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Validation of Predictive Score of 30-day Hospital Readmission or Death among Patients with Heart Failure

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Abstract

Existing prediction algorithms for the identification of heart failure (HF) patients at high risk of readmission or death after hospital discharge are only modestly effective. We sought to validate a recently developed predictive model of 30-day readmission or death in HF using an Australia-wide sample of patients. This study used data from 1046 HF patients at teaching hospitals in five Australian capital cities to validate a predictive model of 30-day readmission or death in HF. Besides standard clinical and administrative data, we collected data on individual socio-demographic and socio-economic status, mental health (PHQ-9 and GAD-7 score), cognitive function (MoCA score), and 2D echocardiograms. The original sample used to develop the predictive model and the validation sample had similar proportions of patients with an adverse event within 30 days (30% vs 29%, p=0.35) and 90 days (52% vs 49%, p=0.36). Applying the predicted risk score to the validation sample provided very good discriminatory power (C-statistic=0.77) in prediction of 30-day readmission or death. This discrimination was greater for predicting 30-day death (C-statistic=0.85) than for predicting 30-day readmission (C-statistic=0.73). There was little difference in the performance of the predictive model among patients with either LVEF<40% or LVEF≥40%, but an attenuation in discrimination when used to predict longer-term adverse outcomes. In conclusion, our findings confirm the generalizability of the predictive model that may be a powerful tool for targeting high-risk HF patients for intensive management.

Key words: algorithm; mortality; rehospitalisation; risk score; quality.

Heart failure (HF) is the leading cause of hospitalization and re-hospitalization for adults aged >65 years.[1, 2] High readmission rates following an index HF admission continue to be a problem in many countries and across different racial and ethnic groups.[3-5] In Australia, approximately 30,000 patients are diagnosed with HF each year and the costs for HF readmissions exceed $1 billion annually.[6] Readmission for HF is a powerful independent predictor of death among patients with HF, as well as being a serious health economic problem.[7, 8] Readmissions shortly after discharge are expensive and often considered preventable.[2] Recently, all-cause mortality and readmission within 30 days of a prior hospitalization for HF has emerged as a major focus of quality improvement and payment reform.[9] However, despite a number of interventions, readmission rates have been difficult to reduce.[10] This may be partly due to failure to target the interventions to patients at high risk of readmission. Financial constraints also become a problem when these interventions are applied indiscriminately to all patients.[11] We have recently developed a predictive model for 30-day readmission or death in HF,[12] which combined both clinical and non-clinical factors to provide excellent discriminatory power (C-statistic 0.82). We now aim to validate this predictive model on an Australia-wide cohort of HF patients.

Methods

This study used data from 1046 consecutive HF patients who were recruited during 2015–2017 in most Australian States (Tasmania, Victoria, New South Wales, Queensland and South Australia). Patients were identified as eligible if their primary diagnosis was confirmed as HF by their treating physicians. Exclusion criteria were: <18 years of age, inability to provide written consent, moderate or worse primary mitral or aortic valve disease, concomitant unstable angina pectoris or acute myocardial infarction as the primary cause of admission, cardiac device malfunction, infective endocarditis, patients with left ventricular assist device, patients with potentially reversible left ventricular (LV) dysfunction including post-partum, alcoholic cardiomyopathy and hyperthyroidism, and concomitant terminal non-cardiac illnesses that could influence 12 month prognosis. All patients

provided written consent. The study was approved by the Tasmanian Human Research Ethics Committee.

Clinical data included past medical history (including chronic kidney disease based on discharge coding), medications, physical measurements and blood tests before discharge. Standard physical measurements included body weight, blood pressure, heart rate, respiratory rate, and electrocardiography. Two-dimensional echocardiographic parameters included LV ejection fraction (EF), LV volume index, left atrial volume index, right atrial pressure, pulmonary arterial systolic pressure and estimated LV filling pressure (E/e'), using standard techniques and procedures following the American Society of Echocardiography guideline.[13] Biochemical measurements included troponin I, C-reactive protein, albumin, blood urea nitrogen, sodium, creatinine, hematocrit, hemoglobin, cholesterol, and B-type natriuretic peptide. HF functional class was defined using the New York Heart Association (NYHA) Class. The Charlson comorbidity index was calculated as previously described.[14] Patients were considered to have a history of life-threatening arrhythmia if they had an episode of ventricular tachycardia or fibrillation shortly prior to (as part of the reasons for the baseline admission) or during their admission with HF. Patients' cognitive function was assessed before discharge by trained personnel using the Montreal Cognitive Assessment (MoCA). The MoCA examines different domains of cognition and was designed to detect mild cognitive impairment with excellent sensitivity (90%) and specificity (87%).[15] A MoCA score <26 was used to define mild cognitive impairment. Patients who did not finish college/grade 12 had one point added as instructed in the MoCA protocol. Depression was assessed using the Patient Health Questionnaire (PHQ-9), with cut-points of 5, 10 and 15 used to define mild, moderate and moderately severe/severe depression respectively.[16] Anxiety was assessed using the Generalized Anxiety Disorder scale (GAD-7), with cut-points of 5, 10 and 15 used to define mild, moderate and severe anxiety respectively.

Non-clinical data included age, sex, language background, marital status, living alone, education, residential address, medical insurance, and any home health care services provided. Socioeconomic status based on residential postcode was derived using the Australian Bureau of Statistics Index of Relative Socioeconomic Disadvantage.[17] The remoteness index - based on

residential address - reflects how far away a geographical area is from service towns of different sizes based on road distance.[18]

This model was developed to predict 30-day all-cause readmission or death in HF.[12] It incorporates social history (living alone or with others), medical data (life-threatening arrhythmia, heart rate, NYHA classification, and whether being discharged in winter), cognitive function, mental health, echocardiographic data (left atrial volume index, right atrial pressure) and lab test (blood urea nitrogen, serum albumin). The development of this model has been previously described.[12] Briefly, logistic regression was used to determine and rank the variables that served as best predictors of readmission or death. A predictor was included in the final model if it contributed ≥0.01 unit to the area under the curve.

For descriptive statistics, we reported categorical variables as the number of patients with percentages, and continuous variables as median with interquartile range. A score of predicted risk was calculated for each patient in the validation sample using the predictive model coefficients and intercept that were previously described in the original publication.[12] These predicted scores were then converted to percentages to reflect how likely a patient was going to have an adverse outcome. We also used this predicted score to estimate the area under the curve and compared against the observed risk of having the adverse outcomes. Plots of the predicted risk vs. the observed risk outcomes were also used to evaluate the model's calibration. Youden's index was used to define the optimal cut-point of the risk score and to accordingly calculate its sensitivity and specificity.

Results

Table 1 compares baseline characteristics between patients in the original sample whose data were used to develop the predictive model and patients in the validation sample. The two samples of patients had similar age at admission and similar male-female ratio. However, there was significantly lower proportion of patients in the validation sample living outside of a major city, having a history of smoking and having a history of arrhythmia. This may explain for the lower use of antiarrhythmic medication in the validation sample compared with that in the original sample, despite of similar use of other HF medications. While the proportion of HF patients with reduced LVEF was similar, the

validation sample had more patients with more severe HF (higher NYHA class) and more dilated LV than the original sample. There was no significant difference in cognitive function and other comorbidities between the two samples.

In general, the two samples had no significant difference in short-term adverse outcomes after discharge. Approximately one in three patients in either sample was readmitted or dead within 30 days of discharge, and one in two patients was readmitted or dead within 90 days (Table 2). Table 3 illustrates how to calculate predicted risk using the coefficients and intercept from the predictive model. The average risk score of the original sample (32%±27%) and the validation sample (34%±27%) were similar (p=0.42).

Figure 1 shows the area under the curve when predicting adverse outcomes within 30 days of discharge. Applying the predicted risk score to the validation sample provided very good discriminatory power (C-statistic=0.77 [95% CI: 0.74, 0.81]) in prediction of the composite outcome within 30 days of discharge in HF. This discrimination was greater for predicting 30-day death (C-statistic=0.85 [95% CI: 0.79, 0.91]) than for predicting 30-day readmission (C-statistic=0.73 [95% CI: 0.69, 0.77]). Figure 2 demonstrates little difference in the performance of the predictive model in patients with either LVEF<40% or LVEF≥40%. However, there was an attenuation in discriminatory power of the model when used to predict outcomes within 90 days of discharge (as shown in Figure 3).

Figure 4 shows very good calibration of the predictive model with observed events by plotting predicted vs. observed risk of 30-day readmission or death within the risk deciles. Although slightly overestimating the absolute values of observed risks, the predictive model has shown excellent accuracy in risk stratification among HF patients (Figure 5).

Youden's index was used to define optimal cut-points of the risk score. A predicted score of 44% risk (sensitivity 65%, specificity 81%) appeared to be optimal for 30-day readmission or death, and a predicted score of 29% risk (sensitivity 64%, specificity 65%) for 90-day readmission or death.

Discussion

The short-term risks of death or readmission after a hospitalization with HF remain very high. These outcomes are important for health care quality improvement, and are a central focus for patients, health care providers, taxpayers and policy makers. Effective targeting of disease management programs is likely to reduce readmissions at the same time as saving money. This, however, requires a reliable tool to identify high-risk patients who are most likely to benefit from the interventions.

This study used an Australia-wide sample of HF patients to validate a previously developed risk score of 30-day readmission or death. This model has shown excellent external validation and calibration, and may be used to predict both short-term mortality and readmission with very good discrimination. The availability of this risk score will facilitate targeting high-risk HF patients for intensive management, and therefore help to reduce readmissions. High-intensity home visiting programs may reduce all-cause readmission or death within 30 days of discharge among HF patients. Such programs are certainly expensive. Although a more detailed cost-effective analysis is required, the availability of our risk score may allow high-risk HF patients to be targeted for these programs and reduce cost. There was little difference in the performance of this model in predicting outcomes for patients with either reduced or preserved LVEF. The discriminatory power of the model was attenuated when used to predict longer-term adverse outcomes.

A systematic review of readmission risk scores in 2008 showed that the strongest prediction models provided only poor discrimination (C-statistic<0.6) in predicting readmissions among HF patients.[19] Several risk scores for the prediction of HF readmission have been developed and validated.[3, 20-24] Despite the use of large samples, these models - which mainly consist of standard clinical parameters and comorbidities – are only modestly effective in predicting short-term outcomes in HF. These findings suggest that some important determinants of readmission were missing in the previous models. Of these previous models, the one developed by Amarasingham[24] combined a range of clinical and non-clinical factors (some of which are similar to those of ours such as living arrangement and mental health) and is therefore most discriminative (C-statistic 0.72). However, this model used data from the electronic medical record, and did not include echocardiographic

parameters and cognitive function that are shown to be very important for 30-day adverse outcomes in our study. This may explain their lower C-statistic than that of our prediction model – which, to the best of our knowledge, has the greatest discriminatory power so far reported for prediction of short-term adverse outcomes among HF patients.

These factors may include readiness for discharge, ability for self-care and family/social support. A discharge echocardiogram to assess the level of congestion may help to determine if a patient is ready for discharge. A cognitive function test reflects a patient's ability for self-care, which is a key to health maintenance and adherence to treatment. Whether a patient is living alone, with family or in a nursing facility indicates how much support the patient may need. All these factors were incorporated in the model that we tested in this study, which resulted in a very good predictability of both 30-day readmission and 30-day death in HF. Our validation of the model using an Australia-wide cohort of HF patients further confirms its generalizability.

Common clinical factors such as prescription of evidence-based medications or Charlson's comorbidity index, which are known to be predictors of long-term adverse outcomes in HF, were associated with the outcome in univariable analysis. However, these associations became weaker in multivariable analysis and did not add incremental value to the discriminatory power of the prediction model. These findings suggest that readmission shortly after discharge may be driven, not only by quality of care or severity of disease, but also by other factors such as social or family support, cognitive function or mental health.

Our findings support the importance of multidisciplinary care to reduce short-term adverse outcomes in HF patients. Some of the risk factors in the model are potentially reversible with appropriate care. Although limited data show that therapeutic interventions to improve cardiac function such as heart transplantation,[25] medications,[26, 27] and exercise training[28] might improve cognition in some HF patients, it is likely that additional support and assistance would help most patients with poor cognitive function. Provision of greater nursing and medical attention to enhance adherence to treatment plan and medications may reduce short-term readmission and mortality risk

among these high risk patients. Depression is also potentially modifiable with pharmaceutical and/or psychological treatment. Although the mechanism underlying the relationship between depression and readmission or death in HF is unknown, data have shown that differences in help-seeking behaviour,[29] health behaviour and treatment adherence[30] may play a role.

This study included a range of patients from a multicenter study of HF, which favors the generalizability of our findings. The prospective nature of this study allowed us to collect a wide range of potential predictors and avoid the known limitations of administrative codes as in retrospective studies. The very good discriminatory power from our external validation further confirms the applicability of the prediction model to an external HF population.

Because of the use of a composite outcome, the prediction model could not differentiate strong predictors of one outcome from those of the other. However, the primary aim of this work was to develop a simple and feasible tool that can quickly and accurately stratify HF patients in the busy setting of clinical practice. This model has proven to have excellent discrimination for both readmission and mortality. Although the predicted risks appear to overestimate the absolute values of observed risk, they are strongly correlated and show consistent risk stratification among HF patients. Our sample however included mostly Caucasian patients, and validation of the model on other ethnic groups is required.

In conclusion, short-term risk of readmission and death after hospitalization for HF remain very high. Preventing such events is complex and requires multidisciplinary efforts. Our previously developed predictive model – which had excellent external validation and calibration – may be a powerful tool for this purpose. The availability of this model will facilitate targeting high-risk HF patients for intensive management, and therefore may help to reduce readmissions.

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Figure legends

Figure 1. Area under the curve of the predictive model with 30-day death (A), 30-day readmission (B) and the composite outcome (C)

Figure 2. Area under the curve of the predictive model with 30-day readmission or death among patients with LVEF<40% (A) and LVEF≥40% (B).

Figure 3. Area under the curve of the predictive model with 90-day death (A), 90-day readmission (B) and the composite outcome (C)

Figure 4. Calibration of the predictive model with observed events. The graph plots the predicted risk vs. observed 30-day readmission or death within the risk deciles (intercept 3.02, slope 0.79, R^2 96%, P<0.001).

Figure 5. Accuracy of the predictive model for risk stratification among HF patients. There is a slight over-estimation of the absolute values of observed risks.

Table 1. Patients' baseline characteristics

	Original sample* (n=430)	Validation sample (n=1046)	
Potential predictors	Description	Description	p
Age at admission (year)	75 [64, 83]	76 [67, 84]	0.72
Men	236 (55%)	607 (58%)	0.78
Completed education (≥ High school)	220 (52%)	523 (50%)	0.31
Living alone	129 (30%)	366 (35%)	0.85
Living outside of a major city	172 (40%)	345 (33%)	0.05
Smoker (ever vs never)	301 (70%)	721 (69%)	0.75
Solid organ tumor	30 (7%)	73 (7%)	0.97
Diabetes mellitus			0.37
Mild, without complications	125 (29%)	293 (28%)	
Complications/End-organ damage	51 (12%)	115 (11%)	
Life-threatening arrhythmia	39 (9%)	67 (6%)	0.003
Cerebrovascular disease or stroke	51 (12%)	105 (10%)	0.13
Discharge during winter	116 (27%)	261 (25%)	0.32
Heart rate	75 [68, 86]	76 [68, 88]	0.50
Charlson comorbidity index	7 [5, 9]	7 [6, 9]	0.74
Chronic kidney disease	155 (36%)	377 (36%)	0.73
Cardiac catheterization (ever vs never)	172 (40%)	408 (39%)	0.87
NYHA class			<0.001
Class II or under	241 (56%)	418 (40%)	
Class III	150 (35%)	408 (39%)	
Class IV	39 (9%)	220 (21%)	
LVEF < 40%	206 (48%)	481 (46%)	0.55
Right atrial pressure (mmHg)	8 [3, 15]	8 [3, 15]	0.45

Left atrial volume index (ml/m^2)	42 [30, 60]	45 [34, 62]	0.77
Pulmonary systolic pressure (mmHg)	38 [30, 48]	38 [30, 48]	0.52
Left ventricular volume index (ml/m^2)	56 [43, 80]	65 [47, 83]	0.001
Blood urea nitrogen (mg/dL)	10.5 [7.6, 16.1]	10.1 [7.4, 15.1]	0.42
B-type natriuretic peptide (pg/mL)	784 [416, 1723]	1352 [788, 3581]	0.003
Serum albumin (g/dL)	35 [31, 38]	33 [30, 36]	0.36
C-reactive protein (mg/L)	10.5 [5.0, 25.4]	13.0 [5.8, 29.0]	0.30
Serum creatinine (μmol/L)	116 [90, 153]	112 [88, 152]	0.21
MoCA score	23 [18, 26]	22 [17, 26]	0.69
GAD-7 score	4 [1, 10]	4 [1, 9]	0.55
PHQ-9 score	9 [4, 15]	8 [4, 14]	0.37
Aldosterone use	202 (47%)	471 (45%)	0.84
ACE-inhibitor/ARB use	348 (81%)	868 (83%)	0.31
Antiarrhythmic medication use	73 (17%)	125 (12%)	0.005
Beta-blocker use	327 (76%)	805 (77%)	0.74

*The sample of patients that was used to developed the risk score of 30-day readmission or death in heart failure.

Data are shown as median [interquartile range] or number (percentage).

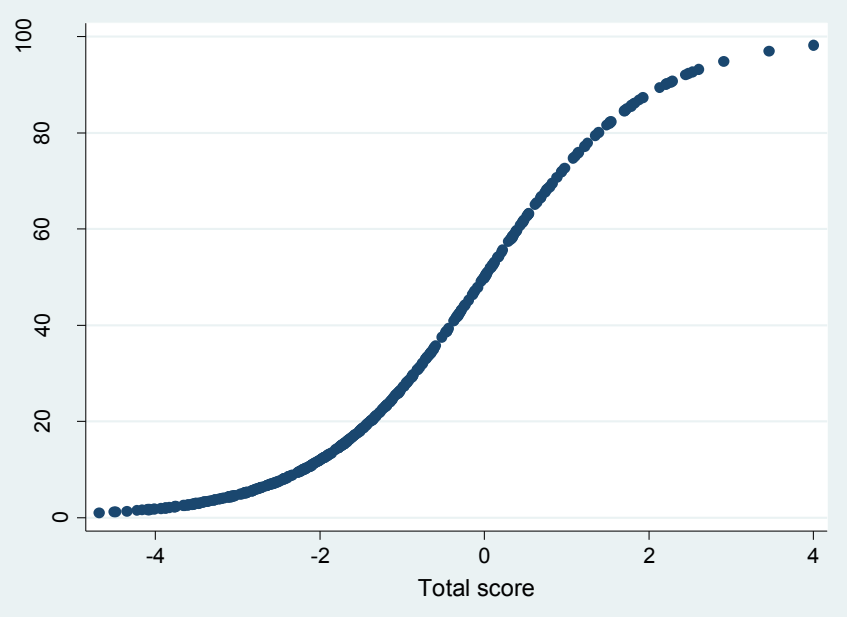
Table 2. Short-term adverse outcomes in heart failure

Observed risk of adverse outcomes		Original sample* (n=430) n (%)	Validation sample (n=1046) n (%)	p
Within 30 days	Death	38 (9%)	72 (7%)	0.09
	Readmission	92 (21%)	249 (24%)	0.11
	Composite outcome	130 (30%)	303 (29%)	0.35
Within 90 days	Death	64 (15%)	135 (13%)	0.15
	Readmission	185 (43%)	439 (42%)	0.36
	Composite outcome	224 (52%)	509 (49%)	0.36

*The sample of patients that was used to developed the risk score of 30-day readmission or death in heart failure.

Table 3. Estimating risk of 30-day readmission or death in heart failure using the prediction model

Predictors	Value		Coefficient		Score
NYHA class	.....	×	0.67	=	.....
MoCA score	.....	×	−0.10	=	.....
Left atrial volume index (ml/m^2)	.....	×	0.02	=	.....
Right atrial pressure (mmHg)	.....	×	0.06	=	.....
Discharge in winter (Y=1 vs N=0)	.....	×	0.49	=	.....
Living alone (Y=1 vs N=0)	.....	×	0.72	=	.....
Blood urea nitrogen (mmol/l)	.....	×	0.04	=	.....
PHQ-9 score	.....	×	0.03	=	.....
Heart rate (per bpm)	.....	×	0.02	=	.....
Albumin (g/dl)	.....	×	−0.05	=	.....
Life-threatening arrhythmia (Y=1 vs N=0)	.....	×	1.07	=	.....
Intercept				=	−3.31
			Total score	=	



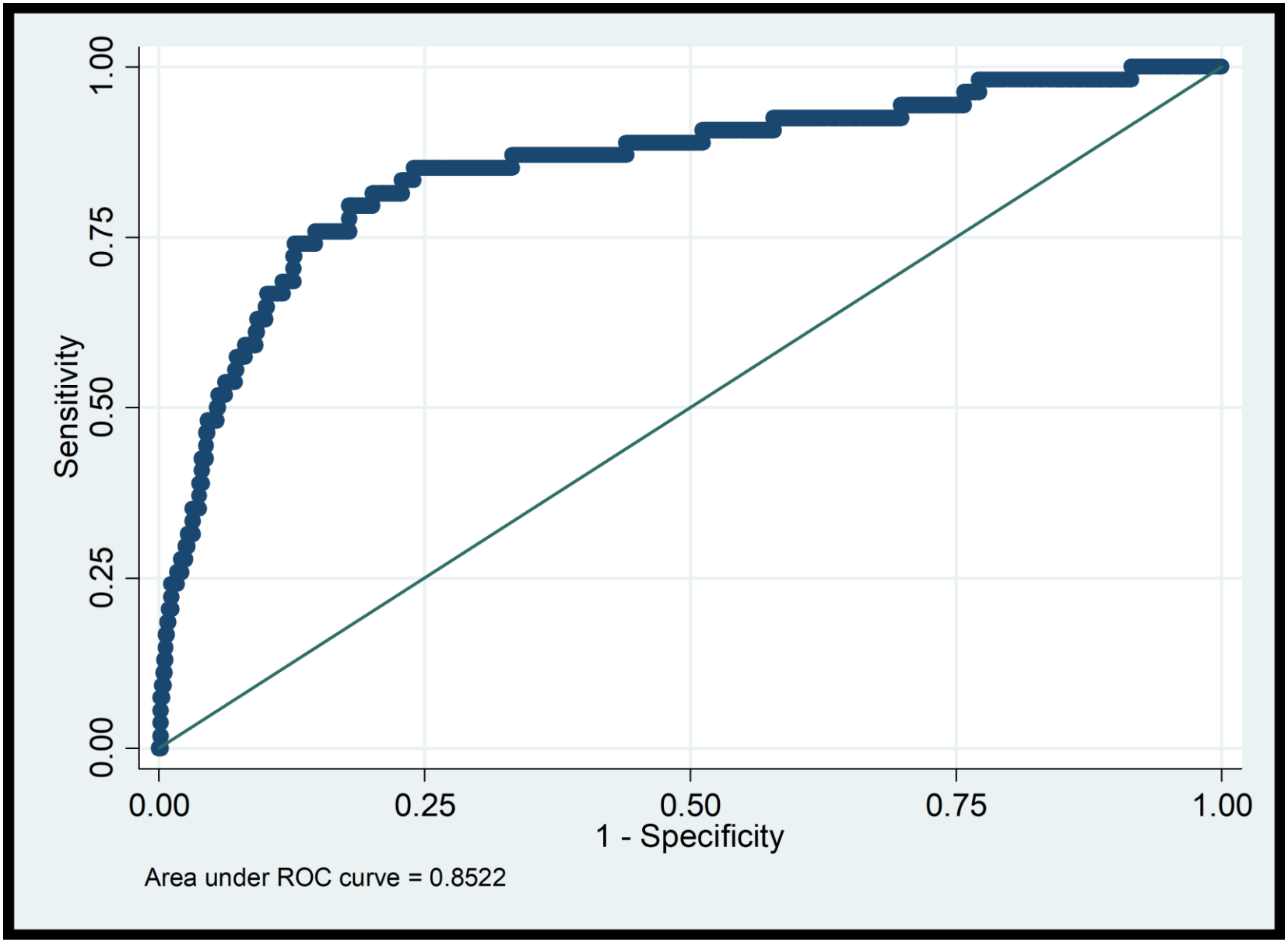


Figure 1A_bestsetConverted.png

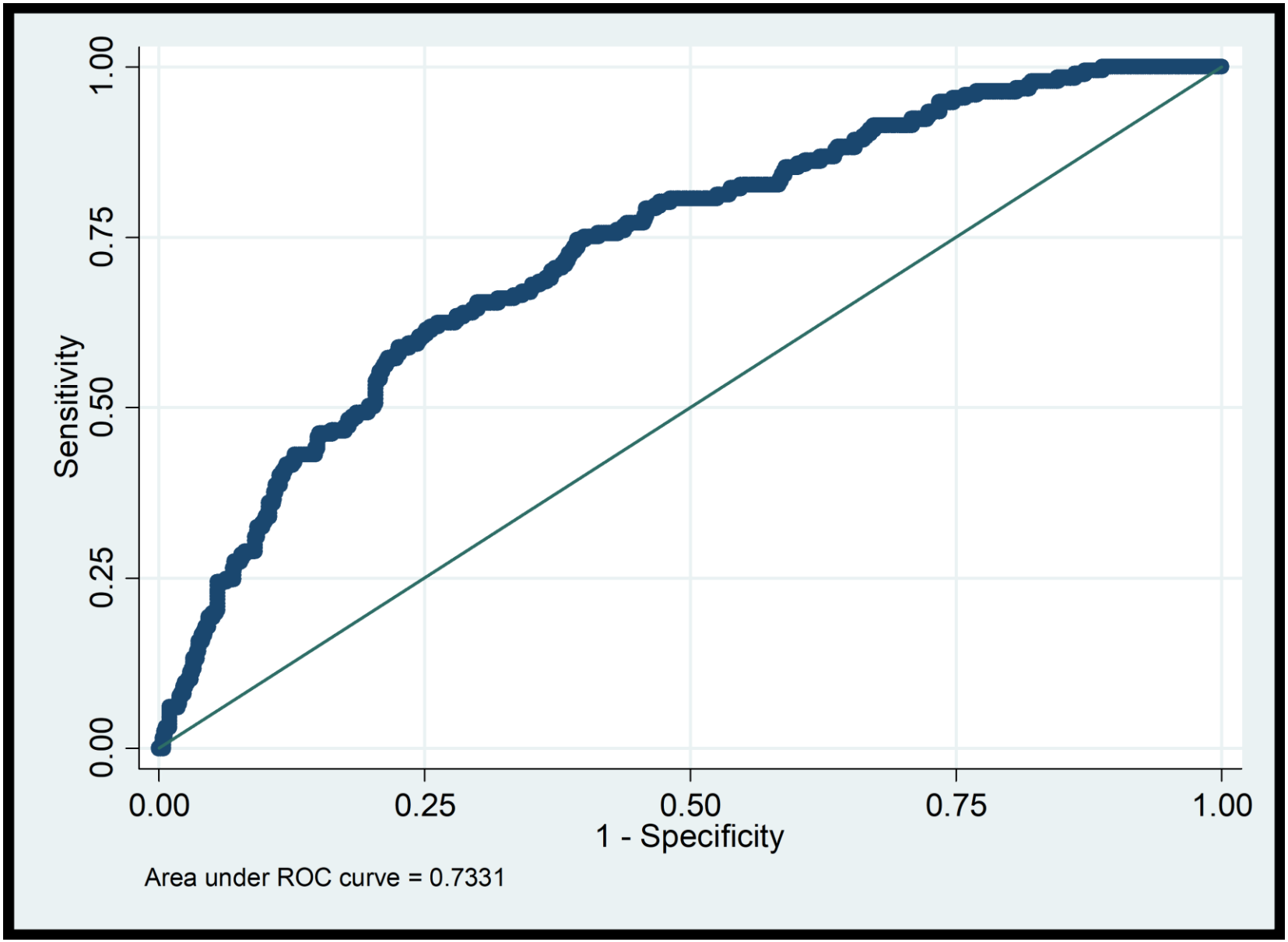


Figure 1B_bestsetConverted.png

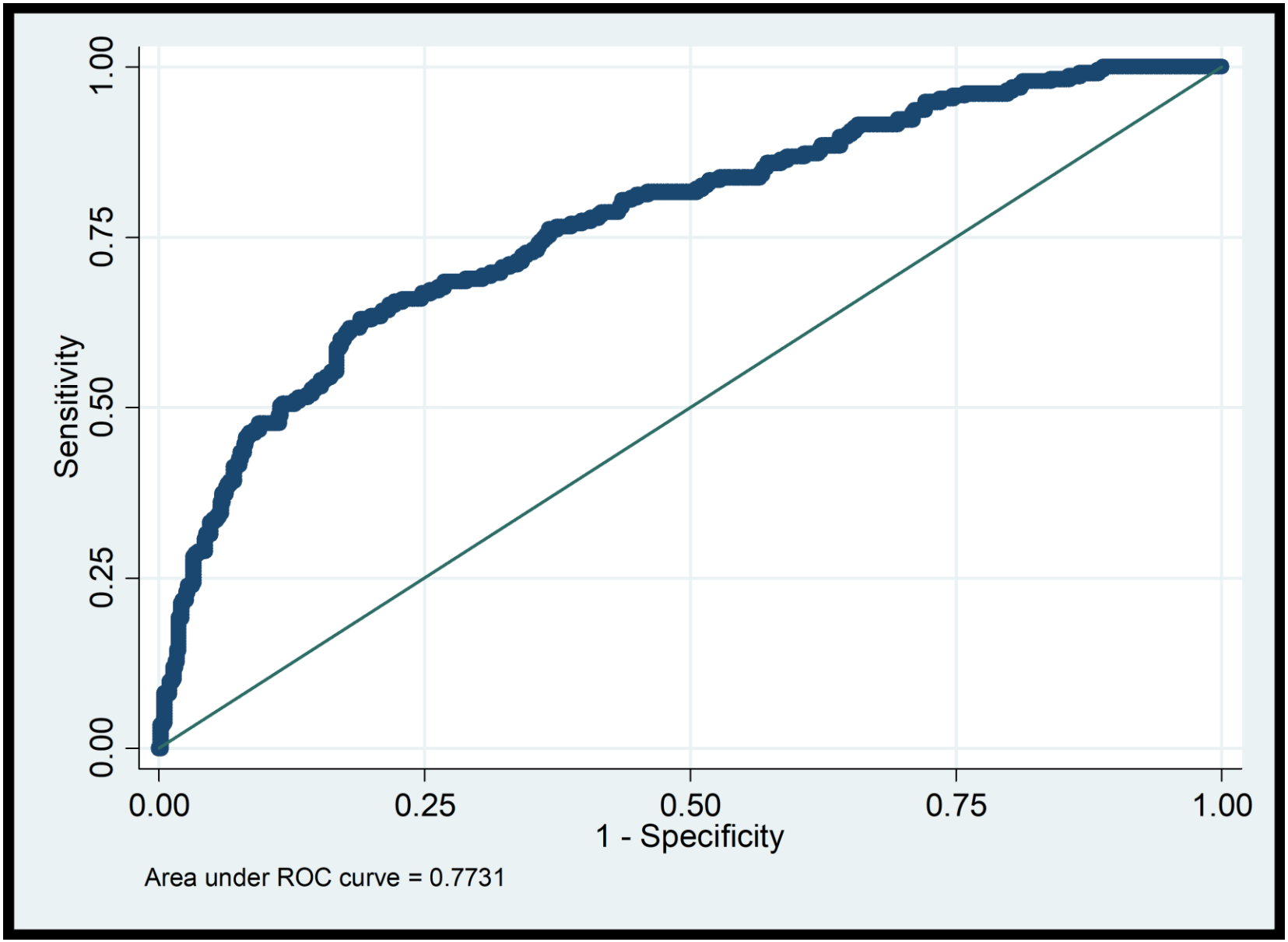


Figure 1C_bestsetConverted.png

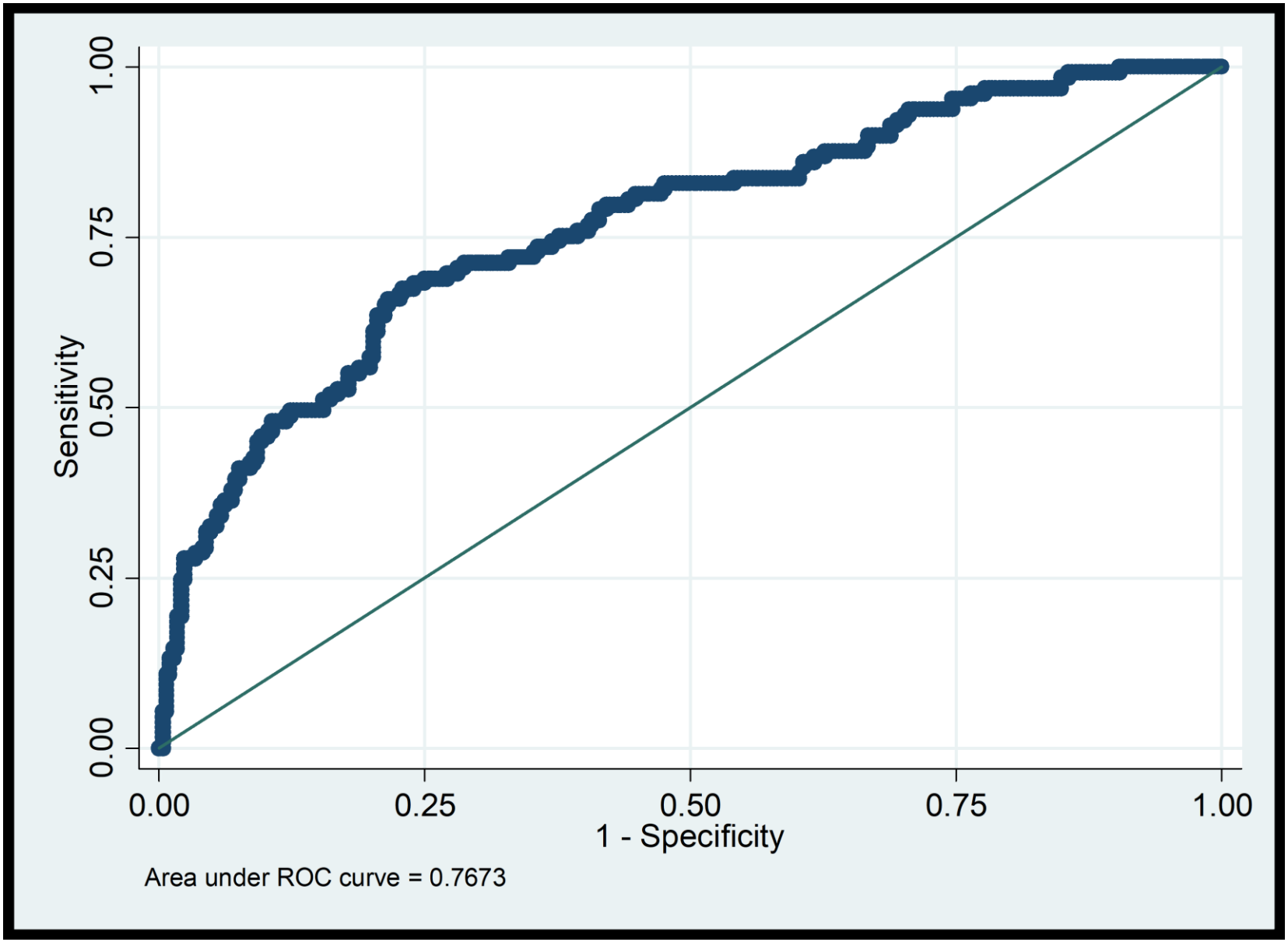


Figure 2A_bestsetConverted.png

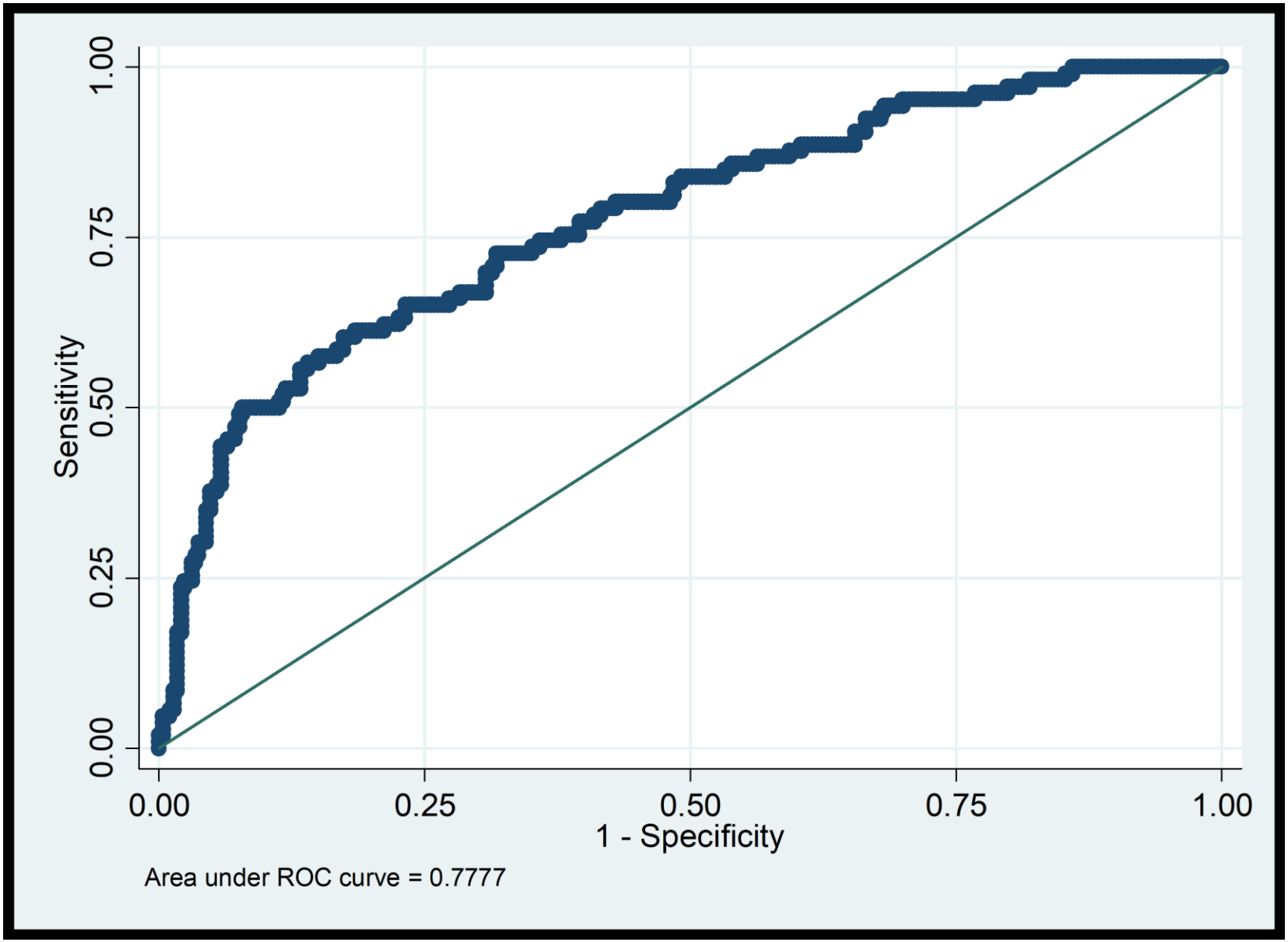


Figure 2B_bestsetConverted.png

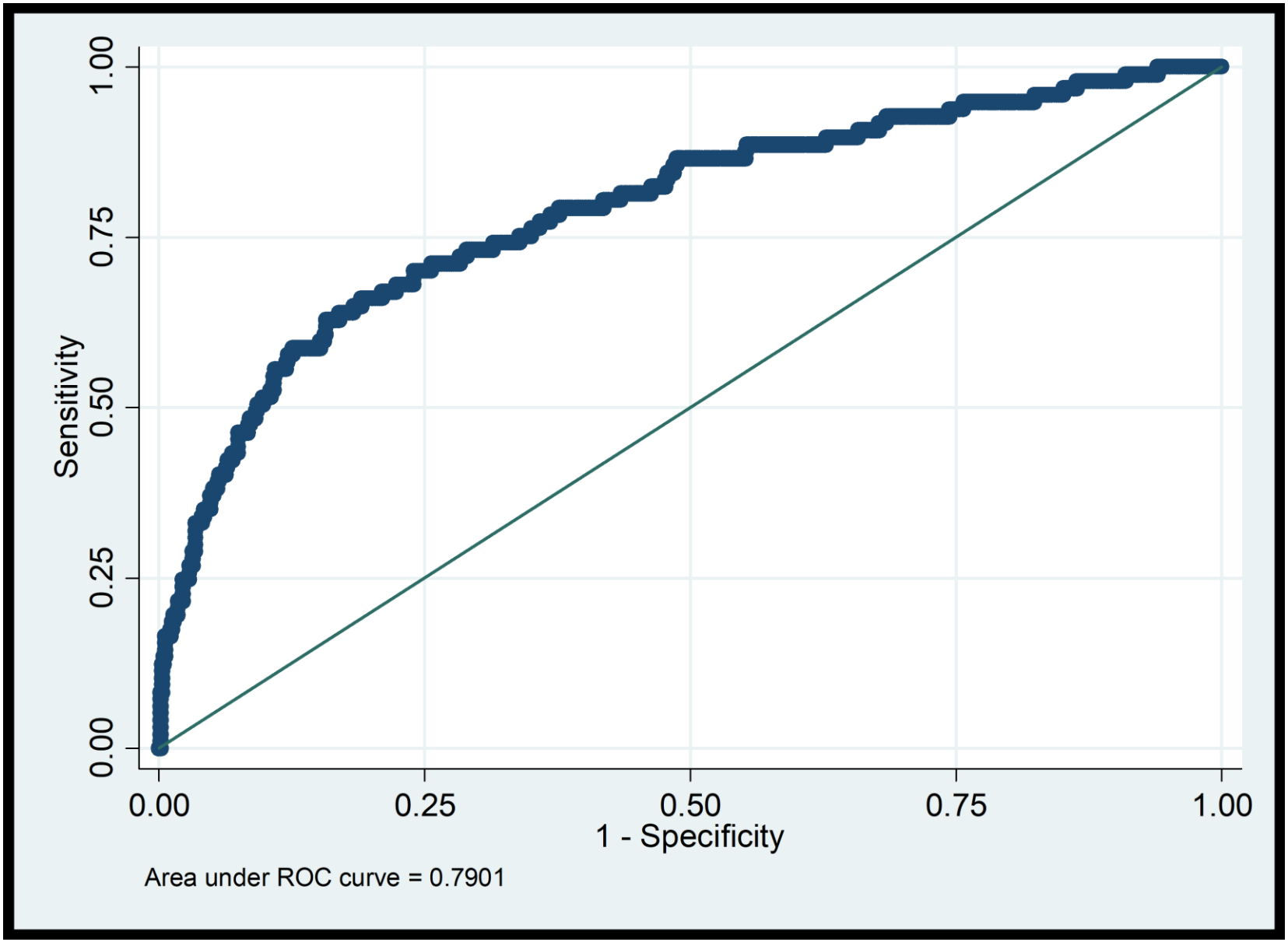


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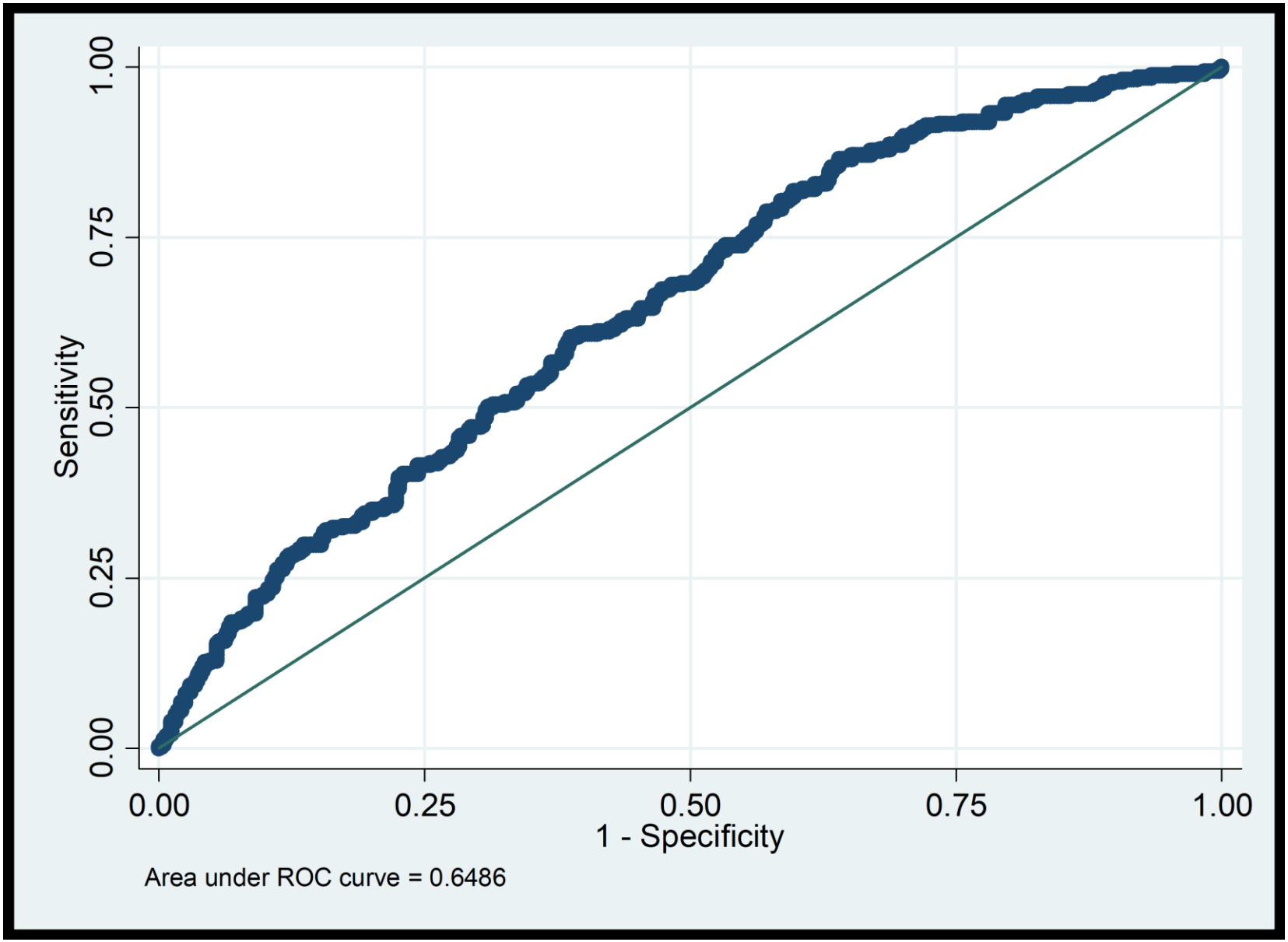
Figure 3A_bestsetConverted.png



30

Figure 3B_bestsetConverted.png

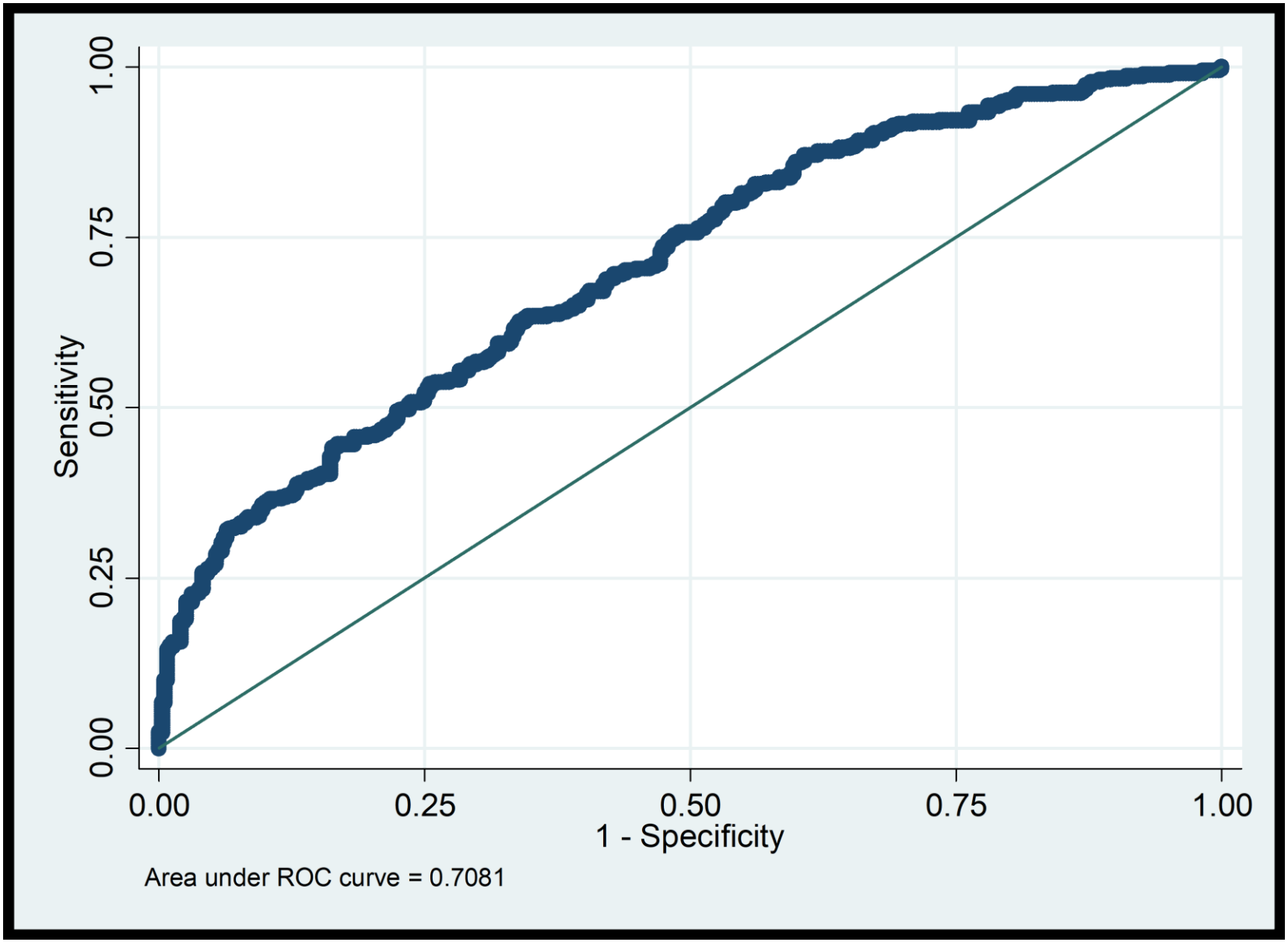


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Figure 3C_bestsetConverted.png

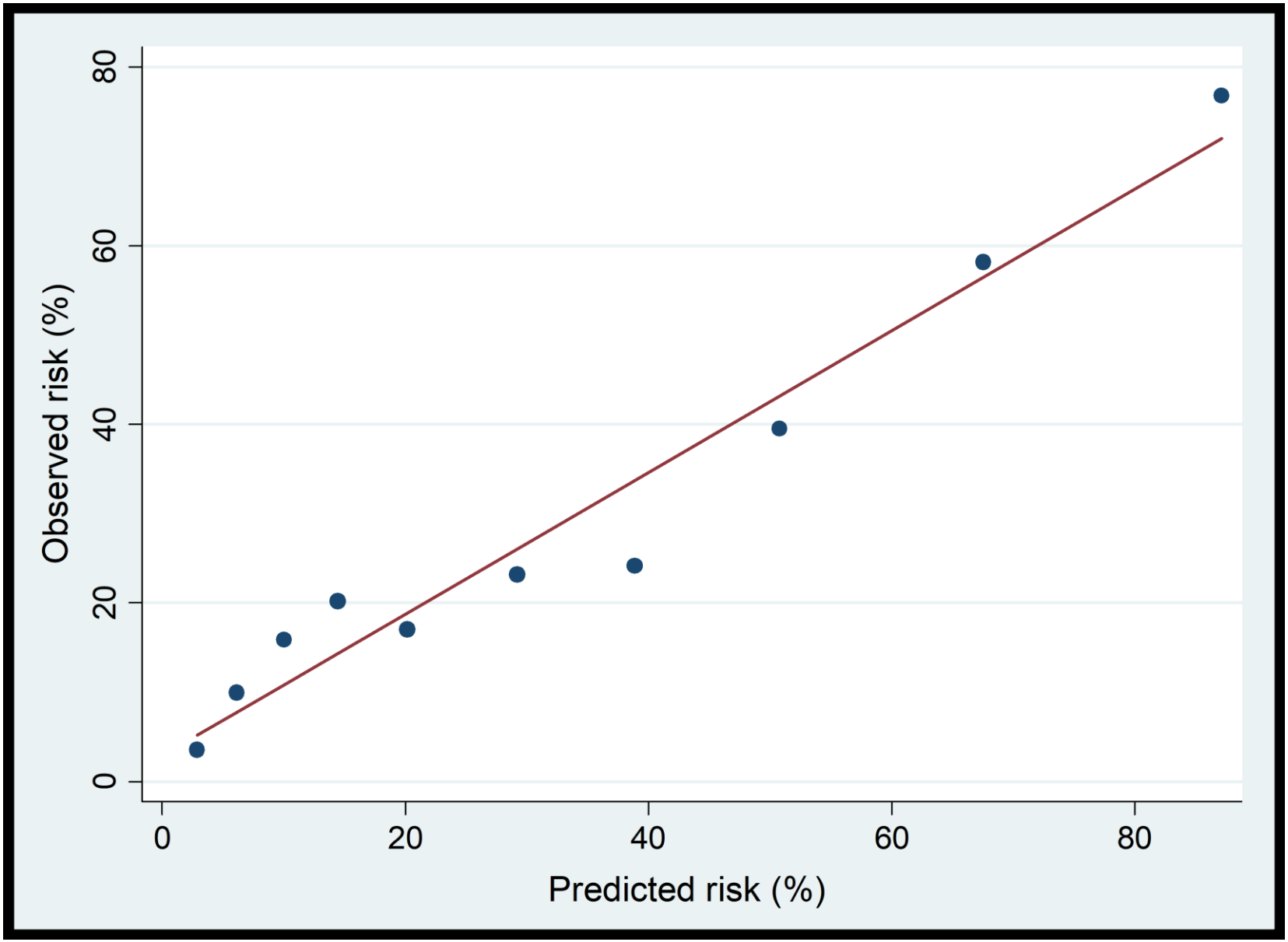

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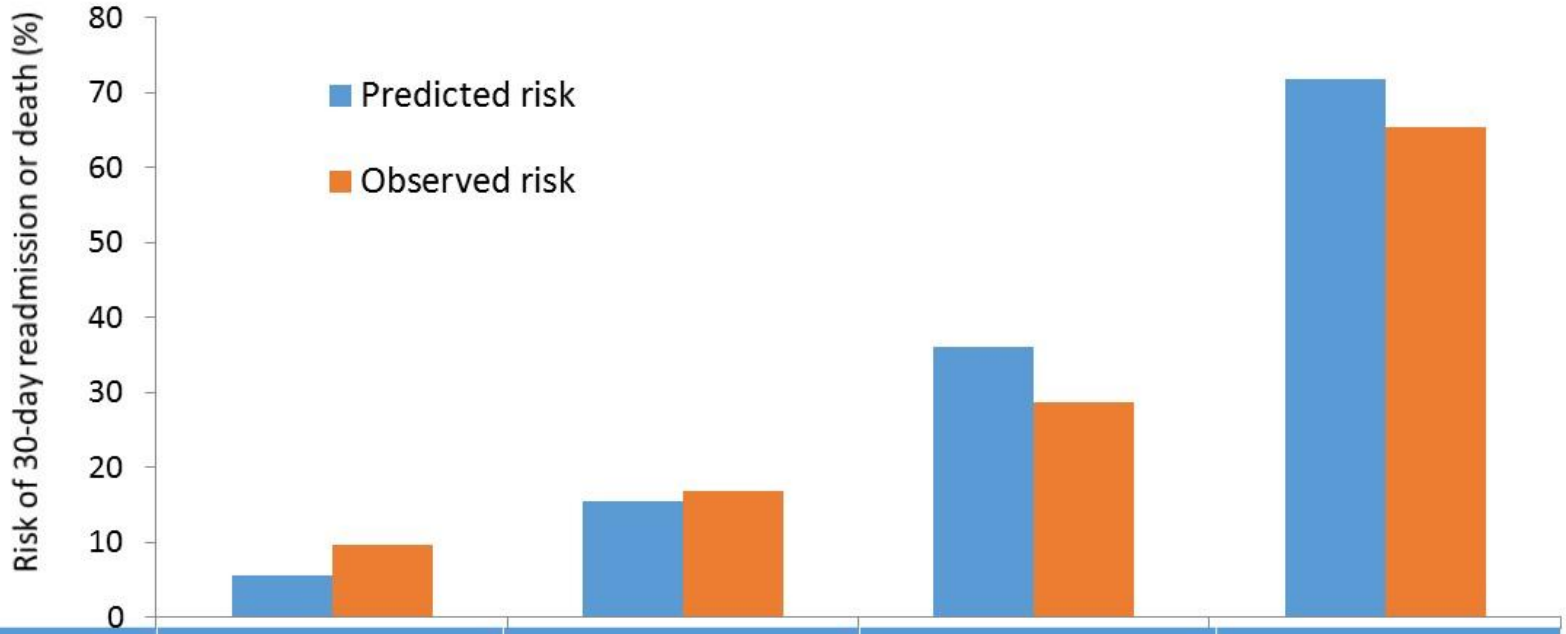
Figure 4_bestsetConverted.png



Risk category	I	II	III	IV
n	262	262	261	261
Predicted score	−2.8 (−3.3, −2.5)	−1.7 (−2.0, −1.4)	−0.6 (−0.8, −0.3)	0.9 (0.4, 1.7)
Predicted risk (%)	5.5 (3.4, 7.4)	15.6 (12.4, 19.3)	36.1 (30.7, 42.7)	71.9 (60.3, 84.8)
Observed risk (%)	9.6 (6.3, 14.6)	16.9 (12.6, 22.9)	28.8 (23.2, 35.7)	65.5 (58.3, 78.6)

Figure 5_bestsetConverted.png