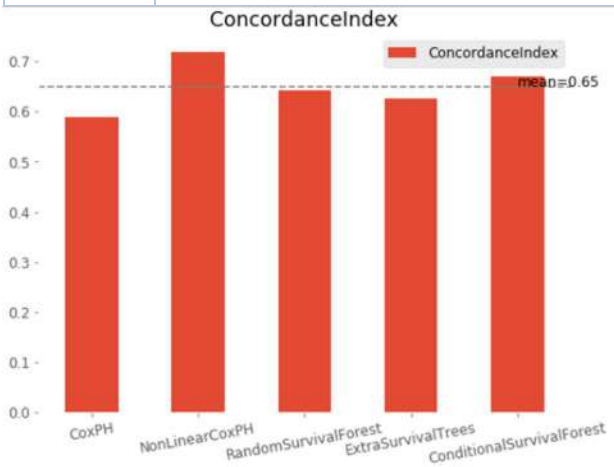
1. has_DIG006 (Gastrointestinal and biliary perforation)
2. has_FAC013 (Contraceptive and procreative management)
3. has_CIR035 (Varicose veins of lower extremity)
4. has_FAC004 (Encounter for prophylactic or other procedures)
5. has_NEO030_Past12Months (Breast cancer - all other types)
6. has_NEO012_Past12Months (Gastrointestinal cancers - esophagus)
7. has_MUS037 (Postprocedural or postoperative musculoskeletal system complication)
8. has_NEO043_Past12Months (Urinary system cancers - bladder)
9. has_NEO065 (Multiple myeloma)
10. has_INJ004_Past12Months (Fracture of the upper limb, initial encounter)
11. has_MBD003_Past12Months (Bipolar and related disorders)
12. has_RSP017 (Postprocedural or postoperative respiratory system complication)
13. has_NVS004 (Parkinson`s disease)
14. has_GEN025 (Other specified female genital disorders)
15. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)
16. has_CIR007_Past12Months (Essential hypertension)
17. Hispanic_or_Latino_ethnicity
18. Male_sex
19. lasthbA1CInPast365Days
20. meandiastolicinPast365Days
21. meansystolicinPast365Days
22. BMI
23. meanhdlcholesterolInPast365Days
24. meanldlcholesterolInPast365Days
25. age
26. meantriglyceroidsInPast365Days

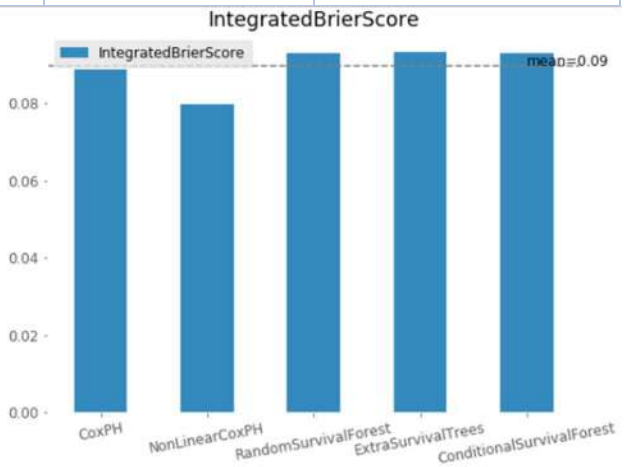


Model Performance

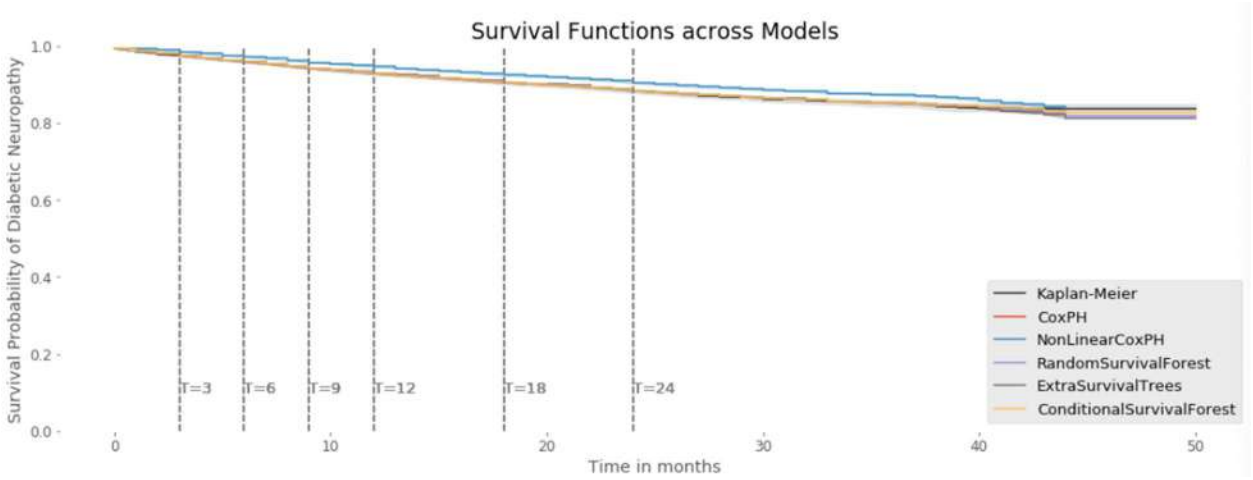
The following table and chart summarize the performance of all candidate models on the test set for this prediction task in terms of the Concordance Index and the Integrated Brier Score.

Model	No. of Parameter Combinations Successfully Tested	Concordance Index	Integrated Brier Score
CoxPH	101	0.59	0.09
DeepSurv	168	**0.72**	**0.08**
RSF	67	0.64	0.09
CSF	36	0.63	0.09
EST	39	0.67	0.09

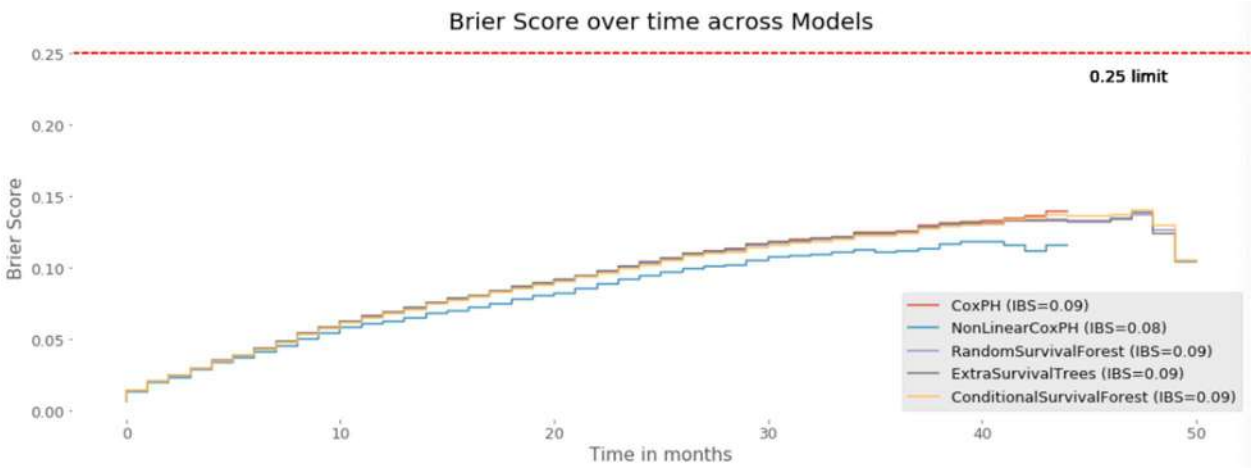




The following chart shows how the average survival function curves of the candidate models compare to the KM survival curve, the more similar their curves are to the KM survival curve the better.



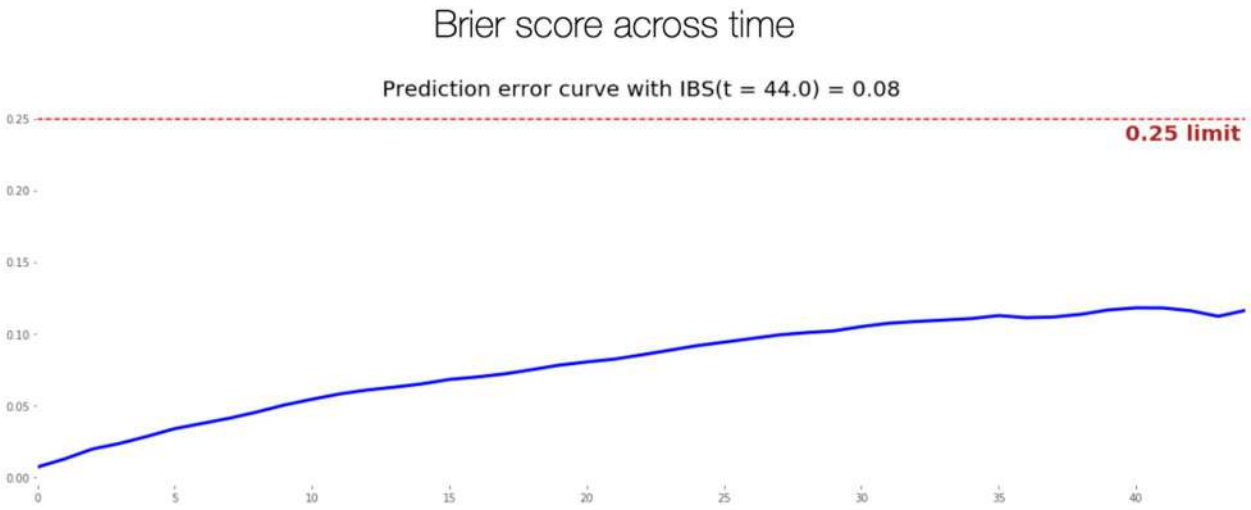
This chart shows the change in the Brier Score over time for all candidate models, the closer the scores are to 0 the better.



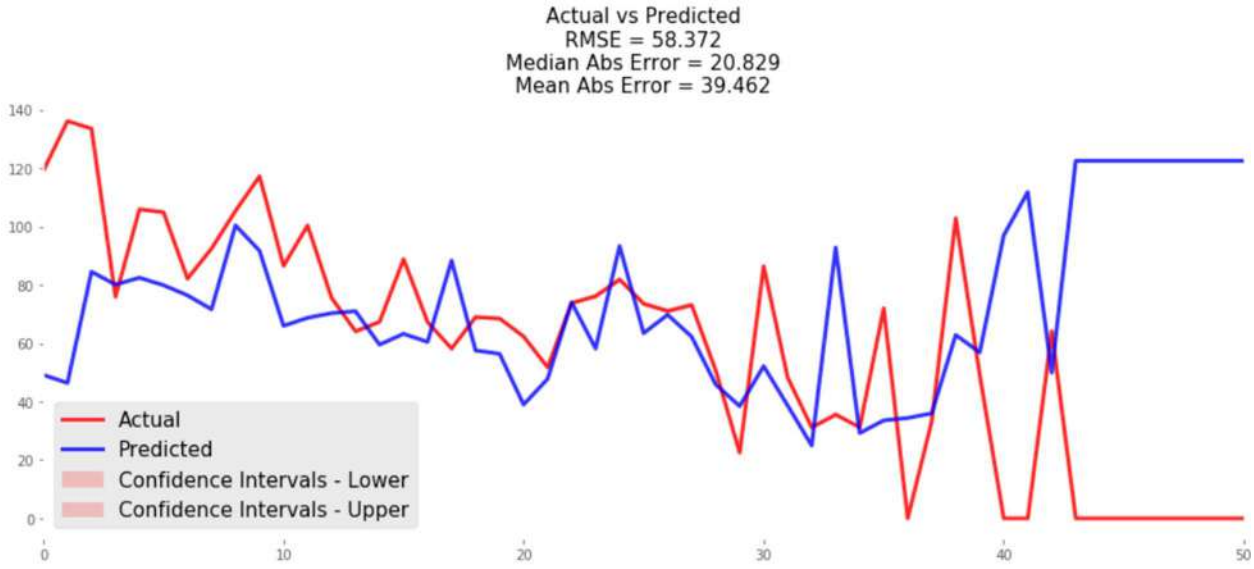
Model Evaluation of Selected Model (DeepSurv)

Overall

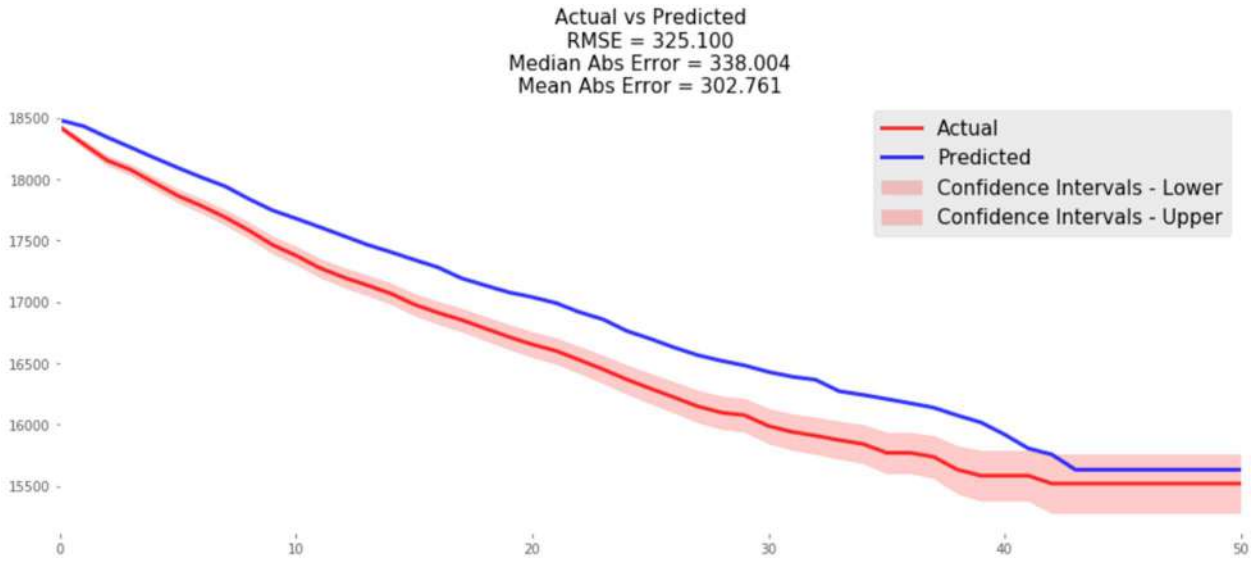
This chart shows the change in the Brier Score over time for the selected model, the closer the scores are to 0 the better.



The following chart shows the actual vs. predicted density functions, i.e. number of instances that get the disease / complication at each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



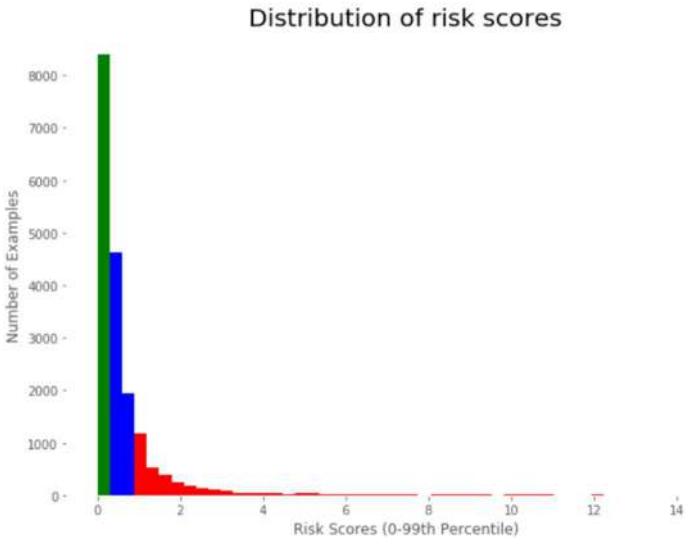
The following chart shows the actual vs. predicted survival functions, i.e. the number of instances that have not had the disease / complication by each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



Risk Stratification

The low, medium and high risk groups are defined as examples with predicted risk scores belonging to the first quartile, second to third quartiles, and fourth quartile respectively.

	Percentile	Risk Scores
Low Risk	0-25th	[0.0,0.11]
Medium Risk	26th-75th	[0.11,0.718]
High Risk	75th-100th	[0.718,433357.625]



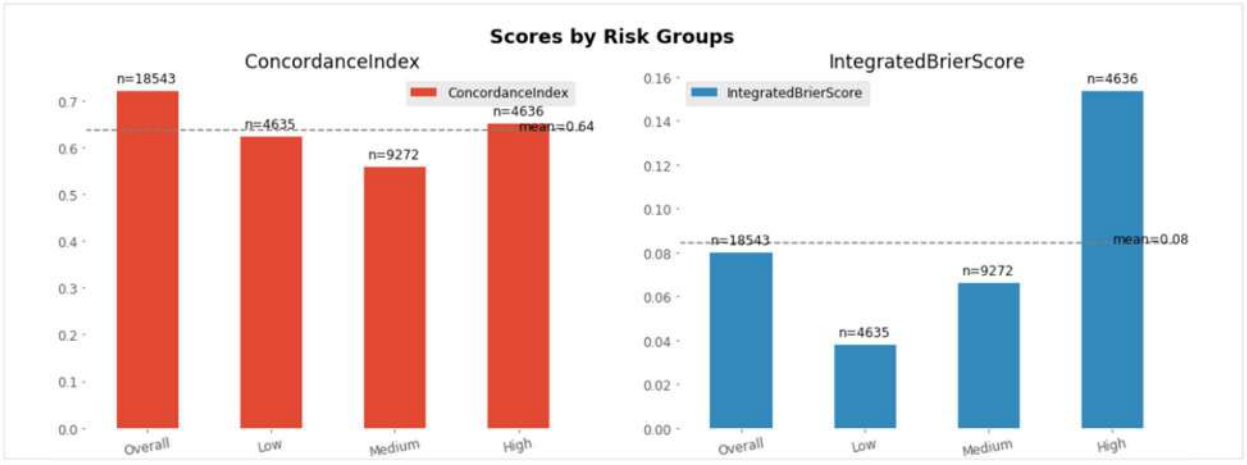
Summary Metrics across Subgroups

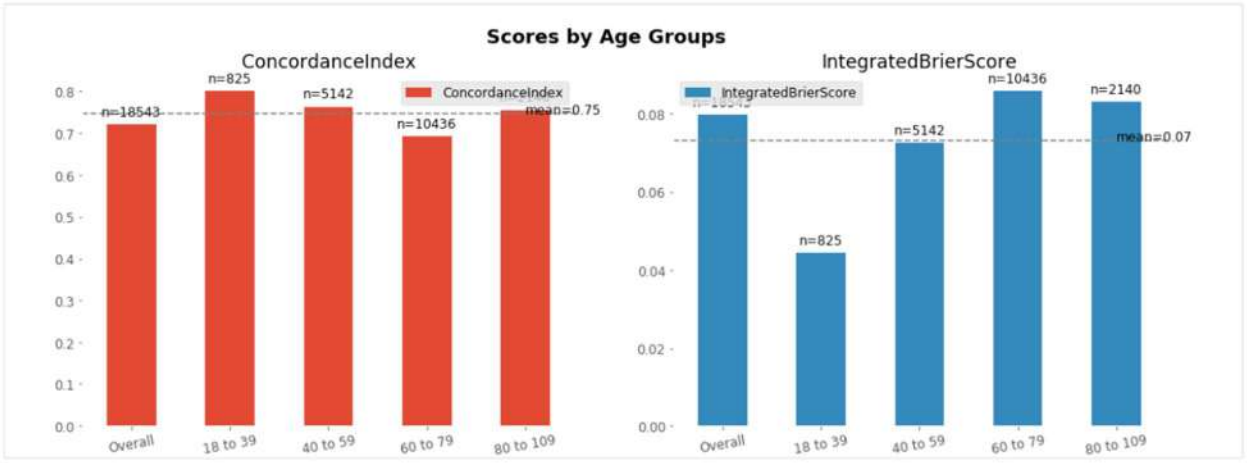
The table below displays the summary metrics across subgroups of risk, age, sex, ethnicity and patient history.

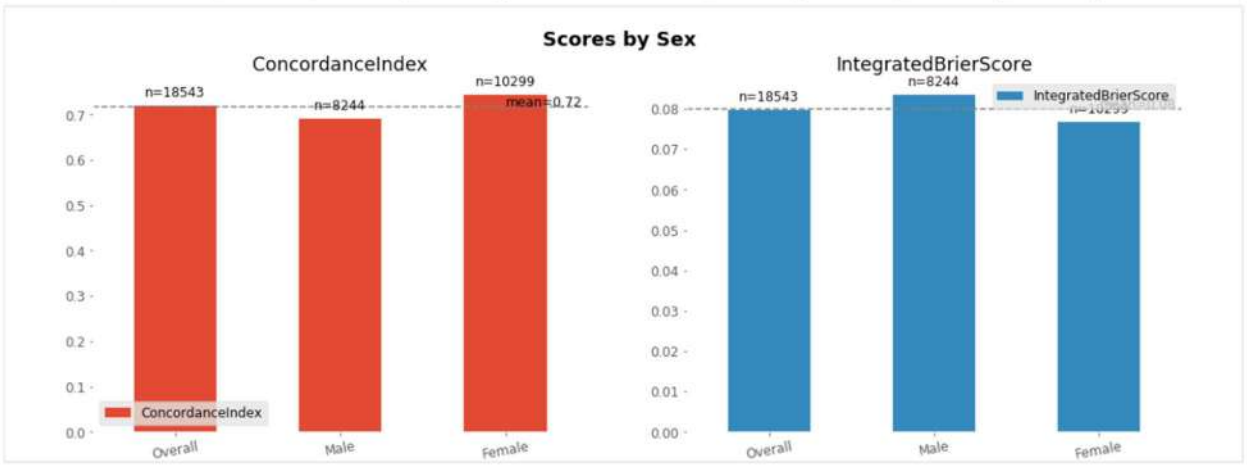
Category	Subgroup	Cohort Size	Concordance Index	Brier Score	Mean AUC	Mean Specificity	Mean Sensitivity	S(t), t=3	S(t), t=6	S(t), t=9	S(t), t=12	S(t), t=18	S(t), t=24
NaN	Overall	18543.00	0.72	0.08	0.73	0.73	0.62	0.97	0.96	0.94	0.93	0.91	0.88
Risk	Low	4635.00	0.62	0.04	0.56	1.00	0.00	1.00	1.00	1.00	1.00	1.00	0.99
Risk	Medium	9272.00	0.56	0.07	0.59	0.89	0.18	0.99	0.99	0.98	0.97	0.96	0.94
Risk	High	4636.00	0.65	0.15	0.71	0.02	0.99	0.95	0.91	0.87	0.84	0.78	0.73
Age Bucket	18 to 39	825.00	0.80	0.04	0.81	0.84	0.65	0.99	0.97	0.96	0.95	0.93	0.91
Age Bucket	40 to 59	5142.00	0.76	0.07	0.74	0.70	0.64	0.99	0.97	0.96	0.95	0.93	0.91
Age Bucket	60 to 79	10436.00	0.69	0.09	0.71	0.73	0.59	0.99	0.97	0.96	0.95	0.93	0.91
Age Bucket	80 to 109	2140.00	0.75	0.08	0.80	0.70	0.71	0.98	0.96	0.94	0.93	0.91	0.88
Sex	Male	8244.00	0.69	0.08	0.71	0.73	0.58	0.98	0.97	0.95	0.94	0.92	0.90
Sex	Female	10299.00	0.74	0.08	0.75	0.72	0.65	0.99	0.97	0.96	0.95	0.93	0.90
Ethnicity	Hispanic or Latino	1360.00	0.85	0.07	0.83	0.60	0.82	0.97	0.95	0.92	0.90	0.87	0.84
Ethnicity	Not Hispanic or Latino	17183.00	0.71	0.08	0.73	0.74	0.61	0.99	0.97	0.96	0.95	0.93	0.91
History Bucket	<= 6	549.00	0.73	0.06	0.62	0.71	0.52	0.99	0.98	0.96	0.95	0.93	0.91
History Bucket	7 to 12	1735.00	0.71	0.07	0.74	0.75	0.64	0.99	0.97	0.96	0.95	0.93	0.91
History Bucket	13 to 24	5206.00	0.70	0.09	0.71	0.72	0.60	0.98	0.96	0.95	0.94	0.91	0.89
History Bucket	25 to 36	5363.00	0.79	0.05	0.76	0.74	0.65	0.99	0.97	0.96	0.95	0.93	0.91
History Bucket	37 to 60	5690.00	0.71	0.04	nan	nan	0.61	0.99	0.98	0.96	0.95	0.93	0.91

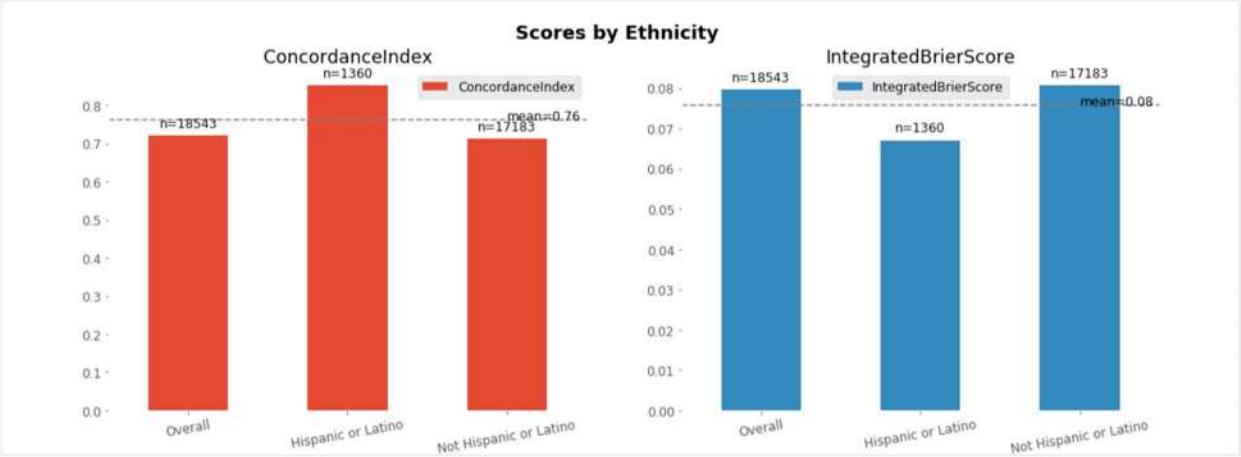
Concordance Index & Integrated Brier Score

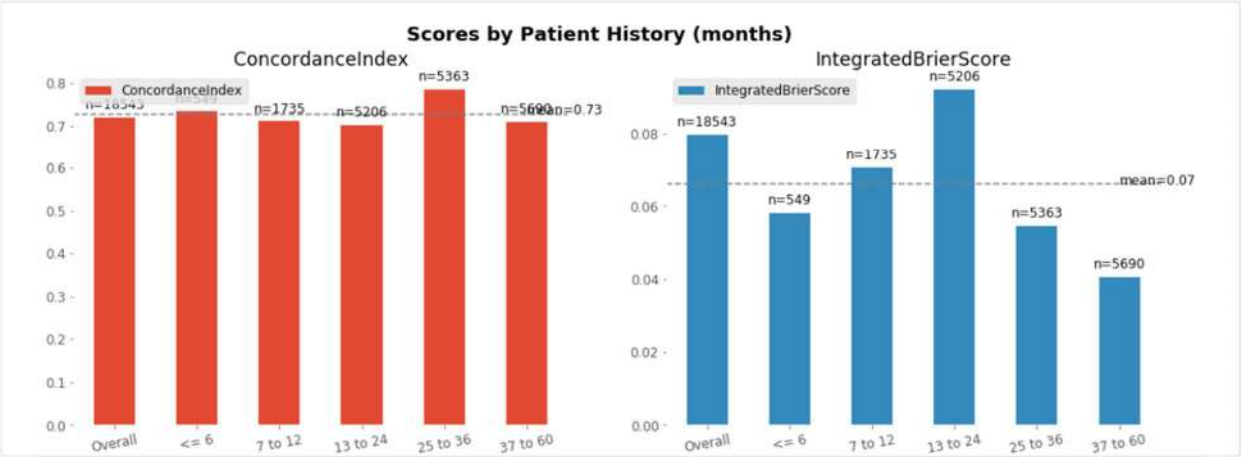
The following charts show how the Concordance Index and Integrated Brier Score varies among subgroups of risk, age, sex, ethnicity and patient history.





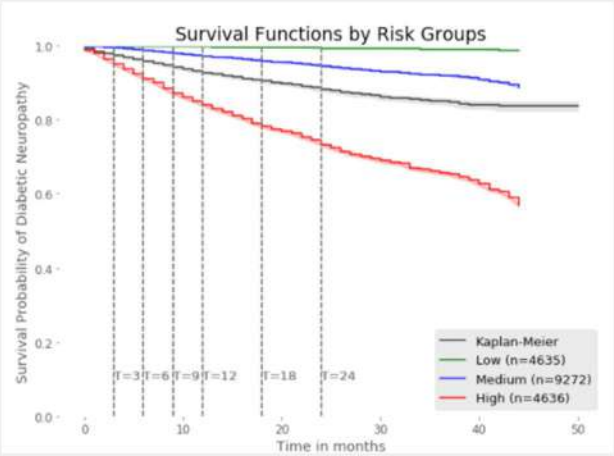


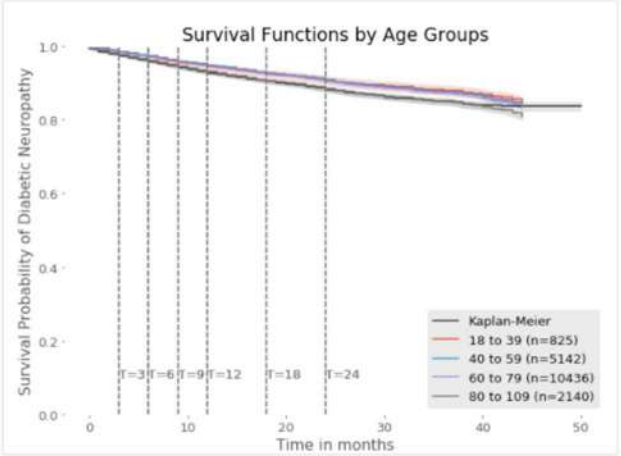

Scores by Ethnicity
ConcordanceIndex
IntegratedBrierScore
n=18543
n=1360
n=17183
mean=0.76
mean=0.08
Overall
Hispanic or Latino
Not Hispanic or Latino

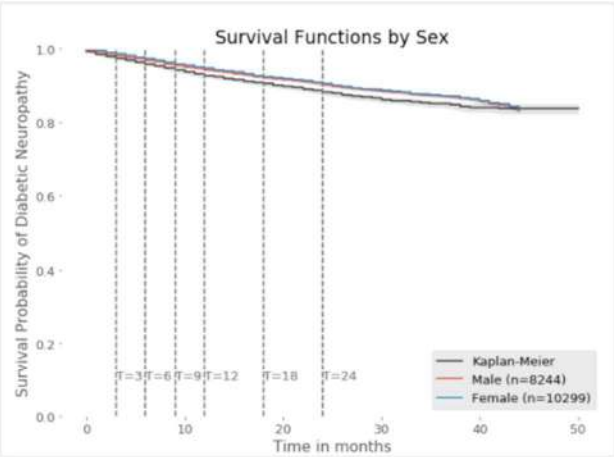

Scores by Patient History (months)
ConcordanceIndex
IntegratedBrierScore
n=18543
n=549
n=1735
n=5206
n=5363
n=5690
mean=0.73
mean=0.07
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60

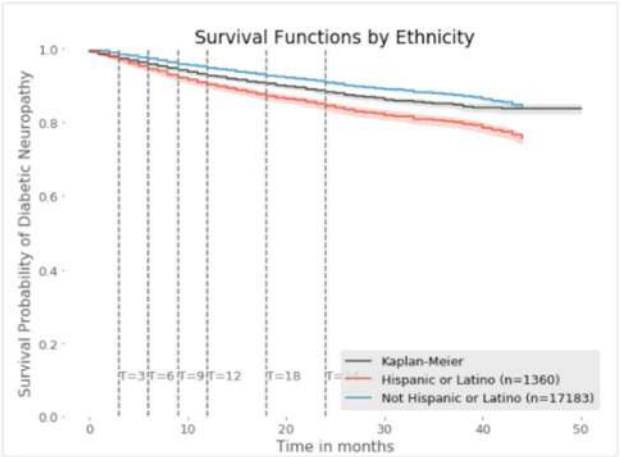
Average Survival Function Curves

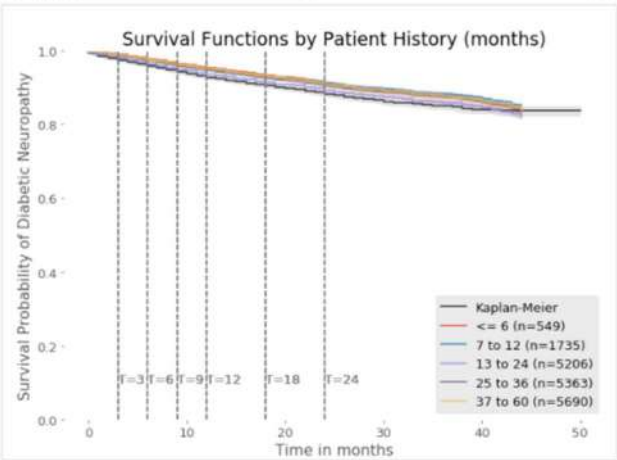
The following charts show how the average survival function curve varies among subgroups of risk, age, sex, ethnicity and patient history.





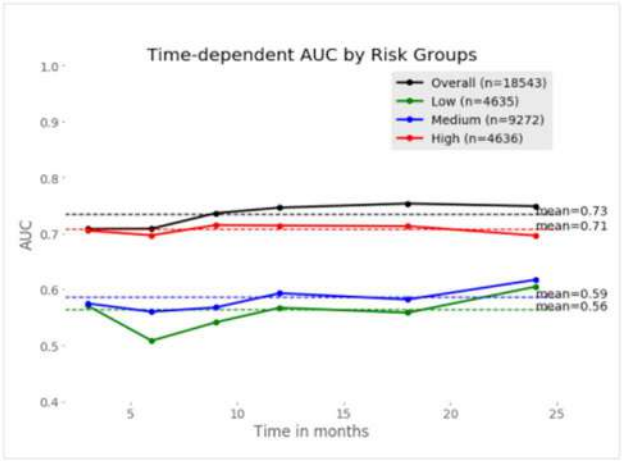


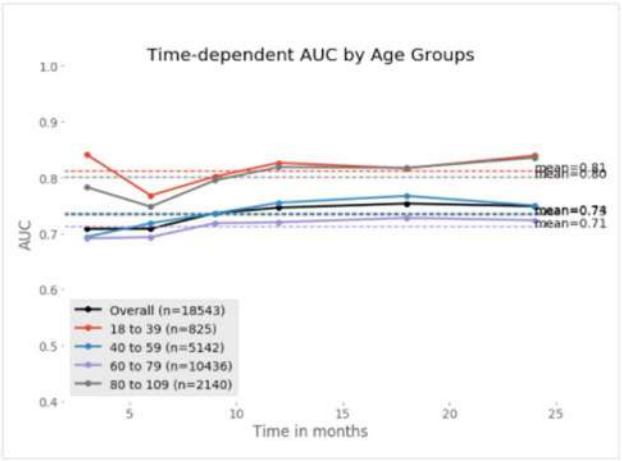


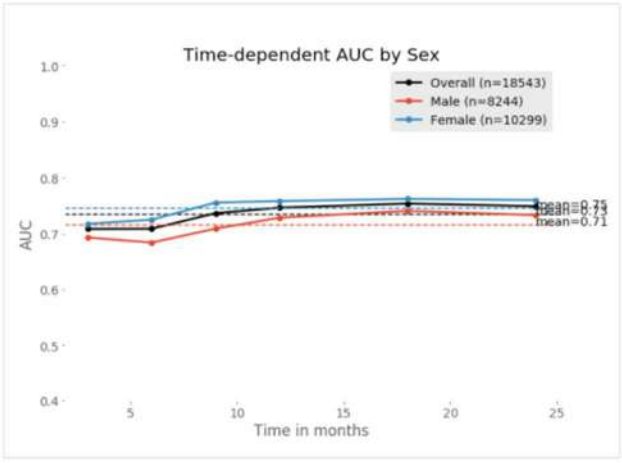


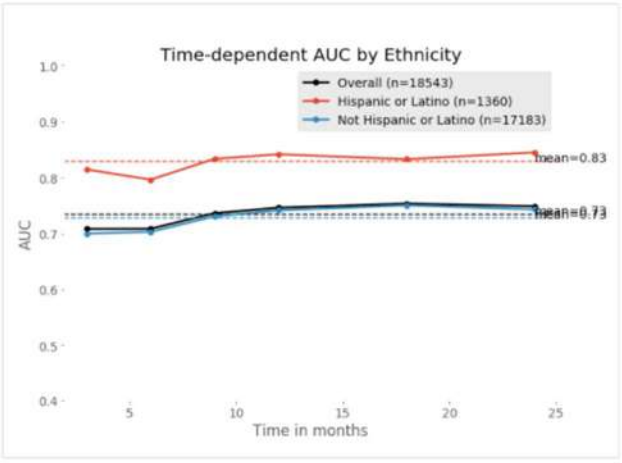
Time-dependent AUC

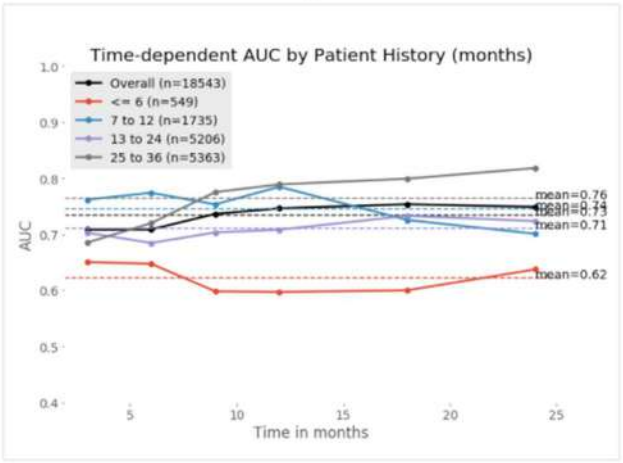
The following charts show how the AUC across time varies among subgroups of risk, age, sex, ethnicity and patient history.





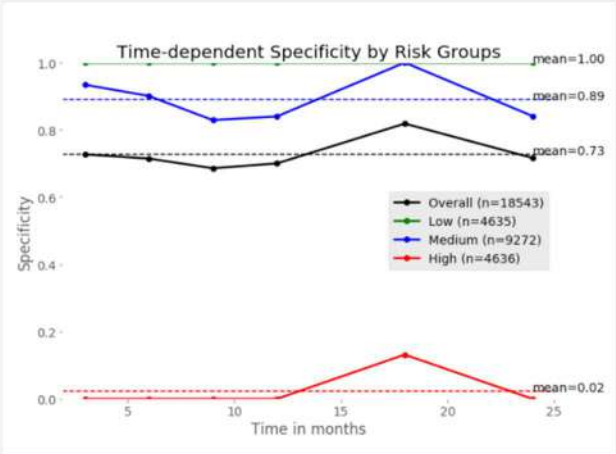


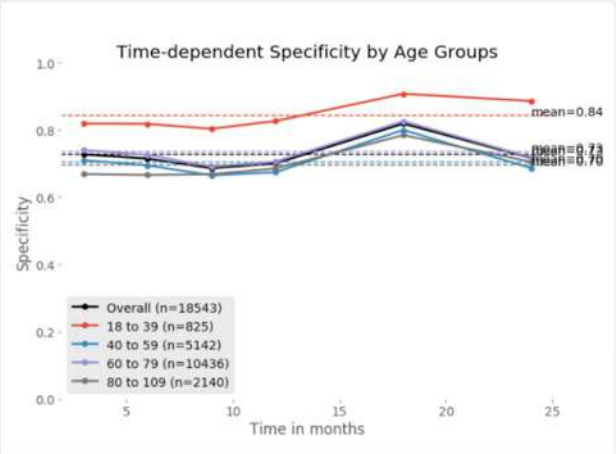


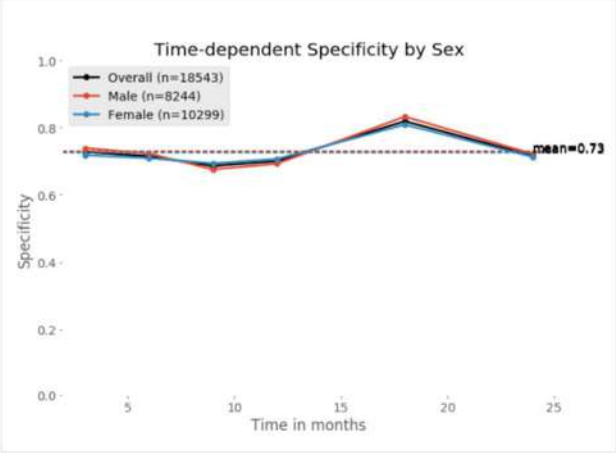


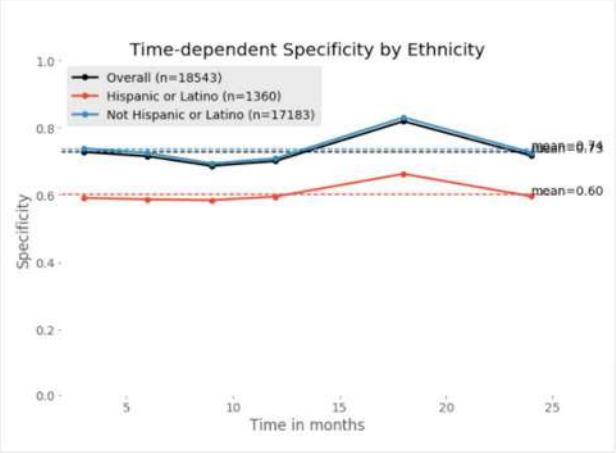
Time-dependent Specificity

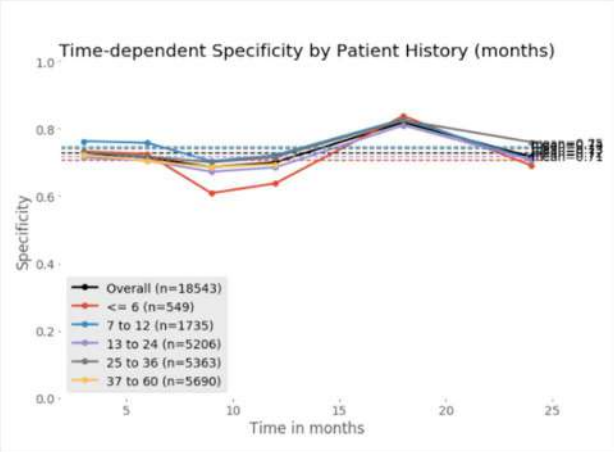
The following charts show how the specificity across time varies among subgroups of risk, age, sex, ethnicity and patient history.





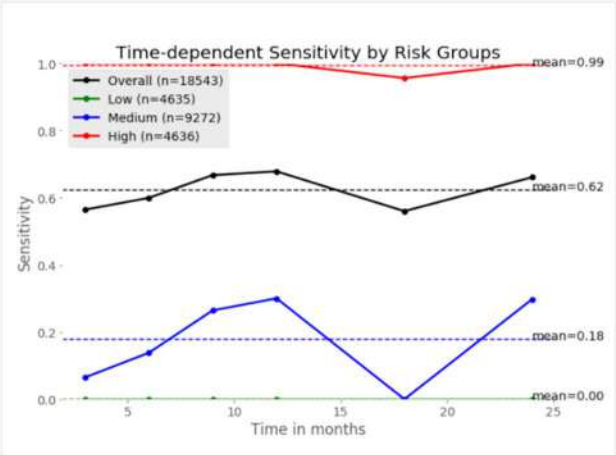


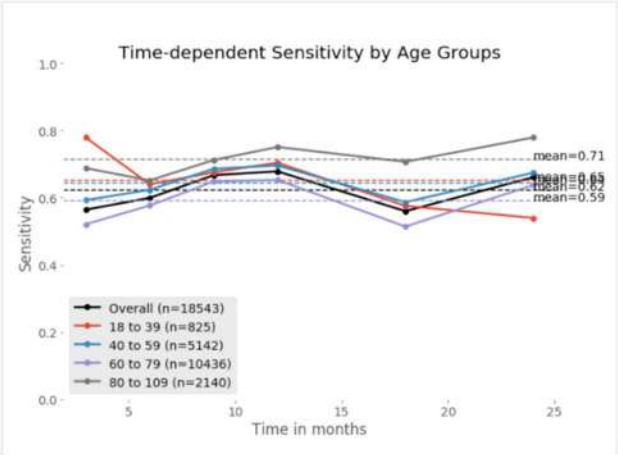


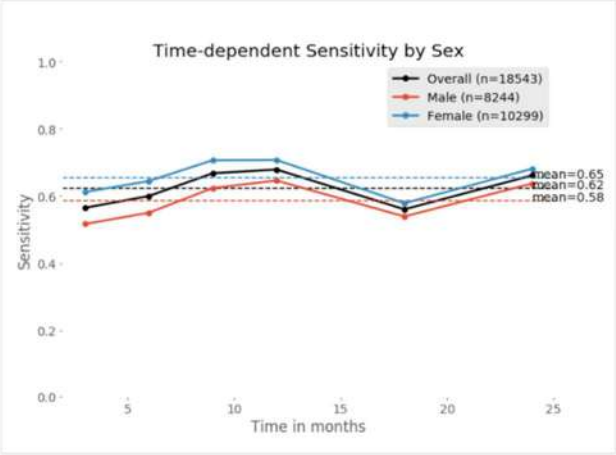


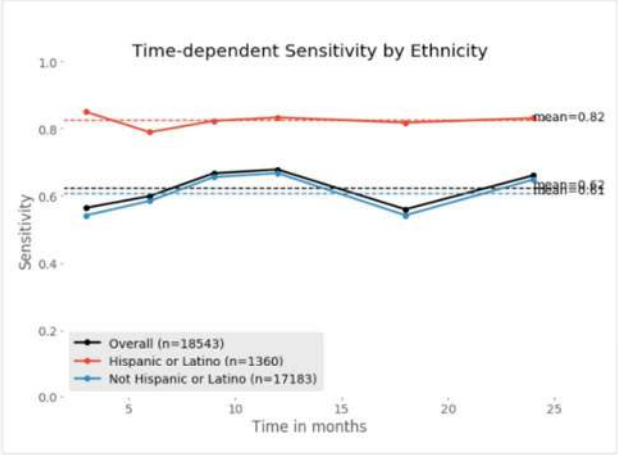
Time-dependent Sensitivity

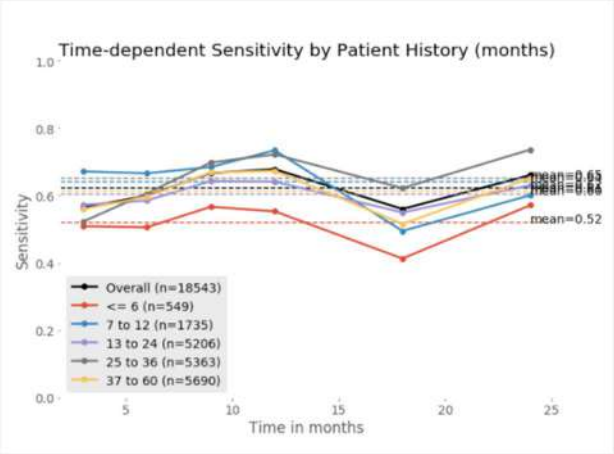
The following charts show how the sensitivity across time varies among subgroups of risk, age, sex, ethnicity and patient history.







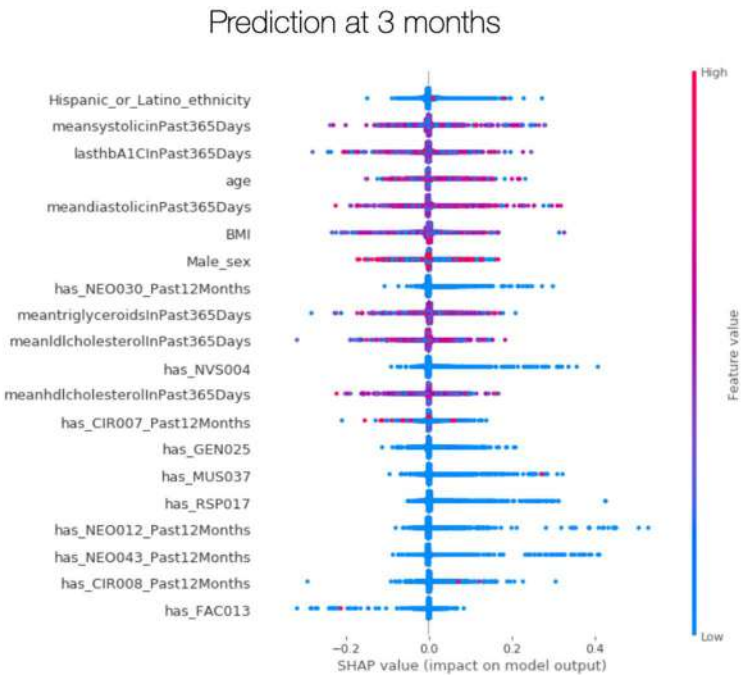


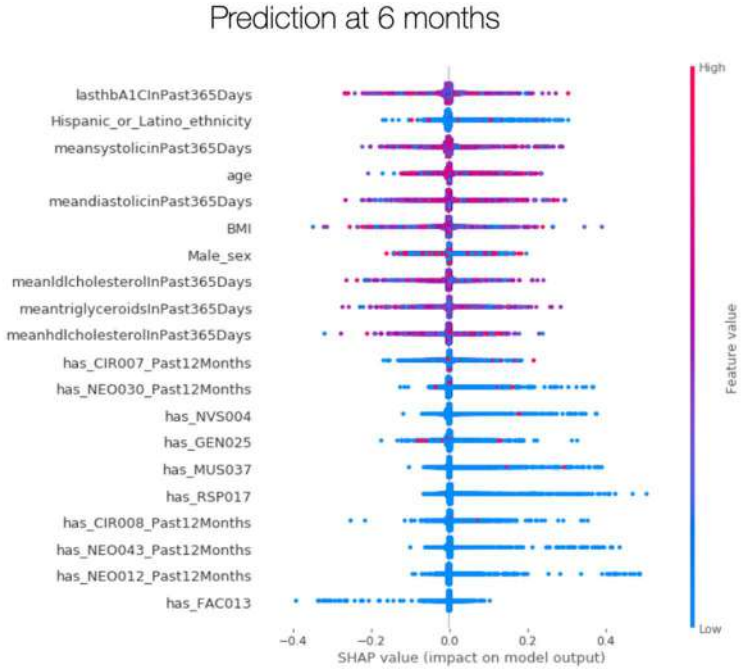


Model Explanation (DeepSurv)

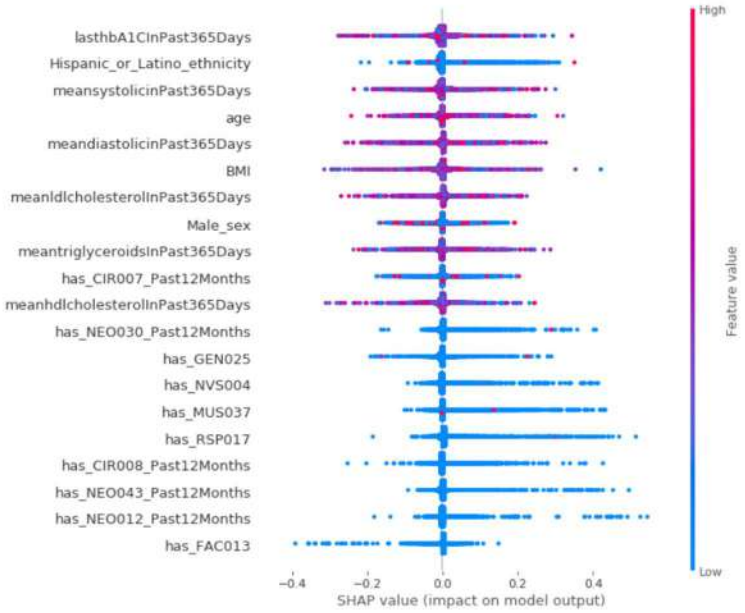
Global

The following plots show the SHAP values of each instance in the training set for each future time (3, 6, 9, 12, 18 and 24 months). The features are sorted by the total magnitude of the SHAP values over all instances and the distribution of the effect that each feature has on the model's output can be observed.

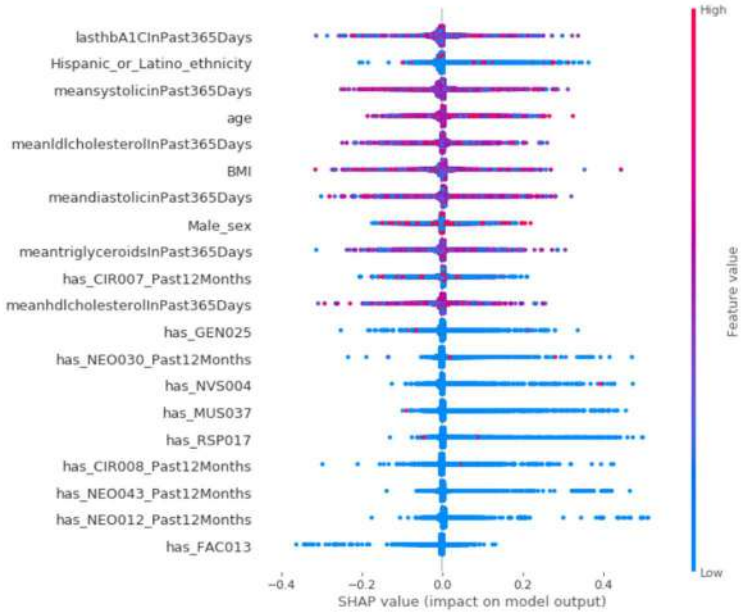


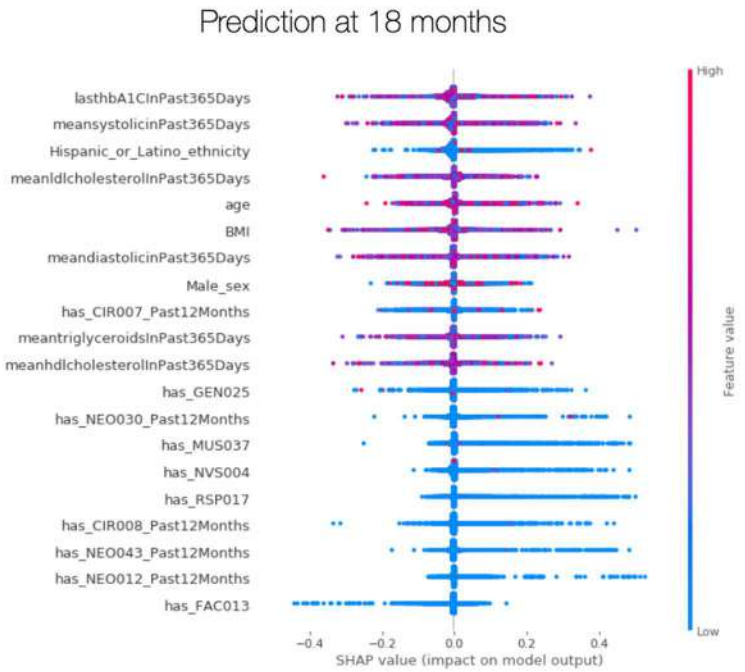


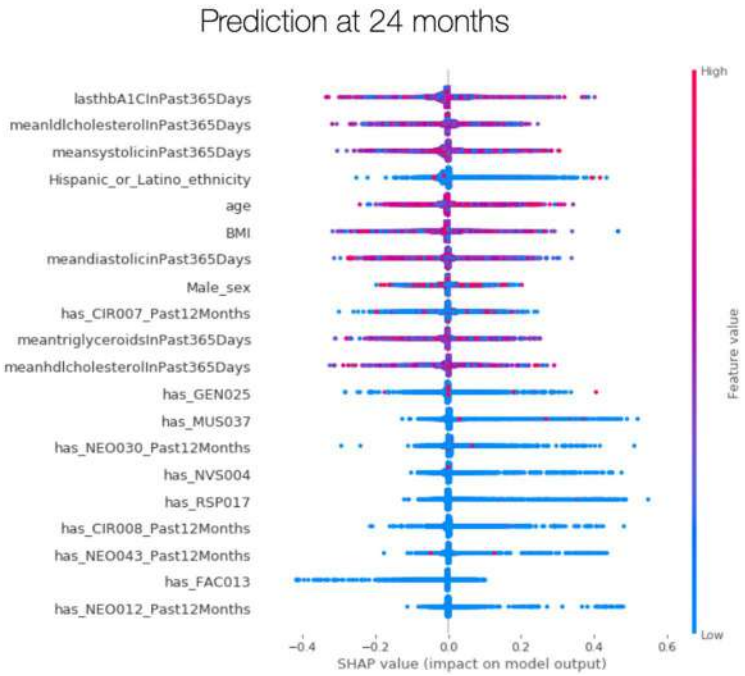
Prediction at 9 months



Prediction at 12 months

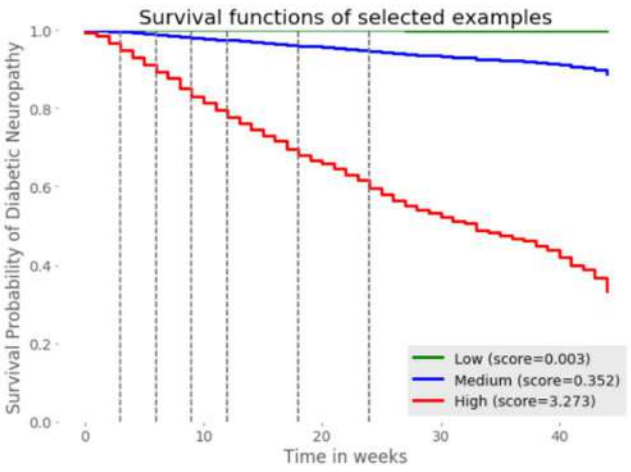






Local

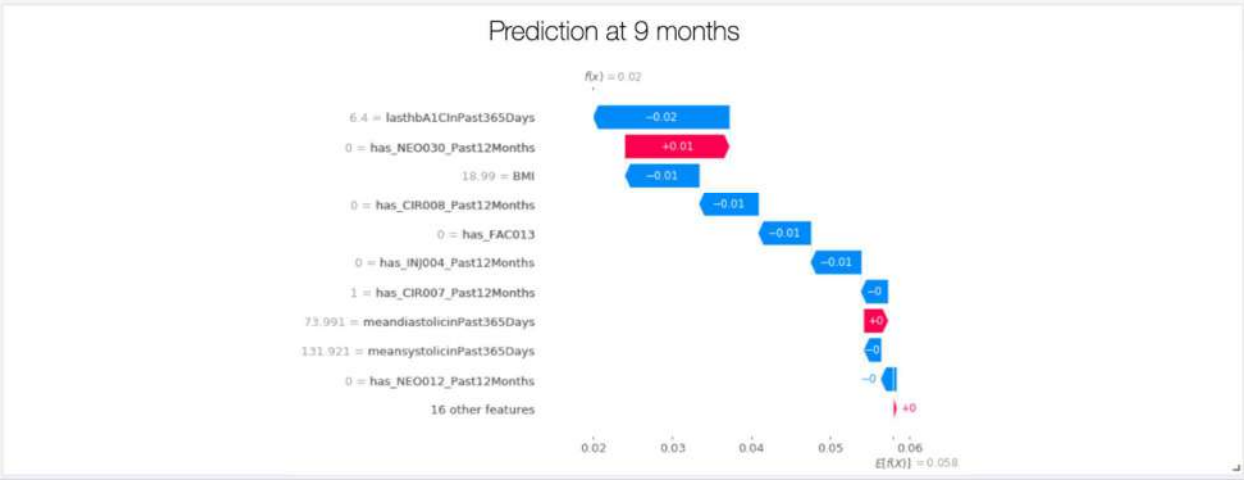
SHAP values were also generated to explain the predictions of individual examples for each future time (3, 6, 9, 12, 18 and 24 months). A total of 3 examples were selected by sampling of risk scores at the 5th, 50th and 95th percentile to represent instances at low, medium and high risks respectively.


Survival functions of selected examples
Survival Probability of Diabetic Neuropathy
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
Time in weeks
Low (score=0.003)
Medium (score=0.352)
High (score=3.273)

Low Risk
Risk Score: 0.003

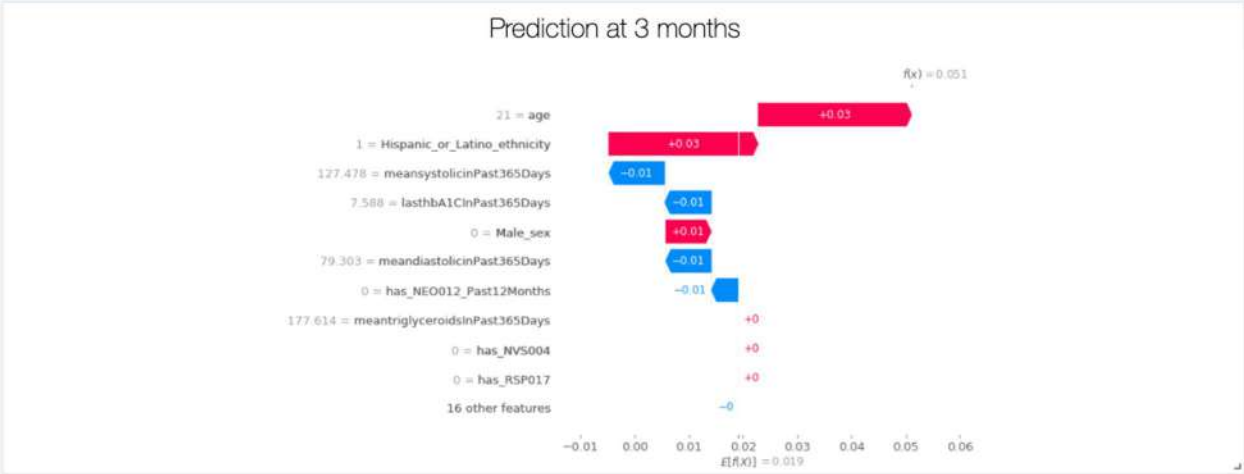
Low Risk
Risk Score: 0.003

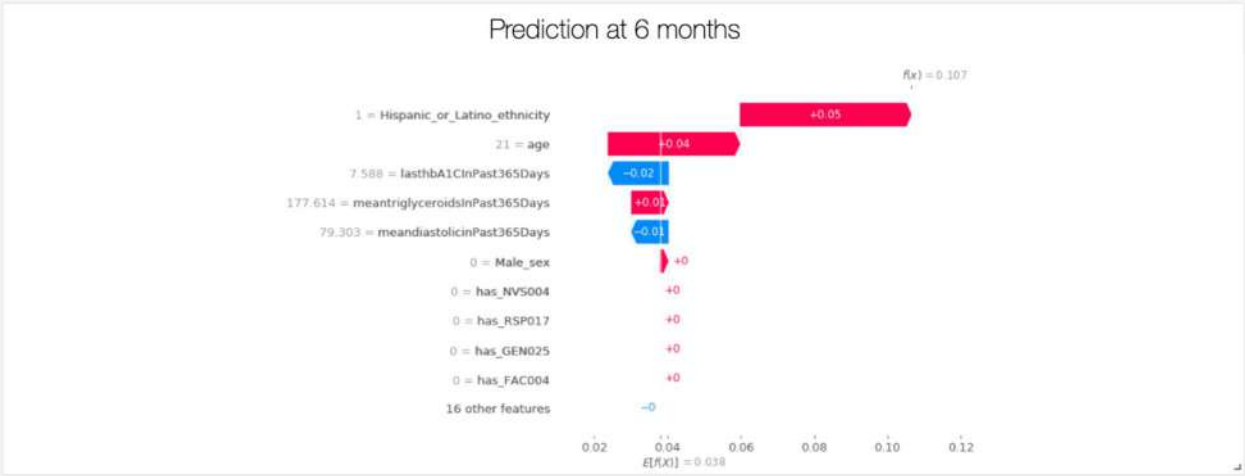
Medium Risk
Risk Score: 0.352

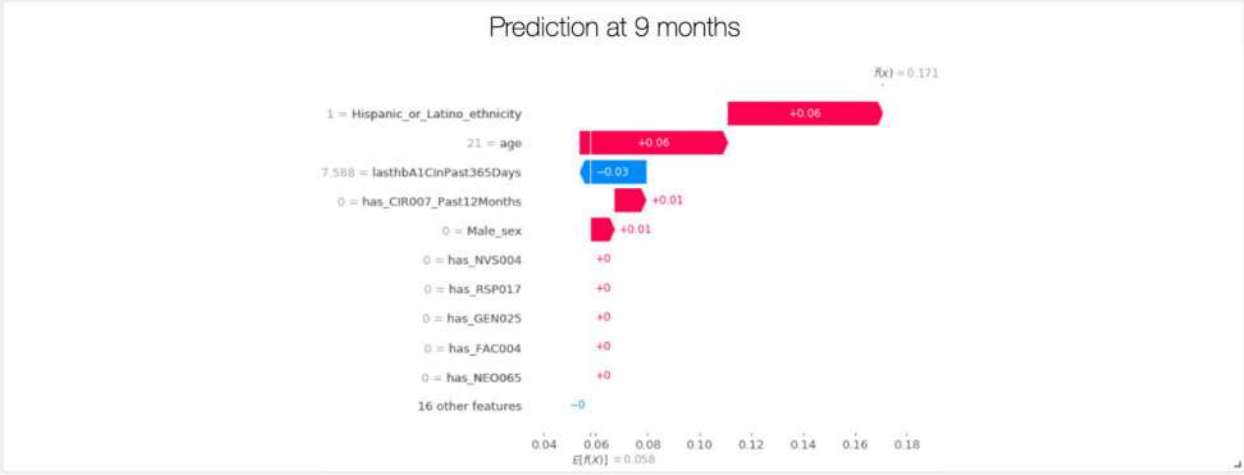


Medium Risk
Risk Score: 0.352

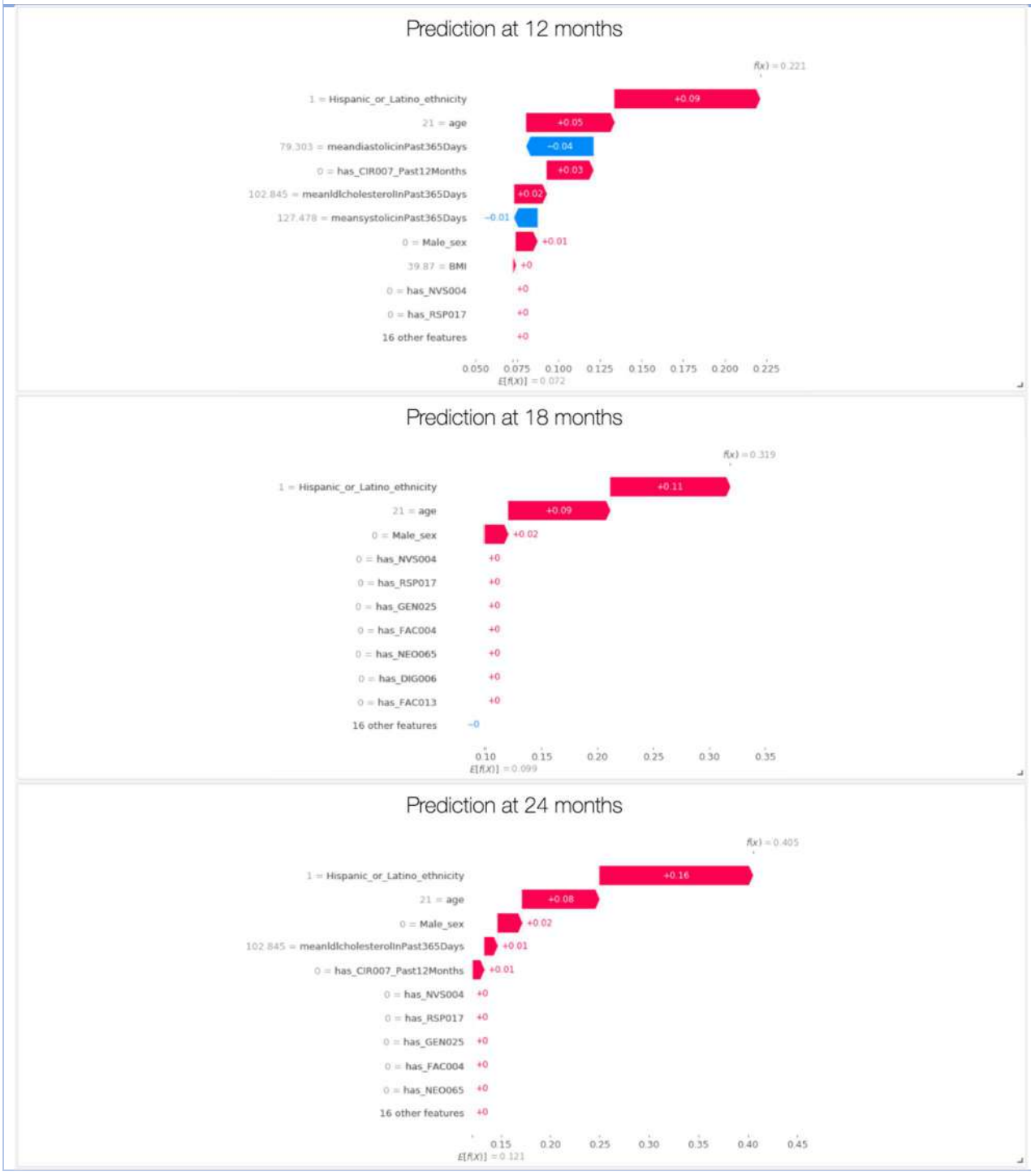
High Risk
Risk Score: 3.273







High Risk
Risk Score: 3.273



DM to Diabetic Retinopathy Prediction

Item	Specification
Business Goal	Enable care managers to identify the patients who are at risk of developing diabetic retinopathy
Usage Setting	Outpatient
ML Task	Predict risk and/or time from DM or uncontrolled DM to diabetic retinopathy
ML Class	Survival
Instances for Prediction	Encounters
Labels for Instances	Binary indicator and time to event or censoring for diabetic retinopathy
Cohort Criteria	• 2016-01-01 ≤ encounter date ≤ 2020-06-30 (available Epic data, excluding outliers) • Encounter date is not within the first 90 days of when the patient entered the data set, to adjust for left-censoring • 18 ≤ age ≤ 110 (adults without outliers) • No T1DM diagnosis • Not pregnant • No "Do Not Resuscitate" diagnosis • DM or uncontrolled DM event before encounter date • No diabetic retinopathy event before encounter date • No diabetic retinopathy event up to 6 days after encounter date (encounters where diagnoses confirm event within the week)

Input Features	• Demographic
	• Diagnosis, except:
	  ○ hasDiabetesRetinopathy*
	  ○ has_EYE002* (cataract and other lens disorders)
	  ○ has_EYE005* (retinal and vitreous conditions)
	• Labs
	• Utilization
	• Vitals
	
	See Appendix E for details.

Evaluation Metrics	• Concordance Index • Integrated Brier Score

Data

The following charts summarize the key characteristics of the data after applying the cohort criteria stated above, along with selected features (see Model Signature below).

Category	summary Variable	count	mean	stddev	min	25%	50%	75%	max
Demographic	AgeBucket_18_to_39	80201.0	0.041994	0.200578	0.00	0.000	0.000	0.000	1.00
	AgeBucket_40_to_59	80201.0	0.273924	0.445973	0.00	0.000	0.000	1.000	1.00
	AgeBucket_60_to_79	80201.0	0.563297	0.495980	0.00	0.000	1.000	1.000	1.00
	AgeBucket_80_to_109	80201.0	0.120784	0.325878	0.00	0.000	0.000	0.000	1.00
	Sex_Female	80201.0	0.554332	0.497042	0.00	0.000	1.000	1.000	1.00
	Sex_Male	80201.0	0.445668	0.497042	0.00	0.000	0.000	1.000	1.00
	Ethnicity_Hispanic_or_Latino	80201.0	0.068154	0.252011	0.00	0.000	0.000	0.000	1.00
	Ethnicity_Not_Hispanic_or_Latino	80201.0	0.931846	0.252011	0.00	1.000	1.000	1.000	1.00
Encounter	EncounterType_Emergency	80201.0	0.223027	0.416279	0.00	0.000	0.000	0.000	1.00
	EncounterType_Inpatient	80201.0	0.114201	0.318057	0.00	0.000	0.000	0.000	1.00
	EncounterType_Outpatient	80201.0	0.662772	0.472766	0.00	0.000	1.000	1.000	1.00
Label	Time	80201.0	15.808593	11.336733	0.00	6.000	14.000	24.000	50.00
	Event	80201.0	0.015436	0.123281	0.00	0.000	0.000	0.000	1.00
Feature	age	80201.0	64.692635	13.071276	18.00	56.000	66.000	74.000	102.00
	Male_sex	80201.0	0.445668	0.497042	0.00	0.000	0.000	1.000	1.00
	Hispanic_or_Latino_ethnicity	80201.0	0.068154	0.252011	0.00	0.000	0.000	0.000	1.00
	lasthbA1ClnPast365Days	80201.0	7.550005	1.225381	3.50	6.800	7.468	8.000	12.70
	meandiastolicinPast365Days	80201.0	73.547908	7.848043	43.62	69.278	73.621	78.210	107.56
	meansystolicinPast365Days	80201.0	132.128908	11.565079	81.00	127.480	131.860	135.970	180.00
	BMI	80201.0	33.674120	6.790728	10.37	29.490	33.600	37.260	157.25
	meantriglyceroidsInPast365Days	80201.0	168.577678	57.720742	19.00	138.000	167.109	182.466	460.50
	meanldlcholesterolInPast365Days	80201.0	88.448366	23.579373	8.00	80.500	88.935	98.338	201.00
	meanhdlcholesterolInPast365Days	80201.0	42.829770	9.193400	5.00	37.500	42.000	47.190	98.00
	has_GEN020_Past12Months	80201.0	0.004377	0.066011	0.00	0.000	0.000	0.000	1.00
	has_CIR009_Past12Months	80201.0	0.018341	0.134184	0.00	0.000	0.000	0.000	1.00
	has_BLD008_Past12Months	80201.0	0.018105	0.133330	0.00	0.000	0.000	0.000	1.00
	has_CIR007_Past12Months	80201.0	0.190609	0.392784	0.00	0.000	0.000	0.000	1.00
	has_NEO008_Past12Months	80201.0	0.001820	0.042628	0.00	0.000	0.000	0.000	1.00
	has_CIR008_Past12Months	80201.0	0.012157	0.109587	0.00	0.000	0.000	0.000	1.00
	has_MBD017	80201.0	0.022818	0.149323	0.00	0.000	0.000	0.000	1.00
	has_INJ026	80201.0	0.003055	0.055186	0.00	0.000	0.000	0.000	1.00
	has_GEN017	80201.0	0.035199	0.184284	0.00	0.000	0.000	0.000	1.00
	has_MAL004	80201.0	0.001696	0.041145	0.00	0.000	0.000	0.000	1.00
	has_NEO022	80201.0	0.037880	0.190907	0.00	0.000	0.000	0.000	1.00
	has_INJ069	80201.0	0.001147	0.033850	0.00	0.000	0.000	0.000	1.00
	has_RSP011	80201.0	0.063428	0.243733	0.00	0.000	0.000	0.000	1.00
	has_INJ023	80201.0	0.002219	0.047059	0.00	0.000	0.000	0.000	1.00
	has_MUS016	80201.0	0.002469	0.049626	0.00	0.000	0.000	0.000	1.00
	has_NVS013	80201.0	0.019040	0.136665	0.00	0.000	0.000	0.000	1.00

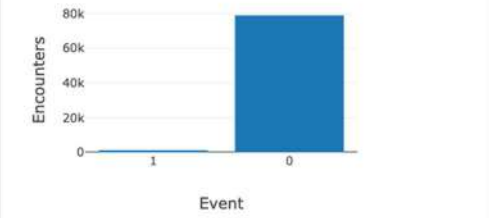
(Percentages for binary variables can be read from the “mean” column.)

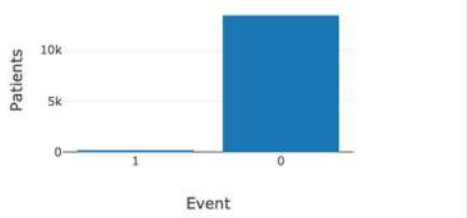
Encounters and Patients

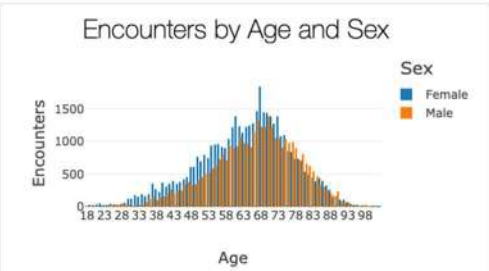
	Examples	Encounters	Patients
1	80201	80201	13624

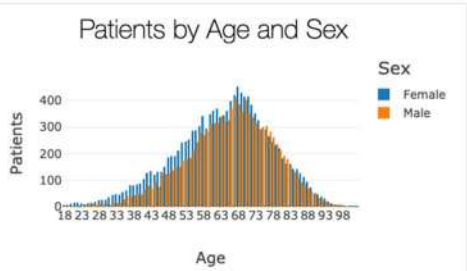
Train and Test Sets

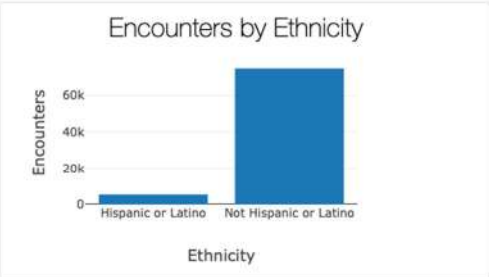
	Set	No Event	No Event %	Event	Event %	Total	Total %
1	Test	23887	30.3	371	30	24258	30.2
2	Train	55076	69.7	867	70	55943	69.8
3	Total	78963	100	1238	100	80201	100

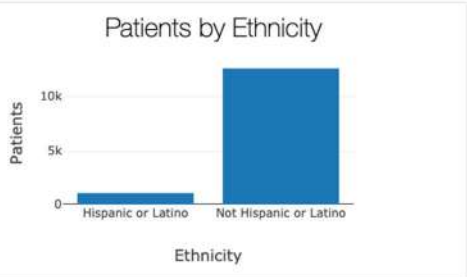


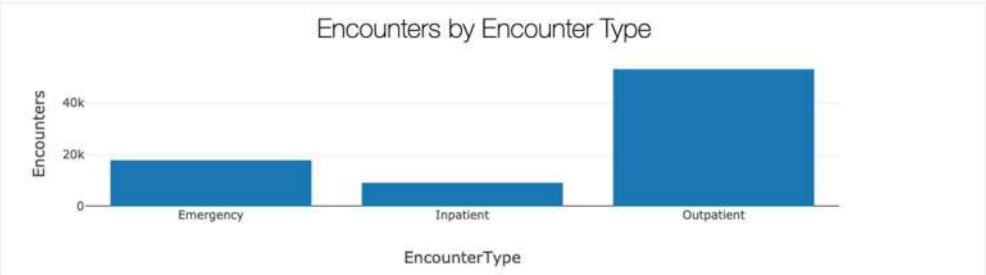


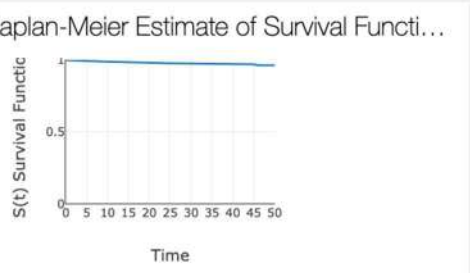








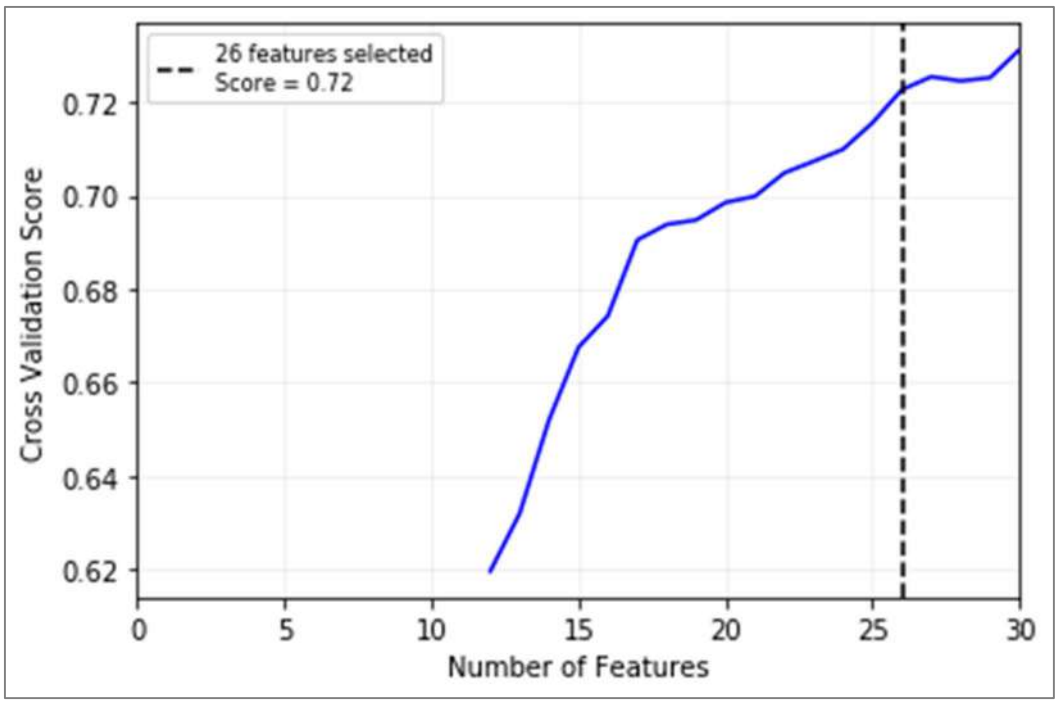




Model Signature

The model signature has 26 features, comprising of 12 mandatory features and 14 other selected features. These are the selected features, in rank order (the last feature to be eliminated is ranked 1):

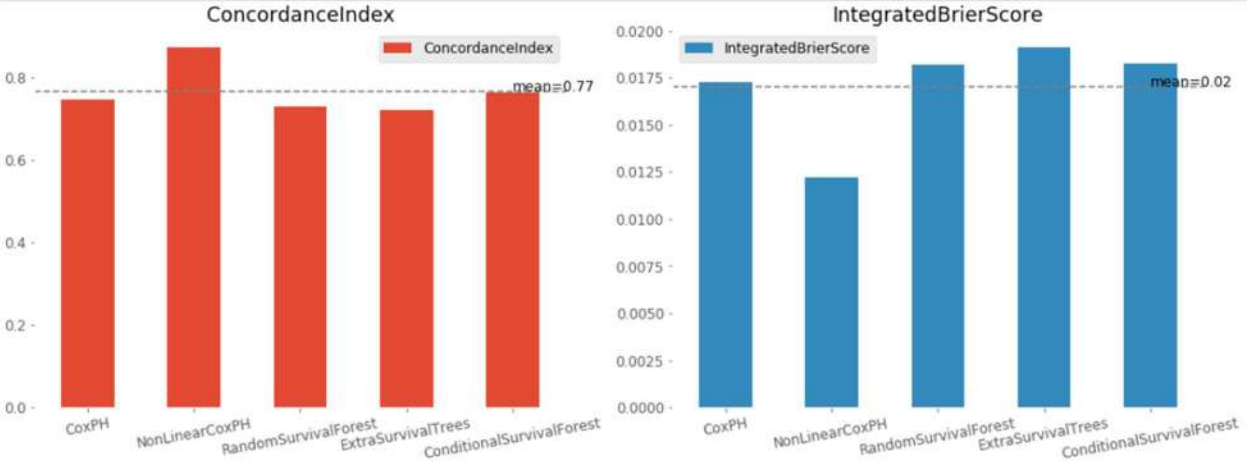
1. has_BLD008_Past12Months (Immunity disorders)
2. has_NEO022 (Respiratory cancers)
3. has_CIR009_Past12Months (Acute myocardial infarction)
4. has_INJ069 (Complication of cardiovascular device, implant or graft, subsequent encounter)
5. has_GEN020_Past12Months (Prolapse of female genital organs)
6. has_MUS016 (Stress fracture, initial encounter)
7. has_INJ023 (Toxic effects, initial encounter)
8. has_MAL004 (Nervous system congenital anomalies)
9. has_NVS013 (Coma; stupor; and brain damage)
10. has_GEN017 (Nonmalignant breast conditions)
11. has_INJ026 (Other specified injury)
12. has_NEO008_Past12Months (Head and neck cancers - laryngeal)
13. has_MBD017 (Alcohol-related disorders)
14. has_RSP011 (Pleurisy, pleural effusion and pulmonary collapse)
15. Hispanic_or_Latino_ethnicity
16. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)
17. lasthbA1CInPast365Days
18. Male_sex
19. has_CIR007_Past12Months (Essential hypertension)
20. meanhdlcholesterolInPast365Days
21. meandiastolicinPast365Days
22. age
23. meansystolicinPast365Days
24. BMI
25. meanldlcholesterolInPast365Days
26. meantriglyceroidsInPast365Days



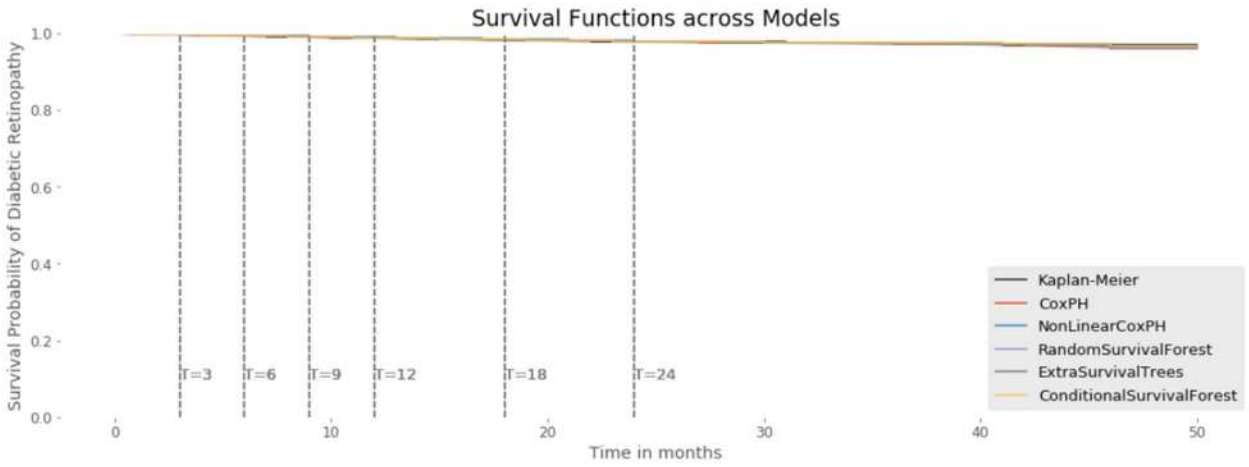
Model Performance

The following table and chart summarize the performance of all candidate models on the test set for this prediction task in terms of the Concordance Index and the Integrated Brier Score.

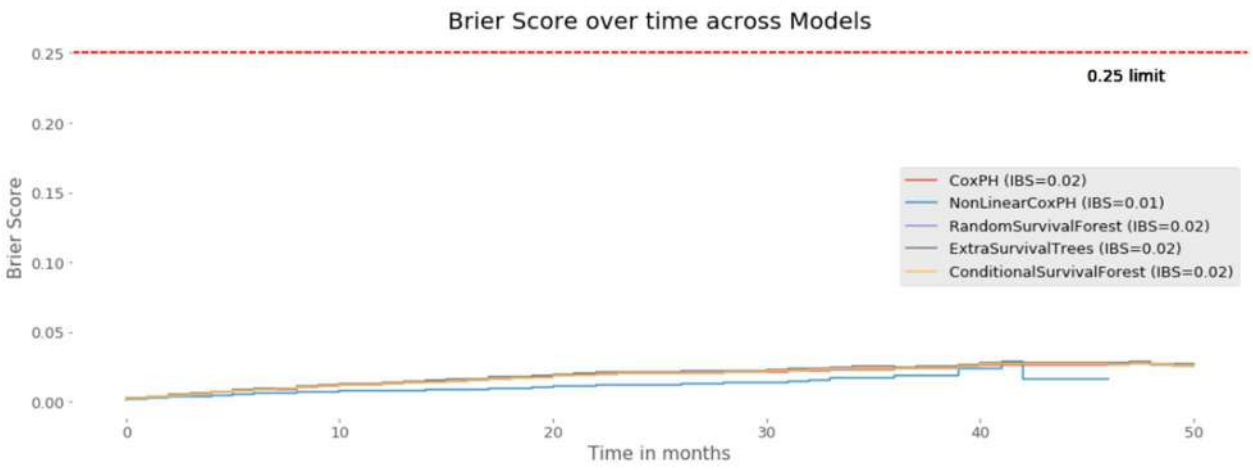
Model	No. of Parameter Combinations Successfully Tested	Concordance Index	Integrated Brier Score
CoxPH	101	0.75	0.02
DeepSurv	169	**0.87**	**0.01**
RSF	31	0.73	0.02
CSF	22	0.72	0.02
EST	36	0.76	0.02



The following chart shows how the average survival function curves of the candidate models compare to the KM survival curve, the more similar their curves are to the KM survival curve the better.



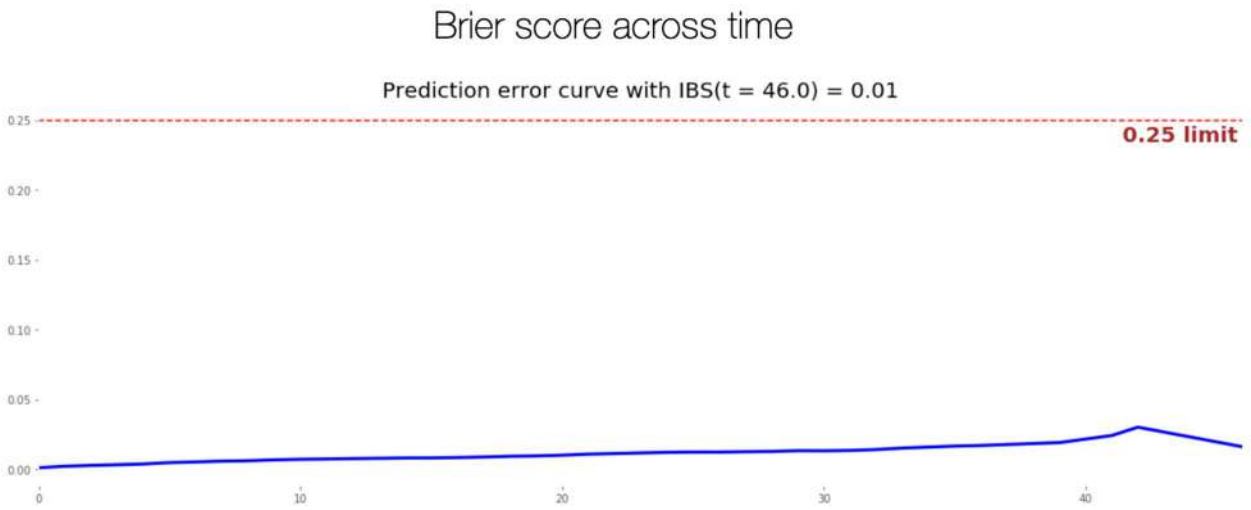
This chart shows the change in the Brier Score over time for all candidate models, the closer the scores are to 0 the better.



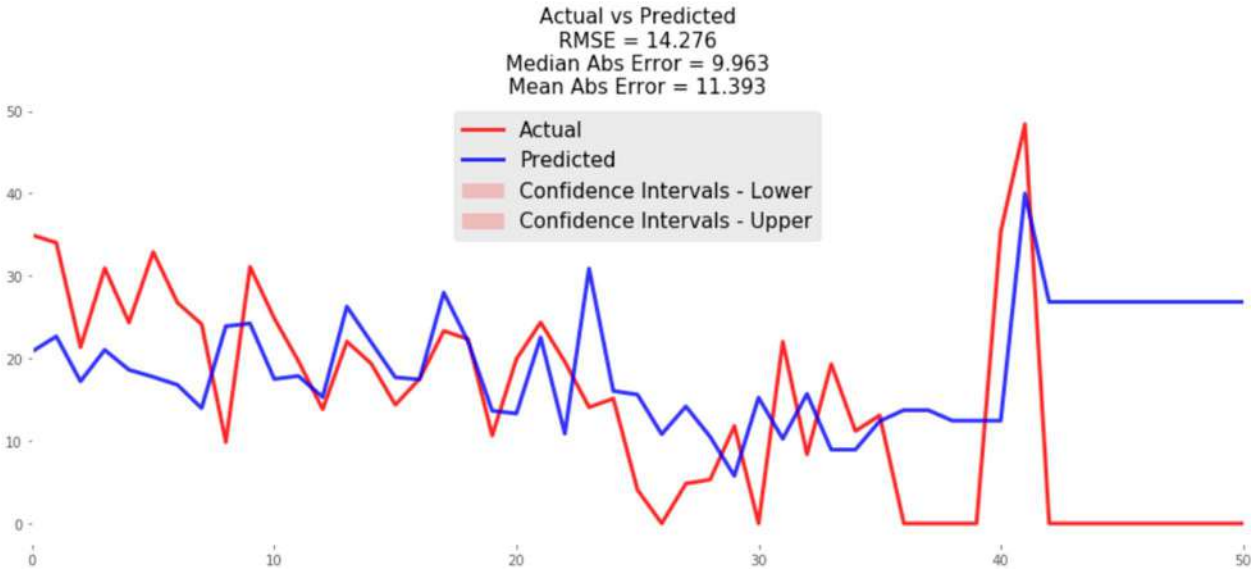
Model Evaluation of Selected Model (DeepSurv)

Overall

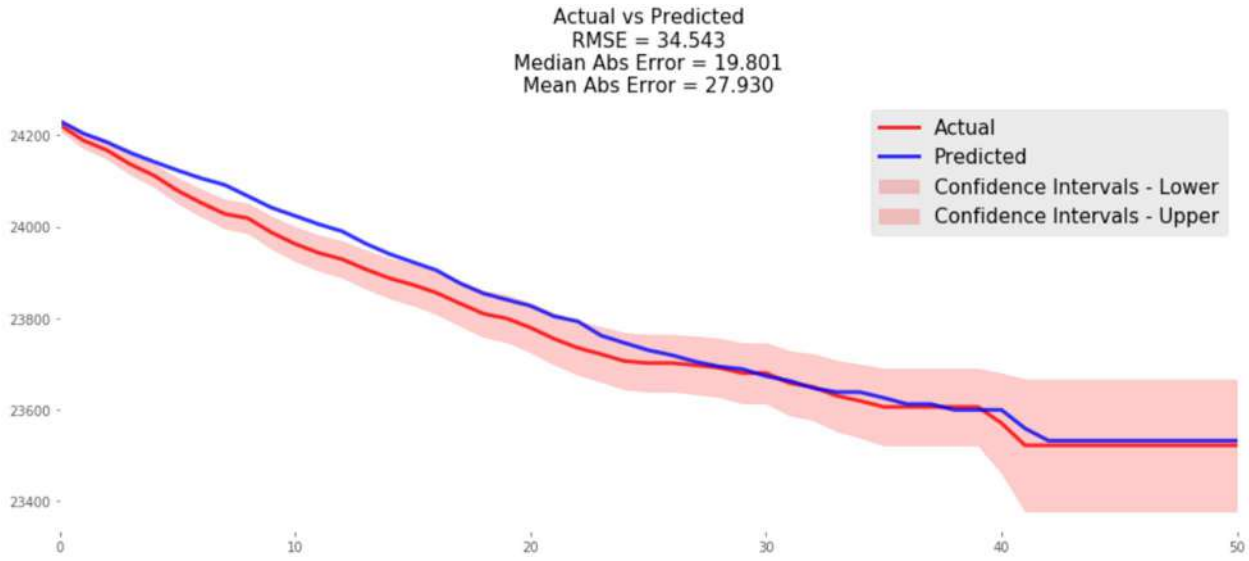
This chart shows the change in the Brier Score over time for the selected model, the closer the scores are to 0 the better.



The following chart shows the actual vs. predicted density functions, i.e. number of instances that get the disease / complication at each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



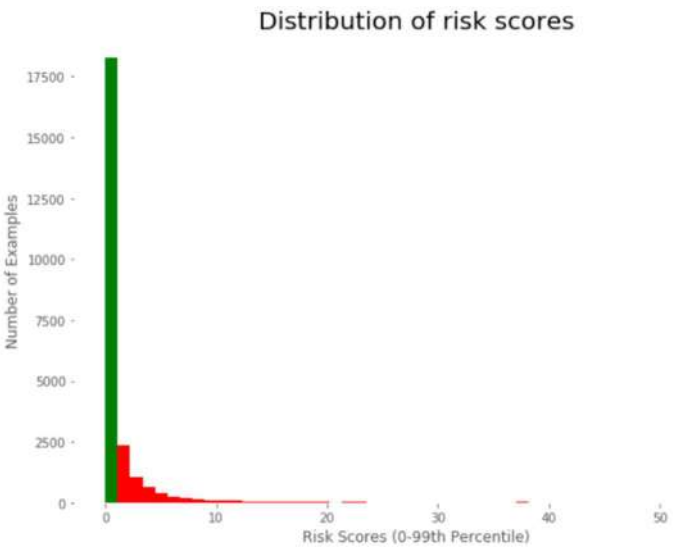
The following chart shows the actual vs. predicted survival functions, i.e. the number of instances that have not had the disease / complication by each time point and the RMSE, Median Absolute Error and Mean Absolute Error across the time points.



Risk Stratification

The low, medium and high risk groups are defined as examples with predicted risk scores belonging to the first quartile, second to third quartiles, and fourth quartile respectively.

	Percentile	Risk Scores
Low Risk	0-25th	[0.0,0.016]
Medium Risk	26th-75th	[0.016,1.098]
High Risk	75th-100th	[1.098,18111.4453125]



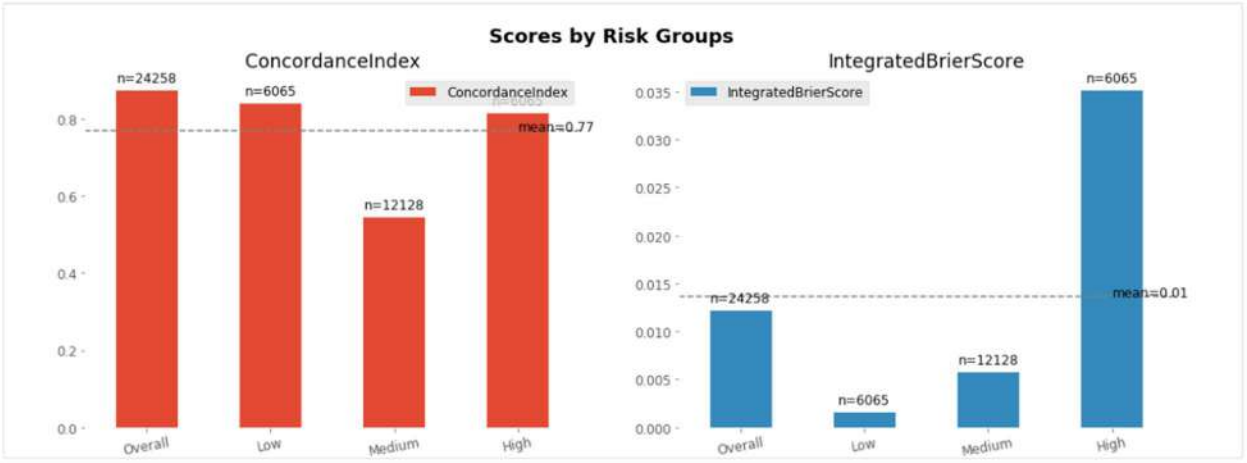
Summary Metrics across Subgroups

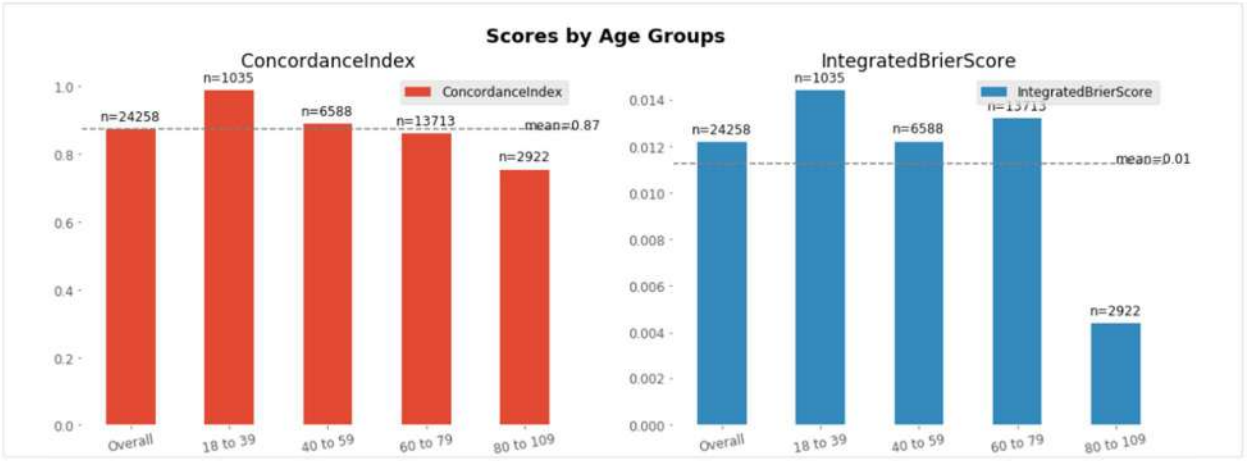
The table below displays the summary metrics across subgroups of risk, age, sex, ethnicity and patient history.

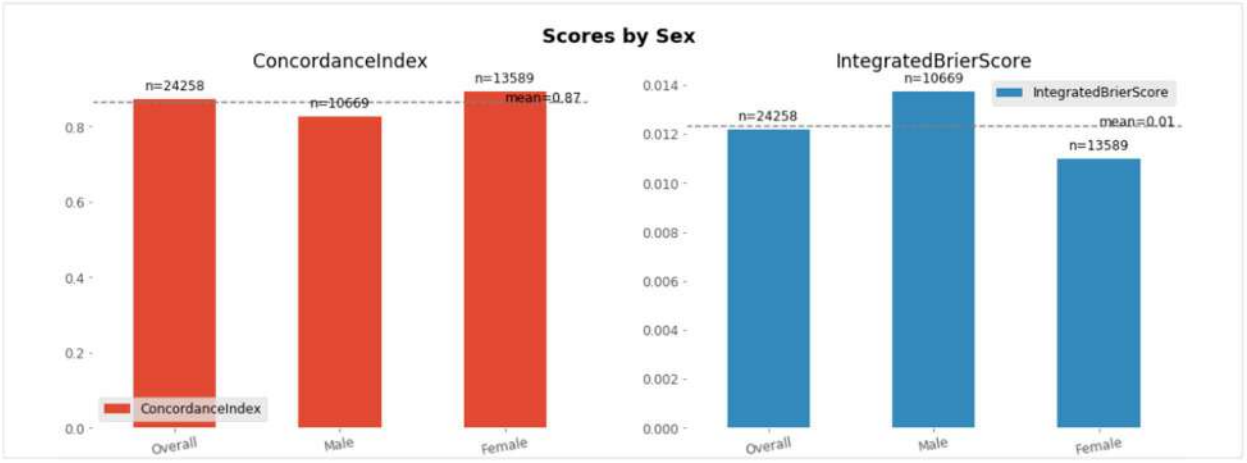
Category	Subgroup	Cohort Size	Concordance Index	Brier Score	Mean AUC	Mean Specificity	Mean Sensitivity	S(t), t=3	S(t), t=6	S(t), t=9	S(t), t=12	S(t), t=18	S(t), t=24
NaN	Overall	24258.00	0.87	0.01	0.90	0.97	0.68	0.99	0.99	0.99	0.99	0.98	0.98
Risk	Low	6065.00	0.84	0.00	0.86	1.00	0.00	1.00	1.00	1.00	1.00	1.00	1.00
Risk	Medium	12128.00	0.55	0.01	0.49	1.00	0.00	1.00	1.00	1.00	1.00	1.00	1.00
Risk	High	6065.00	0.81	0.04	0.87	0.88	0.80	0.98	0.98	0.97	0.96	0.94	0.92
Age Bucket	18 to 39	1035.00	0.99	0.01	0.99	0.99	0.75	1.00	1.00	1.00	0.99	0.99	0.99
Age Bucket	40 to 59	6588.00	0.89	0.01	0.93	0.96	0.77	0.99	0.99	0.99	0.98	0.98	0.97
Age Bucket	60 to 79	13713.00	0.86	0.01	0.89	0.97	0.64	1.00	0.99	0.99	0.99	0.98	0.98
Age Bucket	80 to 109	2922.00	0.75	0.00	0.72	0.98	0.36	1.00	1.00	1.00	0.99	0.99	0.99
Sex	Male	10669.00	0.83	0.01	0.85	0.97	0.60	1.00	0.99	0.99	0.99	0.99	0.98
Sex	Female	13589.00	0.89	0.01	0.92	0.97	0.73	1.00	0.99	0.99	0.99	0.98	0.98
Ethnicity	Hispanic or Latino	1674.00	0.94	0.02	0.88	0.95	0.67	0.99	0.99	0.98	0.98	0.97	0.96
Ethnicity	Not Hispanic or Latino	22584.00	0.86	0.01	0.90	0.97	0.68	1.00	0.99	0.99	0.99	0.98	0.98
History Bucket	<= 6	607.00	0.92	0.01	0.92	0.98	0.59	1.00	1.00	0.99	0.99	0.99	0.98
History Bucket	7 to 12	2035.00	0.82	0.01	0.88	0.97	0.64	1.00	0.99	0.99	0.99	0.98	0.98
History Bucket	13 to 24	6532.00	0.84	0.01	0.87	0.97	0.58	1.00	0.99	0.99	0.99	0.98	0.98
History Bucket	25 to 36	7005.00	0.92	0.01	0.91	0.97	0.74	1.00	0.99	0.99	0.99	0.98	0.98
History Bucket	37 to 60	8079.00	0.90	0.01	nan	nan	0.75	0.99	0.99	0.99	0.99	0.98	0.98

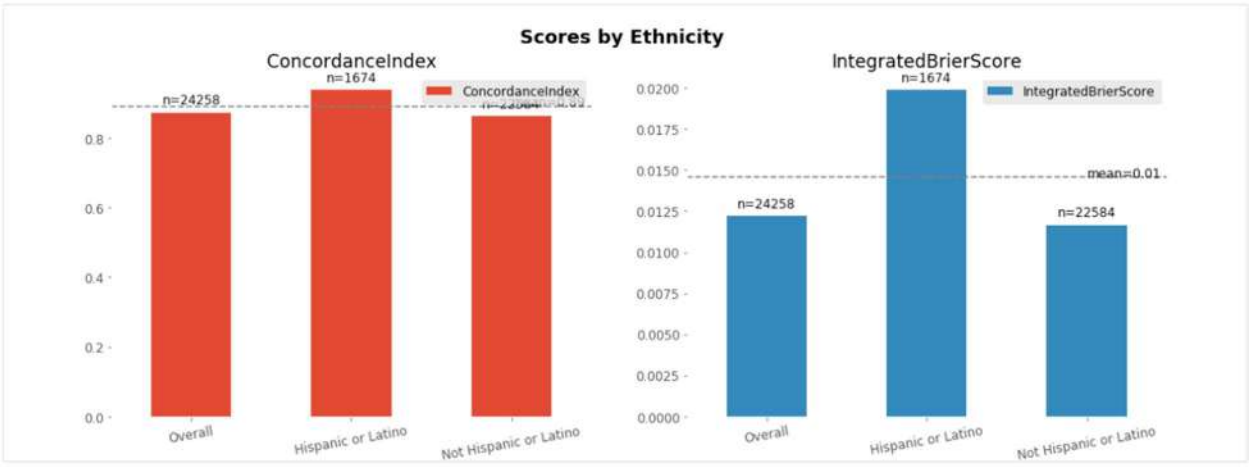
Concordance Index & Integrated Brier Score

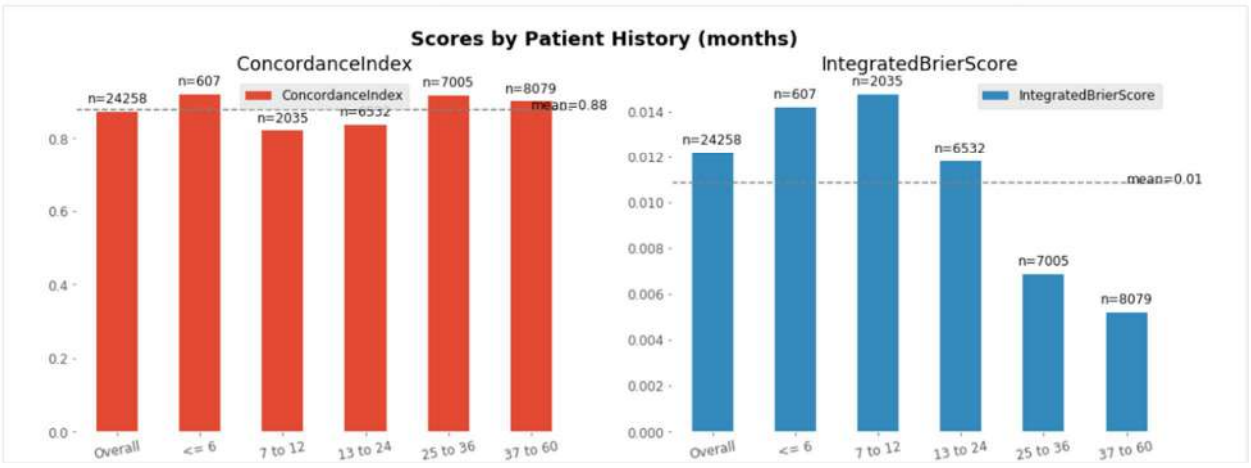
The following charts show how the Concordance Index and Integrated Brier Score varies among subgroups of risk, age, sex, ethnicity and patient history.





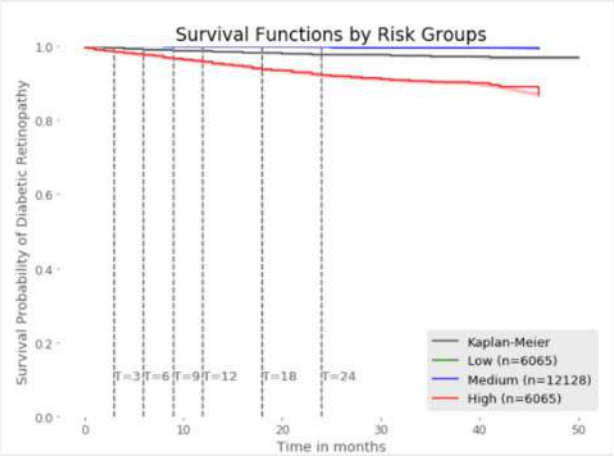


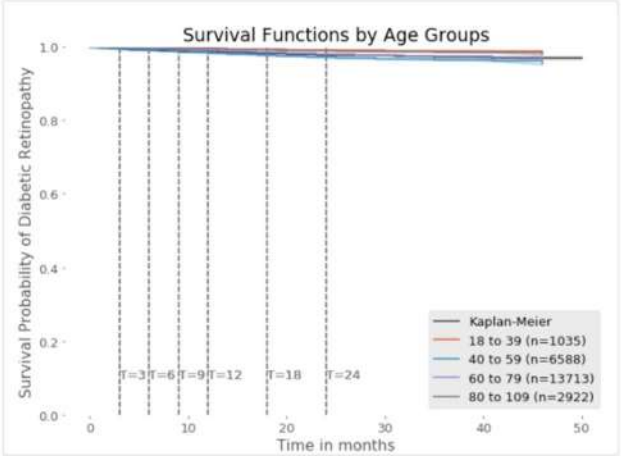

Scores by Ethnicity
ConcordanceIndex
IntegratedBrierScore
n=24258
n=1674
n=22584
mean=0.01
Overall
Hispanic or Latino
Not Hispanic or Latino

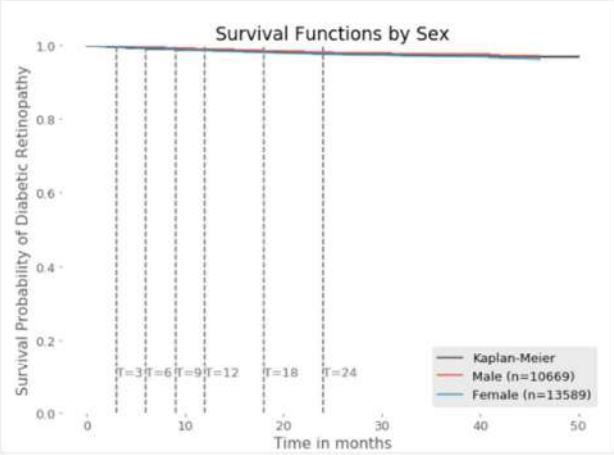

Scores by Patient History (months)
ConcordanceIndex
IntegratedBrierScore
n=24258
n=607
n=2035
n=6532
n=7005
n=8079
mean=0.88
mean=0.01
Overall
<= 6
7 to 12
13 to 24
25 to 36
37 to 60

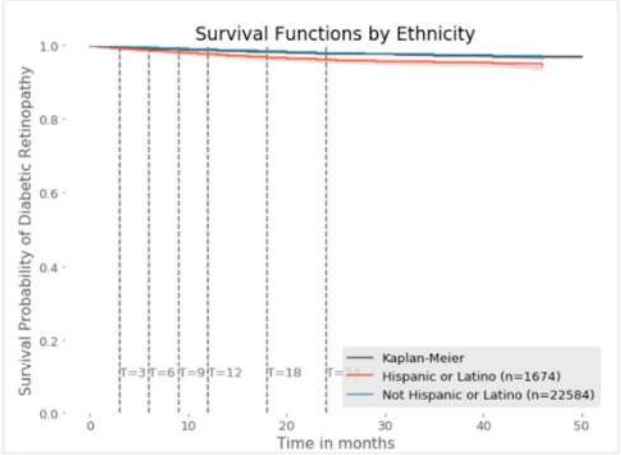
Average Survival Function Curves

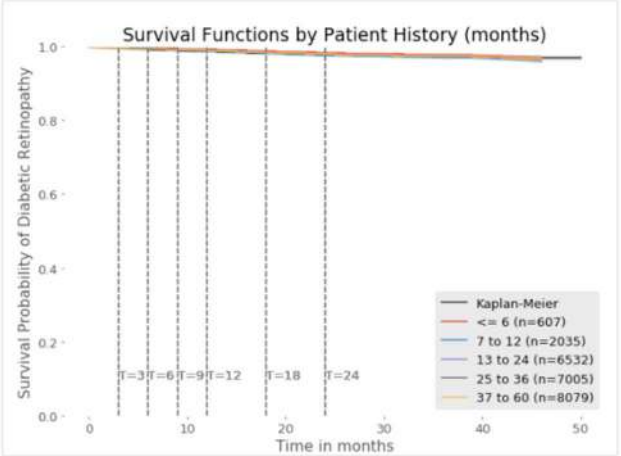
The following charts show how the average survival function curve varies among subgroups of risk, age, sex, ethnicity and patient history.





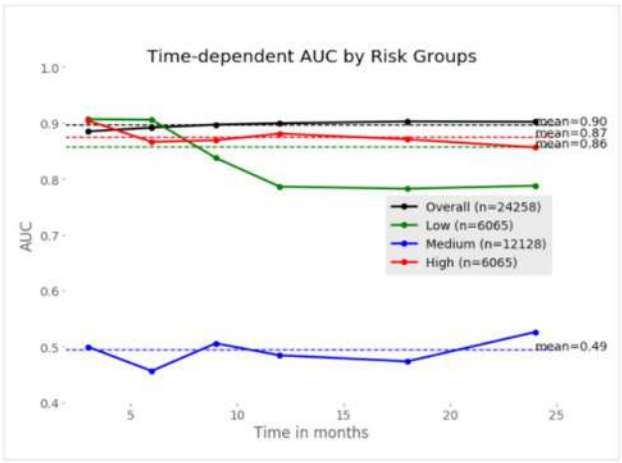


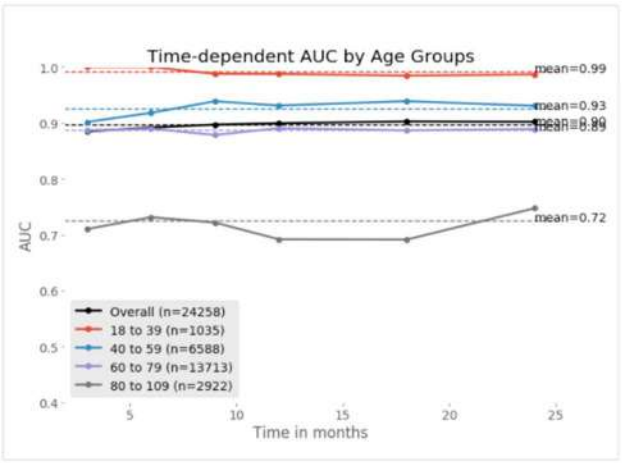


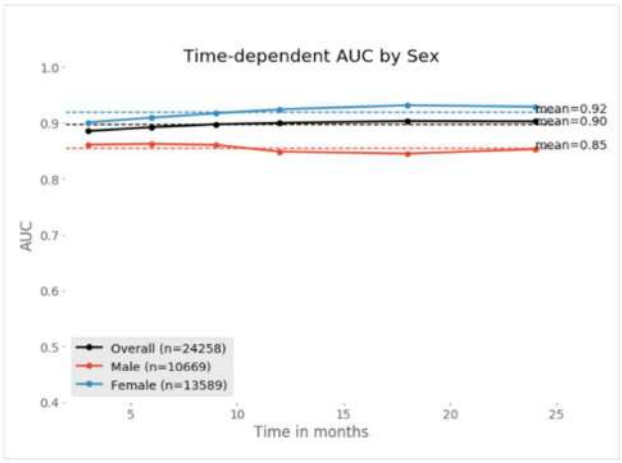


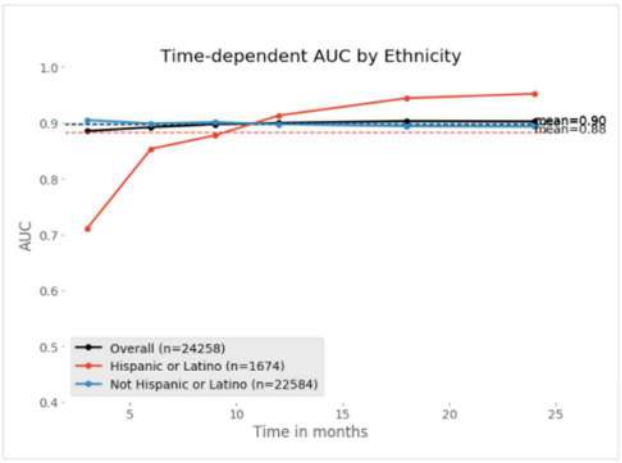
Time-dependent AUC

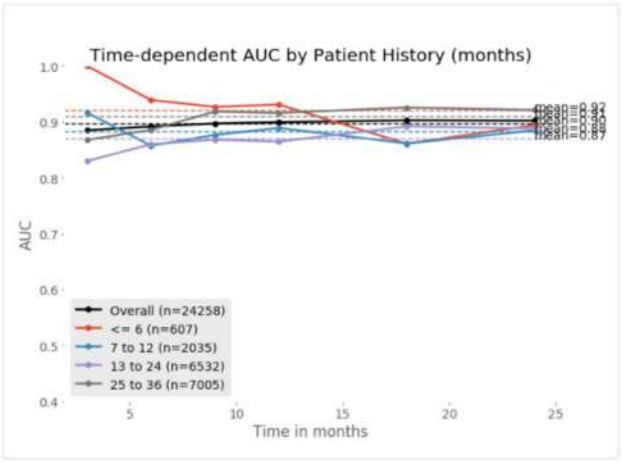
The following charts show how the AUC across time varies among subgroups of risk, age, sex, ethnicity and patient history.





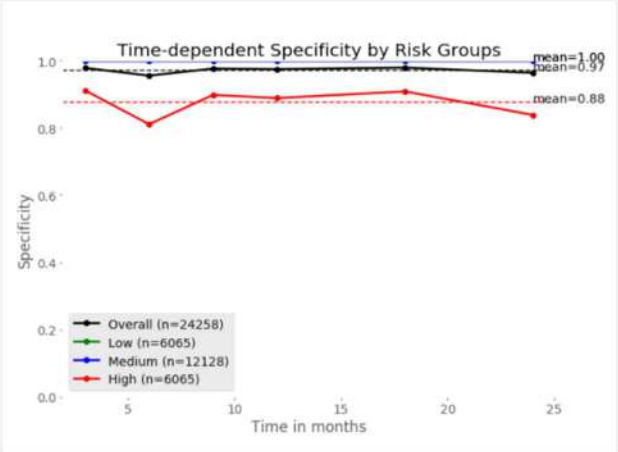


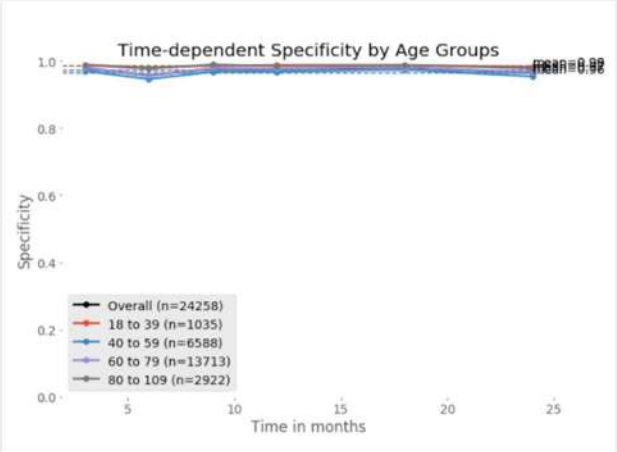


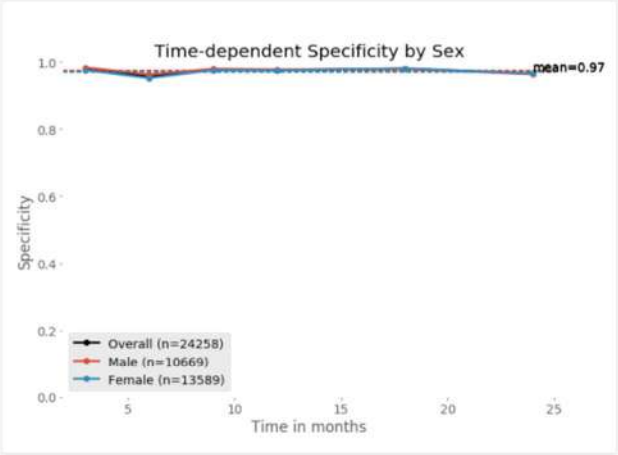


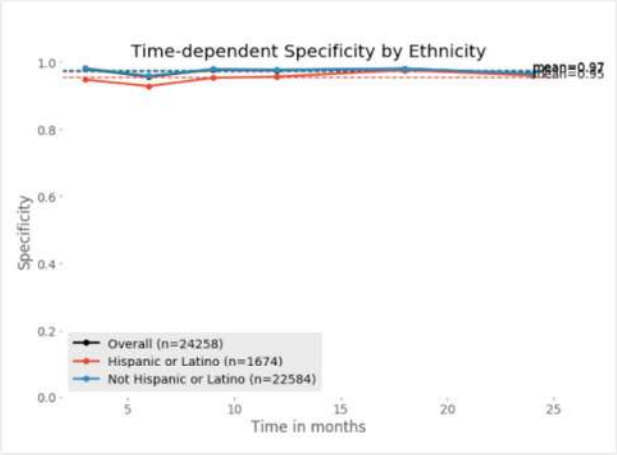
Time-dependent Specificity

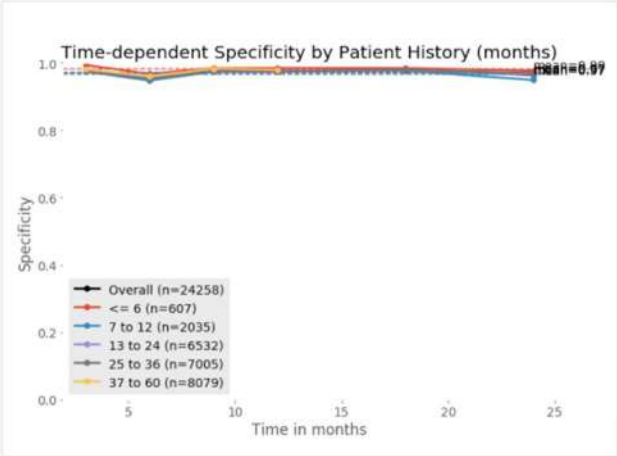
The following charts show how the specificity across time varies among subgroups of risk, age, sex, ethnicity and patient history.





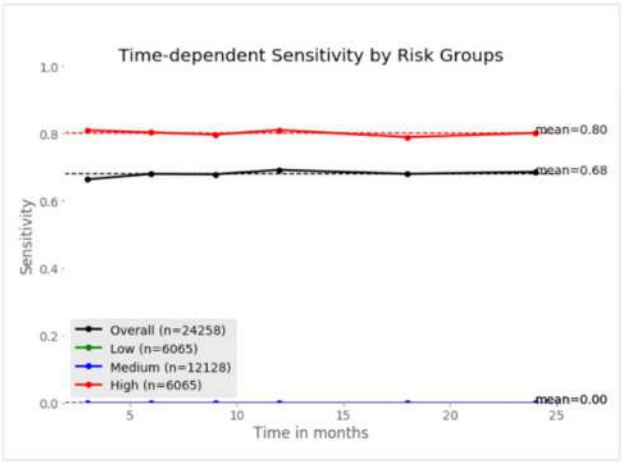


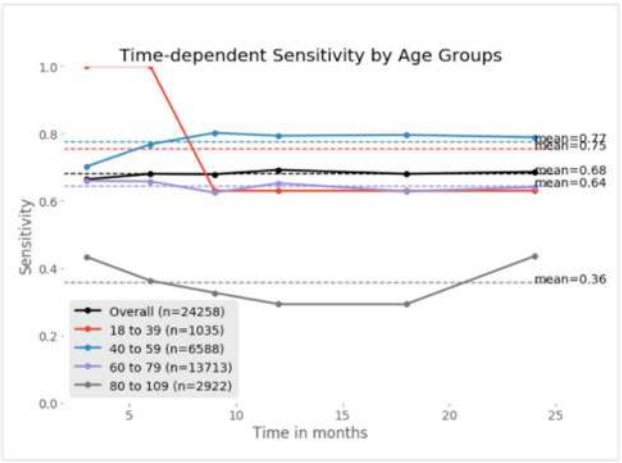


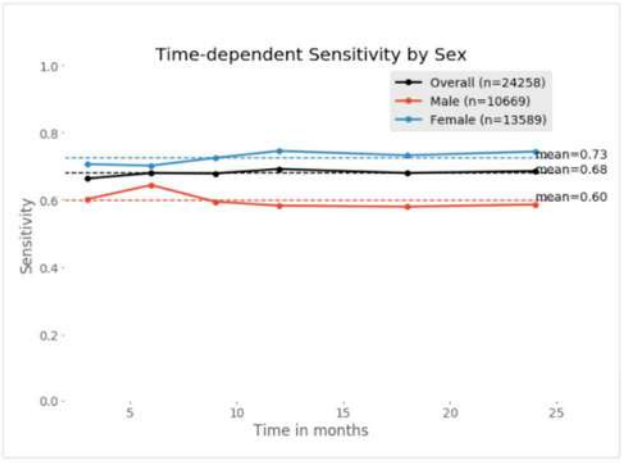


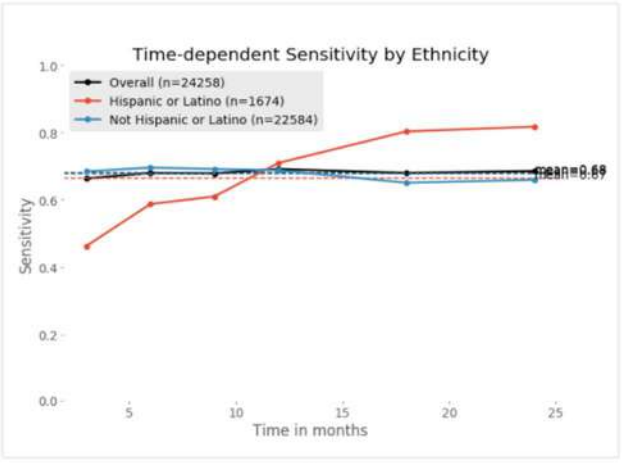
Time-dependent Sensitivity

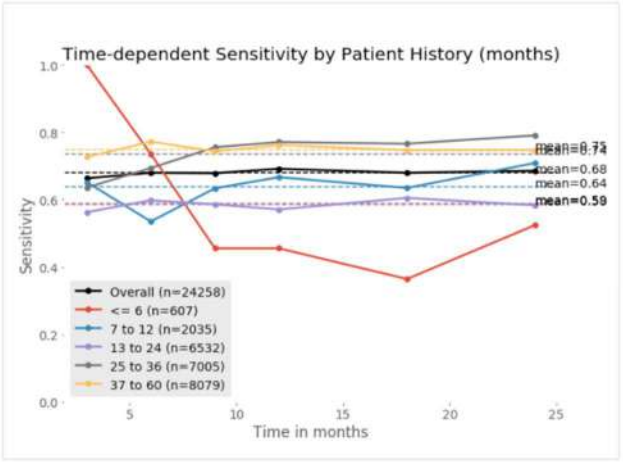
The following charts show how the sensitivity across time varies among subgroups of risk, age, sex, ethnicity and patient history.









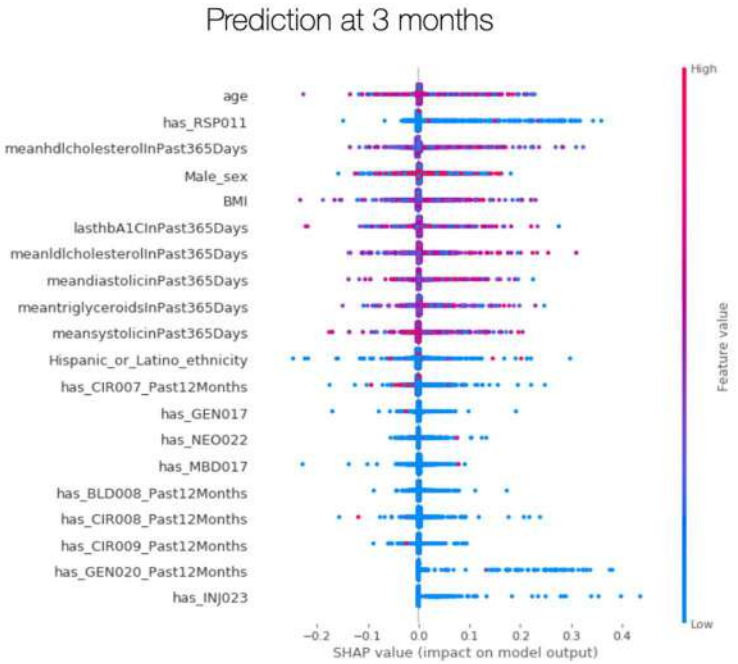


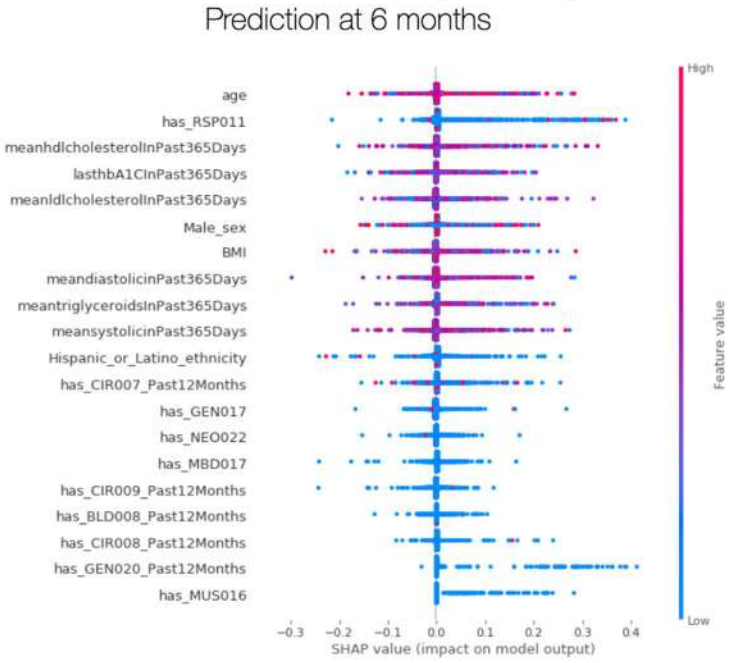
s

Model Explanation (DeepSurv)

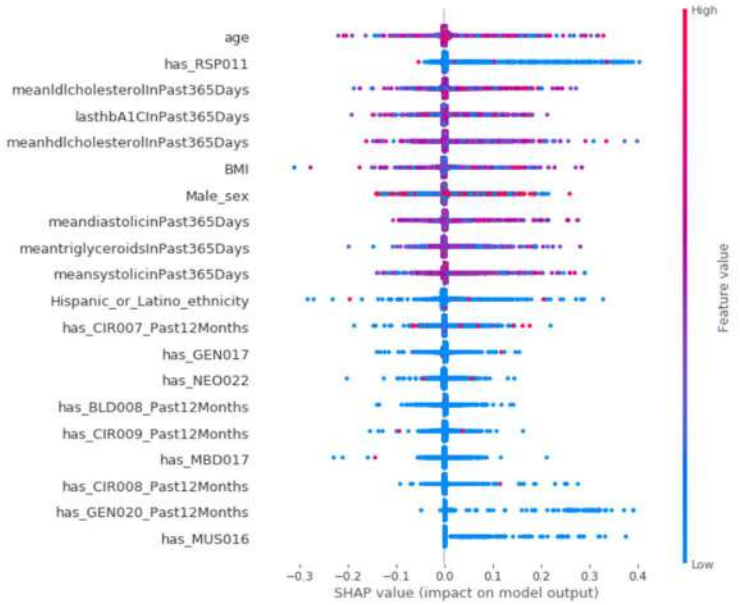
Global

The following plots show the SHAP values of each instance in the training set for each future time (3, 6, 9, 12, 18 and 24 months). The features are sorted by the total magnitude of the SHAP values over all instances and the distribution of the effect that each feature has on the model's output can be observed.

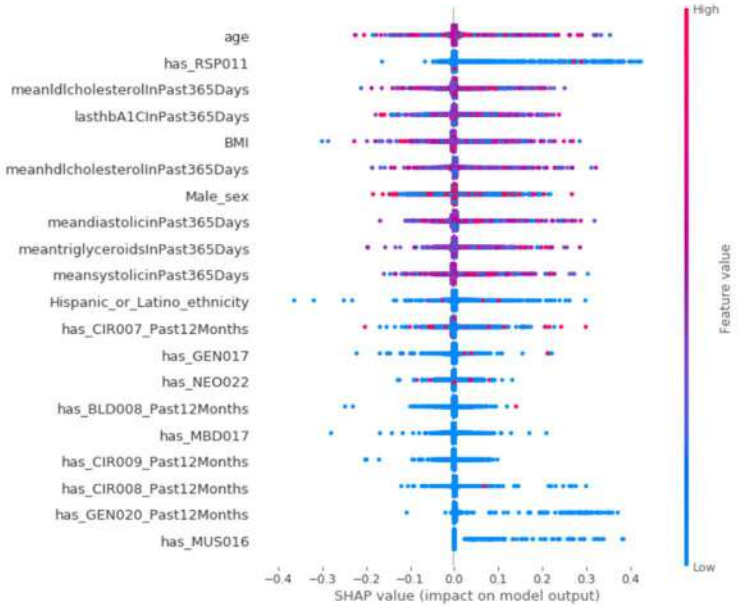




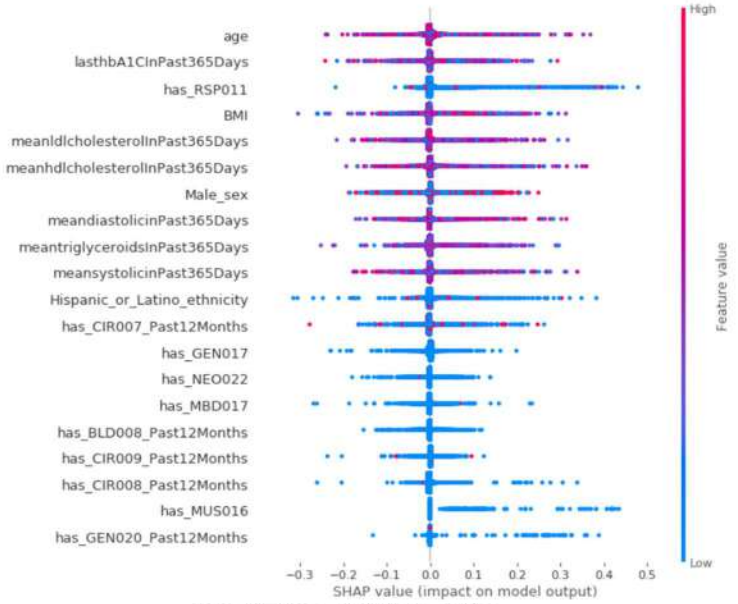
Prediction at 9 months



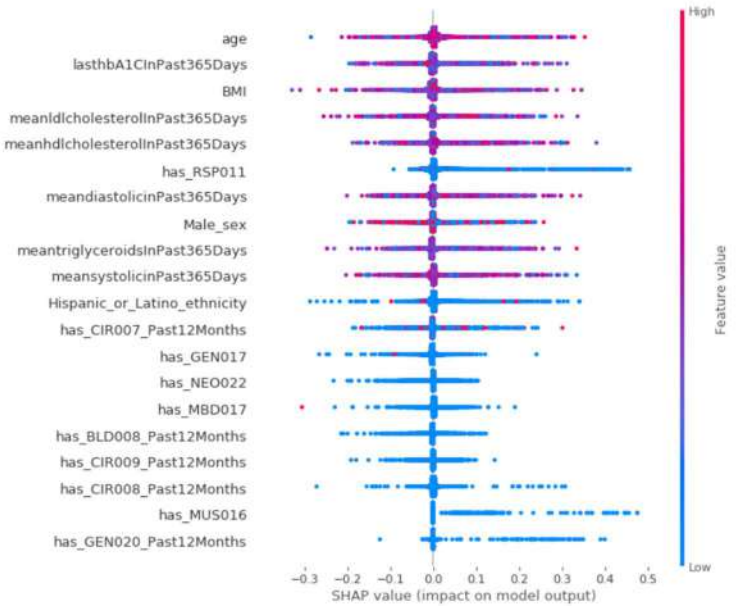
Prediction at 12 months



Prediction at 18 months

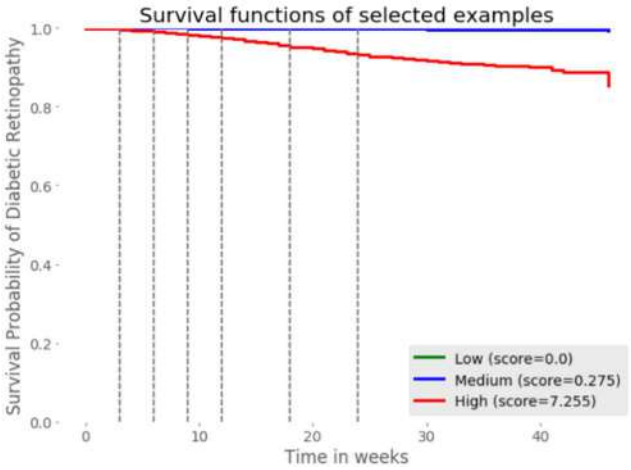


Prediction at 24 months

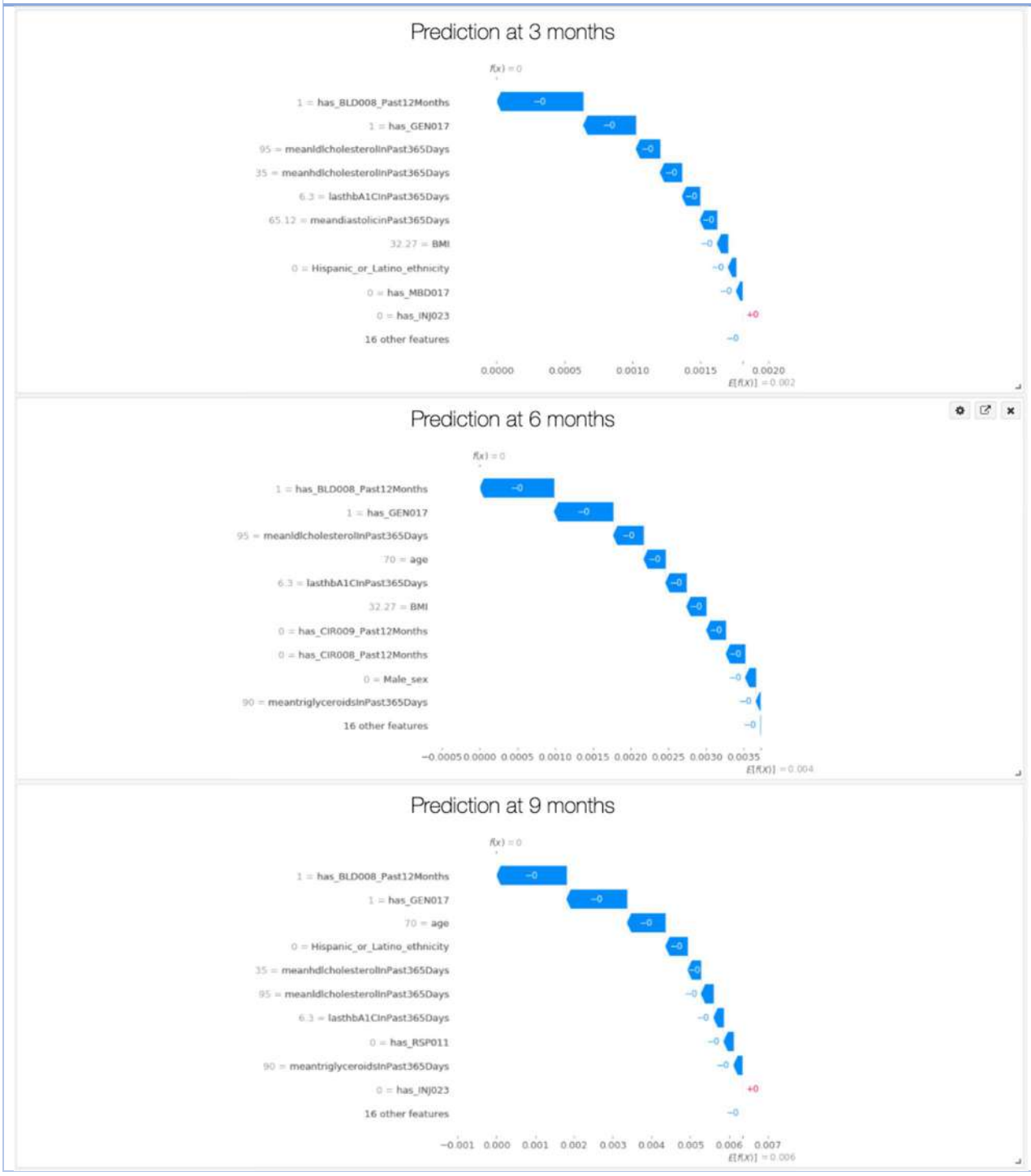


Local

SHAP values were also generated to explain the predictions of individual examples for each future time (3, 6, 9, 12, 18 and 24 months). A total of 3 examples were selected by sampling of risk scores at the 5th, 50th and 95th percentile to represent instances at low, medium and high risks respectively.

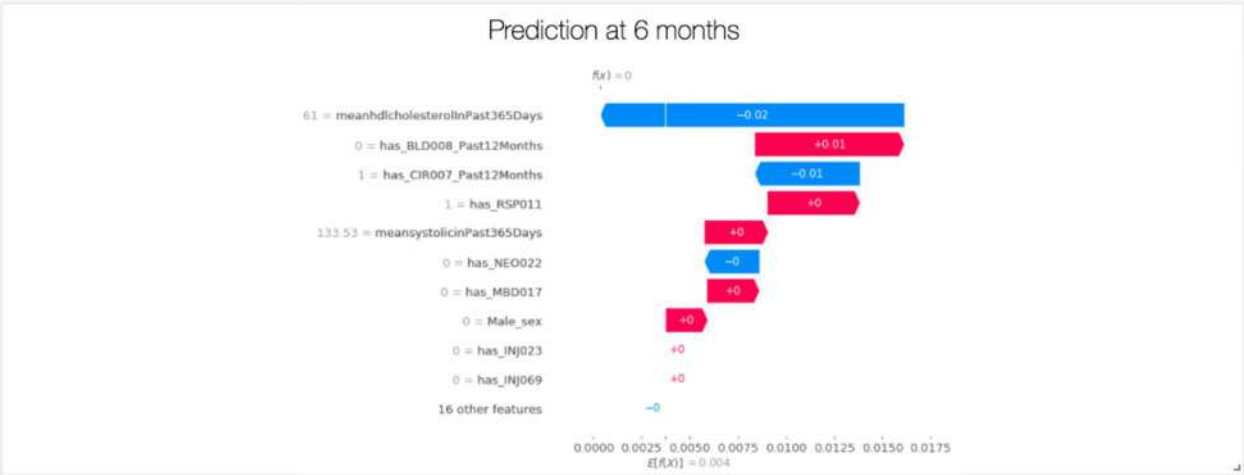


Low Risk
Risk Score: 0.0

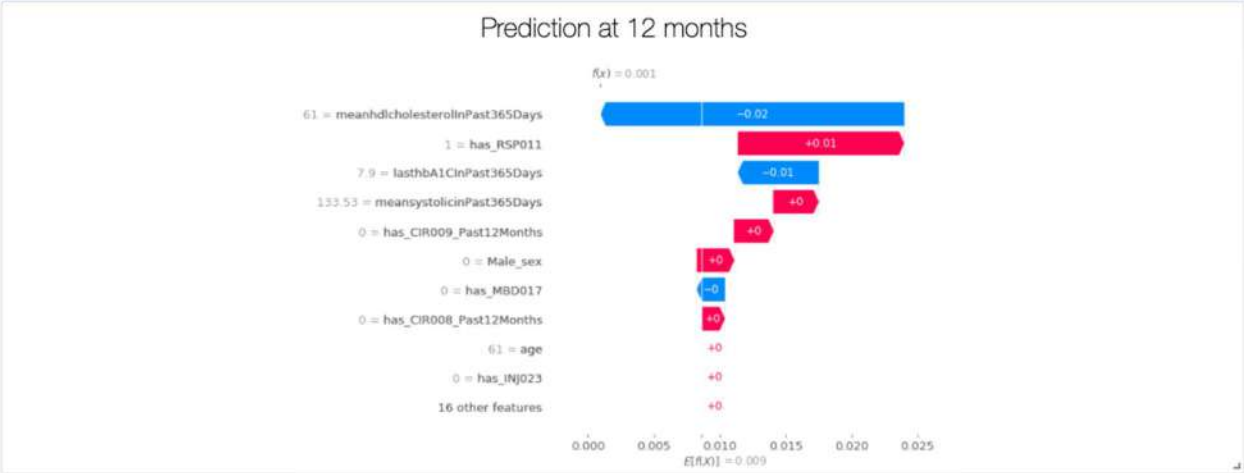


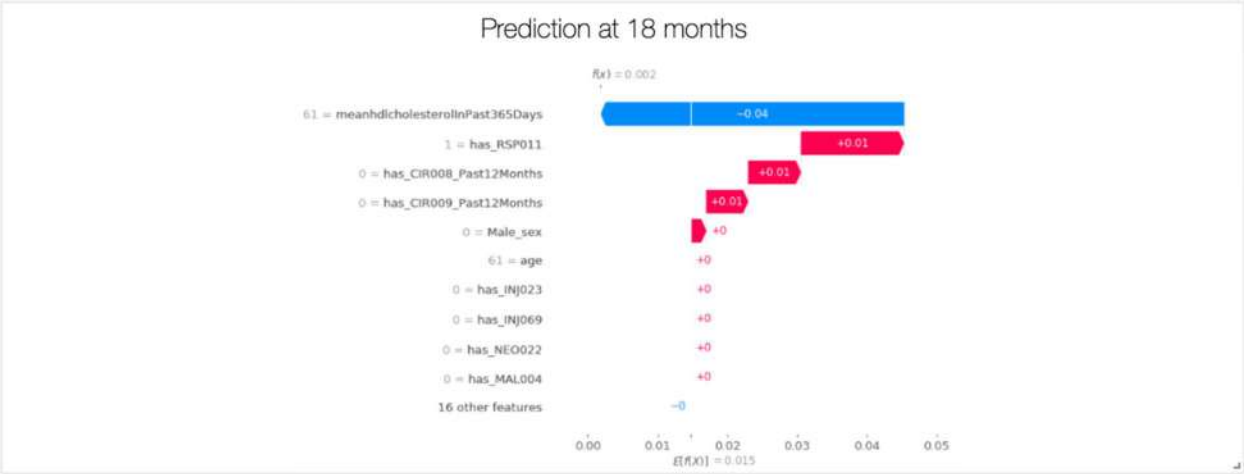
Low Risk
Risk Score: 0.0

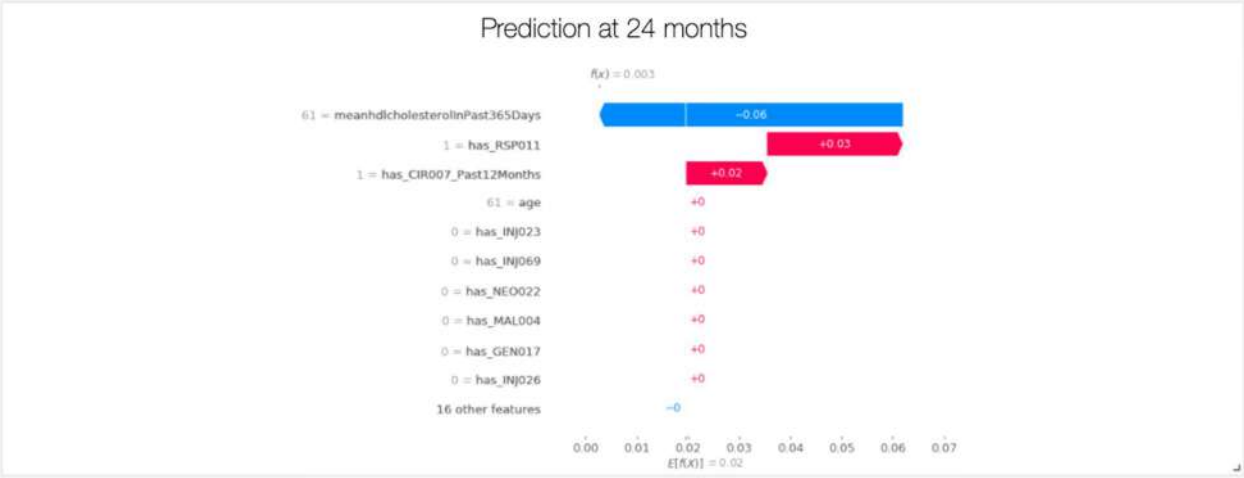
Medium Risk
Risk Score: 0.275



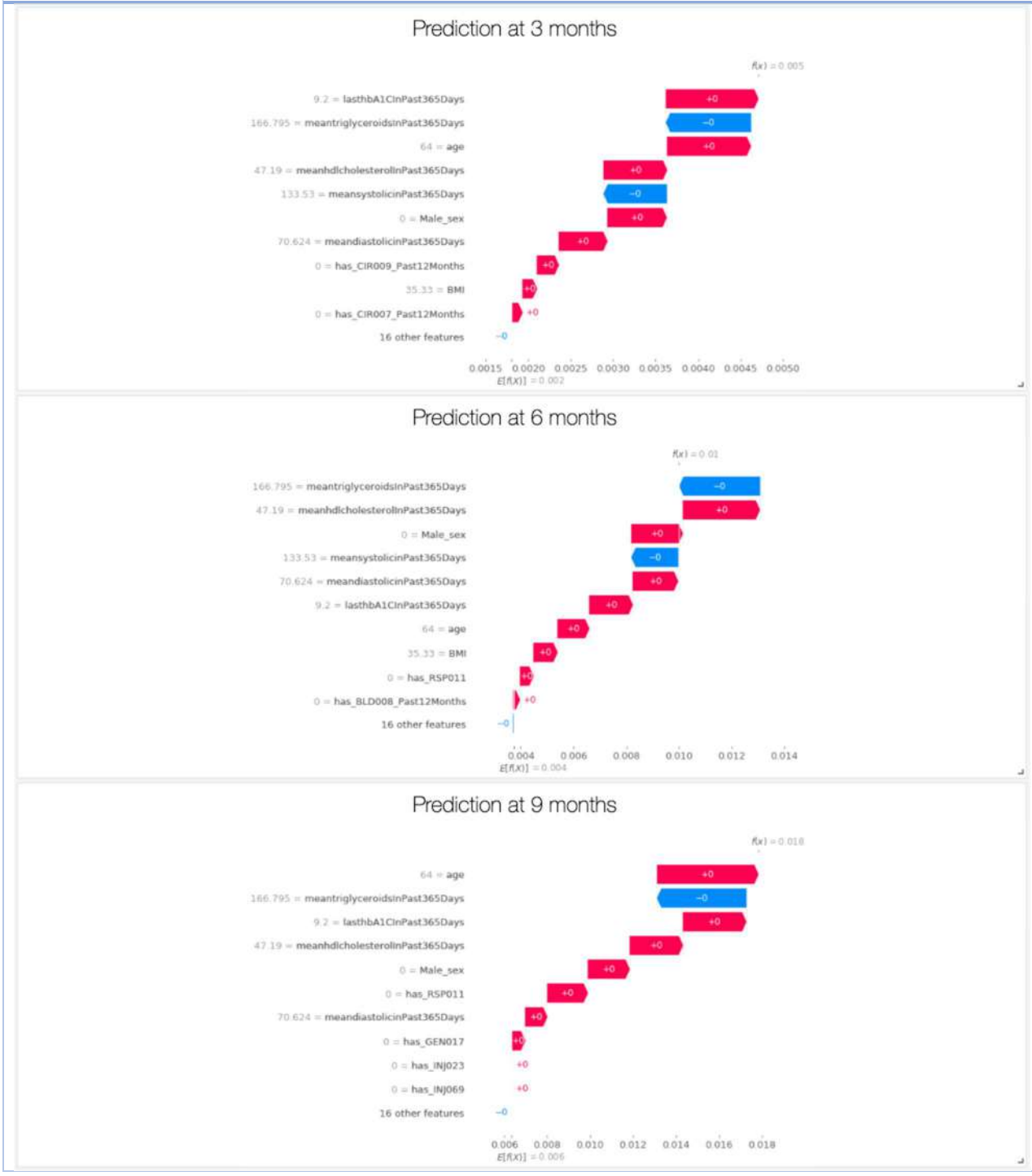
Medium Risk
Risk Score: 0.275



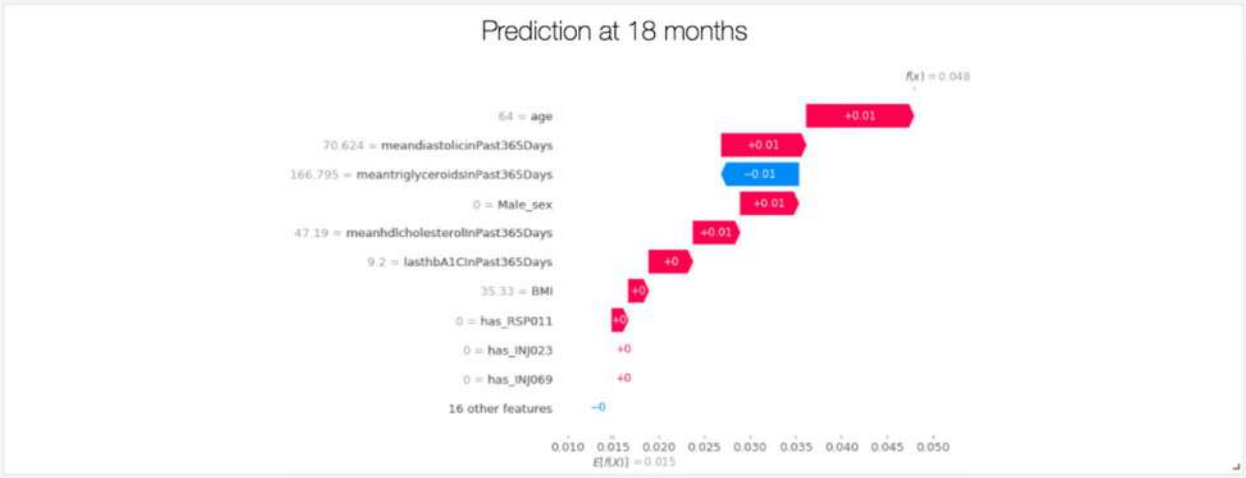


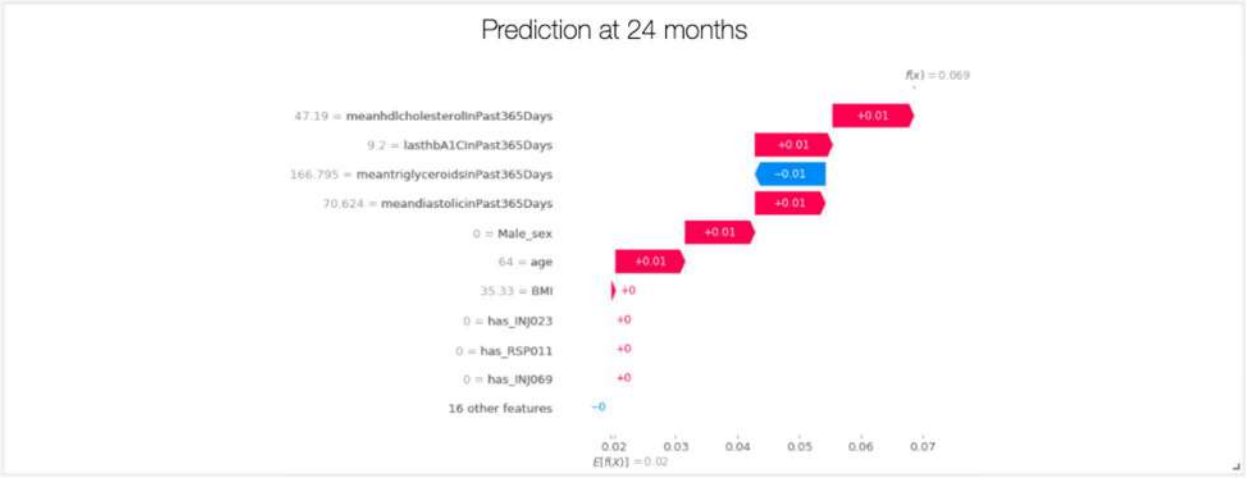


High Risk
Risk Score: 7.255



High Risk
Risk Score: 7.255





Conclusion

In this document we presented an overview of problem settings for diabetes prediction and care management. We gave a detailed literature survey of various problems related to prediction of diabetes as well as management of diabetes. We note that often in literature the two are decoupled while in reality, prediction should always be mindful of disease management. We also specify the various ways to describe the problem and detailed descriptions of feature set that we later employ to build the prediction models. Additionally, we also provided detailed results of experiments for predicting diabetes complications, model calibration, optimization methods, baselines, model evaluation and model results. It is our hope that these results could be used as foundations and guidelines for model building for diabetes research in machine learning.

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Appendix A: Features for Model Training

The following table lists the candidate features for model training.

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Age	Demographic	Integer	In years, at time of encounter	1	No	Yes
Age Above 65	Demographic	Boolean	Whether the patient's age is above 65	1	No	
Ethnicity	Demographic	Categorical	• Hispanic or Latino • Not Hispanic or Latino	1	No	Yes
Sex	Demographic	Categorical	• Female • Male	1	No	Yes
CCSR Category (12 mth)	Diagnosis	Boolean	Presence of CCSR Category in past 12 months	540	Depends	
CCSR Category (Encounter)	Diagnosis	Boolean	Presence of CCSR Category in the patient's whole history	540	Depends	
Days Since Gestational Diabetes	Diagnosis	Integer	Number of days since the patient's most recent diagnosis of gestational diabetes	1	No	
Albumin	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Alkaline Phosphatase	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Bun	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
HBA1C	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		Mean
Neutrophils	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Potassium	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Sodium	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
WBC	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Days Since Last ED Visit	Utilization	Integer	In days	1		
Days Since Last Inpatient Visit	Utilization	Integer	In days	1		
Previous ED Visits Count	Utilization	Integer	For days before current encounter: • 90 days • 180 days • 365 days	3		
Previous Inpatient Encounters Count	Utilization	Integer	For days before current encounter: • 90 days • 180 days • 365 days	3		
ALT	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	Mean
Diastolic	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	Mean
Systolic	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	Mean
LDL Cholesterol	Vitals	Continuous	365-day aggregates:	6	Yes	Mean

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
			• Min • Mean • Median • Max • SD • Last			
HDL Cholesterol	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	Mean
Creatine	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	Mean
Triglyceroids	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	Mean

Appendix B: Baseline Comparison using the Last A1C Value

In this section, we compare the performance of our models against a baseline. The last A1C value of the patients were used as a baseline to match the method which care managers have been using to identify high risk patients. The following metrics were compared using both the risk scores generated by our models and the last A1C value of the patients:

- Concordance Index and
- Time-dependent AUC

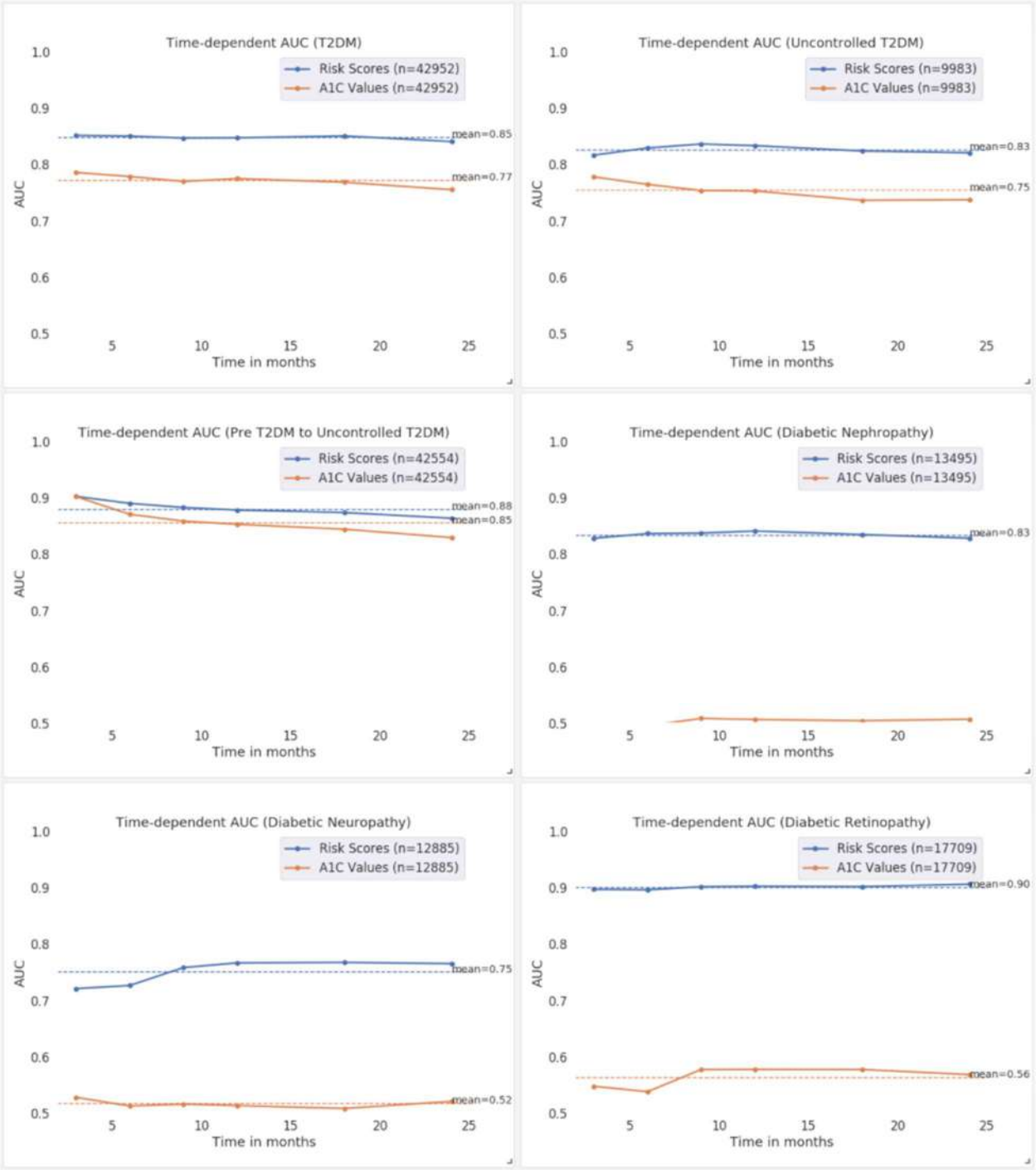
The table below shows the percentage of test instances with a last A1C value for each task which also represents the proportion of the test cohort which we will be carrying out the comparison on.

	% of instances with last A1C value
T2DM	55.55
Uncontrolled T2DM	66.76
Pre T2DM to Uncontrolled T2DM	55.30
Diabetic Nephropathy	70.81
Diabetic Neuropathy	69.49
Diabetic Retinopathy	73.00

For all tasks except T2DM and Diabetic Neuropathy, the use of Risk Scores resulted in a higher Concordance Index, indicating that most of our models were able to beat the baseline in terms of ranking the instances correctly according to their risk levels.

	Concordance Index (Risk Scores)	Concordance Index (A1C Values)
T2DM	0.825329	0.868744
Uncontrolled T2DM	0.804390	0.782126
Pre T2DM to Uncontrolled T2DM	0.832033	0.825503
Diabetic Nephropathy	0.809212	0.767832
Diabetic Neuropathy	0.737294	0.759065
Diabetic Retinopathy	0.868380	0.737511

Using AUC as the metric gives a different perspective. The charts below show that in general, across different prediction tasks and points in time, the survival risks predicted by the ML models achieve higher AUC than the baseline of last A1C value.


Time-dependent AUC (T2DM)
Risk Scores (n=42952)
A1C Values (n=42952)
mean=0.85
mean=0.77
Time-dependent AUC (Uncontrolled T2DM)
Risk Scores (n=9983)
A1C Values (n=9983)
mean=0.83
mean=0.75
Time-dependent AUC (Pre T2DM to Uncontrolled T2DM)
Risk Scores (n=42554)
A1C Values (n=42554)
mean=0.88
mean=0.85
Time-dependent AUC (Diabetic Nephropathy)
Risk Scores (n=13495)
A1C Values (n=13495)
mean=0.83
Time-dependent AUC (Diabetic Neuropathy)
Risk Scores (n=12885)
A1C Values (n=12885)
mean=0.75
mean=0.52
Time-dependent AUC (Diabetic Retinopathy)
Risk Scores (n=17709)
A1C Values (n=17709)
mean=0.90
mean=0.56
AUC
Time in months

Appendix B2: Baseline Comparison using Last A1C Values within 3 Months

In this section, we compare the performance of our models against a baseline. The last A1C value of the patients within 3 months from their encounter date were used as a baseline to match the method which care managers have been using to identify high risk patients. The following metrics were compared using both the risk scores generated by our models and the last A1C value of the patients:

- Concordance Index and
- Time-dependent AUC

The table below shows the percentage of test instances with missing A1C value (or A1C value > 20), last A1C value greater than 3 months from the encounter date and last A1C value within months of the encounter date which also represents the proportion of the test cohort which we will be carrying out the comparison on.

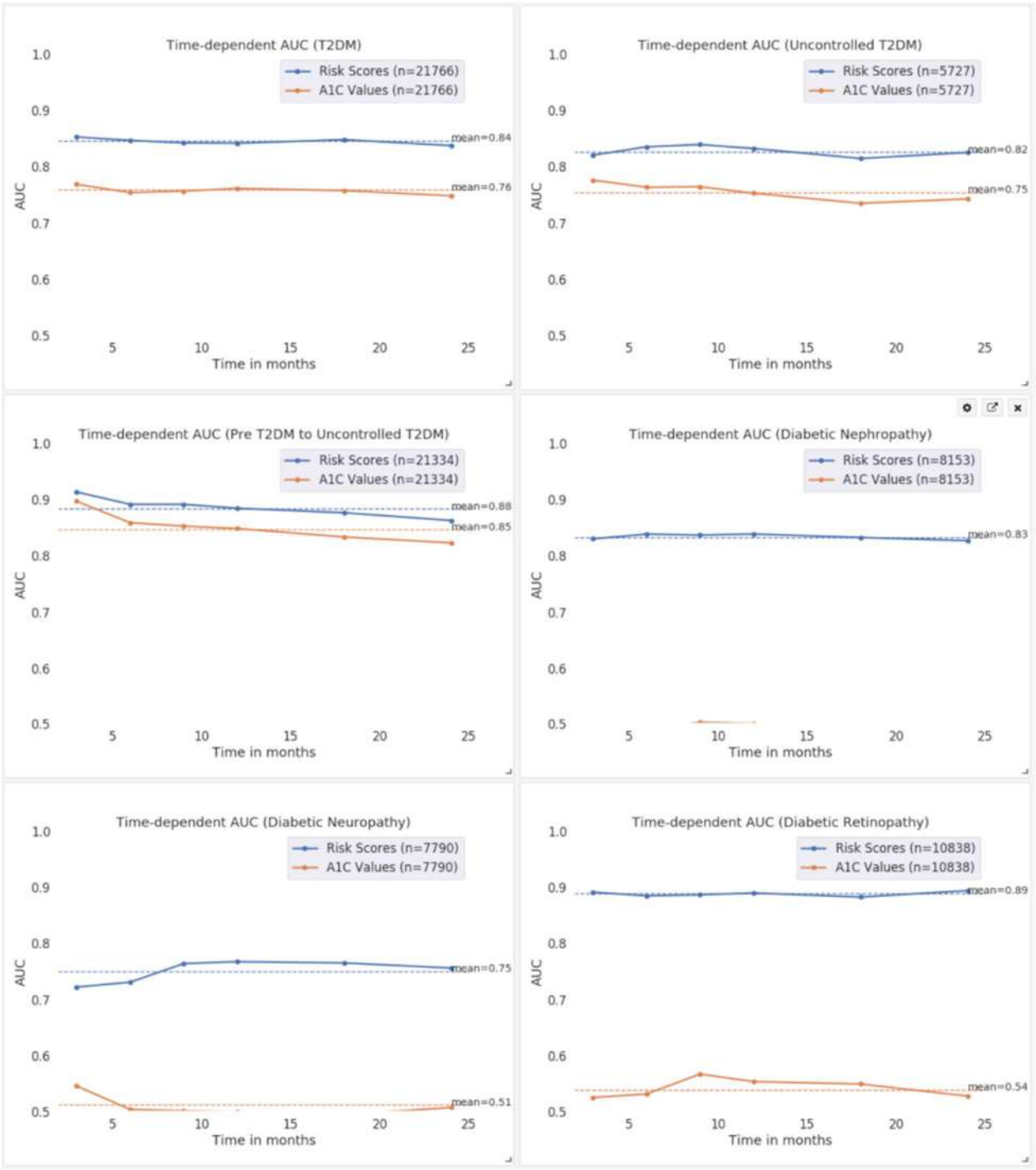
	% with missing A1C value	% with A1C value > 3 months	% with A1C value <= 3 months
T2DM	27.76	44.09	28.15
Uncontrolled T2DM	18.02	43.68	38.30
Pre T2DM to Uncontrolled T2DM	27.88	44.39	27.73
Diabetic Nephropathy	13.86	43.36	42.78
Diabetic Neuropathy	14.44	43.55	42.01
Diabetic Retinopathy	12.07	43.25	44.68

For all tasks except Diabetic Retinopathy, the use of the Risk Scores resulted in a lower Concordance Index, indicating that most of our models were not able to beat the baseline in terms of ranking the instances correctly according to their risk levels.

	Concordance Index (Risk Scores)	Concordance Index (A1C Values)
T2DM	0.808911	0.959292
Uncontrolled T2DM	0.802203	0.919095
Pre T2DM to Uncontrolled T2DM	0.801713	0.968062
Diabetic Nephropathy	0.804889	0.910083
Diabetic Neuropathy	0.729231	0.910516
Diabetic Retinopathy	0.859881	0.857972

Using AUC as the metric gives a different perspective. The charts below show that in general, across different prediction tasks and points in time, the survival risks predicted by the ML models achieve higher AUC than the baseline of last A1C value.

This indicates that an A1C reading within the last 3 months provides a good indication of *relative* risks for DM and its complications between patients, i.e. who is likely to get a disease first, but the ML predicted risk scores are a more accurate predictor of *absolute* risk at specific points in time, i.e. who is likely to get a disease by a certain time.

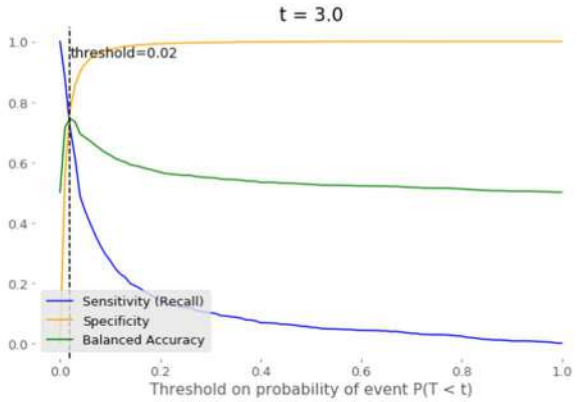


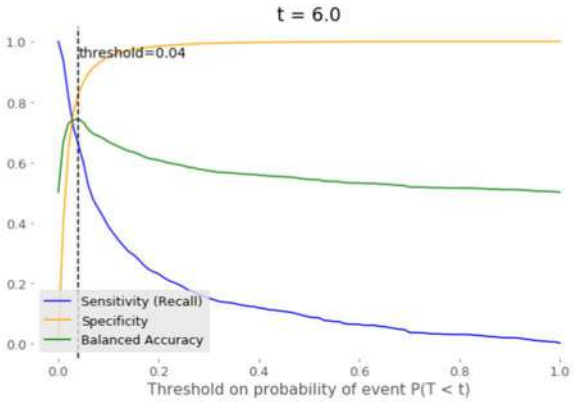
Appendix C: Threshold Optimization for each Time Point

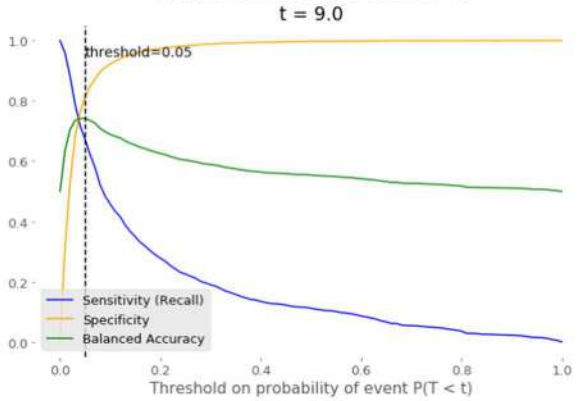
This section shows how the thresholds for the probability of experiencing the event were determined. The thresholds were optimized by maximizing the balanced accuracy score, which is the average of sensitivity and specificity. The table and charts below display the optimal threshold at each time point and for each task.

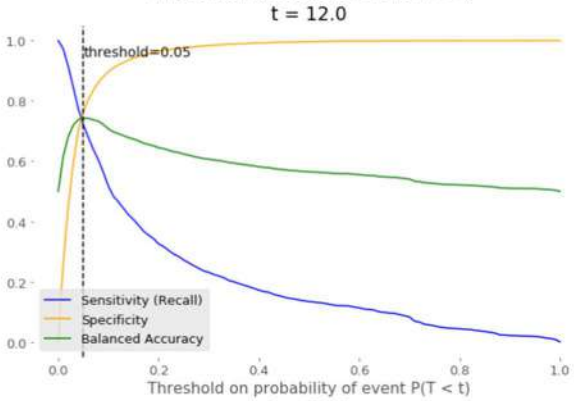
	3	6	9	12	18	24
T2DM	0.02	0.04	0.05	0.05	0.08	0.10
Uncontrolled T2DM	0.02	0.04	0.06	0.07	0.11	0.15
Pre T2DM to Uncontrolled T2DM	0.01	0.01	0.01	0.02	0.03	0.03
Diabetic Nephropathy	0.03	0.04	0.06	0.08	0.13	0.15
Diabetic Neuropathy	0.01	0.02	0.03	0.04	0.09	0.08
Diabetic Retinopathy	0.01	0.01	0.03	0.04	0.08	0.07

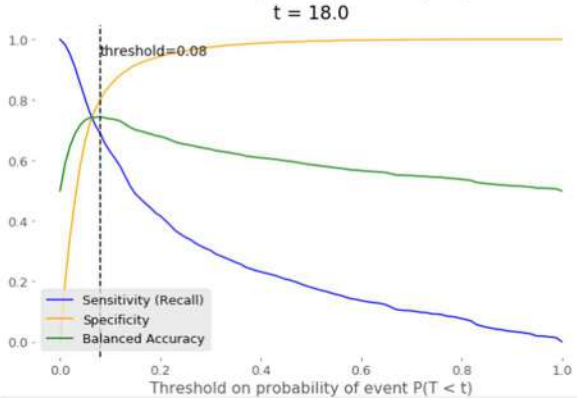
Pre-DM to DM Prediction

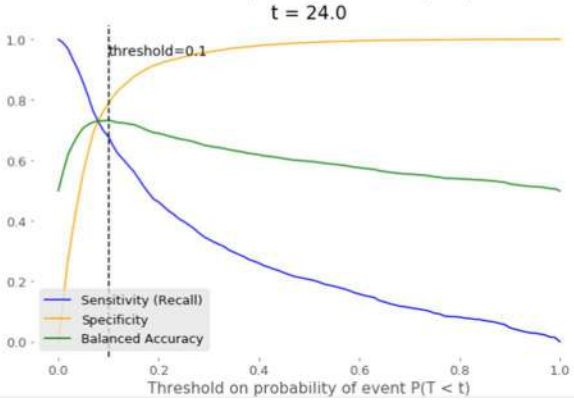




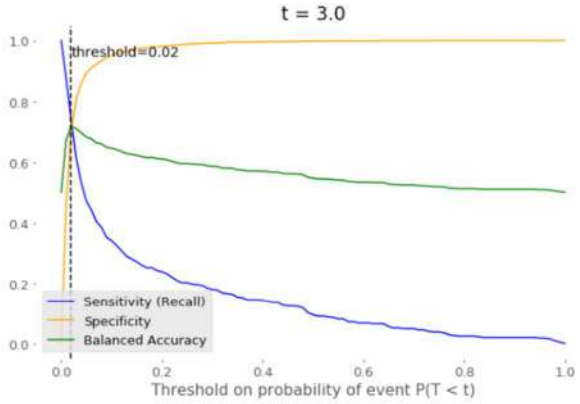


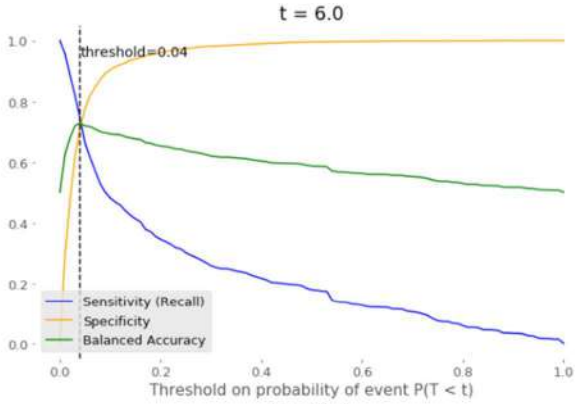


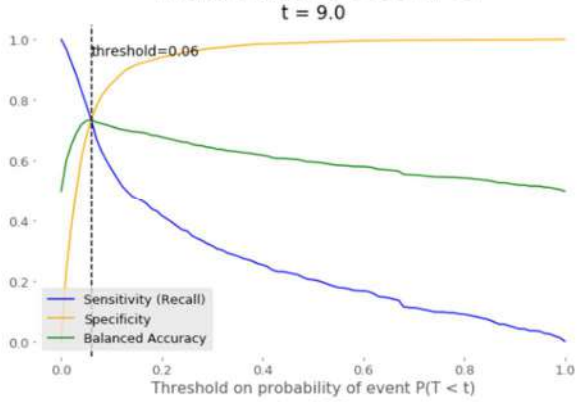


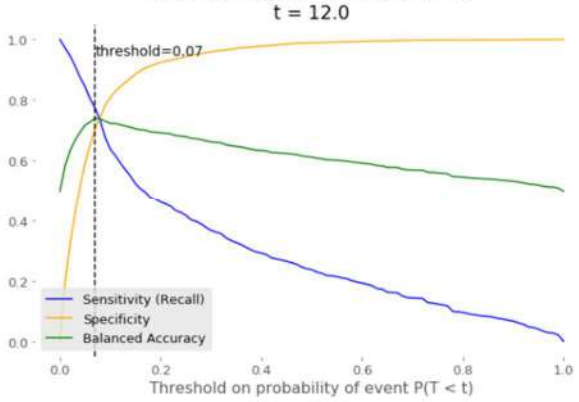


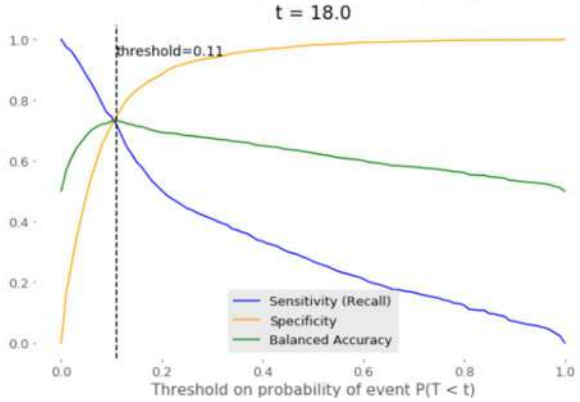
DM to Uncontrolled DM Prediction

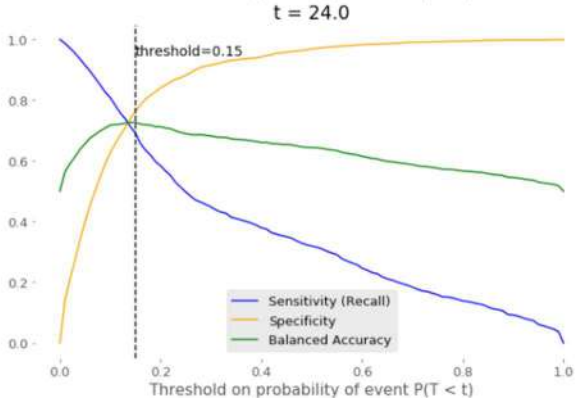




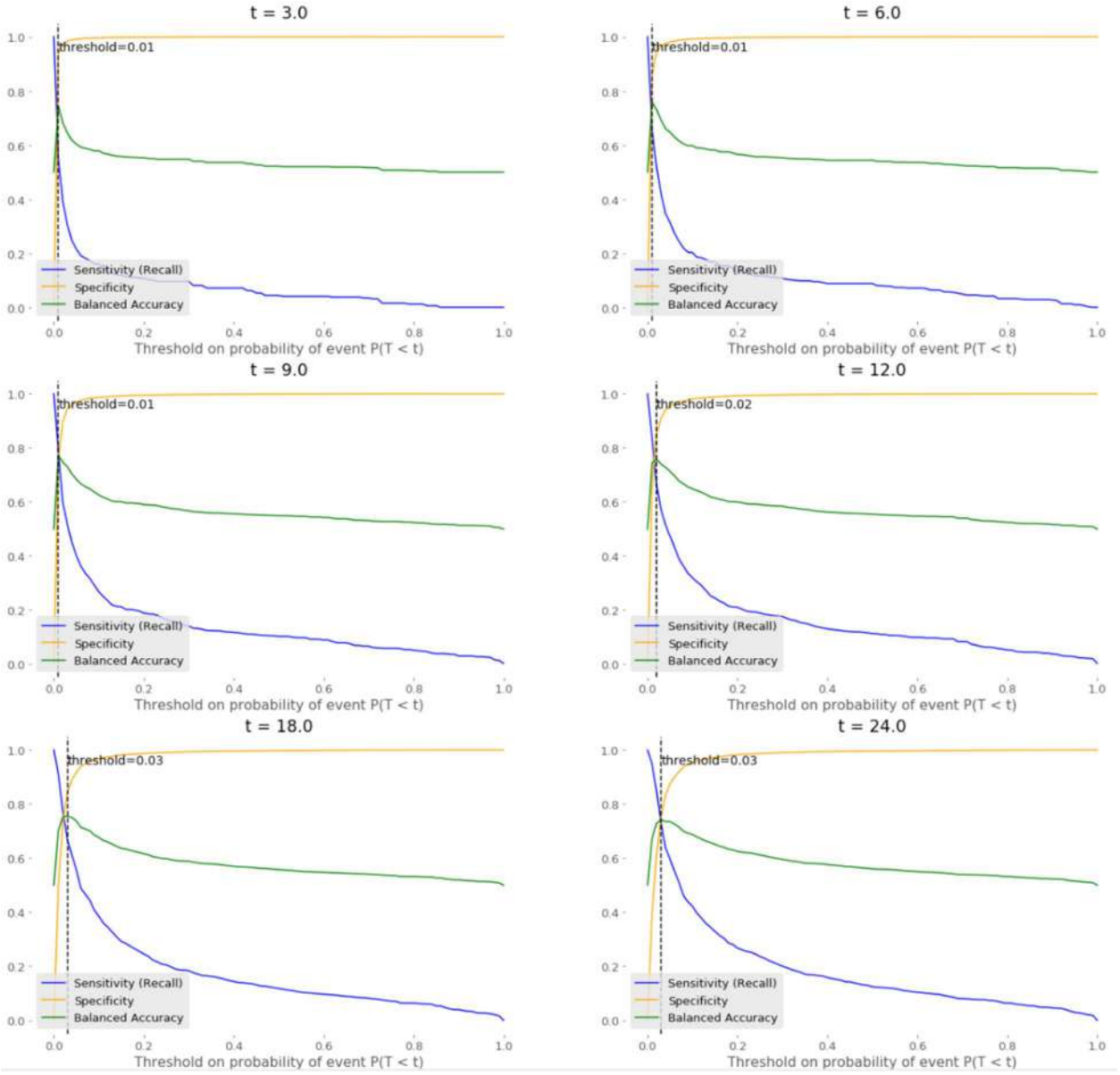




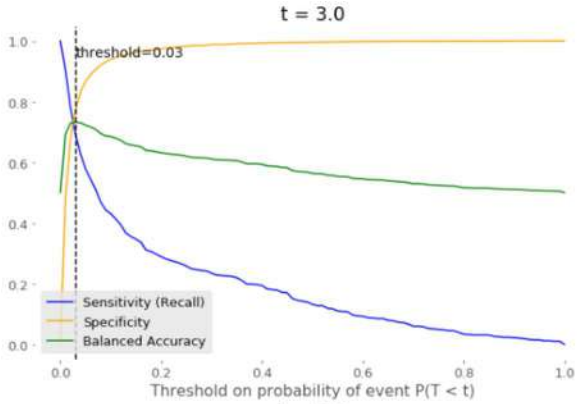


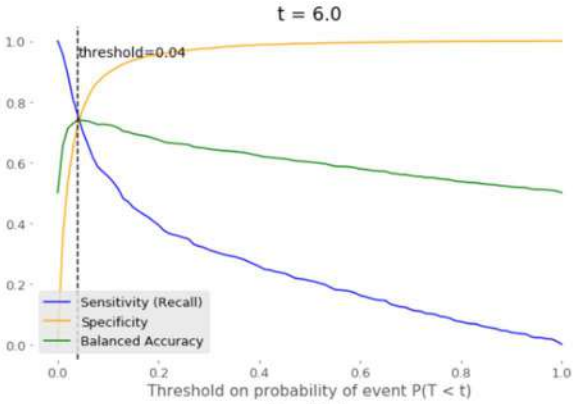


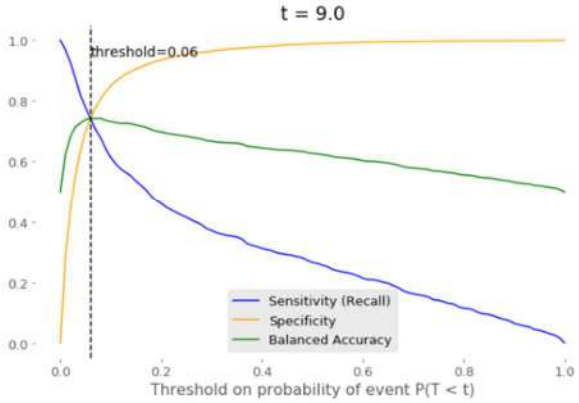
Pre-DM to Uncontrolled DM Prediction

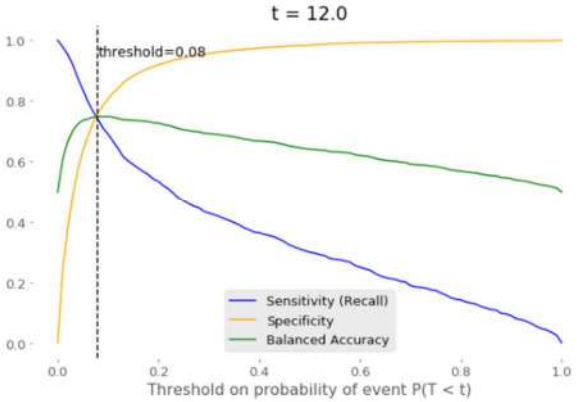


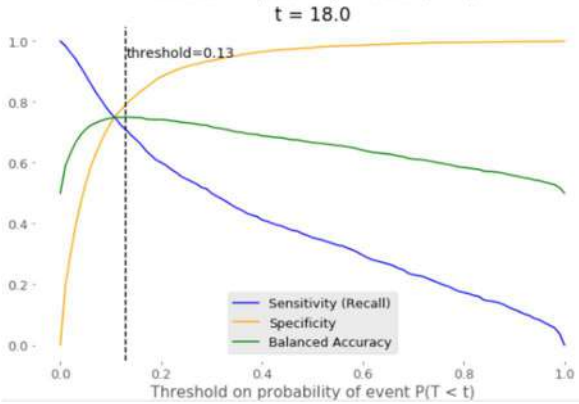
DM to Diabetic Nephropathy Prediction

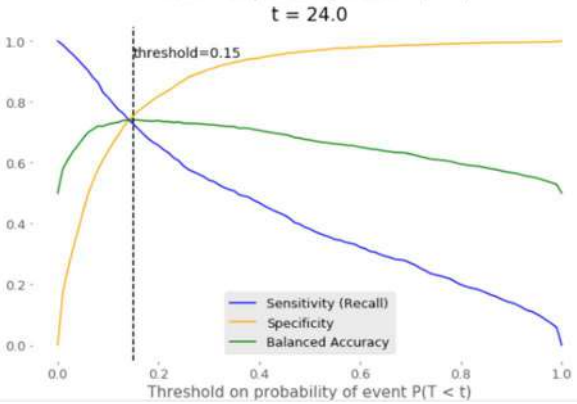




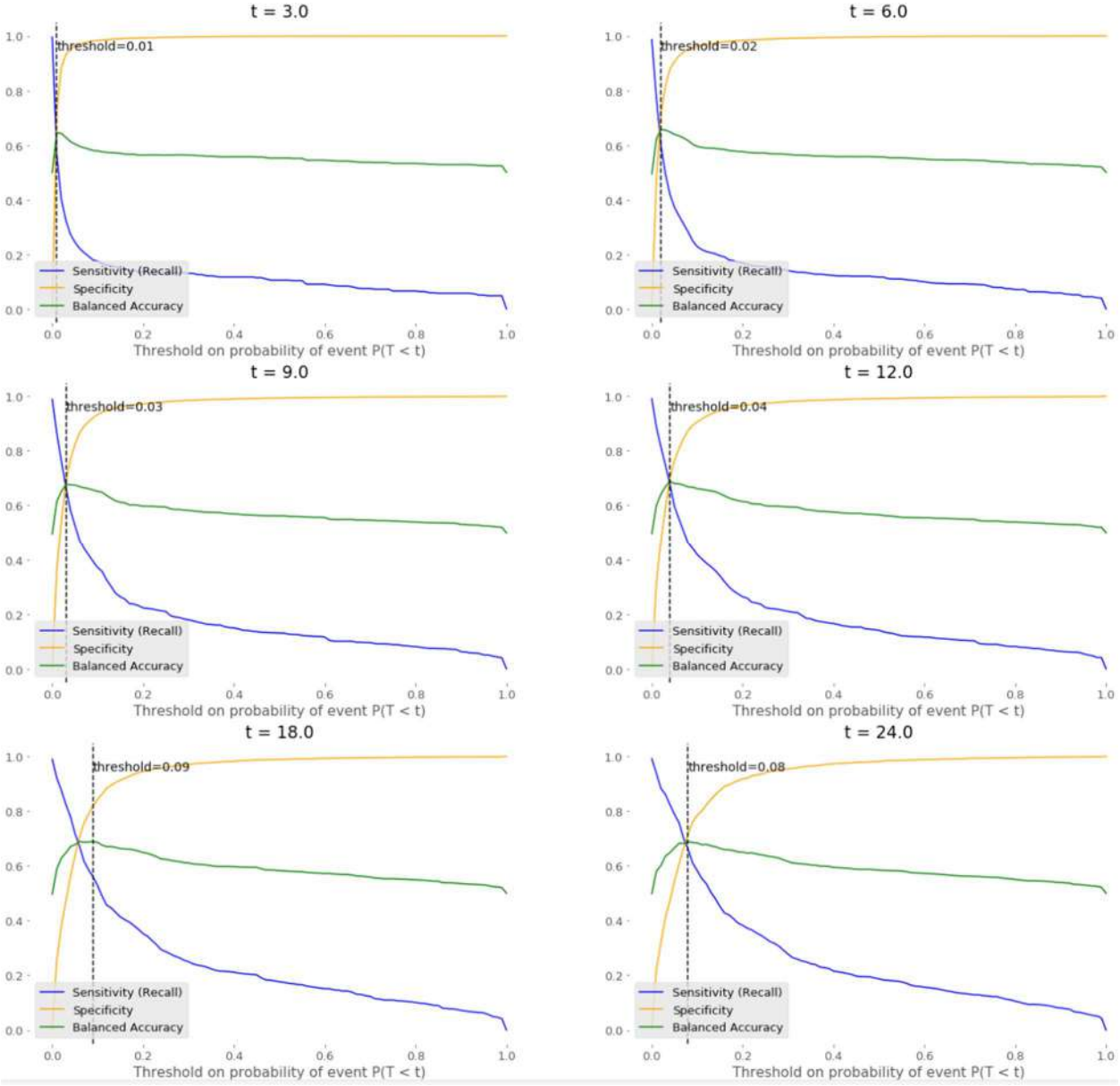




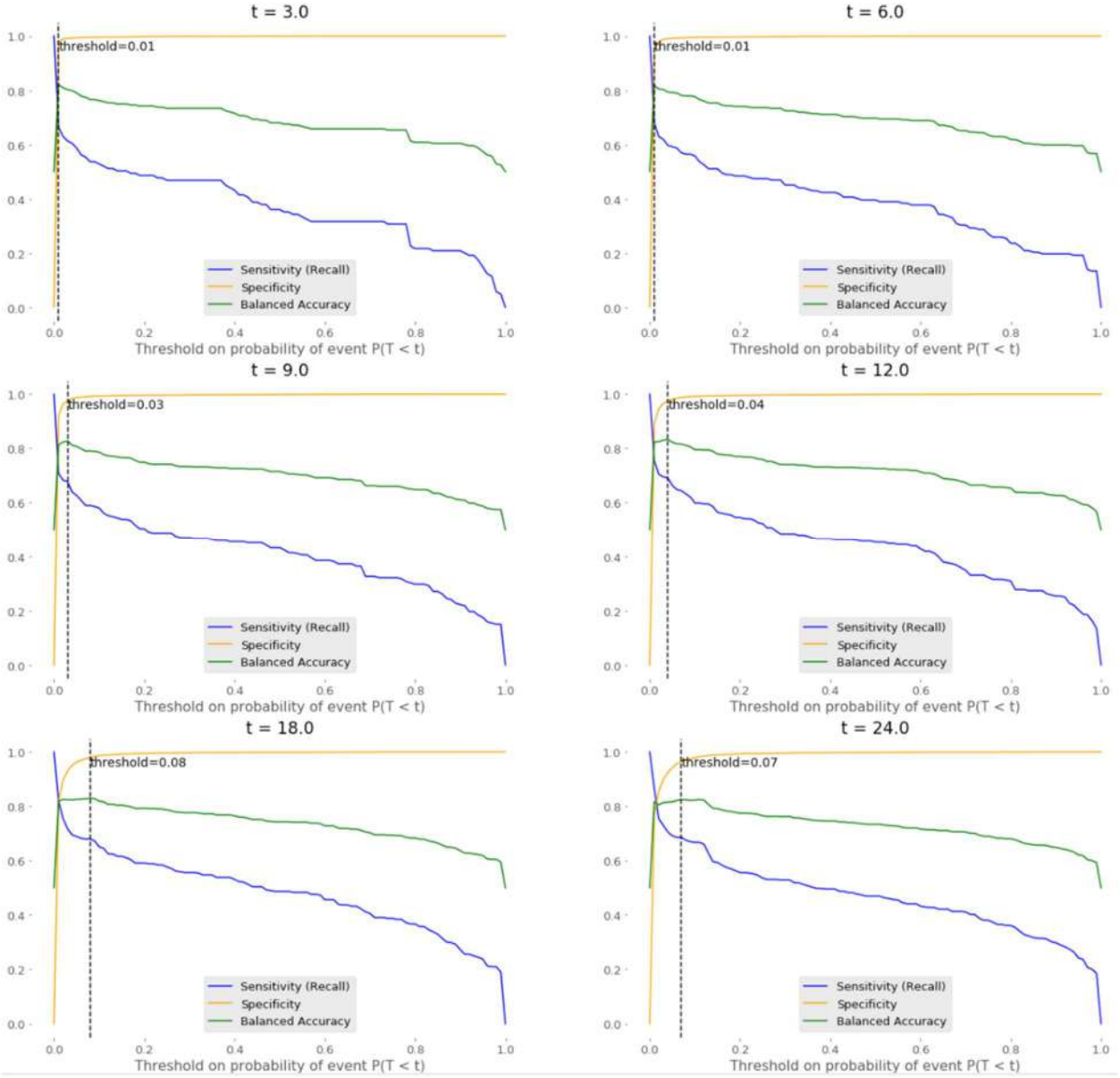




DM to Diabetic Neuropathy Prediction



DM to Diabetic Retinopathy Prediction



Appendix D: Model Calibration Experiment

This model calibration approach was proposed by [15] and adopted by [16], [17], where a set of models predicting diabetes complications was trained on one population (U.S., 1980s), and calibrated for a different population (U.K., 2000s). This approach may be useful for the diabetes models in this document, where models pre-trained by KenSci can be quickly deployed at multiple customers, and calibrated for each target patient population.

Methodology

1. Split data into in-sample (2016-01-01 to 2019-06-30; 2.5 years) and out-of-sample (2019-07-01 to 2020-06-30; 1 year).
2. Further split in-sample data into a 70% training set and 30% in-sample test set.
3. Train model on in-sample training set based on selected features and hyperparameters from Iteration 3.
4. Test model on in-sample test set.
5. Test model on out-of-sample test set, without calibration.
6. Calibrate model using the method in [1].
7. Re-test model on out-of-sample test set, after calibration.

Summary of Results

Model metrics on the out-of-sample test sets, before and after calibration:

Task	**Concordance Index**[2]	**Integrated Brier Score**		**Median Absolute Error of Survival Curves**		**Calibration Coefficient**
		Before	**After**	**Before**	**After**	
Pre-DM to DM	0.62	0.033	0.030	1,815	5.8	0.032
DM to U-DM	0.60	0.052	0.047	837	5.3	0.053
Pre-DM to U-DM	0.71	0.0099	0.0088	144	0.2	-0.090
D. Nephropathy	0.69	0.051	0.044	266	3.2	-0.012
D. Neuropathy	0.54	0.040	0.029	43	0.9	-0.957

[2] Concordance index is not affected by calibration, because no covariates were added to the calibration model in this experiment, thus the rank order of predictions between instances remains the same.

D. Retinopathy	0.67	0.0099	0.0075	152	0.2	0.015

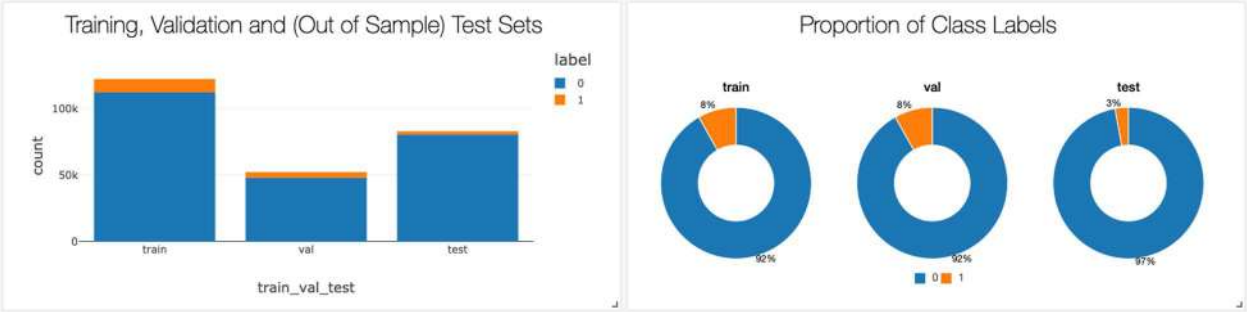
The following sections report the detailed results of model calibration for each task. Although the models are trained on the same features and using the same parameters, they are trained using a different sub-set of data (limited by date range), so the reported metrics will not be the same as those in the main document.

Key Observations & Learnings

1. Calibration reduced Integrated Brier Score and Median Absolute Error for all tasks, and closed the gap between the predicted and actual survival functions in the target population. This can be clearly seen in the charts comparing the predicted survival curve before and after calibration versus the actual survival curve. Thus, the calibrated models can provide more accurate estimates of a patient's survival (or disease) probability over time. Thus, calibration is useful where it is important to know the survival (or disease) probability (e.g. probability of a patient getting diabetic retinopathy in 12 months) for a specific patient.
2. On the other hand, when no additional covariates are added to the calibration model (as in this experiment), calibration has no effect on the rank order of the predictions, nor the Concordance Index. Without additional covariates, the calibration model is a linear function of the risk predicted by the original model. Therefore, while the calibration model may predict different absolute risks for each instance, the relative predicted risks between instances does not change. By extension, Concordance Index is identical for both models. Hence, calibration is not necessary if (a) there are no new covariates, and (b) the primary use case is to rank patients from high to low risk but absolute probabilities are not important.
3. In order to further optimize Concordance Index (i.e. correct rank order of predicted risks for the target population), additional covariates must be added to the calibration model – these can be covariates existing in the original model (effectively calibrating the coefficients of selected covariates), or new covariates that become available (adding new information).
4. The amount of data used for calibration should be at least as long as the intended prediction horizon. For example, if the model is to be used to predict risks up to 18 months in the future, then at least 18 months of data will be needed. This is because the calibration model needs to be able to estimate the baseline hazard function for the target population at least up to that time period.

Pre-DM to DM

Number of instances and proportion of class labels in training, validation and test sets:



Distribution of features in training set:

	count	mean	std	min	25%	50%	75%	max
age	122501.0	64.264839	14.672148	18.00	56.000	66.000	75.000	107.00
Male_sex	122501.0	0.375336	0.484211	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	122501.0	0.056302	0.230504	0.00	0.000	0.000	0.000	1.00
maxhbA1ClnPast365Days	122501.0	6.145194	0.542504	3.80	5.900	6.121	6.228	9.80
lasthbA1ClnPast365Days	122501.0	6.032503	0.494381	3.80	5.800	6.022	6.103	8.90
meandiastolicinPast365Days	122501.0	74.578806	8.462522	43.63	69.900	74.600	79.696	107.50
meansystolicinPast365Days	122501.0	130.583874	12.925398	81.00	123.100	130.162	136.930	180.00
BMI	122501.0	32.062367	6.950208	11.66	28.009	31.894	35.243	273.52
meantriglyceroidsInPast365Days	122501.0	142.243926	48.492521	22.00	119.839	142.732	148.000	466.00
meanldlcholesterolInPast365Days	122501.0	95.220383	23.718540	3.78	84.968	97.608	107.000	201.00
meanhdlcholesterolInPast365Days	122501.0	47.528001	10.470784	6.00	42.000	46.000	52.436	98.00
has_BLD005_Past12Months	122501.0	0.001673	0.040874	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	122501.0	0.195484	0.396575	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	122501.0	0.008980	0.094334	0.00	0.000	0.000	0.000	1.00
has_NEO016_Past12Months	122501.0	0.002498	0.049917	0.00	0.000	0.000	0.000	1.00
has_PRG029	122501.0	0.015151	0.122153	0.00	0.000	0.000	0.000	1.00
has_FAC006	122501.0	0.040906	0.198073	0.00	0.000	0.000	0.000	1.00
has_DIG018	122501.0	0.023894	0.152719	0.00	0.000	0.000	0.000	1.00
has_SKN003	122501.0	0.055763	0.229464	0.00	0.000	0.000	0.000	1.00
has_RSP015	122501.0	0.002327	0.048178	0.00	0.000	0.000	0.000	1.00
has_NEO017	122501.0	0.012457	0.110914	0.00	0.000	0.000	0.000	1.00
has_INJ057	122501.0	0.001747	0.041760	0.00	0.000	0.000	0.000	1.00

Distribution of features in out-of-sample test set:

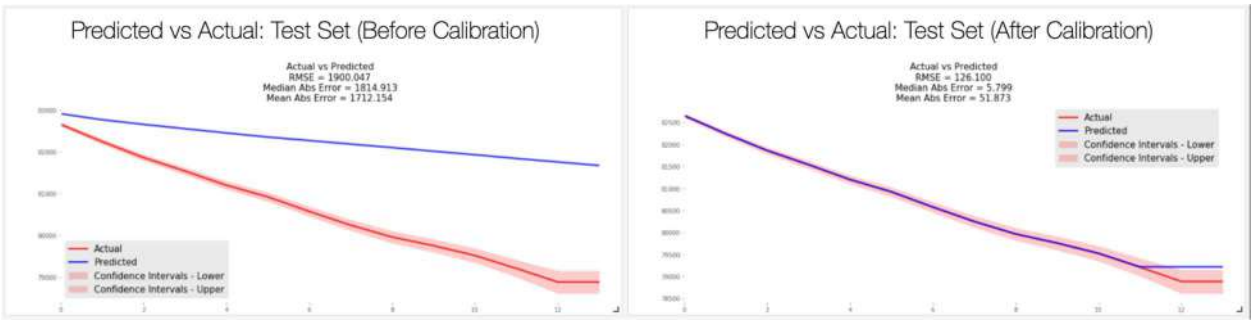
	count	mean	std	min	25%	50%	75%	max
age	83169.0	64.928050	14.577695	18.00	57.000	67.000	75.000	103.00
Male_sex	83169.0	0.371004	0.483076	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	83169.0	0.050848	0.219689	0.00	0.000	0.000	0.000	1.00
maxhbA1CInPast365Days	83169.0	6.144681	0.521625	3.00	5.900	6.121	6.228	8.90
lasthbA1CInPast365Days	83169.0	6.040098	0.482872	2.20	5.800	6.022	6.103	8.90
meandiastolicinPast365Days	83169.0	74.433770	4.714079	44.00	72.425	74.678	77.667	107.00
meansystolicinPast365Days	83169.0	130.417804	6.406752	82.00	127.945	130.162	131.494	180.00
BMI	83169.0	32.058567	7.273502	2.71	27.876	31.690	35.243	326.11
meantriglyceroidsInPast365Days	83169.0	139.865553	46.986997	11.00	119.839	142.732	147.721	468.50
meanldlcholesterolInPast365Days	83169.0	95.183594	23.392690	2.80	84.968	97.608	107.302	201.00
meanhdlcholesterolInPast365Days	83169.0	48.551459	10.051132	8.00	42.348	49.000	52.436	98.00
has_BLD005_Past12Months	83169.0	0.000385	0.019612	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	83169.0	0.101781	0.302362	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	83169.0	0.010028	0.099636	0.00	0.000	0.000	0.000	1.00
has_NEO016_Past12Months	83169.0	0.004365	0.065921	0.00	0.000	0.000	0.000	1.00
has_PRG029	83169.0	0.016845	0.128692	0.00	0.000	0.000	0.000	1.00
has_FAC006	83169.0	0.040075	0.196136	0.00	0.000	0.000	0.000	1.00
has_DIG018	83169.0	0.018853	0.136007	0.00	0.000	0.000	0.000	1.00
has_SKN003	83169.0	0.045365	0.208106	0.00	0.000	0.000	0.000	1.00
has_RSP015	83169.0	0.003547	0.059451	0.00	0.000	0.000	0.000	1.00
has_NEO017	83169.0	0.010677	0.102777	0.00	0.000	0.000	0.000	1.00
has_INJ057	83169.0	0.001515	0.038894	0.00	0.000	0.000	0.000	1.00

Calibration coefficient β (confidence interval): 0.032 (0.031, 0.032)

Model metrics:

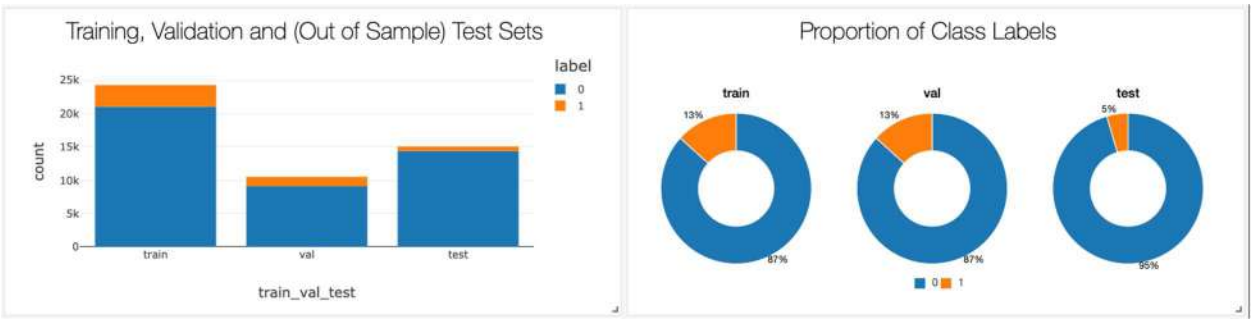
Set	Concordance Index	Integrated Brier Score
Train	0.56	0.079
Validation	0.59	0.079
Test (before calibration)	0.63	0.033
Test (after calibration)	0.63	0.030

Predicted vs Actual survival curves for test set, before and after calibration:



DM to Uncontrolled DM

Number of instances and proportion of class labels in training, validation and test sets:



Distribution of features in training set:

	count	mean	std	min	25%	50%	75%	max
age	24277.0	65.975697	12.953298	18.00	58.00	68.000	75.000	102.00
Male_sex	24277.0	0.453969	0.497887	0.00	0.00	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	24277.0	0.057585	0.232963	0.00	0.00	0.000	0.000	1.00
lasthbA1ClnPast365Days	24277.0	6.868240	0.775740	4.00	6.50	6.866	7.200	8.90
meandiastolicinPast365Days	24277.0	72.817306	8.881113	44.00	67.77	73.000	78.400	107.56
meansystolicinPast365Days	24277.0	131.733696	13.430075	83.00	123.82	131.065	138.500	180.00
BMI	24277.0	32.698618	6.376725	10.37	29.40	32.400	35.320	72.56
meantriglyceroidsInPast365Days	24277.0	161.643379	52.089780	20.00	140.50	163.096	170.874	456.50
meanldlcholesterolInPast365Days	24277.0	85.460050	21.733265	8.00	80.72	85.917	95.000	200.00
meanhdlcholesterolInPast365Days	24277.0	43.260053	9.102808	5.00	39.00	42.000	47.864	97.00
has_MAL004_Past12Months	24277.0	0.000206	0.014350	0.00	0.00	0.000	0.000	1.00
has_CIR007_Past12Months	24277.0	0.228611	0.419947	0.00	0.00	0.000	0.000	1.00
has_NEO061_Past12Months	24277.0	0.001442	0.037943	0.00	0.00	0.000	0.000	1.00
has_CIR008_Past12Months	24277.0	0.009309	0.096036	0.00	0.00	0.000	0.000	1.00
has_EXT030	24277.0	0.001524	0.039010	0.00	0.00	0.000	0.000	1.00
has_NEO029	24277.0	0.003336	0.057667	0.00	0.00	0.000	0.000	1.00
has_END013	24277.0	0.004613	0.067767	0.00	0.00	0.000	0.000	1.00
has_CIR038	24277.0	0.007414	0.085789	0.00	0.00	0.000	0.000	1.00
has_MUS029	24277.0	0.007291	0.085076	0.00	0.00	0.000	0.000	1.00

Distribution of features in out-of-sample test set:

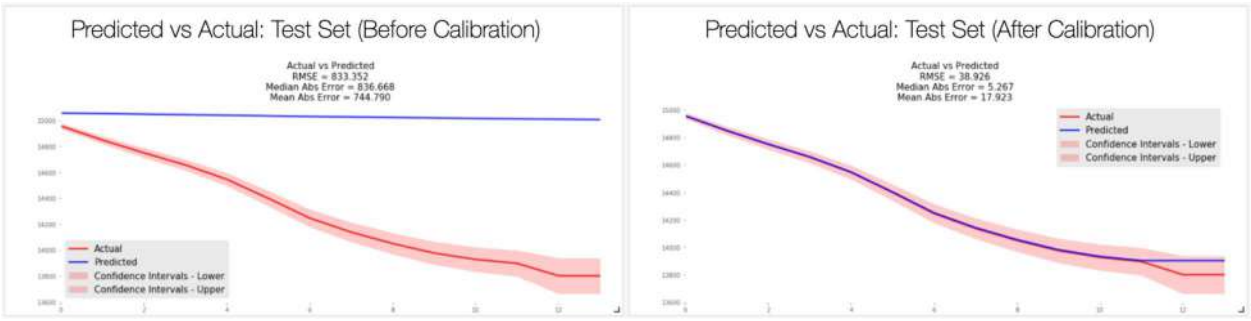
	count	mean	std	min	25%	50%	75%	max
age	15060.0	67.176228	13.144581	19.000	59.000	69.000	77.0000	100.00
Male_sex	15060.0	0.451328	0.497642	0.000	0.000	0.000	1.0000	1.00
Hispanic_or_Latino_ethnicity	15060.0	0.072776	0.259776	0.000	0.000	0.000	0.0000	1.00
lasthbA1CinPast365Days	15060.0	6.882857	0.749252	3.600	6.600	6.866	7.2000	8.90
meandiastolicinPast365Days	15060.0	72.492741	5.145955	43.620	70.137	73.154	75.9140	104.21
meansystolicinPast365Days	15060.0	131.365176	6.472913	90.000	129.358	131.065	133.0550	179.42
BMI	15060.0	32.707763	6.722531	13.430	28.978	32.420	36.0825	80.03
meantriglyceroidsInPast365Days	15060.0	159.501333	52.165235	27.000	132.000	160.500	170.8740	458.00
meanldlcholesterolInPast365Days	15060.0	85.987783	21.523274	11.000	80.000	85.917	96.0710	200.00
meanhdlcholesterolInPast365Days	15060.0	44.188717	8.854655	10.333	39.813	44.000	47.8640	97.00
has_MAL004_Past12Months	15060.0	0.001594	0.039890	0.000	0.000	0.000	0.0000	1.00
has_CIR007_Past12Months	15060.0	0.121846	0.327119	0.000	0.000	0.000	0.0000	1.00
has_NEO061_Past12Months	15060.0	0.000000	0.000000	0.000	0.000	0.000	0.0000	0.00
has_CIR008_Past12Months	15060.0	0.015405	0.123161	0.000	0.000	0.000	0.0000	1.00
has_EXT030	15060.0	0.000531	0.023043	0.000	0.000	0.000	0.0000	1.00
has_NEO029	15060.0	0.007769	0.087801	0.000	0.000	0.000	0.0000	1.00
has_END013	15060.0	0.005378	0.073143	0.000	0.000	0.000	0.0000	1.00
has_CIR038	15060.0	0.003652	0.060324	0.000	0.000	0.000	0.0000	1.00
has_MUS029	15060.0	0.007437	0.085919	0.000	0.000	0.000	0.0000	1.00

Calibration coefficient β (confidence interval): 0.053 (0.050, 0.056)

Model metrics:

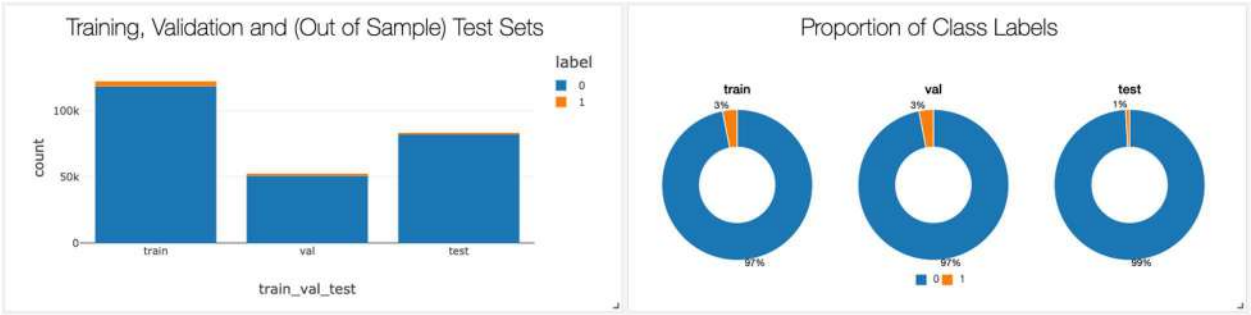
Set	Concordance Index	Integrated Brier Score
Train	0.55	0.128
Validation	0.55	0.127
Test (before calibration)	0.60	0.052
Test (after calibration)	0.60	0.047

Predicted vs Actual survival curves for test set, before and after calibration:



Pre-DM to Uncontrolled DM

Number of instances and proportion of class labels in training, validation and test sets:



Distribution of features in training set:

	count	mean	std	min	25%	50%	75%	max
age	122342.0	64.313506	14.659463	18.00	56.000	66.000	75.000	107.00
Male_sex	122342.0	0.373453	0.483723	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	122342.0	0.055991	0.229904	0.00	0.000	0.000	0.000	1.00
lasthbA1CInPast365Days	122342.0	6.032703	0.494929	3.70	5.800	6.022	6.103	8.90
meandiastolicinPast365Days	122342.0	74.523529	8.456022	43.63	69.860	74.520	79.620	107.67
meansystolicinPast365Days	122342.0	130.536081	12.899920	81.00	123.000	130.162	136.820	180.00
BMI	122342.0	32.047383	6.861005	11.66	28.009	31.894	35.243	273.52
meantriglyceroidsInPast365Days	122342.0	142.364649	49.023127	22.00	119.839	142.732	148.000	466.00
meanldlcholesterolInPast365Days	122342.0	95.223014	23.739237	3.78	84.968	97.608	107.000	201.00
meanhdlcholesterolInPast365Days	122342.0	47.592181	10.548001	6.00	42.000	46.333	52.436	98.00
has_BLD005_Past12Months	122342.0	0.001594	0.039892	0.00	0.000	0.000	0.000	1.00
has_SKN005_Past12Months	122342.0	0.005354	0.072974	0.00	0.000	0.000	0.000	1.00
has_INJ014_Past12Months	122342.0	0.000490	0.022140	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	122342.0	0.196081	0.397033	0.00	0.000	0.000	0.000	1.00
has_NEO022_Past12Months	122342.0	0.028012	0.165007	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	122342.0	0.008926	0.094054	0.00	0.000	0.000	0.000	1.00
has_NEO029_Past12Months	122342.0	0.004406	0.066229	0.00	0.000	0.000	0.000	1.00
has_BLD005	122342.0	0.002501	0.049949	0.00	0.000	0.000	0.000	1.00
has_INJ007	122342.0	0.004962	0.070263	0.00	0.000	0.000	0.000	1.00
has_INJ054	122342.0	0.001782	0.042175	0.00	0.000	0.000	0.000	1.00
has_GEN018	122342.0	0.015056	0.121777	0.00	0.000	0.000	0.000	1.00
has_NEO044	122342.0	0.001177	0.034288	0.00	0.000	0.000	0.000	1.00
has_INJ035	122342.0	0.007340	0.085360	0.00	0.000	0.000	0.000	1.00
has_INJ049	122342.0	0.001954	0.044156	0.00	0.000	0.000	0.000	1.00
has_NEO012	122342.0	0.006261	0.078880	0.00	0.000	0.000	0.000	1.00

Distribution of features in out-of-sample test set:

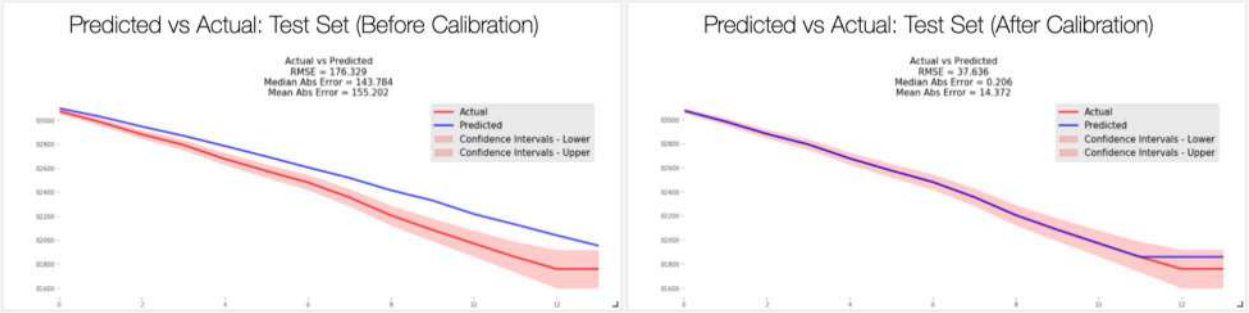
	count	mean	std	min	25%	50%	75%	max
age	83169.0	64.928050	14.577695	18.00	57.000	67.000	75.000	103.00
Male_sex	83169.0	0.371004	0.483076	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	83169.0	0.050848	0.219689	0.00	0.000	0.000	0.000	1.00
lasthbA1ClnPast365Days	83169.0	6.040098	0.482872	2.20	5.800	6.022	6.103	8.90
meandiastolicinPast365Days	83169.0	74.433770	4.714079	44.00	72.425	74.678	77.667	107.00
meansystolicinPast365Days	83169.0	130.417804	6.406752	82.00	127.945	130.162	131.494	180.00
BMI	83169.0	32.058567	7.273502	2.71	27.876	31.690	35.243	326.11
meantriglyceroidsInPast365Days	83169.0	139.865553	46.986997	11.00	119.839	142.732	147.721	468.50
meanldlcholesterolInPast365Days	83169.0	95.183594	23.392690	2.80	84.968	97.608	107.302	201.00
meanhdlcholesterolInPast365Days	83169.0	48.551459	10.051132	8.00	42.348	49.000	52.436	98.00
has_BLD005_Past12Months	83169.0	0.000385	0.019612	0.00	0.000	0.000	0.000	1.00
has_SKN005_Past12Months	83169.0	0.004870	0.069613	0.00	0.000	0.000	0.000	1.00
has_INJ014_Past12Months	83169.0	0.000902	0.030016	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	83169.0	0.101781	0.302362	0.00	0.000	0.000	0.000	1.00
has_NEO022_Past12Months	83169.0	0.023831	0.152523	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	83169.0	0.010028	0.099636	0.00	0.000	0.000	0.000	1.00
has_NEO029_Past12Months	83169.0	0.004292	0.065377	0.00	0.000	0.000	0.000	1.00
has_BLD005	83169.0	0.001335	0.036508	0.00	0.000	0.000	0.000	1.00
has_INJ007	83169.0	0.004377	0.066012	0.00	0.000	0.000	0.000	1.00
has_INJ054	83169.0	0.001238	0.035170	0.00	0.000	0.000	0.000	1.00
has_GEN018	83169.0	0.014597	0.119933	0.00	0.000	0.000	0.000	1.00
has_NEO044	83169.0	0.001130	0.033600	0.00	0.000	0.000	0.000	1.00
has_INJ035	83169.0	0.006529	0.080538	0.00	0.000	0.000	0.000	1.00
has_INJ049	83169.0	0.001816	0.042571	0.00	0.000	0.000	0.000	1.00
has_NEO012	83169.0	0.004244	0.065011	0.00	0.000	0.000	0.000	1.00

Calibration coefficient β (confidence interval): -0.09 (-0.096, -0.083)

Model metrics:

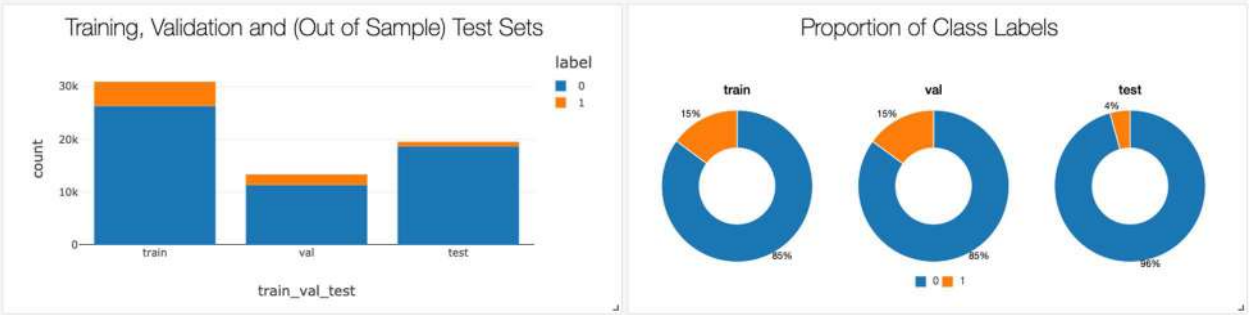
Set	Concordance Index	Integrated Brier Score
Train	0.67	0.0359
Validation	0.58	0.0355
Test (before calibration)	0.71	0.0099
Test (after calibration)	0.71	0.0088

Predicted vs Actual survival curves for test set, before and after calibration:



Diabetic Nephropathy

Number of instances and proportion of class labels in training, validation and test sets:



Distribution of features in training set:

	count	mean	std	min	25%	50%	75%	max
age	30891.0	63.458192	12.980580	18.00	55.000	65.000	72.000	99.00
Male_sex	30891.0	0.432003	0.495363	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	30891.0	0.072125	0.258698	0.00	0.000	0.000	0.000	1.00
lasthbA1ClnPast365Days	30891.0	7.591038	1.215052	3.90	6.900	7.529	8.000	12.70
meandiastolicinPast365Days	30891.0	74.101690	8.748834	44.00	69.110	74.041	79.528	107.00
meansystolicinPast365Days	30891.0	131.945299	13.249303	84.33	124.000	131.574	138.420	180.00
BMI	30891.0	33.759723	6.744802	13.49	29.960	33.718	37.340	76.98
meantriglyceroidsInPast365Days	30891.0	169.731001	57.312733	19.00	144.500	167.131	182.483	457.00
meanldlcholesterolInPast365Days	30891.0	89.362962	23.555869	8.00	81.282	89.776	97.772	201.00
meanhdlcholesterolInPast365Days	30891.0	42.784989	9.134578	5.00	37.685	42.780	47.646	97.00
has_NEO024_Past12Months	30891.0	0.001780	0.042159	0.00	0.000	0.000	0.000	1.00
has_RSP010_Past12Months	30891.0	0.005762	0.075691	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	30891.0	0.221294	0.415125	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	30891.0	0.006928	0.082945	0.00	0.000	0.000	0.000	1.00
has_NVS018	30891.0	0.010456	0.101721	0.00	0.000	0.000	0.000	1.00
has_NEO050	30891.0	0.004241	0.064984	0.00	0.000	0.000	0.000	1.00
has_INJ026	30891.0	0.003788	0.061427	0.00	0.000	0.000	0.000	1.00
has_EXT017	30891.0	0.004111	0.063988	0.00	0.000	0.000	0.000	1.00
has_CIR034	30891.0	0.005568	0.074412	0.00	0.000	0.000	0.000	1.00
has_EYE012	30891.0	0.005180	0.071783	0.00	0.000	0.000	0.000	1.00
has_FAC023	30891.0	0.051148	0.220302	0.00	0.000	0.000	0.000	1.00
has_NEO008	30891.0	0.001975	0.044394	0.00	0.000	0.000	0.000	1.00
has_NVS005	30891.0	0.005180	0.071783	0.00	0.000	0.000	0.000	1.00
has_GEN010	30891.0	0.015797	0.124693	0.00	0.000	0.000	0.000	1.00
has_END011	30891.0	0.244861	0.430012	0.00	0.000	0.000	0.000	1.00
has_CIR008	30891.0	0.031239	0.173965	0.00	0.000	0.000	0.000	1.00

Distribution of features in out-of-sample test set:

	count	mean	std	min	25%	50%	75%	max
age	19522.0	63.255916	13.163093	18.00	55.0000	64.000	72.000	100.00
Male_sex	19522.0	0.411945	0.492198	0.00	0.0000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	19522.0	0.076375	0.265605	0.00	0.0000	0.000	0.000	1.00
lasthbA1ClnPast365Days	19522.0	7.616567	1.217427	3.50	6.9000	7.500	8.000	12.70
meandiastolicinPast365Days	19522.0	74.077505	5.176443	44.00	71.0570	74.041	76.744	106.00
meansystolicinPast365Days	19522.0	131.543621	6.478437	90.00	130.0630	131.574	133.391	179.42
BMI	19522.0	33.938474	6.983243	13.43	29.6325	33.718	37.340	85.68
meantriglyceroidsInPast365Days	19522.0	168.050660	59.142183	27.00	136.0000	167.131	182.483	460.50
meanldlcholesterolInPast365Days	19522.0	90.381401	23.498278	10.00	81.2820	89.776	97.772	200.00
meanhdlcholesterolInPast365Days	19522.0	43.631889	9.058859	12.00	38.5000	43.734	47.646	98.00
has_NEO024_Past12Months	19522.0	0.000922	0.030352	0.00	0.0000	0.000	0.000	1.00
has_RSP010_Past12Months	19522.0	0.003534	0.059348	0.00	0.0000	0.000	0.000	1.00
has_CIR007_Past12Months	19522.0	0.120940	0.326066	0.00	0.0000	0.000	0.000	1.00
has_CIR008_Past12Months	19522.0	0.013062	0.113544	0.00	0.0000	0.000	0.000	1.00
has_NVS018	19522.0	0.007171	0.084382	0.00	0.0000	0.000	0.000	1.00
has_NEO050	19522.0	0.003330	0.057608	0.00	0.0000	0.000	0.000	1.00
has_INJ026	19522.0	0.002459	0.049526	0.00	0.0000	0.000	0.000	1.00
has_EXT017	19522.0	0.004047	0.063487	0.00	0.0000	0.000	0.000	1.00
has_CIR034	19522.0	0.003073	0.055355	0.00	0.0000	0.000	0.000	1.00
has_EYE012	19522.0	0.004200	0.064676	0.00	0.0000	0.000	0.000	1.00
has_FAC023	19522.0	0.028122	0.165326	0.00	0.0000	0.000	0.000	1.00
has_NEO008	19522.0	0.004354	0.065843	0.00	0.0000	0.000	0.000	1.00
has_NVS005	19522.0	0.003381	0.058048	0.00	0.0000	0.000	0.000	1.00
has_GEN010	19522.0	0.012652	0.111772	0.00	0.0000	0.000	0.000	1.00
has_END011	19522.0	0.223850	0.416833	0.00	0.0000	0.000	0.000	1.00
has_CIR008	19522.0	0.032271	0.176724	0.00	0.0000	0.000	0.000	1.00

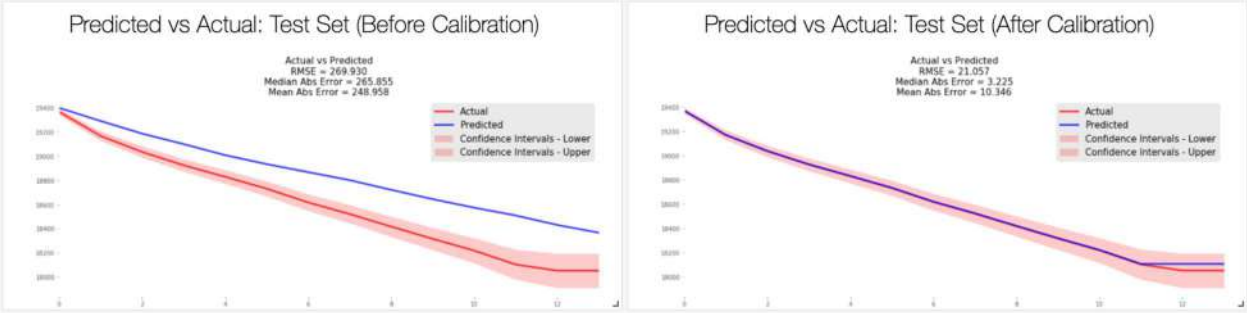
Calibration coefficient β (confidence interval): -0.012 (-0.023, -0.002)

Model metrics:

Set	Concordance Index	Integrated Brier Score
Train	0.54	0.142

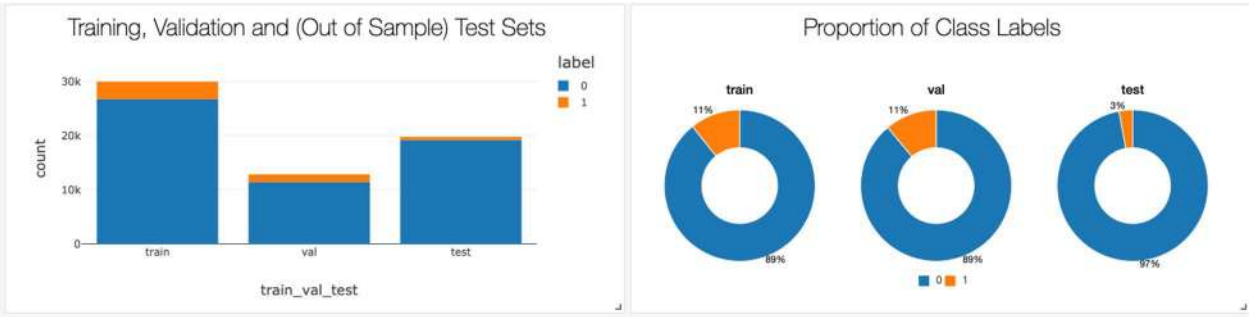
Validation	0.54	0.141
Test (before calibration)	0.69	0.051
Test (after calibration)	0.69	0.044

Predicted vs Actual survival curves for test set, before and after calibration:



Diabetic Neuropathy

Number of instances and proportion of class labels in training, validation and test sets:



Distribution of features in training set:

	count	mean	std	min	25%	50%	75%	max
age	30020.0	64.242405	13.243568	18.00	56.000	66.000	73.000	102.00
Male_sex	30020.0	0.442971	0.496745	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	30020.0	0.070586	0.256137	0.00	0.000	0.000	0.000	1.00
lasthbA1CInPast365Days	30020.0	7.484320	1.180872	3.90	6.800	7.437	7.900	12.70
meandiastolicinPast365Days	30020.0	73.888056	8.770684	44.00	68.600	73.991	79.400	107.56
meansystolicinPast365Days	30020.0	132.179451	13.500032	82.00	124.120	131.921	139.000	180.00
BMI	30020.0	33.406013	6.671339	13.49	29.480	33.677	36.820	157.25
meantriglyceroidsInPast365Days	30020.0	166.541346	56.116023	19.00	141.750	164.470	180.836	457.00
meanldicholesterolInPast365Days	30020.0	88.532380	23.117171	8.00	81.915	89.011	98.902	201.00
meanhdicholesterolInPast365Days	30020.0	43.018117	9.043842	5.00	38.000	42.145	47.634	97.00
has_INJ004_Past12Months	30020.0	0.007229	0.084714	0.00	0.000	0.000	0.000	1.00
has_NEO043_Past12Months	30020.0	0.005863	0.076345	0.00	0.000	0.000	0.000	1.00
has_NEO012_Past12Months	30020.0	0.002831	0.053137	0.00	0.000	0.000	0.000	1.00
has_NEO030_Past12Months	30020.0	0.040640	0.197457	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	30020.0	0.218588	0.413295	0.00	0.000	0.000	0.000	1.00
has_MBD003_Past12Months	30020.0	0.007328	0.085294	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	30020.0	0.007628	0.087008	0.00	0.000	0.000	0.000	1.00
has_FAC013	30020.0	0.009560	0.097310	0.00	0.000	0.000	0.000	1.00
has_DIG006	30020.0	0.007795	0.087945	0.00	0.000	0.000	0.000	1.00
has_NEO065	30020.0	0.004497	0.066910	0.00	0.000	0.000	0.000	1.00
has_FAC004	30020.0	0.002132	0.046124	0.00	0.000	0.000	0.000	1.00
has_GEN025	30020.0	0.042538	0.201817	0.00	0.000	0.000	0.000	1.00
has_RSP017	30020.0	0.011492	0.106586	0.00	0.000	0.000	0.000	1.00
has_NVS004	30020.0	0.010826	0.103486	0.00	0.000	0.000	0.000	1.00
has_MUS037	30020.0	0.012891	0.112808	0.00	0.000	0.000	0.000	1.00
has_CIR035	30020.0	0.008594	0.092308	0.00	0.000	0.000	0.000	1.00

Distribution of features in out-of-sample test set:

	count	mean	std	min	25%	50%	75%	max
age	19815.0	64.536563	13.452568	18.00	56.000	66.000	74.000	100.00
Male_sex	19815.0	0.440676	0.496481	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	19815.0	0.077921	0.268054	0.00	0.000	0.000	0.000	1.00
lasthbA1ClnPast365Days	19815.0	7.522502	1.201356	3.60	6.900	7.437	7.900	12.70
meandiastolicinPast365Days	19815.0	73.814812	5.148202	43.62	70.866	73.991	76.775	104.21
meansystolicinPast365Days	19815.0	131.816459	6.264638	90.50	130.099	131.921	133.683	179.70
BMI	19815.0	33.484880	6.827066	13.43	29.139	33.600	37.041	85.68
meantriglyceroidsInPast365Days	19815.0	164.367480	56.735835	27.00	134.000	164.470	180.836	460.50
meanldlcholesterolInPast365Days	19815.0	89.276920	23.364085	10.00	81.915	89.011	98.902	201.00
meanhdlcholesterolInPast365Days	19815.0	43.888438	8.990077	14.00	39.000	43.333	47.634	98.00
has_INJ004_Past12Months	19815.0	0.004592	0.067614	0.00	0.000	0.000	0.000	1.00
has_NEO043_Past12Months	19815.0	0.004693	0.068349	0.00	0.000	0.000	0.000	1.00
has_NEO012_Past12Months	19815.0	0.004845	0.069438	0.00	0.000	0.000	0.000	1.00
has_NEO030_Past12Months	19815.0	0.020338	0.141158	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	19815.0	0.129851	0.336148	0.00	0.000	0.000	0.000	1.00
has_MBD003_Past12Months	19815.0	0.004895	0.069797	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	19815.0	0.013576	0.115724	0.00	0.000	0.000	0.000	1.00
has_FAC013	19815.0	0.005703	0.075303	0.00	0.000	0.000	0.000	1.00
has_DIG006	19815.0	0.005753	0.075633	0.00	0.000	0.000	0.000	1.00
has_NEO065	19815.0	0.004996	0.070509	0.00	0.000	0.000	0.000	1.00
has_FAC004	19815.0	0.000101	0.010046	0.00	0.000	0.000	0.000	1.00
has_GEN025	19815.0	0.040273	0.196603	0.00	0.000	0.000	0.000	1.00
has_RSP017	19815.0	0.010194	0.100453	0.00	0.000	0.000	0.000	1.00
has_NVS004	19815.0	0.005753	0.075633	0.00	0.000	0.000	0.000	1.00
has_MUS037	19815.0	0.009387	0.096432	0.00	0.000	0.000	0.000	1.00
has_CIR035	19815.0	0.011406	0.106188	0.00	0.000	0.000	0.000	1.00

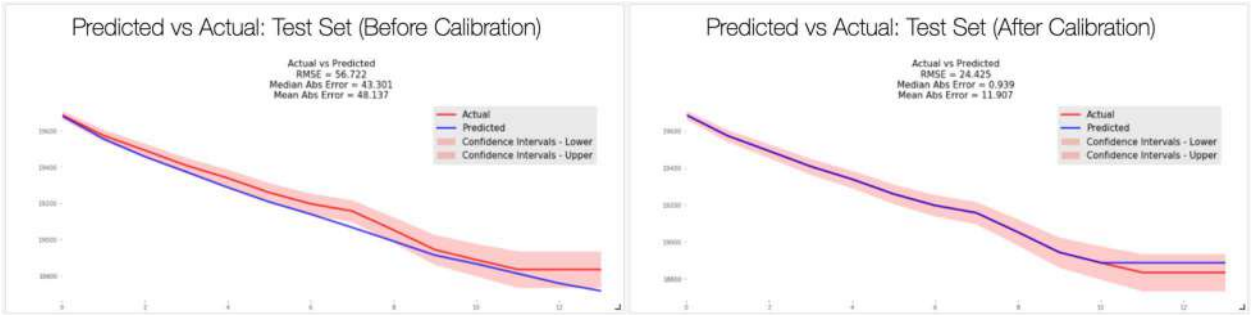
Calibration coefficient β (confidence interval): -0.957 (-1.076, -0.839)

Model metrics:

Set	Concordance Index	Integrated Brier Score
Train	0.53	0.114

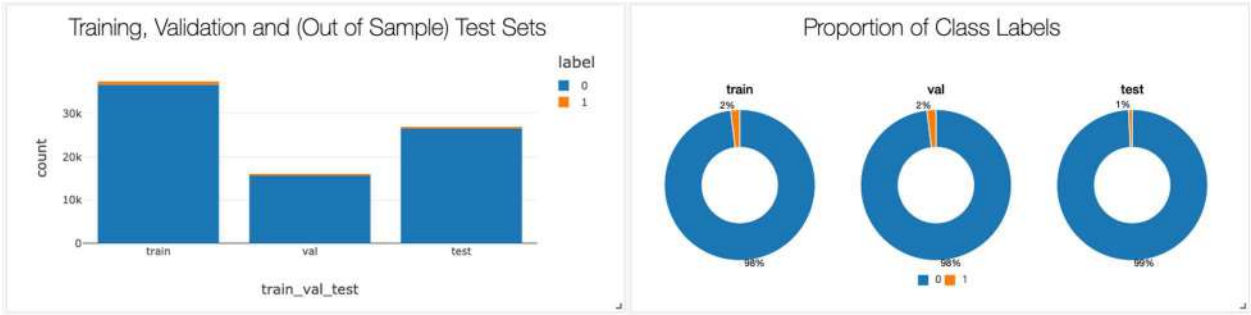
Validation	0.54	0.115
Test (before calibration)	0.54	0.040
Test (after calibration)	0.54	0.029

Predicted vs Actual survival curves for test set, before and after calibration:



Diabetic Retinopathy

Number of instances and proportion of class labels in training, validation and test sets:



Distribution of features in training set:

	count	mean	std	min	25%	50%	75%	max
age	37393.0	64.558901	12.941430	18.00	56.000	66.000	73.000	102.00
Male_sex	37393.0	0.447945	0.497290	0.00	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	37393.0	0.066563	0.249267	0.00	0.000	0.000	0.000	1.00
lasthbA1ClnPast365Days	37393.0	7.552167	1.220510	4.00	6.800	7.468	8.000	12.70
meandiastolicinPast365Days	37393.0	73.574956	8.815770	44.21	68.490	73.621	79.330	107.56
meansystolicinPast365Days	37393.0	132.126932	13.325088	81.00	124.080	131.860	138.940	180.00
BMI	37393.0	33.616739	6.690984	10.37	29.530	33.630	37.000	77.74
meantriglyceroidsInPast365Days	37393.0	169.113035	57.513464	19.00	140.000	167.109	182.466	456.50
meanldlcholesterolInPast365Days	37393.0	88.090462	23.545214	8.00	80.500	88.935	98.338	201.00
meanhdlcholesterolInPast365Days	37393.0	42.549205	9.268495	5.00	37.199	41.093	47.190	97.00
has_GEN020_Past12Months	37393.0	0.003316	0.057491	0.00	0.000	0.000	0.000	1.00
has_CIR009_Past12Months	37393.0	0.017249	0.130200	0.00	0.000	0.000	0.000	1.00
has_BLD008_Past12Months	37393.0	0.023347	0.151004	0.00	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	37393.0	0.223518	0.416608	0.00	0.000	0.000	0.000	1.00
has_NEO008_Past12Months	37393.0	0.001524	0.039014	0.00	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	37393.0	0.009253	0.095748	0.00	0.000	0.000	0.000	1.00
has_MBD017	37393.0	0.022411	0.148017	0.00	0.000	0.000	0.000	1.00
has_INJ026	37393.0	0.003985	0.062999	0.00	0.000	0.000	0.000	1.00
has_GEN017	37393.0	0.036986	0.188729	0.00	0.000	0.000	0.000	1.00
has_MAL004	37393.0	0.001230	0.035053	0.00	0.000	0.000	0.000	1.00
has_NEO022	37393.0	0.042414	0.201535	0.00	0.000	0.000	0.000	1.00
has_INJ069	37393.0	0.000963	0.031014	0.00	0.000	0.000	0.000	1.00
has_RSP011	37393.0	0.067339	0.250611	0.00	0.000	0.000	0.000	1.00
has_INJ023	37393.0	0.001899	0.043534	0.00	0.000	0.000	0.000	1.00
has_MUS016	37393.0	0.003049	0.055132	0.00	0.000	0.000	0.000	1.00
has_NVS013	37393.0	0.020137	0.140472	0.00	0.000	0.000	0.000	1.00

Distribution of features in out-of-sample test set:

	count	mean	std	min	25%	50%	75%	max
age	26753.0	64.982918	13.204143	18.000	57.000	66.000	74.000	100.00
Male_sex	26753.0	0.442268	0.496665	0.000	0.000	0.000	1.000	1.00
Hispanic_or_Latino_ethnicity	26753.0	0.071319	0.257362	0.000	0.000	0.000	0.000	1.00
lasthbA1CInPast365Days	26753.0	7.555745	1.232550	3.500	6.800	7.463	8.000	12.70
meandiastolicinPast365Days	26753.0	73.432272	5.394946	43.620	70.624	73.621	76.480	107.28
meansystolicinPast365Days	26753.0	132.019994	6.519579	90.000	130.446	131.860	133.530	180.00
BMI	26753.0	33.756473	6.892561	13.430	29.485	33.600	37.348	85.68
meantriglyceroidsInPast365Days	26753.0	167.661845	58.104449	27.000	136.888	166.795	182.466	460.50
meanldlcholesterolInPast365Days	26753.0	89.047429	23.607218	10.000	80.000	88.935	98.338	201.00
meanhdlcholesterolInPast365Days	26753.0	43.403549	9.055841	10.333	39.000	43.000	47.190	98.00
has_GEN020_Past12Months	26753.0	0.005719	0.075409	0.000	0.000	0.000	0.000	1.00
has_CIR009_Past12Months	26753.0	0.019362	0.137797	0.000	0.000	0.000	0.000	1.00
has_BLD008_Past12Months	26753.0	0.008784	0.093313	0.000	0.000	0.000	0.000	1.00
has_CIR007_Past12Months	26753.0	0.125481	0.331270	0.000	0.000	0.000	0.000	1.00
has_NEO008_Past12Months	26753.0	0.002691	0.051809	0.000	0.000	0.000	0.000	1.00
has_CIR008_Past12Months	26753.0	0.017120	0.129719	0.000	0.000	0.000	0.000	1.00
has_MBD017	26753.0	0.025418	0.157393	0.000	0.000	0.000	0.000	1.00
has_INJ026	26753.0	0.002355	0.048471	0.000	0.000	0.000	0.000	1.00
has_GEN017	26753.0	0.032707	0.177871	0.000	0.000	0.000	0.000	1.00
has_MAL004	26753.0	0.002467	0.049609	0.000	0.000	0.000	0.000	1.00
has_NEO022	26753.0	0.030688	0.172475	0.000	0.000	0.000	0.000	1.00
has_INJ069	26753.0	0.001570	0.039592	0.000	0.000	0.000	0.000	1.00
has_RSP011	26753.0	0.057414	0.232637	0.000	0.000	0.000	0.000	1.00
has_INJ023	26753.0	0.003102	0.055614	0.000	0.000	0.000	0.000	1.00
has_MUS016	26753.0	0.001383	0.037164	0.000	0.000	0.000	0.000	1.00
has_NVS013	26753.0	0.016895	0.128882	0.000	0.000	0.000	0.000	1.00

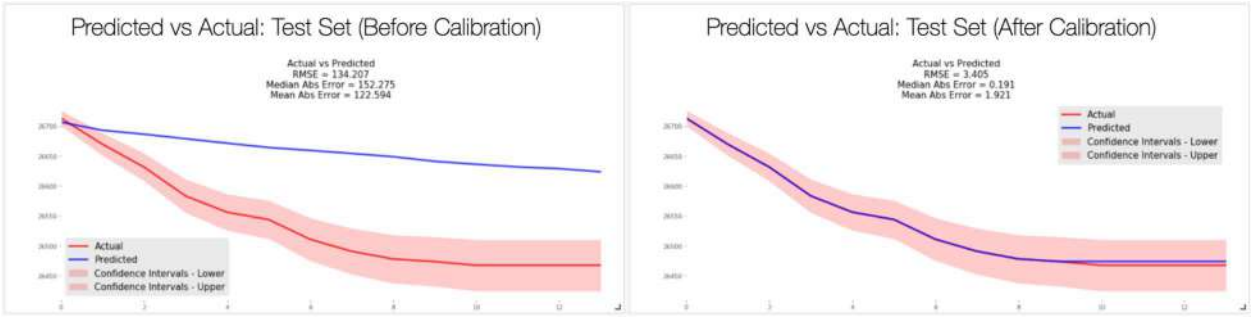
Calibration coefficient β (confidence interval): 0.015 (0.015, 0.015)

Model metrics:

Set	Concordance Index	Integrated Brier Score
Train	0.51	0.0209

Validation	0.53	0.0209
Test (before calibration)	0.67	0.0099
Test (after calibration)	0.67	0.0075

Predicted vs Actual survival curves for test set, before and after calibration:



Appendix E: Model Signatures Excluding Extremely Unbalanced Binary Features

The model signatures generated via feature selection in this evaluation included several features that were surprising or seemed out of place. It was not clear, from a clinical perspective, why these features would be found to be important for predicting the various conditions and complications.

It turned out that most of these features were binary features with extremely low proportions, < 1%, of positives. This could indicate that the models were learning from very strong associations between these features and the target variables, even though they were present only in a very small number of training instances.

A number of issues arise:

a. It may be difficult to explain to clinicians or customers why certain features are important for predicting diabetes and its complications.
b. The usefulness of these features is limited to a very small proportion (< 1%) of the proportion.
c. These feature associations may be a result of spurious correlations present in the training data set, and not universally applicable to other populations; i.e. the models may have been overfit to one population and if so, performance will decrease when they are deployed elsewhere.

In this investigation, we re-generated the model signatures for each task excluding extremely unbalanced binary features. The following procedure was used:

1. Input: The same set of encounters, features and cohort criteria as in the current iteration (Iteration 3) reported in the main body of this document.
2. Detect and remove all binary features where the instances comprise < 2% (extremely low) or > 98% (extremely high) positive values.
3. Re-run recursive feature elimination using the same procedure used in this iteration.

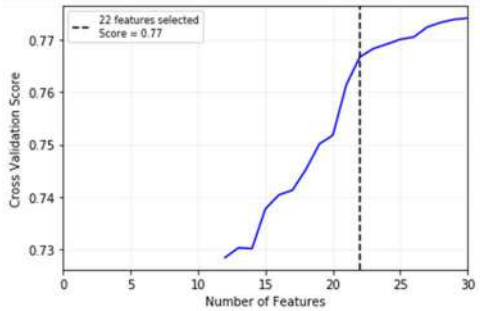
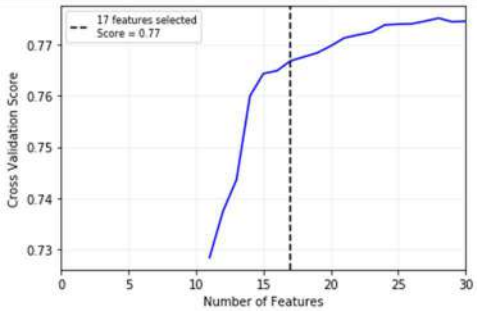
In the tables below, features in grey were selected in the original model signatures but not in the new ones. Conversely, features in green were selected in the new model signatures but were not in the original ones.

Observations:

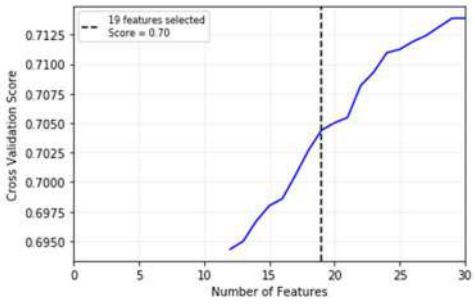
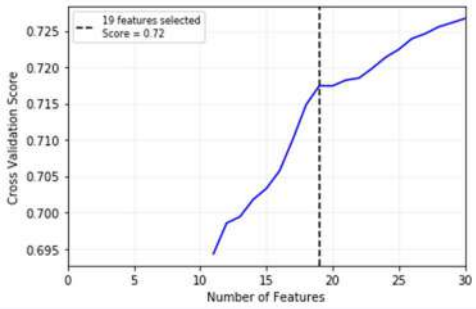
1. Depending on task, between 67% to 71% of features were removed from the candidate list as they were found to be extremely imbalanced with respect to the selected cohorts.
2. Apart from the mandatory features, the other selected features were quite different for most tasks. Whether these new sets of features make sense clinically is to be validated.

3. Selected features remain largely based on diagnoses (as represented by CSSR categories), except for nephropathy, where albumin and potassium features were added to the model signature.
4. There was no detrimental effect on cross-validation scores during feature selection (which are indicative of final model performance); in fact, the cross-validation scores improved for nephropathy, neuropathy and retinopathy.

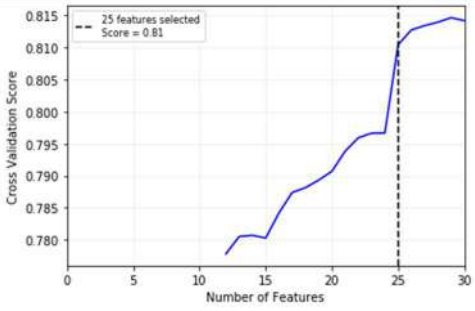
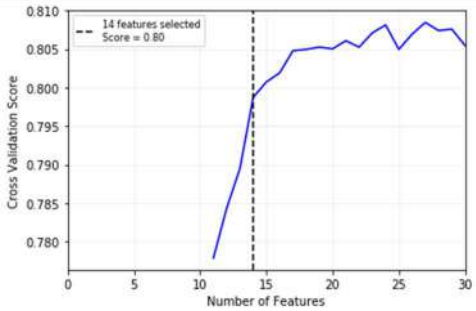
Pre-DM to DM

	With Full List of Candidate Features	**Excluding 828 / 1,174 Extremely Imbalanced Binary Features**
Model Signature	1. has_BLD005_Past12Months (Sickle cell trait/anemia) 2. has_PRG029 (Uncomplicated pregnancy, delivery or puerperium) 3. has_NEO016_Past12Months (Gastrointestinal cancers - anus) 4. has_INJ057 (Effect of foreign body entering opening, subsequent encounter) 5. has_DIG018 (Hepatic failure) 6. maxhbA1CInPast365Days 7. has_RSP015 (Mediastinal disorders) 8. has_NEO017 (Gastrointestinal cancers - liver) 9. has_SKN003 (Pressure ulcer of skin) 10. has_FAC006 (Encounter for antineoplastic therapies) 11. Male_sex 12. lasthbA1CInPast365Days 13. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension) 14. Hispanic_or_Latino_ethnicity 15. has_CIR007_Past12Months (Essential hypertension) 16. meanhdlcholesterolInPast365Days 17. meansystolicinPast365Days 18. BMI 19. meandiastolicinPast365Days 20. age 21. meanldlcholesterolInPast365Days 22. meantriglyceroidsInPast365Days	1. has_DIG018 (Hepatic failure) 2. maxhbA1CInPast365Days 3. has_SKN003 (Pressure ulcer of skin) 4. has_FAC006 (Encounter for antineoplastic therapies) 5. has_SYM002 (Fever) 6. has_FAC023 (Organ transplant status) 7. Male_sex 8. lasthbA1CInPast365Days 9. has_CIR007_Past12Months (Essential hypertension) 10. meanhdlcholesterolInPast365Days 11. meansystolicinPast365Days 12. BMI 13. meandiastolicinPast365Days 14. age 15. meanldlcholesterolInPast365Days 16. meantriglyceroidsInPast365Days 17. Hispanic_or_Latino_ethnicity
Cross-Validation Plot		

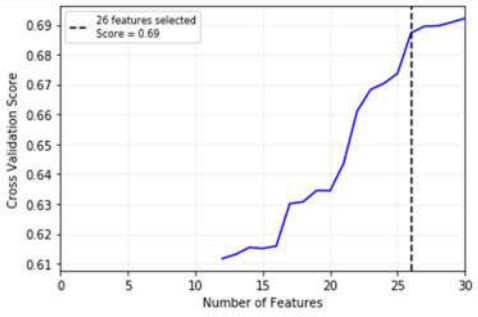
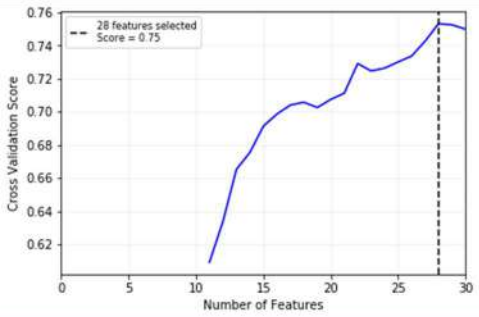
DM to Uncontrolled DM

	With Full List of Candidate Features	Excluding 794 / 1,182 Extremely Imbalanced Binary Features
Model Signature	1. has_CIR038 (Postprocedural or postoperative circulatory system complication) 2. has_END013 (Pituitary disorders) 3. has_MAL004_Past12Months (Nervous system congenital anomalies) 4. has_EXT030 (External cause codes: sequela) 5. has_NEO061_Past12Months (Leukemia - chronic lymphocytic leukemia (CLL)) 6. has_MUS029 (Disorders of jaw) 7. has_NEO029 (Breast cancer - ductal carcinoma in situ (DCIS)) 8. lasthbA1CInPast365Days 9. Hispanic_or_Latino_ethnicity 10. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension) 11. has_CIR007_Past12Months (Essential hypertension) 12. BMI 13. Male_sex 14. age 15. meansystolicinPast365Days 16. meanhdlcholesterolInPast365Days 17. meandiastolicinPast365Days 18. meanldlcholesterolInPast365Days 19. meantriglyceroidsInPast365Days	1. lasthbA1CInPast365Days 2. has_NEO070 (Secondary malignancies) 3. has_NEO070_Past12Months (Secondary malignancies) 4. has_DIG007 (Gastritis and duodenitis) 5. has_FAC022 (Acquired absence of limb or organ) 6. has_CIR024 (Other and ill-defined cerebrovascular disease) 7. has_SYM001 (Syncope) 8. has_CIR036 (Postthrombotic syndrome and venous insufficiency/hypertension) 9. has_SYM015 (General sensation/perception signs and symptoms) 10. Hispanic_or_Latino_ethnicity 11. has_CIR007_Past12Months (Essential hypertension) 12. BMI 13. age 14. meansystolicinPast365Days 15. Male_sex 16. meanhdlcholesterolInPast365Days 17. meandiastolicinPast365Days 18. meanldlcholesterolInPast365Days 19. meantriglyceroidsInPast365Days
Cross-Validation Plot		

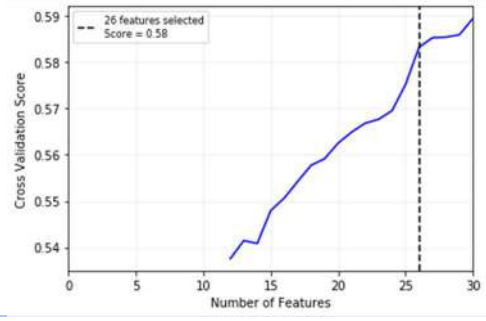
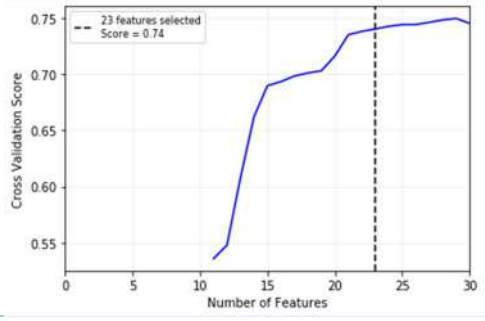
Pre-DM to Uncontrolled DM

	With Full List of Candidate Features	Excluding 830 / 1,182 Extremely Imbalanced Binary Features
Model Signature	1. has_BLD005_Past12Months (Sickle cell trait/anemia) 2. has_INJ035 (Complication of internal orthopedic device or implant, initial encounter) 3. has_INJ014_Past12Months (Amputation of a limb, initial encounter) 4. has_INJ049 (Open wounds to limbs, subsequent encounter) 5. has_NEO022_Past12Months (Respiratory cancers) 6. has_INJ054 (Superficial injury; contusion, subsequent encounter) 7. has_NEO044 (Urinary system cancers - ureter and renal pelvis) 8. lasthbA1CInPast365Days 9. has_SKN005_Past12Months (Contact dermatitis) 10. has_NEO029_Past12Months (Breast cancer - ductal carcinoma in situ (DCIS)) 11. has_BLD005 (Sickle cell trait/anemia) 12. has_NEO012 (Gastrointestinal cancers - esophagus) 13. has_INJ007 (Dislocations, initial encounter) 14. has_GEN018 (Inflammatory diseases of female pelvic organs) 15. Male_sex 16. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension) 17. Hispanic_or_Latino_ethnicity 18. age 19. BMI 20. meanhdlcholesterolInPast365Days 21. has_CIR007_Past12Months (Essential hypertension) 22. meansystolicinPast365Days 23. meantriglyceroidsInPast365Days 24. meandiastolicinPast365Days 25. meanldlcholesterolInPast365Days	1. maxhbA1CInPast365Days 2. has_SYM002 (Fever) 3. has_NEO022_Past12Months (Respiratory cancers) 4. lasthbA1CInPast365Days 5. Male_sex 6. Hispanic_or_Latino_ethnicity 7. age 8. meansystolicinPast365Days 9. BMI 10. meanhdlcholesterolInPast365Days 11. meandiastolicinPast365Days 12. meantriglyceroidsInPast365Days 13. has_CIR007_Past12Months (Essential hypertension) 14. meanldlcholesterolInPast365Days
Cross-Validation Plot		

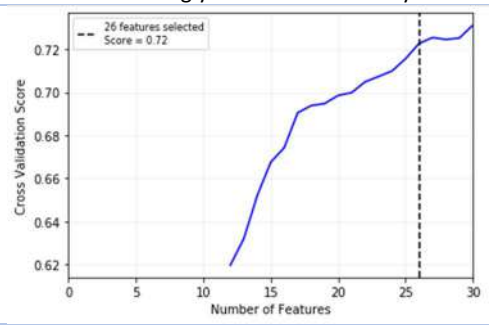
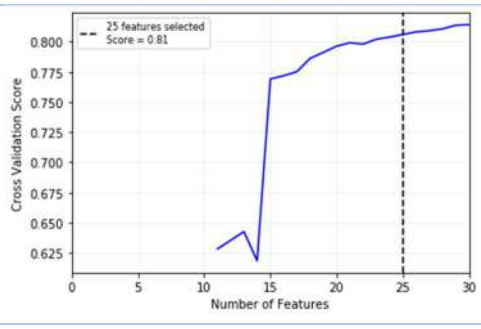
DM to Diabetic Nephropathy

	With Full List of Candidate Features	Excluding 822 / 1,182 Extremely Imbalanced Binary Features
Model Signature	1. has_NEO008 (Head and neck cancers - laryngeal) 2. has_EXT017 (External cause codes: suffocation/inhalation; initial encounter) 3. has_NEO024_Past12Months (Sarcoma) 4. has_EYE012 (Other specified eye disorders) 5. has_CIR034 (Chronic phlebitis; thrombophlebitis and thromboembolism) 6. has_NVS005 (Multiple sclerosis) 7. has_INJ026 (Other specified injury) 8. has_CIR008 (Hypertension with complications and secondary hypertension) 9. has_RSP010_Past12Months (Aspiration pneumonitis) 10. has_GEN010 (Proteinuria) 11. has_END011 (Fluid and electrolyte disorders) 12. has_NVS018 (Myopathies) 13. has_NEO050 (Endocrine system cancers - thyroid) 14. has_FAC023 (Organ transplant status) 15. Hispanic_or_Latino_ethnicity 16. Male_sex 17. has_CIR007_Past12Months (Essential hypertension) 18. lasthbA1CInPast365Days 19. age 20. BMI 21. meandiastolicinPast365Days 22. meansystolicinPast365Days 23. meanhdlcholesterolInPast365Days 24. meanldlcholesterolInPast365Days 25. meantriglyceroidsInPast365Days 26. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension)	1. has_CIR019 (Heart failure) 2. has_CIR008 (Hypertension with complications and secondary hypertension) 3. has_GEN017 (Nonmalignant breast conditions) 4. has_INF003 (Bacterial infections) 5. has_INF003_Past12Months (Bacterial infections) 6. has_FAC023 (Organ transplant status) 7. has_CIR009 (Acute myocardial infarction) 8. has_NEO030_Past12Months (Breast cancer - all other types) 9. stdalbuminInPast365Days 10. minalbuminInPast365Days 11. minpotassiumInPast365Days 12. has_INJ005 (Fracture of the lower limb (except hip), initial encounter) 13. has_FAC010 (Other aftercare encounter) 14. has_CIR029 (Aortic; peripheral; and visceral artery aneurysms) 15. has_MUS033 (Gout) 16. has_INF008_Past12Months (Viral infection) 17. has_INF007 (Hepatitis) 18. Hispanic_or_Latino_ethnicity 19. has_CIR007_Past12Months (Essential hypertension) 20. lasthbA1CInPast365Days 21. meandiastolicinPast365Days 22. Male_sex 23. meansystolicinPast365Days 24. age 25. BMI 26. meanldlcholesterolInPast365Days 27. meantriglyceroidsInPast365Days 28. meanhdlcholesterolInPast365Days
Cross-Validation Plot		

DM to Diabetic Neuropathy

	With Full List of Candidate Features	Excluding 822 / 1,184 Extremely Imbalanced Binary Features
Model Signature	1. has_DIG006 (Gastrointestinal and biliary perforation) 2. has_FAC013 (Contraceptive and procreative management) 3. has_CIR035 (Varicose veins of lower extremity) 4. has_FAC004 (Encounter for prophylactic or other procedures) 5. has_NEO030_Past12Months (Breast cancer - all other types) 6. has_NEO012_Past12Months (Gastrointestinal cancers - esophagus) 7. has_MUS037 (Postprocedural or postoperative musculoskeletal system complication) 8. has_NEO043_Past12Months (Urinary system cancers - bladder) 9. has_NEO065 (Multiple myeloma) 10. has_INJ004_Past12Months (Fracture of the upper limb, initial encounter) 11. has_MBD003_Past12Months (Bipolar and related disorders) 12. has_RSP017 (Postprocedural or postoperative respiratory system complication) 13. has_NVS004 (Parkinson`s disease) 14. has_GEN025 (Other specified female genital disorders) 15. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension) 16. has_CIR007_Past12Months (Essential hypertension) 17. Hispanic_or_Latino_ethnicity 18. Male_sex 19. lasthbA1CInPast365Days 20. meandiastolicinPast365Days 21. meansystolicinPast365Days 22. BMI 23. meanhdlcholesterolInPast365Days 24. meanldlcholesterolInPast365Days 25. age 26. meantriglyceroidsInPast365Days	1. has_NEO030_Past12Months (Breast cancer - all other types) 2. has_SKN003 (Pressure ulcer of skin) 3. has_END003 (Diabetes mellitus with complication) 4. has_INJ012 (Open wounds to limbs, initial encounter) 5. has_GEN006_Past12Months (Other specified and unspecified diseases of kidney and ureters) 6. has_FAC022 (Acquired absence of limb or organ) 7. has_GEN025 (Other specified female genital disorders) 8. has_DIG008 (Other specified and unspecified disorders of stomach and duodenum) 9. has_INF002 (Septicemia) 10. has_CIR019 (Heart failure) 11. has_RSP012_Past12Months (Respiratory failure; insufficiency; arrest) 12. has_SYM004 (Nausea and vomiting) 13. lasthbA1CInPast365Days 14. Hispanic_or_Latino_ethnicity 15. has_CIR007_Past12Months (Essential hypertension) 16. meansystolicinPast365Days 17. meandiastolicinPast365Days 18. BMI 19. meanldlcholesterolInPast365Days 20. meanhdlcholesterolInPast365Days 21. meantriglyceroidsInPast365Days 22. age 23. Male_sex
Cross-Validation Plot		

DM to Diabetic Retinopathy

	With Full List of Candidate Features	Excluding 801 / 1,186 Extremely Imbalanced Binary Features
Model Signature	1. has_BLD008_Past12Months (Immunity disorders) 2. has_NEO022 (Respiratory cancers) 3. has_CIR009_Past12Months (Acute myocardial infarction) 4. has_INJ069 (Complication of cardiovascular device, implant or graft, subsequent encounter) 5. has_GEN020_Past12Months (Prolapse of female genital organs) 6. has_MUS016 (Stress fracture, initial encounter) 7. has_INJ023 (Toxic effects, initial encounter) 8. has_MAL004 (Nervous system congenital anomalies) 9. has_NVS013 (Coma; stupor; and brain damage) 10. has_GEN017 (Nonmalignant breast conditions) 11. has_INJ026 (Other specified injury) 12. has_NEO008_Past12Months (Head and neck cancers - laryngeal) 13. has_MBD017 (Alcohol-related disorders) 14. has_RSP011 (Pleurisy, pleural effusion and pulmonary collapse) 15. Hispanic_or_Latino_ethnicity 16. has_CIR008_Past12Months (Hypertension with complications and secondary hypertension) 17. lasthbA1CInPast365Days 18. Male_sex 19. has_CIR007_Past12Months (Essential hypertension) 20. meanhdlcholesterolInPast365Days 21. meandiastolicinPast365Days 22. age 23. meansystolicinPast365Days 24. BMI 25. meanldlcholesterolInPast365Days 26. meantriglyceroidsInPast365Days	1. has_NEO022 (Respiratory cancers) 2. has_CIR001 (Chronic rheumatic heart disease) 3. has_GEN017 (Nonmalignant breast conditions) 4. has_MBD017 (Alcohol-related disorders) 5. has_RSP011 (Pleurisy, pleural effusion and pulmonary collapse) 6. has_END003 (Diabetes mellitus with complication) 7. has_CIR013 (Acute pulmonary embolism) 8. has_FAC010 (Other aftercare encounter) 9. has_END006 (Diabetes mellitus, due to underlying condition, drug or chemical induced, or other specified type) 10. has_INF008 (Viral infection) 11. has_INF008_Past12Months (Viral infection) 12. has_BLD008 (Immunity disorders) 13. has_SYM003 (Shock) 14. has_GEN010 (Proteinuria) 15. Hispanic_or_Latino_ethnicity 16. lasthbA1CInPast365Days 17. has_CIR007_Past12Months (Essential hypertension) 18. meandiastolicinPast365Days 19. age 20. meansystolicinPast365Days 21. meanhdlcholesterolInPast365Days 22. meanldlcholesterolInPast365Days 23. BMI 24. Male_sex 25. meantriglyceroidsInPast365Days
Cross-Validation Plot		

Appendix F: Features for Model Training

The following table lists the relevant features for model training that are available from existing Patient Flow features.

- Many of the features also have "Unknown" or "Other" as possible values, but these are omitted from this table for brevity, as they would be treated as missing values.
- Calendar features were omitted (e.g., admission hour, day and month) as these are less relevant for predicting diabetes and its complications.

Name	Category	Type	Description	Number of Features	Modifiable	Remarks
Age	Demographic	Integer	In years, at time of encounter	1	No	
Ethnicity	Demographic	Categorical	• Hispanic or Latino • Not Hispanic or Latino	1	No	How does this overlap with Race?
Race	Demographic	Categorical	• American Indian or Alaska Native • Asian • Black or African American • Native Hawaiian or Other Pacific Islander • White or Caucasian	1	No	
Sex	Demographic	Categorical	• Female • Male	1	No	
Chronic Conditions	Diagnosis	Boolean	Presence of chronic condition(s) in the last 365 days	40	Depends	
Diagnosis Group	Diagnosis	Boolean	Presence of diagnosis group(s) for the encounter	358	Depends	
Albumin	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Alkaline Phosphatase	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Bilirubin	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Bun	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		

Name	Category	Type	Description	Number of Features	Modifiable	Remarks
HBA1C	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Neutrophils	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Potassium	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Serum Bicarbonate	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Sodium	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
WBC	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Smoking	Lifestyle	Categorical	• Current Every Day Smoker • Current Some Day Smoker • Former Smoker • Heavy Tobacco Smoker • Light Tobacco Smoker • Never Assessed • Never Smoker • Passive Smoke Exposure - Never Smoker • Smoker, Current Status Unknown	1	Yes	May not be useful, as definitions of each category are not clearly specified, and may not be the same for all providers

Name	Category	Type	Description	Number of Features	Modifiable	Remarks
Specialty Received	Specialty	Boolean	0, 1 or more of 121 specialties for the encounter	121		Is this consistently defined across providers?
Specialty Requested	Specialty	Boolean	0, 1 or more of 121 specialties for the encounter	121		Is this consistently defined across providers?
Admission Type	Utilization	Integer	• Emergency • Inpatient • Outpatient • Not a Hospital Encounter	1		May need to convert into an aggregate, e.g., number of each type in last 90, 180, 365 days
Days Since Last ED Visit	Utilization	Integer	In days	1		
Days Since Last Inpatient Visit	Utilization	Integer	In days	1		
Discharge Disposition	Utilization	Categorical	For the encounter • home • pac • home-health • other • None	1	No	May need to convert into an aggregate, e.g., number of each type in last 90, 180, 365 days
Is Admission	Utilization	Boolean	For the encounter • 0: outpatient • 1: inpatient	1	No	Use Previous Inpatient / Outpatient Encounters Count instead
Length of Stay	Utilization	Integer	In days, for the encounter	1	No	
Previous ED Visits Count	Utilization	Integer	For days before current encounter: • 90 days • 180 days • 365 days	3		
Previous Inpatient Encounters Count	Utilization	Integer	For days before current encounter: • 90 days • 180 days • 365 days	3		Add another feature for outpatient encounters
Diastolic	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	

Name	Category	Type	Description	Number of Features	Modifiable	Remarks
Systolic	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
Glasgow Coma Scale Score	Vitals	Integer	During encounter	1		
O2 Device Usage	Vitals	Integer	• aerosolmask • artificialnose • bagvalvemask • bipap • blowby • bubblecpap • cpap • endotrachealtube • ett • facetent • heliox80/20 • highflownasalcannula • hood • lma • misttent • nasalcannula • neonasalcannula • neopuff • noneroomair • nonrebreather • nonrebreathermask • othercomment • oxymask • oxymizer • pednasalcannula • ramcannula • simplemask • tpiece • trachcollar • tracheostomy • trachmask • ventilator • venturimask	33		
O2 Flow Flowsheet Value	Vitals	Integer	Max during encounter	1		

ED Utilization / Visit Non-Compliance / Medication Non-Adherence

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Age	Demographic	Integer	In years, at time of appointment	1	No	Yes
Age Above 65	Demographic	Boolean	Whether the patient's age is above 65	1	No	
Ethnicity	Demographic	Categorical	• Hispanic or Latino • Not Hispanic or Latino	1	No	Yes
Sex	Demographic	Categorical	• Female • Male	1	No	Yes
Marital Status	Demographic	Categorical	• Married • Single • Divorced • Widowed			
Insurance Status	Demographic	Boolean	Whether the patient is insured	1		
Income Level	Demographic	Categorical				
Educational Level	Demographic	Categorical				
Employment Status	Demographic	Categorical				
English Proficiency	Demographic	Boolean	Whether the patient's primary language is English	1		
Distance to Clinic	Demographic	Continuous	How far is the patient's home from the clinic	1		
Smoking Status	Demographic	Categorical	• Never • Former • Current			
Elixhauser Comorbidity Index	Diagnosis	Integer	Comorbidity of the patient	1		
CCSR Category (12 mth)	Diagnosis	Boolean	Presence of CCSR Category in past 12 months	540	Depends	
CCSR Category	Diagnosis	Boolean	Presence of CCSR Category in the patient's whole history	540	Depends	
Albumin	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Alkaline Phosphatase	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Bilirubin	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Bun	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
HBA1C	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Neutrophils	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Potassium	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Serum Bicarbonate	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
Sodium	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
WBC	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • Last	5		
BMI	Vitals	Continuous	BMI of the patient calculated using height and weight	1		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
AST	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
ALT	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
Diastolic	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
Systolic	Vitals	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
LDL Cholesterol	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
HDL Cholesterol	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
Creatine	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Triglyceroids	Lab	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6	Yes	
Days Since Last ED Visit	Utilization	Integer	In days	1		
Days Since Last Inpatient Visit	Utilization	Integer	In days	1		
Days Since Last Outpatient Visit	Utilization	Integer	In days	1		
Days Since Last PCP Visit	Utilization	Integer	In days	1		
Previous ED Visits Count	Utilization	Integer	For days before current appointment: • 90 days • 180 days • 365 days	3		
Previous Inpatient Encounters Count	Utilization	Integer	For days before current appointment: • 90 days • 180 days • 365 days	3		
Previous Outpatient Encounters Count	Utilization	Integer	For days before current appointment: • 90 days • 180 days • 365 days	3		
Previous Outpatient Primary Care Encounters Count	Utilization	Integer	For days before current appointment: • 90 days • 180 days • 365 days	3		
Previous Outpatient Specialist Type Count	Utilization	Integer	Number of distinct specialist type For days before current appointment: • 90 days • 180 days • 365 days	3		
Number of Previous No-shows	Utilization	Integer	For days before current appointment: • 90 days • 180 days • 365 days	3		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Number of Previous Late Appointments	Utilization	Integer	For days before current appointment: • 90 days • 180 days • 365 days	3		
Trend in Missed Appointments	Utilization	Continuous	Increasing or decreasing trend with more weight given to the most recent appointments	1		
Past Appointment Lead Time	Utilization	Continuous	365-day aggregates: • Min • Mean • Median • Max • SD • Last	6		
Past Appointment Cancel Reason Count	Utilization	Integer	e.g. Patient, Provider, Scheduled from Wait List, Error, Lack of Transportation, Weather			
Past Kept Appointment of Day of Week	Utilization	Continuous	Percentage of kept appointments on the same day of week as current appointment	1		
Provider Type	Utilization	Categorical	• Physician • Licensed practical nurse • Technician • Medical assistant • Resident • Psychologist • Registered dietitian • Social worker			
Has History of Medication Side Effects	Utilization	Boolean	Whether the patient has had any history of medication side effects	1		
Appointment Lead Time	Current Appointment	Continuous	Duration between when appointment was made and actual appointment date	1		
Appointment Category	Current Appointment	Categorical	• Follow Up • Routine • Consult • Urgent • Procedure • Preventive			
Appointment Hour of Day	Current Appointment	Categorical	Hour of day of current appointment	1		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Appointment Day of Week	Current Appointment	Categorical	Day of week of current appointment	1		
Appointment Month	Current Appointment	Categorical	Month of current appointment	1		
Multiple Same-day Appointments	Current Appointment	Boolean	Whether patient has multiple appointments on the same day	1		
Estimated Appointment Length	Current Appointment	Integer	Estimated length of appointment	1		
Appointment Rescheduled	Current Appointment	Boolean	Whether appointment was rescheduled	1		
Appointment Change Count	Current Appointment	Integer	Number of changes	1		
Appointment Calls Count	Current Appointment	Integer	Number of calls	1		
Appointment Referral	Current Appointment	Boolean	Whether appointment was referred	1		
Appointment Confirm Status	Current Appointment	Categorical	• Confirmed • Not Confirmed • Removed	2		
Appointment Phone Confirmation Status	Current Appointment	Categorical	e.g. Answered not confirmed, hang up, busy, no answer			
Copayment Due	Current Appointment	Continuous	Amount of copayment due	1		
FEATURES SPECIFIC TO DM PATIENTS						
Has Diabetes	DM Condition	Boolean	• Past 90 days • Past 365 days	2		
Has Diabetes Nephropathy	DM Condition	Boolean	• Past 90 days • Past 365 days	2		
Has Diabetes Neuropathy	DM Condition	Boolean	• Past 90 days • Past 365 days	2		
Has Diabetes Retinopathy	DM Condition	Boolean	• Past 90 days • Past 365 days	2		
Has Diabetes Other Complications	DM Condition	Boolean	• Past 90 days • Past 365 days	2		
Time Since Diabetes Diagnosis	DM Condition	Continuous	Number of days since diabetes diagnosis	1		
Time Since Diabetes Nephropathy Diagnosis	DM Condition	Continuous	Number of days since diabetes nephropathy diagnosis	1		
Time Since Diabetes Neuropathy Diagnosis	DM Condition	Continuous	Number of days since diabetes neuropathy diagnosis	1		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Time Since Diabetes Retinopathy Diagnosis	DM Condition	Continuous	Number of days since diabetes retinopathy diagnosis	1		
Time Since Diabetes Other Complications Diagnosis	DM Condition	Continuous	Number of days since diabetes other complications diagnosis	1		
Has Hypoglycemia Event	DM Condition	Boolean	Whether patient has experienced a hypoglycemic event	1		
Past Hypoglycemia Event Count	DM Condition	Integer	• 90 days • 180 days • 365 days	3		
Has Hyperglycemia Event	DM Condition	Boolean	Whether patient has experienced a hyperglycemic event	1		
Past Hyperglycemia Event Count	DM Condition	Integer	• 90 days • 180 days • 365 days	3		
DM-related ED Visit Count	DM Condition	Integer	• 90 days • 180 days • 365 days	3		
DM-related Hospitalization Count	DM Condition	Integer	• 90 days • 180 days • 365 days	3		
New Diabetes Medication	Medication	Boolean	• Whether patient has any new diabetes medication dispensed in the past 6 months	1		
Diabetes Insulin Treatment	Medication	Boolean	Whether patient is under insulin treatment	1		
Diabetes Insulin Type	Medication	Categorical	• Rapid acting • Short acting • Intermediate (NPH) acting insulin • Long acting Mixed action			
Insulin Treatment by Pen or Pump	Medication	Boolean	• Whether patient uses a pen-injector or pump instead of syringe or needles	1		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Diabetes OAD Treatment	Medication	Boolean	Whether patient given treatment for each class of OAD • Biguanides • Sulfonylureas • Meglitinides • Thiazolidinediones (TZDs) • Glucagonlike peptide-1 (GLP-1) agonists • Dipeptidyl peptidase IV (DPP-4) inhibitors Alpha-glucosidase inhibitors	7		
Dosage Count	Medication	Integer	• Number of current dosages required in a day	1		
Average Frequency of Current Medication	Medication	Continuous	Average frequency across all medications	1		
Current Medication Class Count	Medication	Integer	Number of current unique medication classes	1		
Chronic Medication Count	Medication	Integer	Number of chronically used medications	1		
Current Medication Route Count	Medication	Integer	Number of current unique medication routes (e.g. Oral, Subcutaneous, Intramuscular)	1		
Average Medication Length of Fill	Medication	Continuous	Average length of fill across all medications	1		
Average Number of Available Refills	Medication	Continuous	Average number of available refills across all medications	1		
Prescribed Medication Count	Medication	Integer	Number of unique medications prescribed in • Past 90 days • Past 180 days Past 365 days	3		

Name	Category	Type	Description	Number of Features	Modifiable	Mandatory
Prescribed Medication Class Count	Medication	Integer	Number of unique medication classes prescribed in • Past 90 days • Past 180 days • Past 365 days	3		
Prescriber Count	Medication	Integer	Number of prescribers in • Past 90 days • Past 180 days • Past 365 days	3		
Rx Fill by Mail	Medication	Boolean	• Whether the patient's prescriptions are filled by mail	1		
Past HbA1c Tests Count	Compliance	Integer	Number of past HbA1c tests in • Past 90 days • Past 180 days Past 365 days	3		
Past Glucose Tests Count	Compliance	Integer	Number of past glucose tests in • Past 90 days • Past 180 days • Past 365 days	3		
Visit Non-Compliance	Compliance	Continuous	Patient's visit compliance rate in • Past 90 days • Past 180 days • Past 365 days	3		
Medication Non-Compliance	Compliance	Continuous	Patient's PDC in • Past 90 days • Past 180 days • Past 365 days	3		

Relevant Medications

Medications identified from [69] which may be used as features

- Glucagon-like peptide-1 agonists
- Dipeptidyl peptidase-4 inhibitor
- Acarbose or Miglitol
- Repaglinide or Nateglinide
- Metformin
- Pramlintide
- ACE-inhibitors
- Angiotensin II blockers
- Beta adrenergic blockers
- Calcium channel blockers

- Thiazides/related diuretics
- Potassium sparing diuretics
- Loop diuretics
- Alpha-adrenergic blockers
- Statin
- Bile acid resins
- Fibrates
- Niacin
- Ezetimibe
- Antidepressant
- Cholinesterase inhibitor
- Benzodiazepines
- Neuroleptics
- Memantine
- Anti-seizure meds
- Anti-arrhythmia meds
- Digoxin
- Estrogen agonist
- Anti-bisphosphonate
- Corticosteroid
- Levothyroxine
- Codeine
- Tramadol
- Quinolone
- Calcitriol
- Epoetin
- Warfarin