Predictive Modeling of Incident Heart Failure in Subjects with Newly Diagnosed Atrial Fibrillation.

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CONFLICT OF INTEREST STATEMENT

BACKGROUND

- The incidence of both atrial fibrillation (AF) and heart failure (HF) have been increasing over the past 20 years in the US.
- It is estimated that by 2030 in the US, there will be 12 million people with AF and over 8 million with heart failure. [1, 2]
- Many studies have demonstrated a relationship between the 2 diseases; those with either one of the conditions are at a higher risk to develop the other condition than those without the condition.
- Negative outcomes including stroke, myocardial infarction, and death are experienced at a higher rate in those with both conditions compared to those with only one of the conditions.
- It is therefore important to be able to predict which newly diagnosed AF patients are most likely to develop HF so that appropriate preventive measures may be taken earlier in the course of the disease.
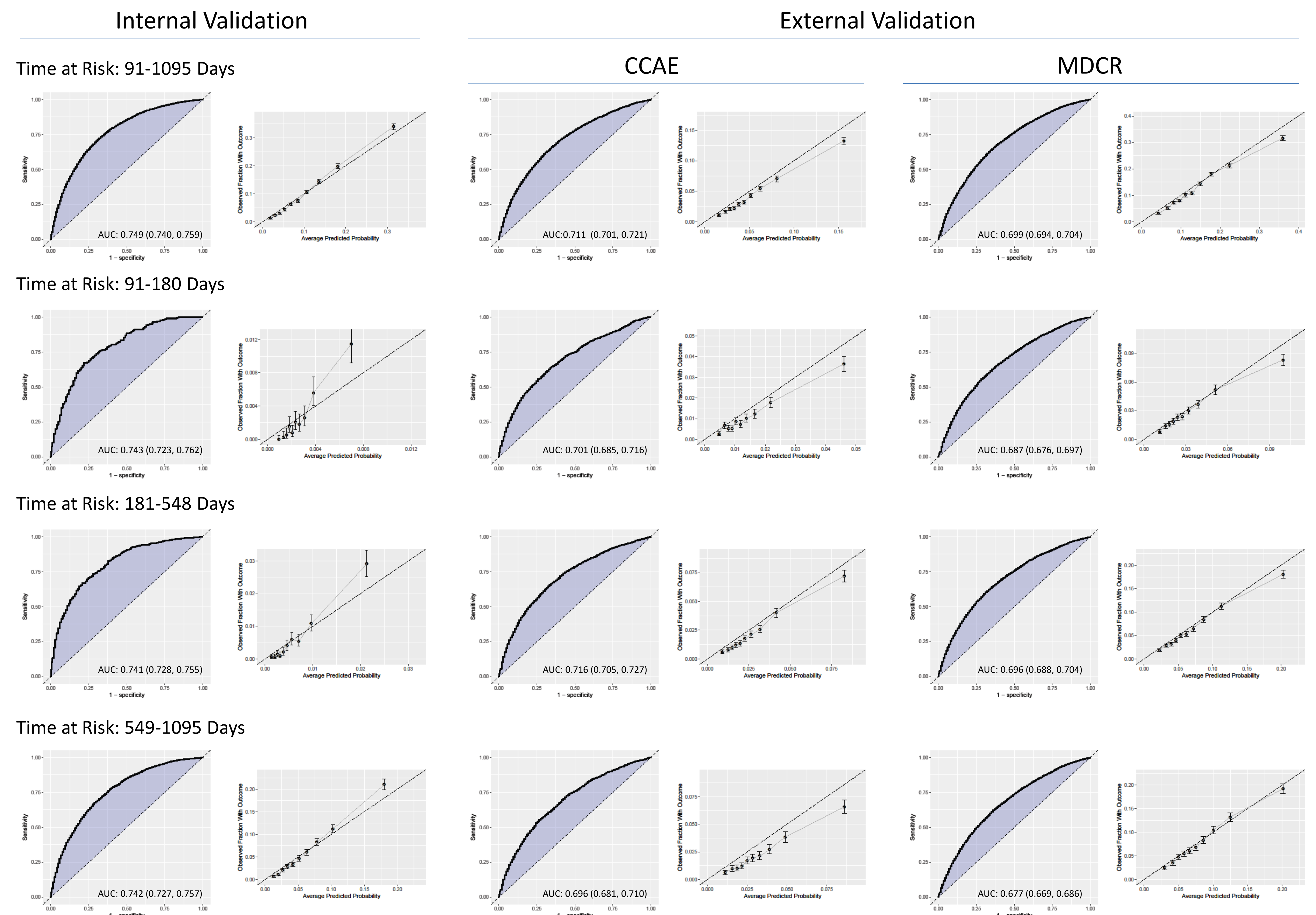
OBJECTIVES

To use machine learning to develop a model for predicting the probability of developing HF in patients with newly diagnosed AF.

METHODS

- Data for this study was collected between January 1, 2000 and December 31, 2016 from 3 data sets: Truven MarketScan Commercial Claims and Encounters (CCAE), Truven Medicare (MDCR), and OptumInsight's de-identified Clinformatics® Datamart (Eden Prairie,MN) (Optum).
- The databases had been transformed from their original form into the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).
- The cohorts were developed using the OHDSI Atlas tool.
- The cohort definitions used were as follows:

1) Target population: Patients ages 40-70 years old with newly diagnosed AF
   - A condition code for AF for the first time in a person's history (index date)
   - A follow-up condition code for AF between 1 and 60 days following the index date
   - No condition codes for HF in the person's history prior to or 90 days after the index date
   - At least one in-patient or out-patient visit occurrence between 1 and 180 days prior to index date and at least one visit occurrence between 181 and 365 days prior to the index date
   - A continuous observation period of at least 365 days prior to the index date

2) Outcome population: Patients with newly diagnosed HF
   - A condition code for HF for the first time in a person's history
   - A follow-up condition code for HF between 1 and 60 days following the initial HF diagnosis

- Models were developed using the Optum dataset for 4 different times-at-risk for incident HF: 3-36 months, 3-6 months, 6-18 months, or 18-36 months after the AF index date.
- For each time-at-risk, we required a minimum continuous observation period after the index date up to the start of the period, e.g., for the 3-6 month time-at-risk window, patients eligibility required having at least 3 months continuous observation after the index date.
- For these analyses, the R PatientLevelPrediction package was used.
- We included covariates for condition occurrence, drug exposure, and clinical observations and measurements within 365 days prior to the index date.
- LASSO (L1) logistic regression models were trained on 75% of the cohort records ("training data set") and tested on the remaining 25% ("test data set").
- Internal validation of model performance was through analysis of the area under the Receiver Operator Characteristic (ROC) curves (AUC) and calibration of the Optum test data set.
- External validation of model performance was through analysis of the AUC and calibration of the CCAE and MDCR datasets.

RESULTS

	Database	Risk Period Start	Risk Period End	Total Population	Number of Outcomes	Percent with Outcome	AUC (95% CI)	Calibration Intercept	Calibration Slope
Internal Validation	Optum	91	1095	114,019	11,779	10.3%	0.749 (0.740, 0.759)	-0.002	1.02
	Optum	91	180	104,858	2,618	2.5%	0.743 (0.723, 0.762)	-0.003	1.13
	Optum	181	548	97,088	5,244	5.4%	0.741 (0.728, 0.755)	0.000	1.00
	Optum	549	1095	63,766	3,893	6.1%	0.742 (0.727, 0.757)	-0.004	1.05
External Validation	CCAE	91	1095	112,184	4,825	4.3%	0.711 (0.701, 0.721)	-0.004	0.89
	MDCR	91	1095	91,369	11,864	13.0%	0.699 (0.694, 0.704)	-0.003	0.92
	CCAE	91	180	108,573	1,213	1.1%	0.701 (0.685, 0.716)	-0.001	0.81
	MDCR	91	180	81,995	2,487	3.0%	0.687 (0.676, 0.697)	0.001	0.86
	CCAE	181	548	97,921	2,204	2.3%	0.716 (0.705, 0.727)	-0.003	0.93
	MDCR	181	548	76,996	5,099	6.6%	0.696 (0.688, 0.704)	-0.001	0.92
	CCAE	549	1095	61,682	1,400	2.3%	0.696 (0.681, 0.710)	-0.004	0.81
	MDCR	549	1095	53,192	4,261	8.0%	0.677 (0.669, 0.686)	-0.004	1.01

Internal Validation

Time at Risk: 91-1095 Days
AUC: 0.749 (0.740, 0.759)

Time at Risk: 91-180 Days
AUC: 0.743 (0.723, 0.762)

Time at Risk: 181-548 Days
AUC: 0.741 (0.728, 0.755)

Time at Risk: 549-1095 Days
AUC: 0.742 (0.727, 0.757)

External Validation

CCAE
- AUC:0.711 (0.701, 0.721)
- AUC: 0.701 (0.685, 0.716)
- AUC: 0.716 (0.705, 0.727)
- AUC: 0.696 (0.681, 0.710)

MDCR
- AUC: 0.699 (0.694, 0.704)
- AUC: 0.687 (0.676, 0.697)
- AUC: 0.696 (0.688, 0.704)
- AUC: 0.677 (0.669, 0.686)

CONCLUSIONS

- The models developed using the OHDSI PatientLevelPrediction package appear to show promise in predicting patients with AF at risk for developing HF between 3 months and 3 years after initial AF diagnosis.
- Future work in this area might include examining models after separating HF patients into the more homogeneous divisions of HF with reduced or preserved ejection fraction as these two types have very different etiologies.

REFERENCES

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