Model Evaluation

Considerations for Time-to-Event Studies

Daniel Saggau

11/15/2020

Overview

- Time to Event Studies:

What is a time to event study ?

- Classical Model Evaluation:

Why cant we use them?

- TTS Model Evaluation:

How do we derive these methods (c-index, ibs)?

- Discussion :

What are the shortcomings of these methods?

- Further Considerations:

What solutions exist?

Time-to Event Studies

- Analysis working with (right) censored data
- Right censored data (event after follow up) vs. left censored data (event was not recorded when it occured intially)
- Highly relevant for clinicians in the field of medical statistics e.g. looking at when a patient dies or when he gets a disease (clinical/epidemiological studies)
- In Economics/Finance e.g. to examine when a subject/borrower will default or when a subject will find/lose a job
- Operations research to predict the time a machine will break

Basic Notations & Concepts

- Time T and Survival S
- From hazard to cumulative hazard to survival
- Hazard h(t,x) is the eminent probability of death a specific point in time
- Capital H is the cumulative hazard
- non-parametric hazard models (KM) vs.semi-parametric proportional hazard model

Model Evaluation - Considerations

(1) *What type of study are we dealing with?*

Diagnostic vs. Prognostic Study

(2) *What are the components of our model evaluation metric?*

Discrimination: Are we able to correctly discriminate between e.g. sick and healthy patients ? **Calibration**: How concise is our prediction accuracy ? **Clinical Usefulness**: Will our model create more benefits than harm?

Classical Model Evaluation Tools for Classification Tasks

Working with *Label* vs. working with *Probability*

- Brier Score (probability from true class label)
-
- AUC/ROC (receiver operating characteristics)
- Mis-classification Error rate (rate of incorrect classification)
- ACC (rate of correct classifications)
- Concordance Statistics

Brier Score

- Based on loss function

MSE for Regression (L2 Loss):

$BS = \frac{1}{n} \sum_{i=1}^{n} (y^{(i)}) - \hat{y}^{(i)})^2$

Where: the $MSE \in [0; \infty)$

The Brier Score is the MSE for Classification:

$BS = \frac{1}{n} \sum_{i=1}^{n} (\hat{\pi}(x^{(i)}) - y^{(i)})^2$

The general version of the brier score looks at a specific point in time

Confusion Matrix

Sensitivity:

- deals with values above the threshold among the subject group which do endure an event
- Another common name for Sensitivity is the true positive rate.

$TPF = \frac{TP}{TP+FN}$

Specificity:

- deals with false negatives, hence patients with a disease we classify as not having any diseases
- Another name for specificity is the true negative rate

$TNR = \frac{TN}{TN+FP}$

Why cant we use traditional model evaluation tools for time to event studies?

- Working with censored data
- Need to estimate survival of patients without having data on e.g. death
- Account for time dependent covariates
-

Early approaches: - excluding subjects with right censored data and only evaluate on the complete data

From Harell's C to time dependent C-index

- Advancement of AUC

$$C^{td} = \frac{\pi_{concordance}}{\pi_{comparable}}$$

$$C^{t,d} = \frac{Pr(z(X_i) > z(X_j) \& T_i < T_j \& E_i = 1}{Pr(Ti < Tj | E_i = 1)}$$

c-index

- studying concordance pairs of subjects
- addressing right censored data via inverse of the probability of censoring weighted estimate (of concordance probability)
- kendall's tau as conservative weight
- Summary measure (over all time) based on the AUC

$$C - index = \frac{\Delta_j \times \sum_{i,j} 1_{Ti>Tj} \times 1_{\eta_i > \eta_j}}{\Delta_j \times \sum_{i,j} 1_{Ti>Tj}}$$

- Where 1 are indicator-functions:

```
##
##  randomForestSRC 2.9.3
##
##  Type rfsrc.news() to see new features, changes, and bug
##

##
## The c-index for right censored event times
##
## Prediction models:
```

IBS

- called cumulative predictive error curves == continuous ranked probability score (crps)
- area under the prediction error curve
- Integral over all points in time to get one summary value henceforth called "integrated" BS
- able to build a R^2 like measure where we divide MSE of a model with a different MSE of reference model
- Where L is a loss function of the S(the probability that the event of interest has not taken place yet) and time
- t is the time of the event (death) and t* the time before death
- G(t) is the P(C>t), so where the censored time is longer than the time (in mlr3proba via survfit == KM Estimate)
- When selecting integrated == FALSE then we looking at specific time

For the population mean:

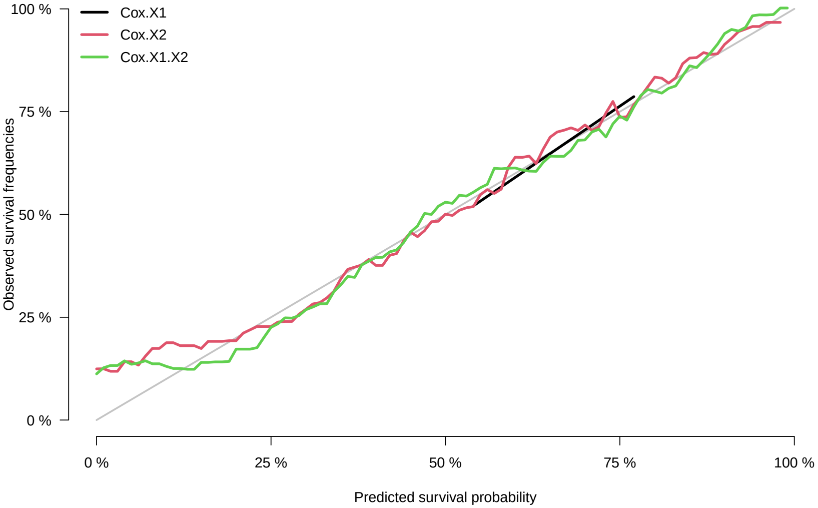
$$L(S, t|t^*) = \frac{1}{N}\sum_{i=1}^{N} L(S_i, t_i|t^*) \tag{9}$$

Mean Population:

$$L(S, t|t^*) = \frac{1}{NT}\sum_{i=1}^{N}\sum_{j=1}^{T} L(S_i, t_i|t^*)$$

- N = Number of observations
- S_i is the predicted survival function

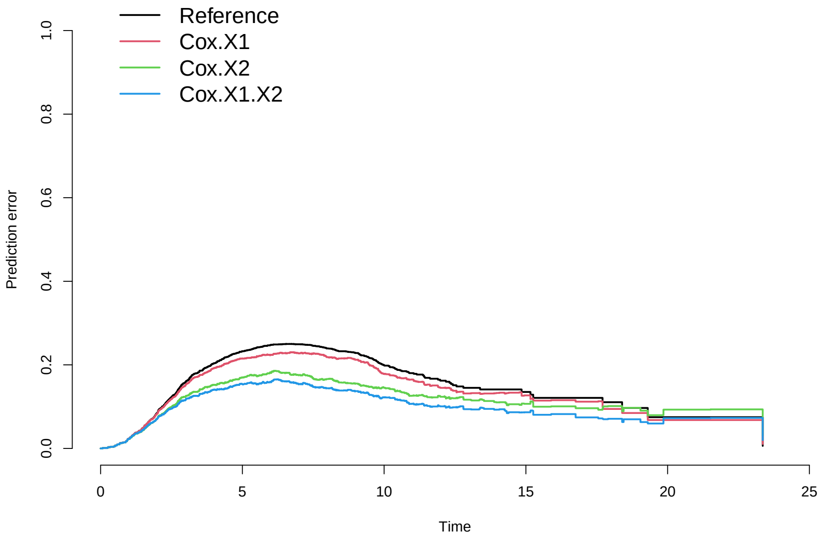
Calibration Plot



Summary Prediction Error Curves

```
##
## Prediction error curves
##
##
## No data splitting: either apparent or independent test s
##
##  AppErr
##   time n.risk Reference Cox.X1 Cox.X2 Cox.X1.X2
## 1    0   1000     0.000  0.000  0.000     0.000
## 2    5    471     0.233  0.215  0.170     0.154
## 3   10    105     0.199  0.178  0.145     0.122
## 4   15     17     0.135  0.127  0.107     0.087
## 5   20      2     0.075  0.068  0.093     0.072
```

Plotting prediction error

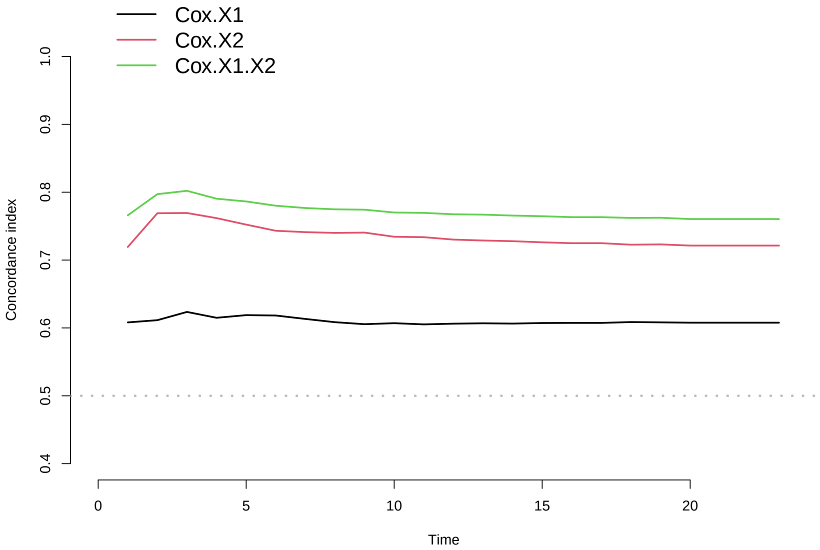


Cumulative Prediction Error

```
##
## Integrated Brier score (crps):
##
##            IBS[0;time=0) IBS[0;time=5) IBS[0;time=10) IBS
## Reference              0         0.117          0.177
## Cox.X1                 0         0.111          0.164
## Cox.X2                 0         0.091          0.129
## Cox.X1.X2              0         0.085          0.116
##            IBS[0;time=20)
## Reference           0.156
## Cox.X1              0.144
## Cox.X2              0.119
## Cox.X1.X2           0.101

##
## Integrated Brier score (crps):
##
##            IBS[0;time=23.4)
## Reference             0.144
```

c-index plot



Cox.X1
Cox.X2
Cox.X1.X2
Concordance index
0.4
0.5
0.6
0.7
0.8
0.9
1.0
0
5
10
15
20
Time

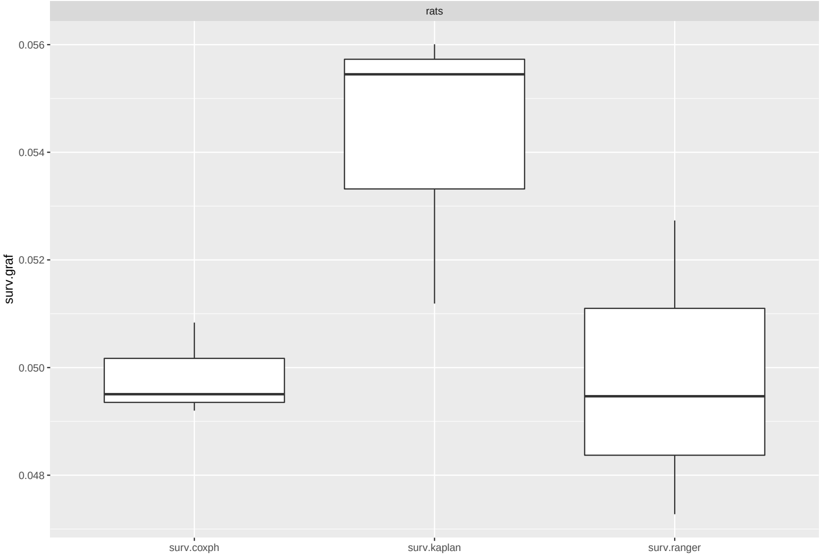
mlr3Proba

- van Houwelingen's Alpha Calibration
- van Houwelingen's Beta Calibration
- Integrated Graf Score (other Name for IBS based on Author Graf)
- Integrated Log Loss
- Log Loss

Further measures via survAUC package:

- Uno's AUC/TPR/TNR
- Song and Zhou's AUC/TNR/TPR
- Chambless and Diao's AUC
- Hung and Chiang's AUC

mlr3Proba Example



Discussion

- Integrated Brier Score accounts for both calibration and discrimination
- Irrespective, neither model accounts and leaves room for improvement

Literature and Recommendations

Introduction:

- Steyerberg, E. W., Vickers, A. J., Cook, N. R., Gerds, T., Gonen, M., Obuchowski, N., ... & Kattan, M. W. (2010). Assessing the performance of prediction models: a framework for some traditional and novel measures. Epidemiology (Cambridge, Mass.), 21(1), 128.

Comparative Study:

- Kattan, M. W., & Gerds, T. A. (2018). The index of prediction accuracy: an intuitive measure useful for evaluating risk prediction models. Diagnostic and prognostic research, 2(1), 7.

Use Cases:

https://rpubs.com/kaz_yos/survival-auc
https://datascienceplus.com/time-dependent-roc-for-survival-prediction-models-in-r/ https://rdrr.io/cran/pec/
https://adibender.github.io/pammtools/