### Risk-Evaluation: Breast Cancer Royston-Altman

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#### 1 Evaluation of RISK survival models

This document highlights the use of

- RRPlot(),
- CoxRiskCalibration(), and
- CalibrationProbPoissonRisk(),

## Loading required package: miscTools

## Loading required package: Hmisc

for the evaluation (RRPlot), and calibration of cox models (CoxRiskCalibration) or logistic models (CalibrationProbPoissonRisk) of survival data.

Furthermore, it can be used to evaluate any Risk index that reruns the probability of a future event on external data-set.

This document will use the survival::rotterdam, and survival::gbsg data-sets to train and predict the risk of cancer recurrence after surgery. Both Cox and Logistic models will be trained and evaluated.

Here are some sample plots returned by the evaluated functions:

#### 1.1 The libraries

```
library(survival)
library(FRESA.CAD)

## Loading required package: Rcpp

## Loading required package: stringr
```

```
##
## Attaching package: 'Hmisc'
## The following objects are masked from 'package:base':
##
##
       format.pval, units
## Loading required package: pROC
## Type 'citation("pROC")' for a citation.
##
## Attaching package: 'pROC'
## The following objects are masked from 'package:stats':
##
##
       cov, smooth, var
op <- par(no.readonly = TRUE)
pander::panderOptions('digits', 3)
pander::panderOptions('table.split.table', 400)
pander::panderOptions('keep.trailing.zeros',TRUE)
```

#### 1.2 Breast Cancer Royston-Altman data

1.2.1 data(gbsg, package="survival") and data(rotterdam, package="survival")

```
gbsgdata <- gbsg
rownames(gbsgdata) <- gbsgdata$pid</pre>
gbsgdata$pid <- NULL</pre>
odata <-rotterdam
rownames(odata) <- odata$pid
odata$pid <- NULL
odata$rfstime <- odata$rtime
odata$status <- odata$recur
odata$rtime <- NULL
odata$recur <- NULL
odata <- odata[,colnames(odata) %in% colnames(gbsgdata)]</pre>
odata$size <- 10*(odata$size=="<=20") +
  35*(odata\$size=="20-50") +
  60*(odata$size==">50")
data <- as.data.frame(model.matrix(Surv(rfstime,status)~.*.,odata))</pre>
data$`(Intercept)` <- NULL</pre>
dataBrestCancerTrain <- cbind(time=odata[rownames(data), "rfstime"], status=odata[rownames(data), "status"]
colnames(dataBrestCancerTrain) <-str_replace_all(colnames(dataBrestCancerTrain),":","_")</pre>
colnames(dataBrestCancerTrain) <-str_replace_all(colnames(dataBrestCancerTrain)," ","")</pre>
colnames(dataBrestCancerTrain) <-str_replace_all(colnames(dataBrestCancerTrain),"\\.","_")</pre>
\verb|colnames| (\texttt{dataBrestCancerTrain})| < -\texttt{str\_replace\_all} (\texttt{colnames} (\texttt{dataBrestCancerTrain}), "-", "\_")|
colnames(dataBrestCancerTrain) <-str replace all(colnames(dataBrestCancerTrain),">"," ")
dataBrestCancerTrain$time <- dataBrestCancerTrain$time/365 ## To years
```

```
pander::pander(table(odata[rownames(data), "status"]), caption="rotterdam")
```

Table 1: rotterdam

0	1
1464	1518

#### 1.2.2 data(gbsg, package="survival") data conditioning

```
gbsgdata <- gbsgdata[,colnames(odata)]
data <- as.data.frame(model.matrix(Surv(rfstime,status)~.*.,gbsgdata))

data$`(Intercept)` <- NULL

dataBrestCancerTest <- cbind(time=gbsgdata[rownames(data),"rfstime"],status=gbsgdata[rownames(data),"st

colnames(dataBrestCancerTest) <-str_replace_all(colnames(dataBrestCancerTest),":","_")
colnames(dataBrestCancerTest) <-str_replace_all(colnames(dataBrestCancerTest),"","")
colnames(dataBrestCancerTest) <-str_replace_all(colnames(dataBrestCancerTest),"\\.","_")
colnames(dataBrestCancerTest) <-str_replace_all(colnames(dataBrestCancerTest),"\\.","_")
colnames(dataBrestCancerTest) <-str_replace_all(colnames(dataBrestCancerTest),"-","_")
dataBrestCancerTest$time <- dataBrestCancerTest$time/365

pander::pander(table(odata[rownames(data),"status"]), caption="gbsg")</pre>
```

Table 2: gbsg

0	1
499	183

#### 1.3 Cox Modeling

```
ml <- BSWiMS.model(Surv(time, status)~., data=dataBrestCancerTrain, loops=1, NumberofRepeats = 5)</pre>
```

```
sm <- summary(ml)
pander::pander(sm$coefficients)</pre>
```

Estimalewer HR upperu.Acc	una <i>e</i> yccurauch.	Accumaty CAUGull.AUOI NRI z.IDI z.NRIDelta.AUQuenc
age_node\$00716001 1.001 1.001 0.626	0.600 0.63	32  0.630  0.601  0.634  0.03040.459412.81  14.37  0.0330561
$\mathbf{size} \underline{\hspace{0.1cm}} \mathbf{gradde} 0564 \underline{0.005}  1.006  1.006  0.598$	0.623  0.63	0.599  0.626  0.634  0.0186  0.39149.82  11.29  0.0079471
$\mathbf{nodes}  0.0865820821.0901.0990.637$	0.642  0.64	43 0.640 0.643 0.644 0.0074 <b>5</b> .05648.33 1.66 0.0001481
<b>size</b> 0.0068880051.0071.0090.595	0.641  0.64	0.5950.6420.6440.0144 $0.0144$ $0.35878.059.970.0013221$
$size\_nodes$ 1.000 1.000 1.000 0.624	0.643  0.64	43 0.629 0.644 0.644 0.00346.34307.25 9.57 - 1
0.000378		0.000377
$age\_size - 1.0001.0001.0000.567$	0.627  0.63	32 0.568 0.630 0.634 0.0063 <b>5</b> .19355.95 5.36 0.0040781
0.000149		
<b>grade</b> 0.2049341461.2271.3140.565	0.637  0.64	43 0.561 0.638 0.644 0.00926.20695.88 6.31 0.0053441

	Estim	na <b>te</b> wer HR	upperu.Accı	ına <i>e</i> yccu	r <b>aul</b> t.Aco	cumaAyCAUGull.A	UMO I NRI	z.IDl	I z.NR	IDelta.A	<b>₩</b> ��quency
age	-	0.9960.997	7 0.998 0.513	0.628	0.643	0.5130.6280.644	0.00416.093	175.27	2.51	0.01546	51
_	0.003										
${f grade}_{-}$	_nodes	0.9810.986	60.9920.635	0.645	0.643	0.6390.6460.644	0.00207 -	5.03	-	-	1
	0.013	784					0.093	10	2.55	0.002609	9

#### 1.4 Cox Model Performance

Here we evaluate the model using the RRPlot() function.

#### 1.4.1 The evaluation of the raw Cox model with RRPlot()

Here we will use the predicted event probability assuming a baseline hazard for events withing 5 years

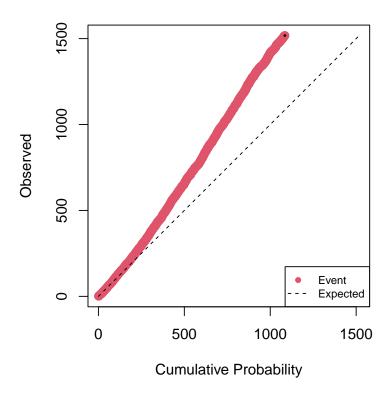
```
timeinterval <- 5 # Five years

h0 <- sum(dataBrestCancerTrain$status & dataBrestCancerTrain$time <= timeinterval)
h0 <- h0/sum((dataBrestCancerTrain$time > timeinterval) | (dataBrestCancerTrain$status==1))
pander::pander(t(c(h0=h0,timeinterval=timeinterval)),caption="Initial Parameters")
```

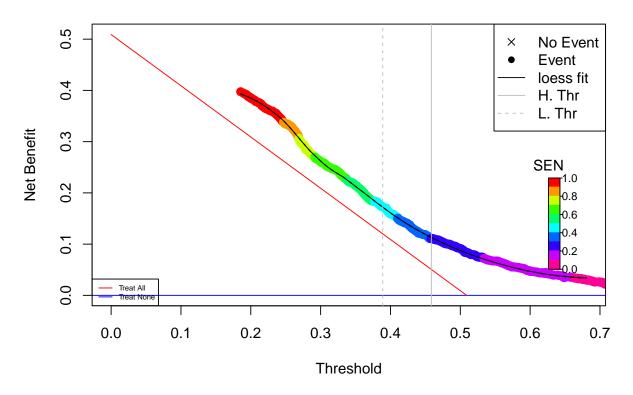
Table 4: Initial Parameters

h0	timeinterval
0.429	5

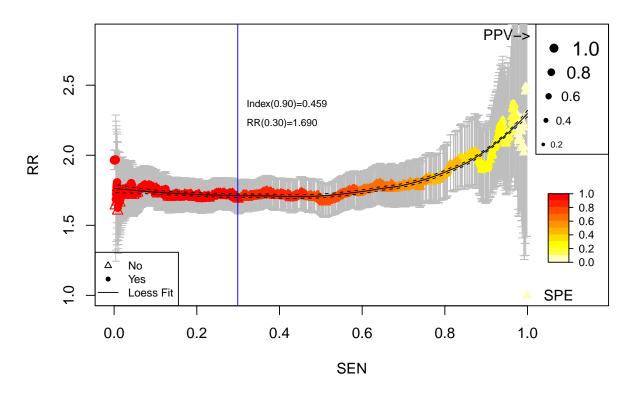
# **Cumulative vs. Observed: Train: Breast Cancer**



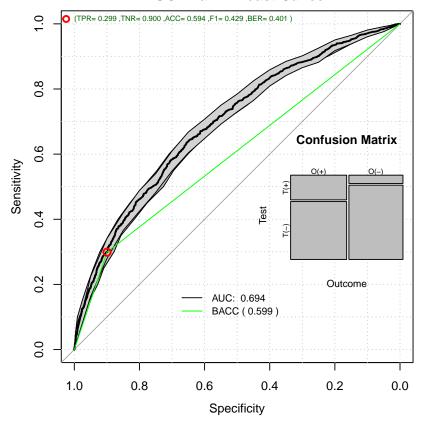
# **Decision Curve Analysis: Train: Breast Cancer**



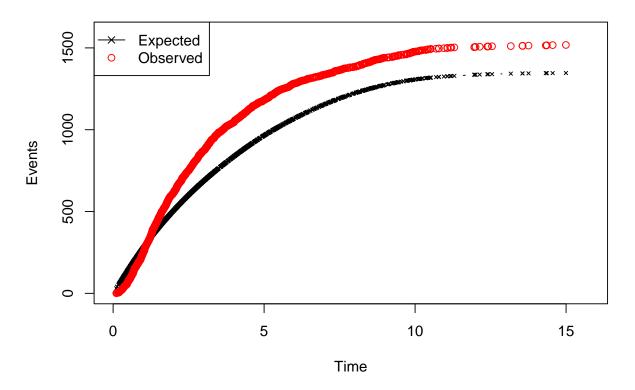
### **Relative Risk: Train: Breast Cancer**



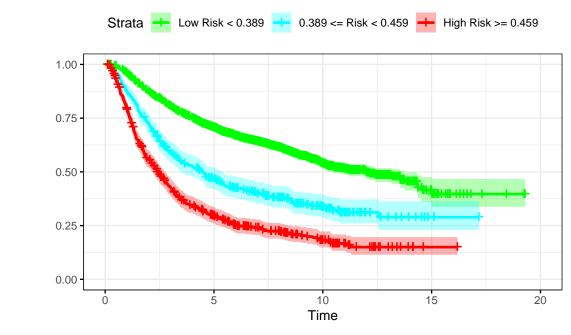
**ROC: Train: Breast Cancer** 



Time vs. Events: Train: Breast Cancer



# Kaplan-Meier: Train: Breast Cancer



### Number at risk

Low Risk < 0.389	1985	1260	393	23	0
0.389 <= Risk < 0.459	396	166	51	2	0
High Risk >= 0.459	601	145	39	1	0

#### 1.4.2 Time to event

```
toinclude <- rdata[,1] == 1
obstiemToEvent <- dataBrestCancerTrain[,"time"]
tmin<-min(obstiemToEvent)
sum(toinclude)</pre>
```

#### [1] 1518

Survival probability

```
timetoEvent <- meanTimeToEvent(rdata[,2],timeinterval)
tmax<-max(c(obstiemToEvent,timetoEvent))
lmfit <- lm(obstiemToEvent[toinclude]~0+timetoEvent[toinclude])
sm <- summary(lmfit)
pander::pander(sm)</pre>
```

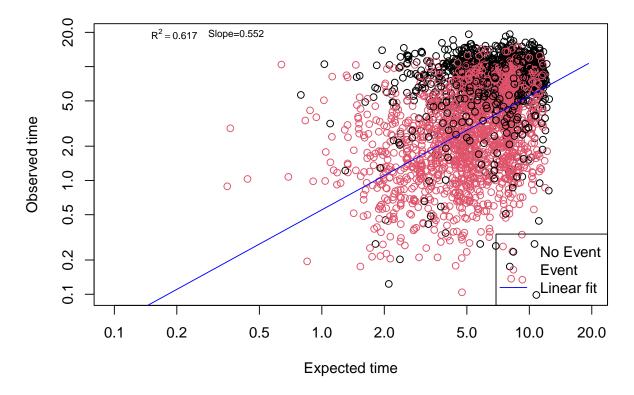
	Estimate	Std. Error	t value	$\Pr(> t )$
${\bf time to Event [to include]}$	0.552	0.0112	49.4	3.39e-318

Table 6: Fitting linear model: obstiem ToEvent[toinclude]  $\sim 0 + {\rm timetoEvent[toinclude]}$ 

Observations	Residual Std. Error	$R^2$	Adjusted $\mathbb{R}^2$
1518	2.67	0.617	0.616

```
plot(timetoEvent,obstiemToEvent,
     col=1+rdata[,1],
     xlab="Expected time",
     ylab="Observed time",
     main="Expected vs. Observed",
     xlim=c(tmin,tmax),
     ylim=c(tmin,tmax),
     log="xy")
lines(x=c(tmin,tmax),y=lmfit$coefficients*c(tmin,tmax),lty=1,col="blue")
txt <- bquote(paste(R^2 == .(round(sm$r.squared,3))))</pre>
text(tmin+0.005*(tmax-tmin),tmax,txt,cex=0.7)
text(tmin+0.015*(tmax-tmin),tmax,sprintf("Slope=%4.3f",sm$coefficients[1]),cex=0.7)
legend("bottomright",legend=c("No Event","Event","Linear fit"),
             pch=c(1,1,-1),
             col=c(1,2,"blue"),
             lty=c(-1,-1,1)
```

### **Expected vs. Observed**



# MADerror2 <- mean(abs(timetoEvent[toinclude]-obstiemToEvent[toinclude])) pander::pander(MADerror2)</pre>

3.12

The Time vs. Events are not calibrated. Lets do the calibration

#### 1.4.3 Uncalibrated Performance Report

pander::pander(t(rrAnalysisTrain\$keyPoints),caption="Threshold values")

Table 7: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.459	0.389	0.320	0.214	0.18549	0.4996
RR	1.690	1.713	1.799	2.376	1.00000	1.7255
$RR\_LCI$	1.586	1.603	1.666	1.869	0.00000	1.6196
$RR\_UCI$	1.802	1.830	1.942	3.019	0.00000	1.8383
$\mathbf{SEN}$	0.299	0.462	0.644	0.965	1.00000	0.2464
$\mathbf{SPE}$	0.900	0.798	0.646	0.125	0.00137	0.9310
$\mathbf{BACC}$	0.599	0.630	0.645	0.545	0.50068	0.5887
${f NetBenefit}$	0.110	0.172	0.246	0.374	0.39742	0.0916

pander::pander(t(rrAnalysisTrain\$0ERatio\$estimate),caption="0/E Ratio")

Table 8: O/E Ratio

O/E	Low	Upper	p.value
1.13	1.07	1.19	4.66e-06

pander::pander(t(rrAnalysisTrain\$0E95ci),caption="0/E Mean")

Table 9: O/E Mean

mean	50%	2.5%	97.5%
1.16	1.16	1.15	1.17

pander::pander(t(rrAnalysisTrain\$OAcum95ci),caption="0/Acum Mean")

Table 10: O/Acum Mean

mean	50%	2.5%	97.5%
1.35	1.35	1.35	1.35

pander::pander(rrAnalysisTrain\$c.index\$cstatCI,caption="C. Index")

mean.C Index	median	lower	upper
0.676	0.676	0.663	0.69

pander::pander(t(rrAnalysisTrain\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 12: ROC AUC

est	lower	upper
0.694	0.675	0.713

pander::pander((rrAnalysisTrain\$ROCAnalysis\$sensitivity), caption="Sensitivity")

Table 13: Sensitivity

est	lower	upper
0.299	0.276	0.323

pander::pander((rrAnalysisTrain\$ROCAnalysis\$specificity), caption="Specificity")

Table 14: Specificity

est	lower	upper
0.9	0.883	0.915

pander::pander(t(rrAnalysisTrain\$thr\_atP),caption="Probability Thresholds")

Table 15: Probability Thresholds

90%	80%
0.459	0.389

pander::pander(rrAnalysisTrain\$surdif,caption="Logrank test")

Table 16: Logrank test Chisq = 465.079317 on 2 degrees of freedom, p = 0.000000

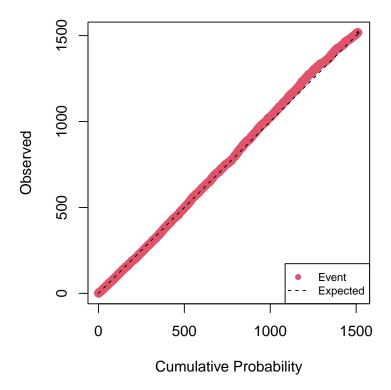
	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1985	816	1144	93.9	385.7
class=1	396	248	177	28.0	31.8
class=2	601	454	197	336.3	391.3

#### 1.4.4 Cox Calibration

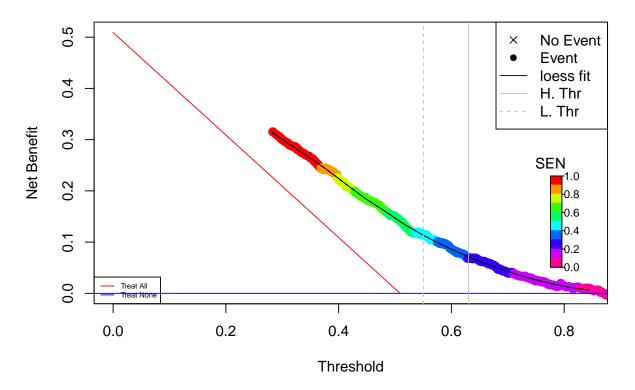
h0	Gain	DeltaTime
0.696	1.62	6.95

#### 1.4.5 The RRplot() of the calibrated model

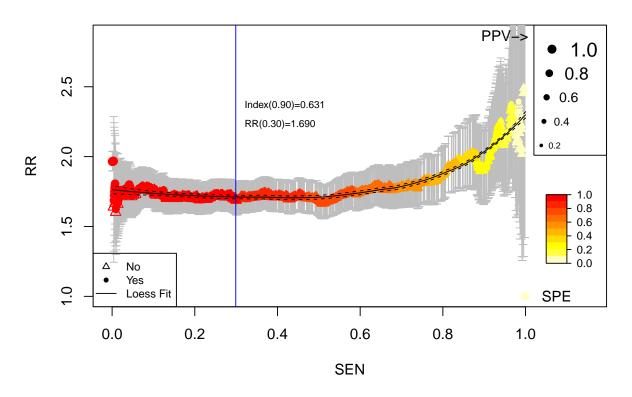
# Cumulative vs. Observed: Cal. Train: Breast Cancer



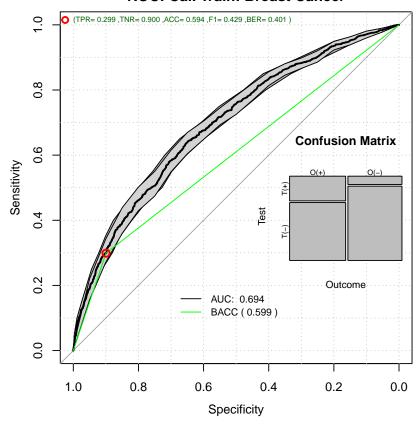
# **Decision Curve Analysis: Cal. Train: Breast Cancer**



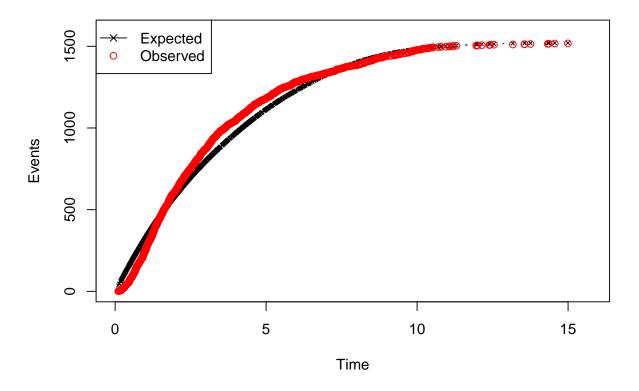
### Relative Risk: Cal. Train: Breast Cancer



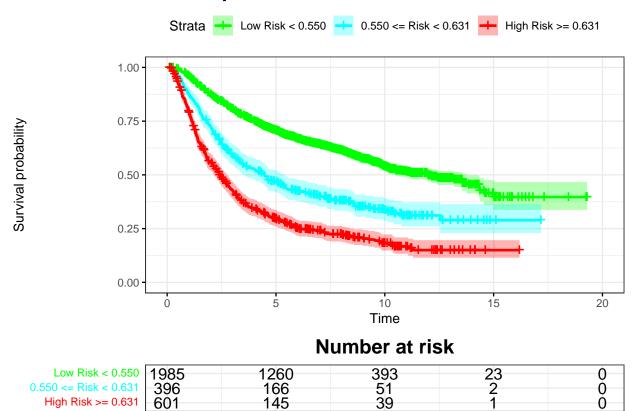
**ROC: Cal. Train: Breast Cancer** 



Time vs. Events: Cal. Train: Breast Cancer



### Kaplan-Meier: Cal. Train: Breast Cancer



#### 1.4.6 Time to event after calibration

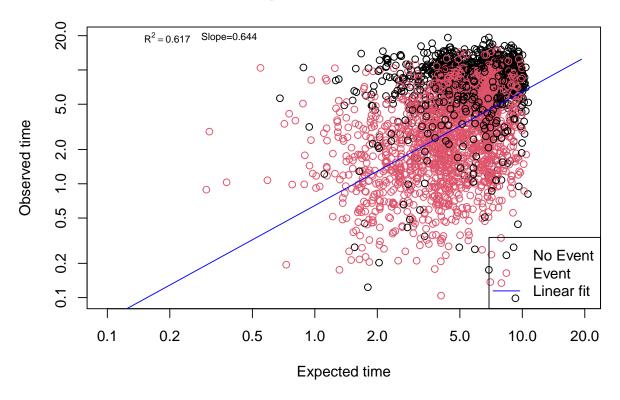
```
timetoEvent <- meanTimeToEvent(rdata[,2],timeinterval)
tmax<-max(c(obstiemToEvent,timetoEvent))
lmfit <- lm(obstiemToEvent[toinclude]~0+timetoEvent[toinclude])
sm <- summary(lmfit)
pander::pander(sm)</pre>
```

	Estimate	Std. Error	t value	$\Pr(> t )$
$ ext{timetoEvent[toinclude]}$	0.644	0.013	49.4	3.39e-318

Table 19: Fitting linear model: obstiem ToEvent[toinclude]  $\sim 0 + timetoEvent[toinclude]$ 

Observations	Residual Std. Error	$R^2$	Adjusted $\mathbb{R}^2$
1518	2.67	0.617	0.616

### **Expected vs. Observed**



MADerror2 <- c(MADerror2,mean(abs(timetoEvent[toinclude]-obstiemToEvent[toinclude])))
pander::pander(MADerror2)</pre>

3.12 and 2.63

#### 1.4.7 Calibrated Train Performance

```
pander::pander(t(rrAnalysisTrain$keyPoints),caption="Threshold values")
```

Table 20: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
$\operatorname{Thr}$	0.631	0.550	0.465	0.323	0.28321	0.500
$\mathbf{R}\mathbf{R}$	1.690	1.713	1.799	2.376	1.00000	1.751
$RR\_LCI$	1.586	1.603	1.666	1.869	0.00000	1.630
$RR\_UCI$	1.802	1.830	1.942	3.019	0.00000	1.881
$\mathbf{SEN}$	0.299	0.462	0.644	0.965	1.00000	0.578
$\mathbf{SPE}$	0.900	0.798	0.646	0.125	0.00137	0.706
$\mathbf{BACC}$	0.599	0.630	0.645	0.545	0.50068	0.642
${\bf Net Benefit}$	0.068	0.114	0.177	0.286	0.31537	0.150

pander::pander(t(rrAnalysisTrain\$0ERatio\$estimate),caption="0/E Ratio")

Table 21: O/E Ratio

O/E	Low	Upper	p.value
0.998	0.949	1.05	0.959

pander::pander(t(rrAnalysisTrain\$0E95ci),caption="0/E Mean")

Table 22: O/E Mean

mean	50%	2.5%	97.5%
1	1	0.995	1.01

pander::pander(t(rrAnalysisTrain\$OAcum95ci),caption="0/Acum Mean")

Table 23: O/Acum Mean

mean	50%	2.5%	97.5%
1.01	1.01	1.01	1.01

pander::pander(rrAnalysisTrain\$c.index\$cstatCI,caption="C. Index")

mean.C Index	median	lower	upper
0.676	0.676	0.662	0.689

pander::pander(t(rrAnalysisTrain\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 25: ROC AUC

est	lower	upper
0.694	0.675	0.713

pander::pander((rrAnalysisTrain\$ROCAnalysis\$sensitivity), caption="Sensitivity")

Table 26: Sensitivity

est	lower	upper
0.299	0.276	0.323

pander::pander((rrAnalysisTrain\$ROCAnalysis\$specificity), caption="Specificity")

Table 27: Specificity

est	lower	upper
0.9	0.883	0.915

pander::pander(t(rrAnalysisTrain\$thr\_atP),caption="Probability Thresholds")

Table 28: Probability Thresholds

90%	80%
0.631	0.55

pander::pander(rrAnalysisTrain\$surdif,caption="Logrank test")

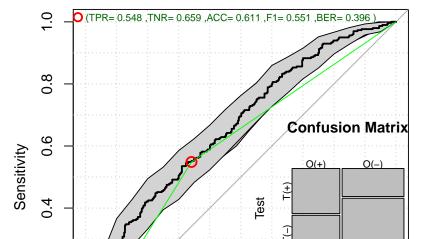
Table 29: Logrank test Chisq = 465.079317 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1985	816	1144	93.9	385.7
class=1	396	248	177	28.0	31.8
class=2	601	454	197	336.3	391.3

#### 1.5 Performance on the external data set

index <- predict(ml,dataBrestCancerTest)</pre>

pp <- predictionStats\_binary(cbind(dataBrestCancerTest\$status,index),plotname="Breast Cancer")</pre>



Outcome

0.2

0.0

AUC: 0.660 BACC (0.604)

0.4

0.2

0.0

1.0

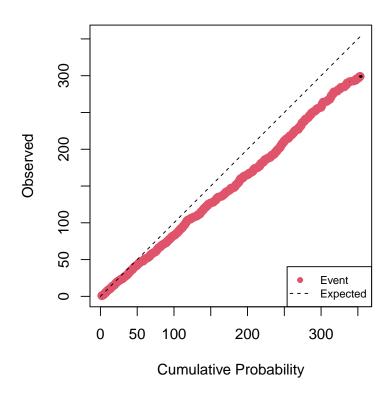
**Breast Cancer** 

0.6

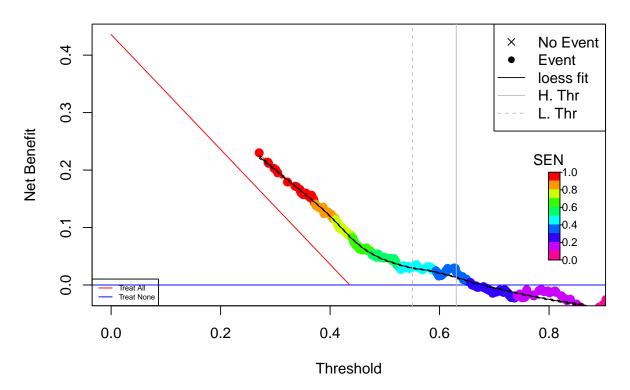
Specificity

8.0

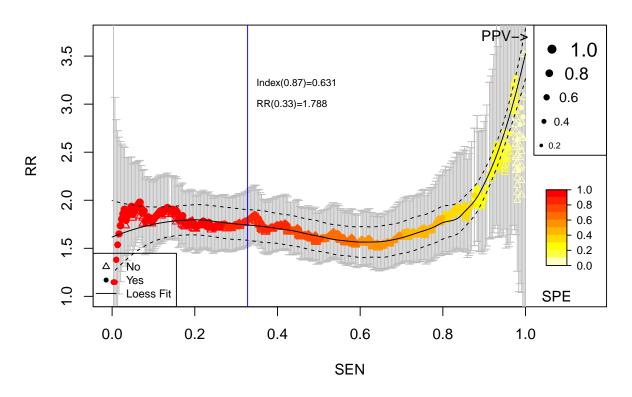
# **Cumulative vs. Observed: Test: Breast Cancer**



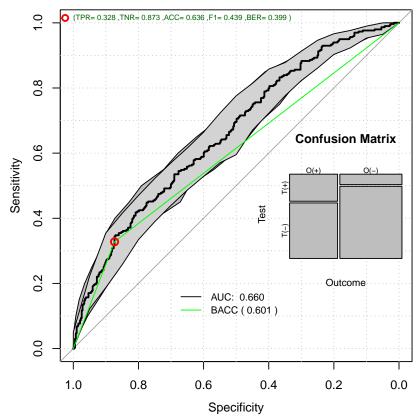
# **Decision Curve Analysis: Test: Breast Cancer**



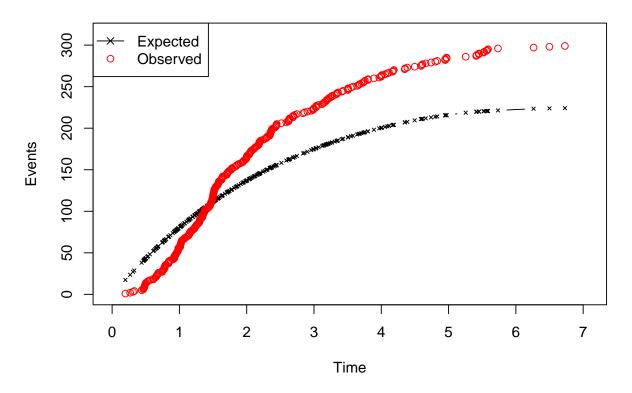
### **Relative Risk: Test: Breast Cancer**



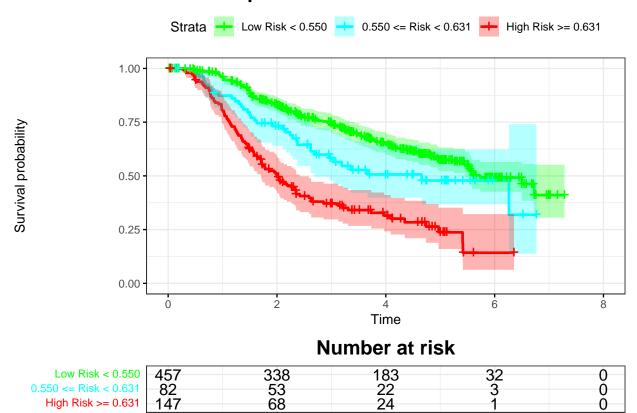




Time vs. Events: Test: Breast Cancer



### Kaplan-Meier: Test: Breast Cancer



par(op)

#### 1.5.1 External Data Report

pander::pander(t(rrCoxTestAnalysis\$keyPoints),caption="Threshold values")

Table 30: Threshold values

	@:0.631	@:0.55	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.6303	0.5507	0.5825	0.336	2.70e-01	0.500
$\mathbf{R}\mathbf{R}$	1.7994	1.6427	1.7581	3.279	2.64e + 01	1.603
$RR\_LCI$	1.5366	1.3951	1.4980	1.641	5.65 e-02	1.352
$RR\_UCI$	2.1071	1.9343	2.0632	6.552	1.23e + 04	1.902
$\mathbf{SEN}$	0.3311	0.4515	0.4181	0.977	1.00e+00	0.552
$\mathbf{SPE}$	0.8734	0.7571	0.8088	0.111	1.55e-02	0.656
$\mathbf{BACC}$	0.6022	0.6043	0.6134	0.544	5.08e-01	0.604
NetBenefit	0.0226	0.0289	0.0318	0.172	2.30e-01	0.047

pander::pander(t(rrCoxTestAnalysis\$0ERatio\$estimate),caption="0/E Ratio")

Table 31: O/E Ratio

O/E	Low	Upper	p.value
1.33	1.19	1.49	1.73e-06

pander::pander(rrCoxTestAnalysis\$c.index,caption="C. Index")

• C Index: 0.664

Dxy: 0.328S.D.: 0.0311

• n: 686

• missing:  $\theta$ 

• uncensored: 299

• Relevant Pairs: 266144

• Concordant: 176738

• Uncertain: 203702

• cstatCI:

mean.C Index	median	lower	upper
0.664	0.664	0.633	0.694

pander::pander(t(rrCoxTestAnalysis\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 33: ROC AUC

est	lower	upper
0.66	0.619	0.7

pander::pander((rrCoxTestAnalysis\$ROCAnalysis\$sensitivity), caption="Sensitivity")

Table 34: Sensitivity

est	lower	upper
0.328	0.275	0.384

pander::pander((rrCoxTestAnalysis\$ROCAnalysis\$specificity)), caption="Specificity")

Table 35: Specificity

est	lower	upper
0.873	0.836	0.905

pander::pander(t(rrCoxTestAnalysis\$thr\_atP),caption="Probability Thresholds")

Table 36: Probability Thresholds

90%	80%
0.631	0.55

pander::pander(rrCoxTestAnalysis\$surdif,caption="Logrank test")

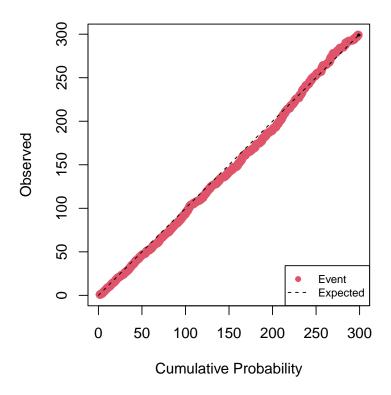
Table 37: Logrank test Chisq = 81.471750 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	457	164	221.4	14.888	58.181
class=1	82	37	33.2	0.438	0.494
class=2	147	98	44.4	64.710	77.254

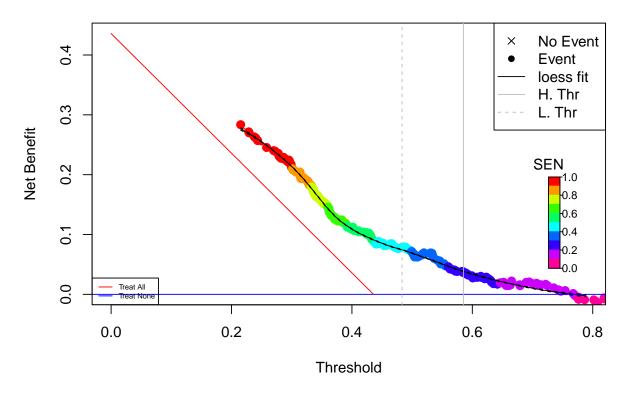
#### 1.5.2 Calibrating the index on the test data

h0	Gain	DeltaTime
0.535	0.925	4.87

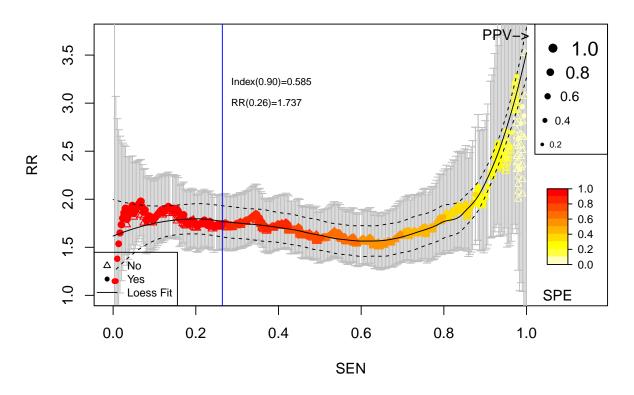
### **Cumulative vs. Observed: Cal. Test: Breast Cancer**



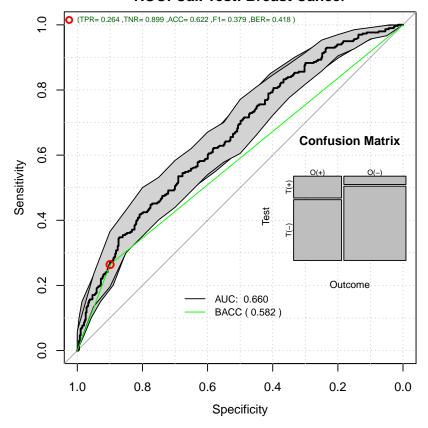
# **Decision Curve Analysis: Cal. Test: Breast Cancer**



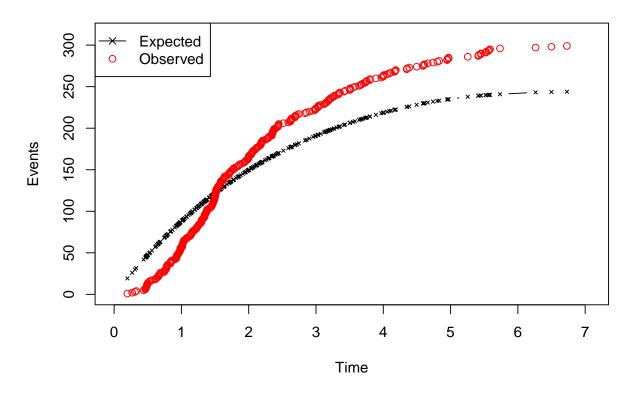
### Relative Risk: Cal. Test: Breast Cancer



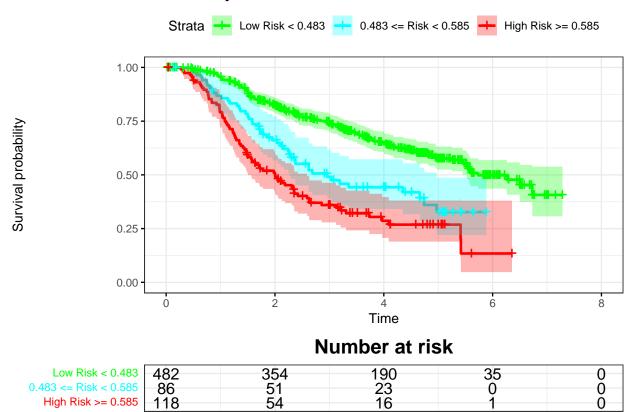
**ROC: Cal. Test: Breast Cancer** 



Time vs. Events: Cal. Test: Breast Cancer



### Kaplan-Meier: Cal. Test: Breast Cancer



#### 1.5.3 After Calibration Report

pander::pander(t(rrAnalysis\$keyPoints),caption="Threshold values")

Table 39: Threshold values

	@:0.9	@:0.8	@MAX_BACC	C @MAX_RR	@SPE100	p(0.5)
Thr	0.5843	0.483	0.489	0.270	2.15e-01	0.4991
$\mathbf{R}\mathbf{R}$	1.7405	1.732	1.758	3.279	2.64e + 01	1.7385
$RR\_LCI$	1.4790	1.475	1.498	1.641	5.65 e-02	1.4816
$RR\_UCI$	2.0483	2.035	2.063	6.552	1.23e + 04	2.0399
$\mathbf{SEN}$	0.2676	0.425	0.418	0.977	1.00e+00	0.3980
$\mathbf{SPE}$	0.8992	0.798	0.809	0.111	1.55e-02	0.8191
$\mathbf{BACC}$	0.5834	0.612	0.613	0.544	5.08e-01	0.6086
NetBenefit	0.0367	0.079	0.079	0.240	2.84e-01	0.0718

pander::pander(t(rrAnalysis\$OERatio\$estimate),caption="0/E Ratio")

Table 40: O/E Ratio

O/E	Low	Upper	p.value
1.23	1.09	1.37	0.000607

pander::pander(rrAnalysis\$c.index, caption="C. Index")

• C Index: 0.664

Dxy: 0.328S.D.: 0.0311

• n: 686

• missing:  $\theta$ 

• uncensored: 299

Relevant Pairs: 266144
 Concordant: 176737
 Uncertain: 203702

• cstatCI:

mean.C Index	median	lower	upper
0.664	0.664	0.632	0.693

pander::pander(t(rrAnalysis\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 42: ROC AUC

est	lower	upper
0.66	0.619	0.7

pander::pander((rrAnalysis\$ROCAnalysis\$sensitivity), caption="Sensitivity")

Table 43: Sensitivity

est	lower	upper
0.264	0.215	0.318

pander::pander((rrAnalysis\$ROCAnalysis\$specificity), caption="Specificity")

Table 44: Specificity

est	lower	upper
0.899	0.865	0.927

pander::pander(t(rrAnalysis\$thr\_atP),caption="Probability Thresholds")

Table 45: Probability Thresholds

90%	80%
0.585	0.483

pander::pander(rrAnalysis\$surdif,caption="Logrank test")

Table 46: Logrank test Chisq = 80.835092 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	482	173	232.4	15.20	69.5
class=1	86	47	32.0	7.02	7.9
class=2	118	79	34.6	57.14	65.4

#### 1.6 Logistic Model

Here we train a logistic model on the same data set

```
## Only label subjects that present event withing five years

dataBrestCancerR <- subset(dataBrestCancerTrain, time>=5 | status==1)

dataBrestCancerR$status <- dataBrestCancerR$status * (dataBrestCancerR$time < 5)

dataBrestCancerR$time <- NULL

#ml <- BSWiMS.model(status~1, data=dataBrestCancerR, loops=20, NumberofRepeats = 5)

mlog <- BSWiMS.model(status~1, data=dataBrestCancerR, loops=1, NumberofRepeats = 5)</pre>
```

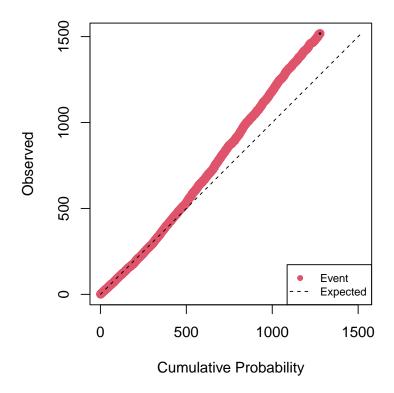
```
sm <- summary(mlog)
pander::pander(sm$coefficients)</pre>
```

Es	stima <b>tø</b> wer OR	upperu.Accu	ına <i>e</i> yccu	r <b>ach</b> Acc	cura&yCAUCull.A	UMOI NRI	z.IDI z.NRIDel	lta. <b>AW</b> quency
size_node		1 1.001 0.669	0.571	0.668	0.6270.5000.628	0.1123 <b>6</b> .636	5547.86 18.8700.1	284901
nodes 4.3	33e- 1.040 1.04	4 1.048 0.676	0.634	0.690	0.639 0.621 0.662	0.07110.571	.064.1316.1790.0	404941
grade_nb		5 1.016 0.682	0.637	0.686	0.649 0.624 0.655	0.0658 <b>0</b> .548	86 <b>d</b> 3.66 15.65@.0	310871
age_nodle(	=	1 1.001 0.678	0.653	0.686	0.6420.6210.657	0.0334 <b>6</b> .213	31 <b>2</b> 0.39 5.710 0.0	358961
size gradi	-	21.0020.632	0.682	0.686	0.6260.6460.655	0.01780.294	116.74 7.728 0.0	086481
0	3				0.5770.6490.657			
0.	5				0.500 0.653 0.662			
0	1							
-	04e-	4 0.996 0.571	0.676	0.686	0.500 0.645 0.657	0.0078 <b>4</b> .080	054.76 2.337 0.0	120651
0:	3							

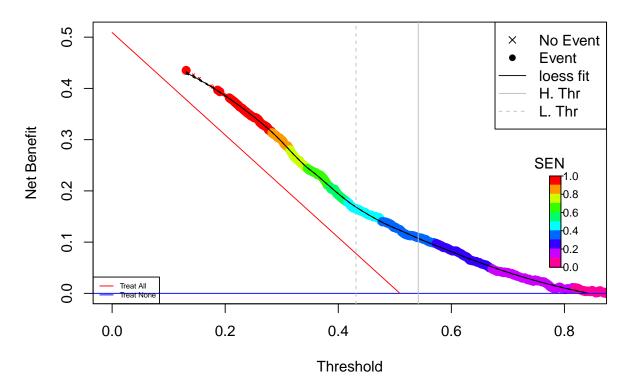
Estima	atower OR	upperu.Accu	ma <i>A</i> yccu	r <b>ach</b> Acc	uura&yCAUGull.A	UMO I NRI z.I	DI z.NRIDelta. A (uenc
<b>age_pgr</b> - 5.42e-06	1.000 1.000	1.000 0.571	0.686	0.686	0.500 0.656 0.657	0.0051 <b>2</b> .0074 <b>3</b> .1	1 0.194 0.0004171
	0.997 0.998	8 0.999 0.574	0.690	0.690	0.507 0.661 0.662	0.0045 <b>4</b> .1137 <b>2</b> .6	0 2.960 0.0003151
	1.045 1.107	7 1.173 0.571	0.683	0.686	0.5000.6520.657	0.0042 <b>6</b> .2042 <b>8</b> .4	7 5.343 0.0044411
nodes_hormo 1.38e- 02	o <b>10</b> .979 0.986	3 0.994 0.587	0.688	0.686	0.5260.6580.655	0.0028 <b>0</b> .4552 <b>2</b> .4	4 12.150 - 1 0.002853
~-	1.002 1.004	11.006 0.611	0.693	0.690	0.618 0.663 0.662	0.0050 <b>7</b> .2105 <b>3</b> .4	2 5.600 - 1 0.001075
<b>meno_pg:i</b> 9e- 04	1.000 1.000	0 1.001 0.571	0.687	0.686	0.500 0.657 0.657	0.0031 <b>6</b> .0597 <b>3</b> .3	5 1.558 - 1 0.000429
<b>pgr</b> - 1.07e- 04	1.000 1.000	1.000 0.571	0.689	0.686	0.500 0.659 0.655	0.0025 <b>7</b> .1975 <b>2</b> .6	4 5.745 - 1 0.004123
meno_nodes 2.60e- 02	0.955 0.974	10.9940.640	0.686	0.686	0.595 0.656 0.657	0.00264 - 2.5 0.06329	9 - 0.0006311 1.645
grade_pgr 3.51e- 05	1.000 1.000	1.000 0.571	0.669	0.668	0.500 0.627 0.628	0.0024 <b>0</b> .1747 <b>2</b> .5	5 5.058 0.0012521
	1.000 1.002	21.0040.604	0.691	0.690	0.578 0.663 0.662	0.0018 <b>5</b> .1022 <b>2</b> .4	3 2.662 - 1 0.001378

#### 1.7 Logistic Model Performance

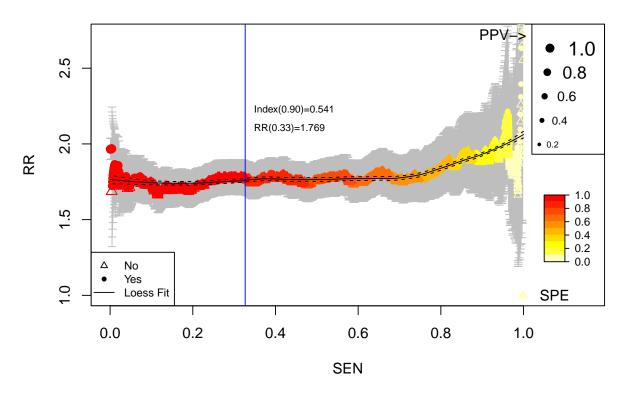
# **Cumulative vs. Observed: Logistic Train: Breast Cancer**



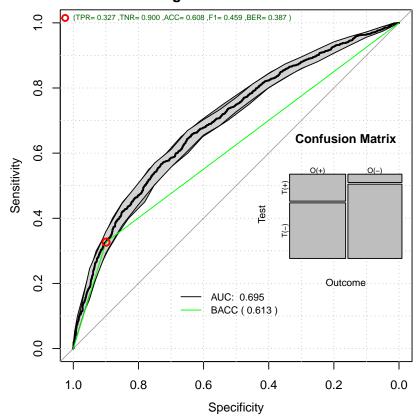
# **Decision Curve Analysis: Logistic Train: Breast Cancer**



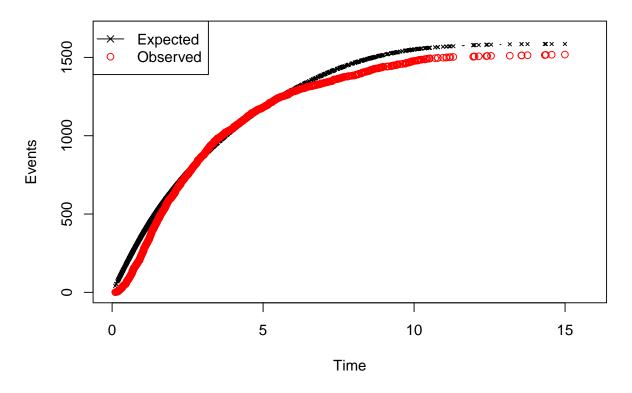
# **Relative Risk: Logistic Train: Breast Cancer**



**ROC: Logistic Train: Breast Cancer** 

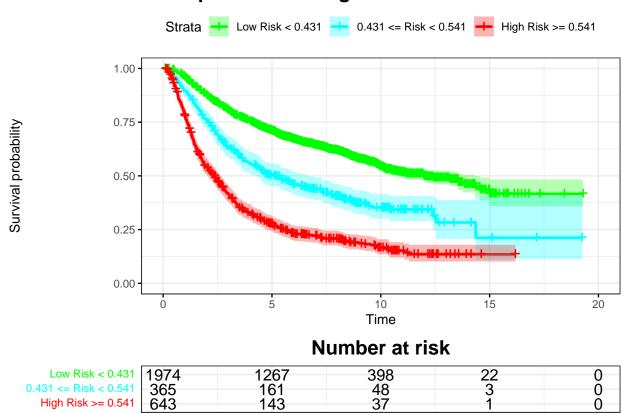


Time vs. Events: Logistic Train: Breast Cancer



### Kaplan-Meier: Logistic Train: Breast Cancer

0



par(op)

#### 1.7.1 Training Report

0.431 <= Risk < 0.541

High Risk >= 0.541

365 643

pander::pander(t(rrAnalysisTrain\$keyPoints),caption="Threshold values")

Table 48: Threshold values

	@:0.9	@:0.8	@MAX_BACC @	MAX_RR	@SPE100	p(0.5)
$\mathbf{Thr}$	0.542	0.431	0.394	0.255	0.130969	0.500
$\mathbf{R}\mathbf{R}$	1.765	1.739	1.799	2.213	1.000000	1.773
$RR\_LCI$	1.659	1.627	1.676	1.764	0.000000	1.665
$RR\_UCI$	1.879	1.858	1.931	2.777	0.000000	1.888
$\mathbf{SEN}$	0.327	0.470	0.566	0.962	1.000000	0.374
$\mathbf{SPE}$	0.900	0.799	0.731	0.125	0.000683	0.874
$\mathbf{BACC}$	0.613	0.635	0.648	0.543	0.500342	0.624
NetBenefit	0.108	0.165	0.202	0.342	0.435125	0.129

pander::pander(t(rrAnalysisTrain\$0ERatio\$estimate),caption="0/E Ratio")

Table 49: O/E Ratio

O/E	Low	Upper	p.value
0.957	0.91	1.01	0.0901

pander::pander(rrAnalysisTrain\$c.index,caption="C. Index")

• C Index: 0.68

Dxy: 0.36S.D.: 0.014

n: 2982missing: 0

1 484

• uncensored: 1518

• Relevant Pairs: 6184528

Concordant: 4206594Uncertain: 2703838

• cstatCI:

mean.C Index	median	lower	upper
0.68	0.68	0.666	0.694

pander::pander(t(rrAnalysisTrain\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 51: ROC AUC

est	lower	upper
0.695	0.677	0.714

pander::pander((rrAnalysisTrain\$ROCAnalysis\$sensitivity),caption="Sensitivity")

Table 52: Sensitivity

est	lower	upper
0.327	0.303	0.351

pander::pander((rrAnalysisTrain\$ROCAnalysis\$specificity), caption="Specificity")

Table 53: Specificity

est	lower	upper
0.9	0.883	0.915

pander::pander(t(rrAnalysisTrain\$thr\_atP),caption="Probability Thresholds")

Table 54: Probability Thresholds

90%	80%
0.541	0.431

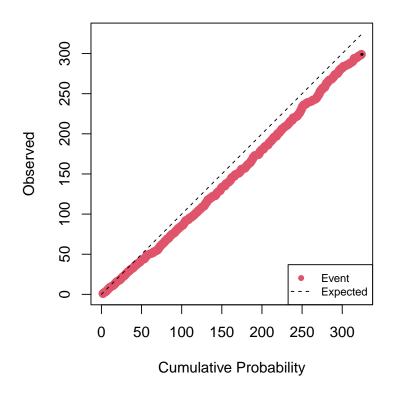
pander::pander(rrAnalysisTrain\$surdif,caption="Logrank test")

Table 55: Logrank test Chisq = 541.976716 on 2 degrees of freedom, p = 0.000000

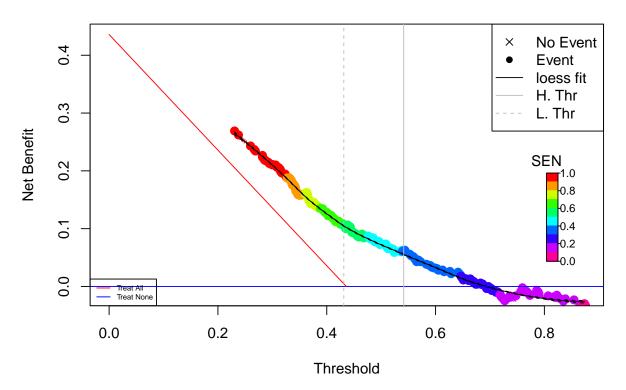
	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$
class=0	1974	804	1144	100.9	415.3
class=1	365	218	170	13.4	15.1
class=2	643	496	204	418.2	490.7

#### 1.7.2 Results on the validation set using Logistic model

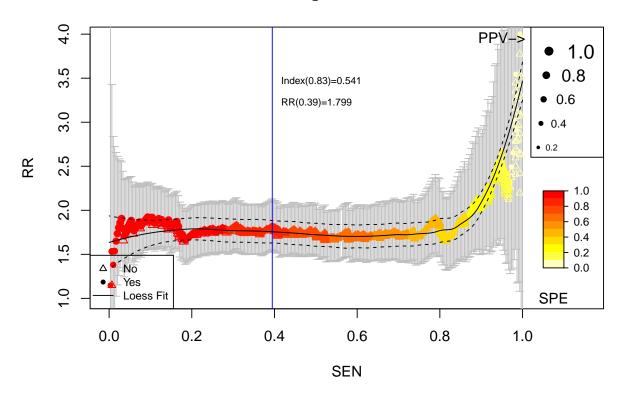
# **Cumulative vs. Observed: Logistic Test: Breast Cancer**



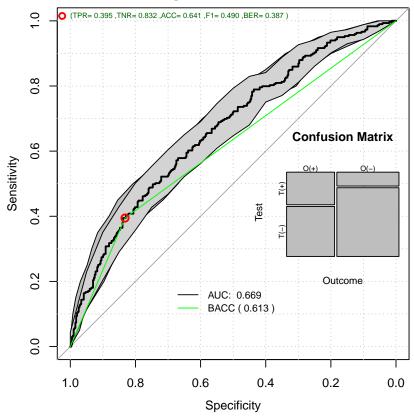
# **Decision Curve Analysis: Logistic Test: Breast Cancer**



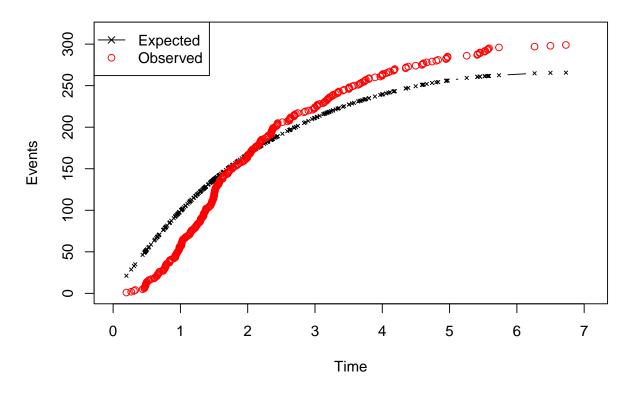
# Relative Risk: Logistic Test: Breast Cancer



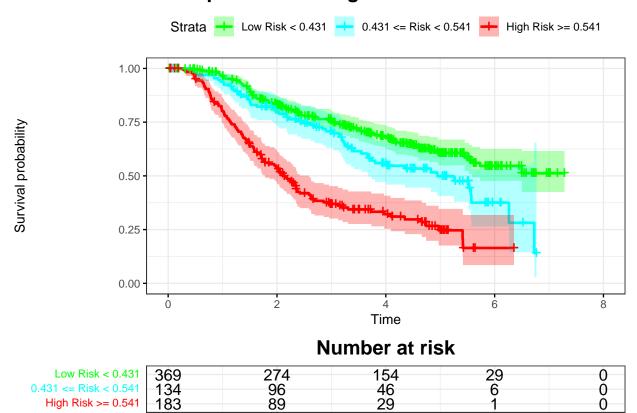
**ROC: Logistic Test: Breast Cancer** 



**Time vs. Events: Logistic Test: Breast Cancer** 



### Kaplan-Meier: Logistic Test: Breast Cancer



par(op)

#### 1.7.3 Validation Report

pander::pander(t(rrAnalysis\$keyPoints),caption="Threshold values")

Table 56: Threshold values

	@:0.541	@:0.431	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.542	0.431	0.439	0.306	2.31e-01	0.4996
$\mathbf{R}\mathbf{R}$	1.792	1.702	1.756	2.678	2.20e+01	1.7318
$RR\_LCI$	1.529	1.428	1.477	1.679	4.75e-02	1.4731
$RR\_UCI$	2.100	2.029	2.088	4.271	1.02e+04	2.0360
$\mathbf{SEN}$	0.395	0.595	0.579	0.950	1.00e+00	0.4482
$\mathbf{SPE}$	0.832	0.638	0.669	0.181	1.29e-02	0.7804
$\mathbf{BACC}$	0.613	0.617	0.624	0.565	5.06e-01	0.6143
NetBenefit	0.060	0.105	0.106	0.210	2.69e-01	0.0717

pander::pander(t(rrAnalysis\$OERatio\$estimate),caption="0/E Ratio")

Table 57: O/E Ratio

O/E	Low	Upper	p.value
1.13	1	1.26	0.0428

pander::pander(rrAnalysis\$c.index,caption="C. Index")

• C Index: 0.669

Dxy: 0.338S.D.: 0.0309

• **n**: 686

• missing:  $\theta$ 

• uncensored: 299

• Relevant Pairs: 266144

• Concordant: 178115

• Uncertain: 203702

• cstatCI:

mean.C Index	median	lower	upper
0.669	0.669	0.638	0.699

pander::pander(t(rrAnalysis\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 59: ROC AUC

est	lower	upper
0.669	0.628	0.709

pander::pander((rrAnalysis\$ROCAnalysis\$sensitivity),caption="Sensitivity")

Table 60: Sensitivity

est	lower	upper
0.395	0.339	0.453

pander::pander((rrAnalysis\$ROCAnalysis\$specificity),caption="Specificity")

Table 61: Specificity

est	lower	upper
0.832	0.791	0.868

```
pander::pander(t(rrAnalysis$thr_atP),caption="Probability Thresholds")
```

Table 62: Probability Thresholds

90%	80%
0.541	0.431

pander::pander(rrAnalysis\$surdif,caption="Logrank test")

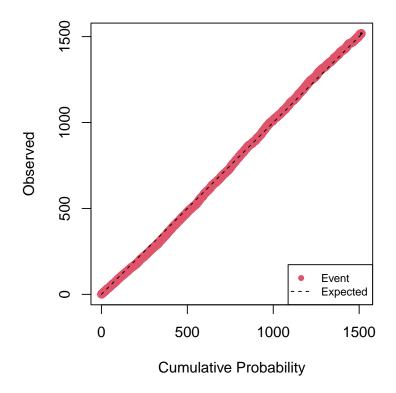
Table 63: Logrank test Chisq = 92.507991 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	369	121	181.7	20.2997	52.3868
class=1	134	60	61.7	0.0479	0.0604
class=2	183	118	55.5	70.2342	88.0195

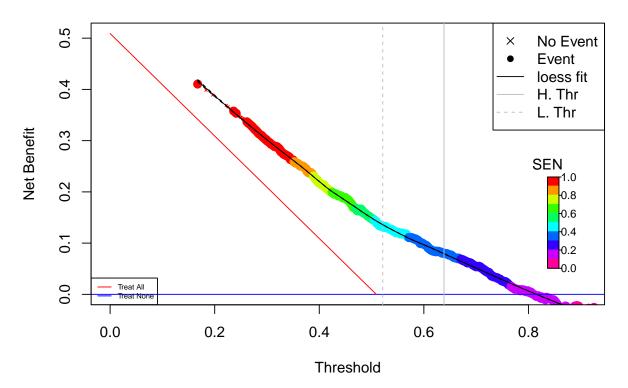
#### 1.8 Logistic Model Poisson Calibration

h0	Gain	DeltaTime
0.676	1.31	7.14

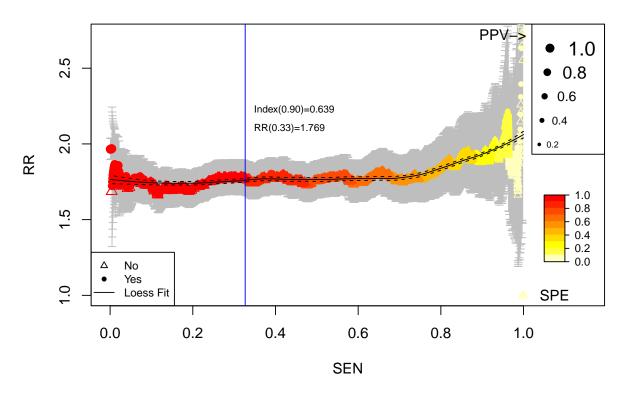
# Cumulative vs. Observed: Cal. Logistic Train: Breast Cancer



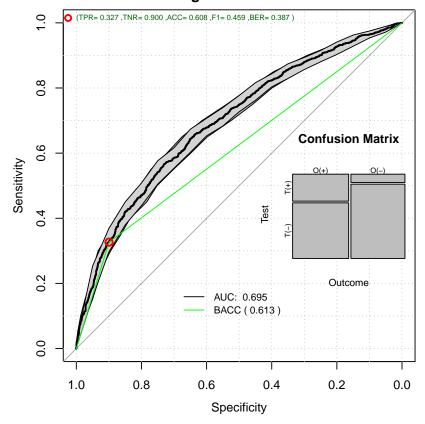
# Decision Curve Analysis: Cal. Logistic Train: Breast Cancer



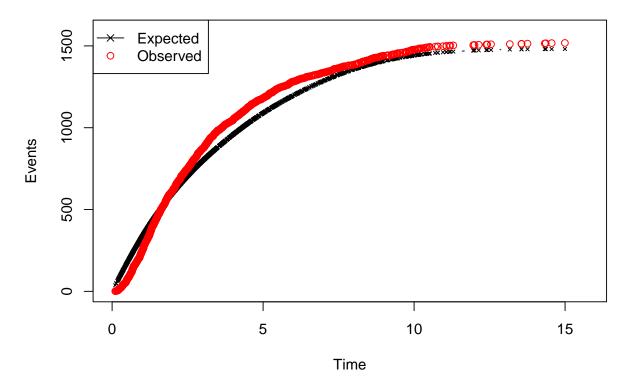
# Relative Risk: Cal. Logistic Train: Breast Cancer



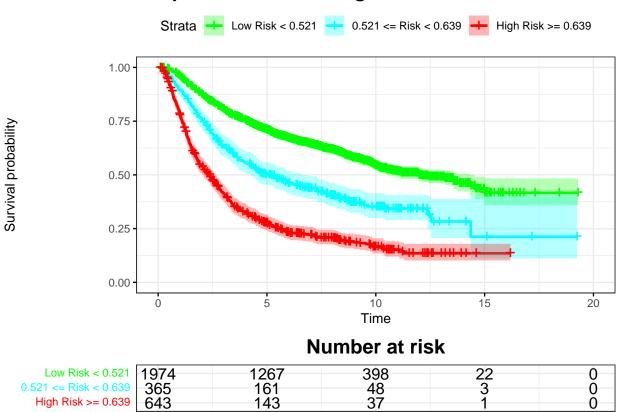
**ROC: Cal. Logistic Train: Breast Cancer** 



Time vs. Events: Cal. Logistic Train: Breast Cancer



### Kaplan-Meier: Cal. Logistic Train: Breast Cancer



par(op)

High Risk >= 0.639

#### 1.8.1 Report of the calibrated logistic: training

pander::pander(t(rrAnalysisTrain\$keyPoints),caption="Threshold values")

Table 65: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
$\mathbf{Thr}$	0.6395	0.521	0.480	0.319	0.167426	0.500
$\mathbf{R}\mathbf{R}$	1.7654	1.739	1.799	2.213	1.000000	1.759
$RR\_LCI$	1.6587	1.627	1.676	1.764	0.000000	1.643
$RR\_UCI$	1.8790	1.858	1.931	2.777	0.000000	1.882
$\mathbf{SEN}$	0.3267	0.470	0.566	0.962	1.000000	0.507
$\mathbf{SPE}$	0.8996	0.799	0.731	0.125	0.000683	0.774
$\mathbf{BACC}$	0.6132	0.635	0.648	0.543	0.500342	0.641
NetBenefit	0.0789	0.132	0.166	0.288	0.410407	0.147

pander::pander(t(rrAnalysisTrain\$0ERatio\$estimate),caption="0/E Ratio")

Table 66: O/E Ratio

O/E	Low	Upper	p.value
1.02	0.974	1.08	0.336

pander::pander(rrAnalysisTrain\$c.index,caption="C. Index")

• C Index: 0.68

Dxy: 0.36S.D.: 0.014

n: 2982missing: 0

• uncensored: 1518

• Relevant Pairs: 6184528

Concordant: 4206588Uncertain: 2703838

• cstatCI:

mean.C Index	median	lower	upper
0.68	0.68	0.666	0.693

pander::pander(t(rrAnalysisTrain\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 68: ROC AUC

est	lower	upper
0.695	0.677	0.714

pander::pander((rrAnalysisTrain\$ROCAnalysis\$sensitivity), caption="Sensitivity")

Table 69: Sensitivity

est	lower	upper
0.327	0.303	0.351

pander::pander((rrAnalysisTrain\$ROCAnalysis\$specificity), caption="Specificity")

Table 70: Specificity

est	lower	upper
0.9	0.883	0.915

pander::pander(t(rrAnalysisTrain\$thr\_atP),caption="Probability Thresholds")

Table 71: Probability Thresholds

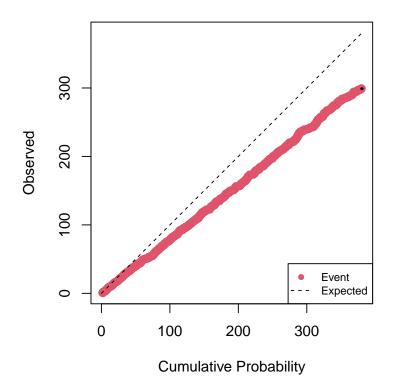
90%	80%
0.639	0.521

pander::pander(rrAnalysisTrain\$surdif,caption="Logrank test")

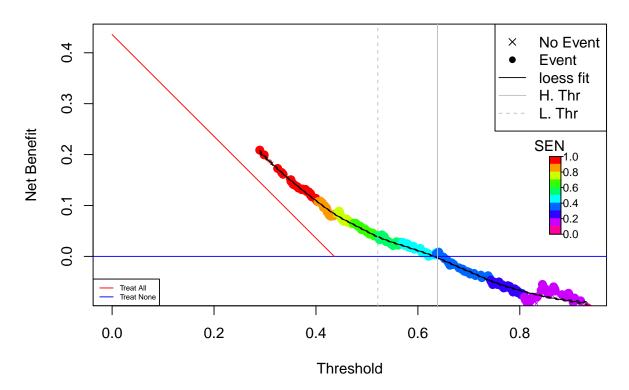
Table 72: Logrank test Chisq = 541.976716 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$
class=0	1974	804	1144	100.9	415.3
class=1	365	218	170	13.4	15.1
class=2	643	496	204	418.2	490.7

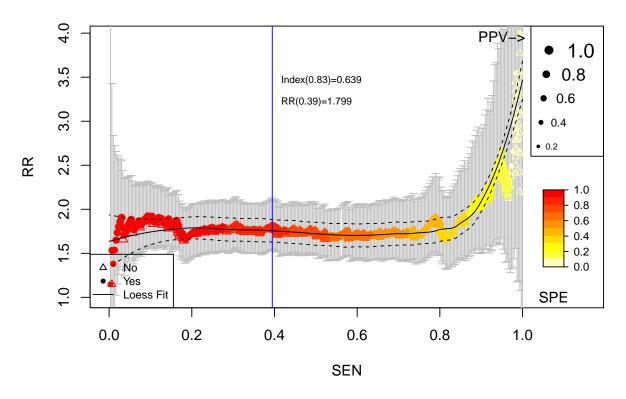
# Cumulative vs. Observed: Cal. Logistic Test: Breast Cancer



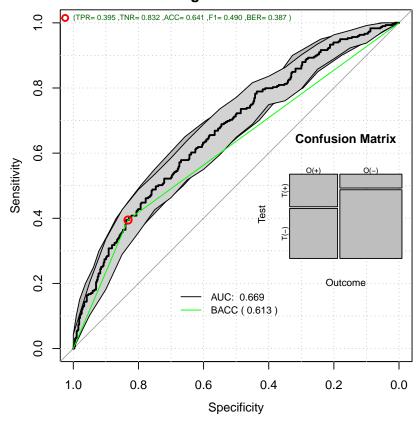
# **Decision Curve Analysis: Cal. Logistic Test: Breast Cancer**



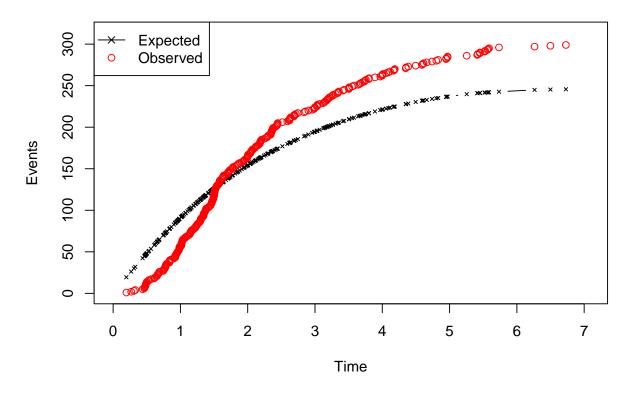
# Relative Risk: Cal. Logistic Test: Breast Cancer



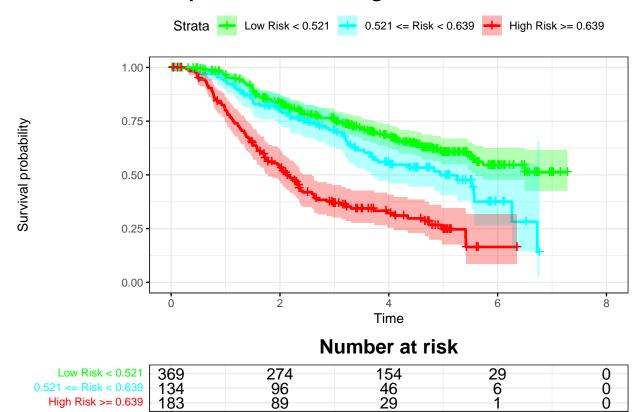
**ROC: Cal. Logistic Test: Breast Cancer** 



Time vs. Events: Cal. Logistic Test: Breast Cancer



### Kaplan-Meier: Cal. Logistic Test: Breast Cancer



par(op)

#### 1.8.2 Report of the calibrated validation

pander::pander(t(rrAnalysisTestLogistic\$keyPoints),caption="Threshold values")

Table 73: Threshold values

	@:0.639	@:0.521	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.63882	0.5212	0.5294	0.379	2.90e-01	0.5001
RR	1.79193	1.7024	1.7562	2.678	2.20e+01	1.7026
$RR\_LCI$	1.52914	1.4283	1.4771	1.679	4.75e-02	1.4179
$RR\_UCI$	2.09988	2.0290	2.0880	4.271	1.02e+04	2.0446
$\mathbf{SEN}$	0.39465	0.5953	0.5786	0.950	1.00e+00	0.6421
$\mathbf{SPE}$	0.83204	0.6382	0.6693	0.181	1.29e-02	0.5866
$\mathbf{BACC}$	0.61335	0.6168	0.6239	0.565	5.06e-01	0.6144
NetBenefit	0.00447	0.0374	0.0423	0.132	2.09e-01	0.0466

pander::pander(t(rrAnalysisTestLogistic\$0ERatio\$estimate),caption="0/E Ratio")

Table 74: O/E Ratio

O/E	Low	Upper	p.value
1.22	1.08	1.36	0.000902

pander::pander(rrAnalysisTestLogistic\$c.index,caption="C. Index")

C Index: 0.669Dxy: 0.338

• **S.D.**: 0.0309

• n: 686

• missing:  $\theta$ 

• uncensored: 299

• Relevant Pairs: 266144

Concordant: 178115Uncertain: 203702

• cstatCI:

 mean.C Index
 median
 lower
 upper

 0.669
 0.67
 0.639
 0.701

pander::pander(t(rrAnalysisTestLogistic\$ROCAnalysis\$aucs),caption="ROC AUC")

Table 76: ROC AUC

est	lower	upper
0.669	0.628	0.709

pander::pander((rrAnalysisTestLogistic\$ROCAnalysis\$sensitivity),caption="Sensitivity")

Table 77: Sensitivity

est	lower	upper
0.395	0.339	0.453

pander::pander((rrAnalysisTestLogistic\$ROCAnalysis\$specificity), caption="Specificity")

Table 78: Specificity

est	lower	upper
0.832	0.791	0.868

pander::pander(t(rrAnalysisTestLogistic\$thr\_atP),caption="Probability Thresholds")

Table 79: Probability Thresholds

90%	80%
0.639	0.521

pander::pander(rrAnalysisTestLogistic\$surdif,caption="Logrank test")

Table 80: Logrank test Chisq = 92.507991 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	369	121	181.7	20.2997	52.3868
class=1	134	60	61.7	0.0479	0.0604
class=2	183	118	55.5	70.2342	88.0195

#### 1.9 Comparing the COX and Logistic Models on the Independent Data

pander::pander(t(rrCoxTestAnalysis\$OAcum95ci))

mean	50%	2.5%	97.5%
0.842	0.842	0.841	0.844

pander::pander(t(rrAnalysisTestLogistic\$OAcum95ci))

mean	50%	2.5%	97.5%
0.791	0.791	0.791	0.792

pander::pander(t(rrCoxTestAnalysis\$0E95ci))

mean	50%	2.5%	97.5%
1.11	1.11	1.08	1.13

pander::pander(t(rrAnalysisTestLogistic\$0E95ci))

mean	50%	2.5%	97.5%
0.989	0.989	0.961	1.02

maxobs <- sum(dataBrestCancerTest\$status)</pre>

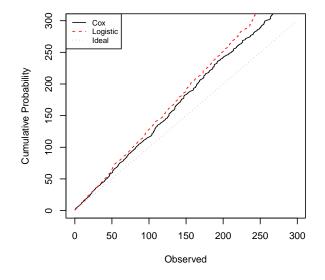
par(mfrow=c(1,2),cex=0.75)

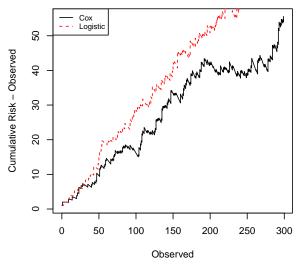
plot(rrCoxTestAnalysis\$CumulativeOvs[,1:2],type="l",lty=1,

```
main="Cumulative Probability",
     xlab="Observed",
     vlab="Cumulative Probability",
     ylim=c(0,maxobs),
     xlim=c(0,maxobs))
lines(rrAnalysisTestLogistic$CumulativeOvs[,1:2],lty=2,col="red")
lines(x=c(0,maxobs),y=c(0,maxobs),lty=3,col="gray")
legend("topleft",legend = c("Cox","Logistic","Ideal"),
       col=c("black","red","gray"),
       lty=c(1,2,3),
       cex=0.75
)
plot(rrCoxTestAnalysis$CumulativeOvs$Observed,
     rrCoxTestAnalysis$CumulativeOvs$Cumulative-
       rrCoxTestAnalysis$CumulativeOvs$Observed,
     main="Cumulative Risk Difference",
     xlab="Observed",
     ylab="Cumulative Risk - Observed",
     type="1",
     lty=1)
lines(rrAnalysisTestLogistic$CumulativeOvs$Observed,
     rrAnalysisTestLogistic$CumulativeOvs$Cumulative-
       rrAnalysisTestLogistic$CumulativeOvs$Observed,
     1ty=2,
     col="red")
legend("topleft",legend = c("Cox","Logistic"),
       col=c("black","red"),
       lty=c(1,2),
       cex=0.75
)
```

#### **Cumulative Probability**

#### **Cumulative Risk Difference**

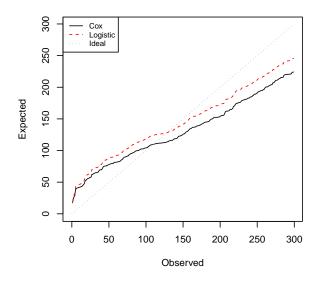


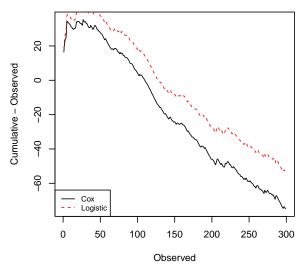


```
plot(rrCoxTestAnalysis$0EData[,2:3],type="1",lty=1,
     main="Expected over Time",
     xlab="Observed",
     ylab="Expected",
     ylim=c(0,maxobs),
     xlim=c(0,maxobs))
lines(rrAnalysisTestLogistic$0EData[,2:3],lty=2,col="red")
lines(x=c(0,maxobs),y=c(0,maxobs),lty=3,col="gray")
legend("topleft",legend = c("Cox","Logistic","Ideal"),
       col=c("black","red","gray"),
       lty=c(1,2,3),
       cex=0.75
)
plot(rrCoxTestAnalysis$0EData$0bserved,
     rrCoxTestAnalysis$0EData$Expected-
       rrCoxTestAnalysis$OEData$Observed,
     main="Expected vs Observed Difference",
     xlab="Observed",
     ylab="Cumulative - Observed",
     type="1",
     lty=1)
lines(rrAnalysisTestLogistic$0EData$0bserved,
     rrAnalysisTestLogistic$OEData$Expected-
       rrAnalysisTestLogistic$0EData$0bserved,
     lty=2,col="red")
legend("bottomleft",legend = c("Cox","Logistic"),
       col=c("black","red"),
       lty=c(1,2),
       cex=0.75
)
```

#### **Expected over Time**

#### **Expected vs Observed Difference**





par(op)