

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()`,

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
## Loading required package: miscTools
## Loading required package: Hmisc
```

```
##
## 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

#source("~/GitHub/FRESA.CAD/R/RRPlot.R")
#source("~/GitHub/FRESA.CAD/R/PoissonEventRiskCalibration.R")
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$pid
gbsgdata$pid <- NULL

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)]

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))

data$`(Intercept)` <- NULL

dataBrestCancerTrain <- cbind(time=odata[rownames(data),"rfstime"],status=odata[rownames(data),"status"])

colnames(dataBrestCancerTrain) <- str_replace_all(colnames(dataBrestCancerTrain),":","_")
colnames(dataBrestCancerTrain) <- str_replace_all(colnames(dataBrestCancerTrain)," ","")
colnames(dataBrestCancerTrain) <- str_replace_all(colnames(dataBrestCancerTrain),"\\.","_")
colnames(dataBrestCancerTrain) <- str_replace_all(colnames(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), "status"])

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")
```

Table 2: gbsg

0	1
499	183

1.3 Cox Modeling

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

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

Table 3: Table continues below

	Estimate	lower	HR	upper	u.Accuracy	r.Accuracy
age_nodes	0.000716	1.001	1.001	1.001	0.626	0.600
size_grade	0.005649	1.005	1.006	1.006	0.598	0.623
nodes	0.086582	1.082	1.090	1.099	0.637	0.642
size	0.006888	1.005	1.007	1.009	0.595	0.641
size_nodes	-0.000378	1.000	1.000	1.000	0.624	0.643

	Estimate	lower	HR	upper	u.Accuracy	r.Accuracy
age_size	-0.000149	1.000	1.000	1.000	0.567	0.627
grade	0.204934	1.146	1.227	1.314	0.565	0.637
age	-0.003113	0.996	0.997	0.998	0.513	0.628
grade_nodes	-0.013784	0.981	0.986	0.992	0.635	0.645

Table 4: Table continues below

	full.Accuracy	u.AUC	r.AUC	full.AUC	IDI	NRI
age_nodes	0.632	0.630	0.601	0.634	0.03040	0.4594
size_grade	0.632	0.599	0.626	0.634	0.01868	0.3914
nodes	0.643	0.640	0.643	0.644	0.00745	0.0564
size	0.643	0.595	0.642	0.644	0.01447	0.3587
size_nodes	0.643	0.629	0.644	0.644	0.00346	0.3430
age_size	0.632	0.568	0.630	0.634	0.00635	0.1935
grade	0.643	0.561	0.638	0.644	0.00926	0.2069
age	0.643	0.513	0.628	0.644	0.00416	0.0917
grade_nodes	0.643	0.639	0.646	0.644	0.00207	-0.0910

	z.IDI	z.NRI	Delta.AUC	Frequency
age_nodes	12.81	14.37	0.033056	1
size_grade	9.82	11.29	0.007947	1
nodes	8.33	1.66	0.000148	1
size	8.05	9.97	0.001322	1
size_nodes	7.25	9.57	-0.000377	1
age_size	5.95	5.36	0.004078	1
grade	5.88	6.31	0.005344	1
age	5.27	2.51	0.015465	1
grade_nodes	5.03	-2.55	-0.002609	1

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 6: Initial Parameters

h0	timeinterval
0.429	5

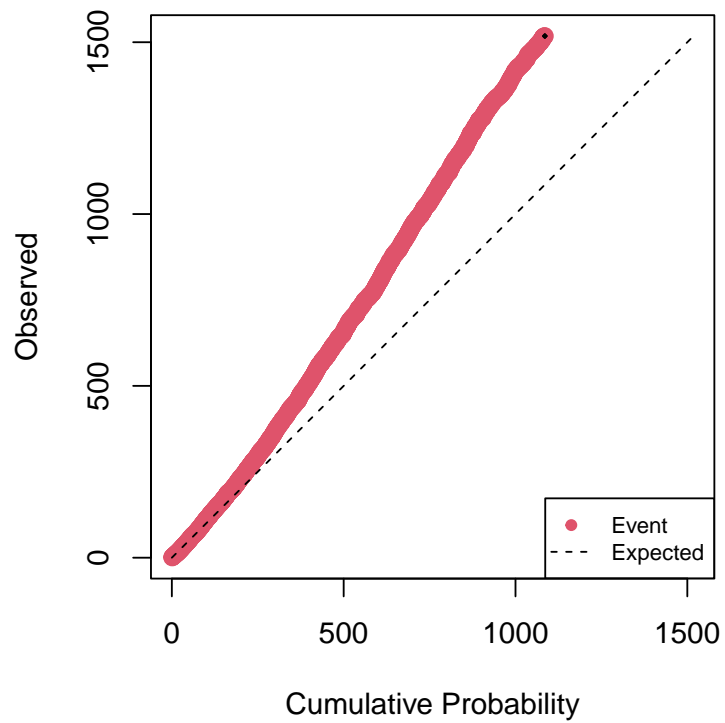
```

index <- predict(ml,dataBrestCancerTrain)
rdata <- cbind(dataBrestCancerTrain$status,ppoisGzero(index,h0))

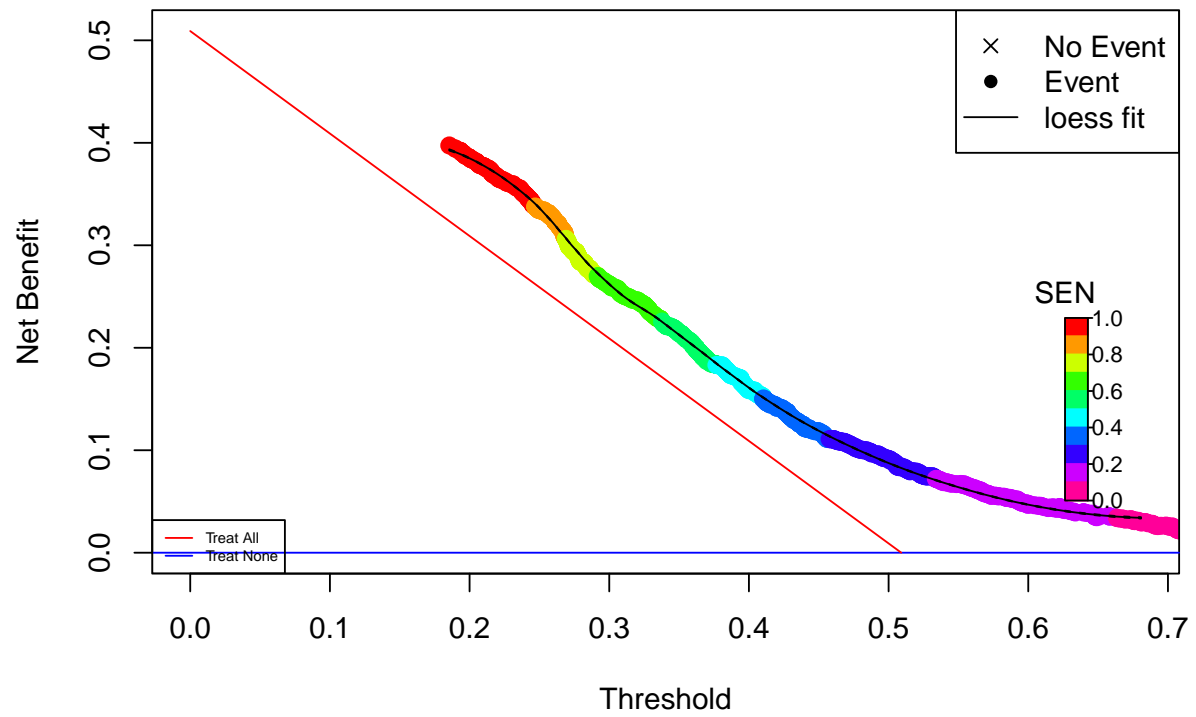
rrAnalysisTrain <- RRPlot(rdata,atProb=c(0.90,0.80),
  timetoEvent=dataBrestCancerTrain$time,
  title="Train: Breast Cancer",
  ysurvlim=c(0.00,1.0),
  riskTimeInterval=timeinterval)

```

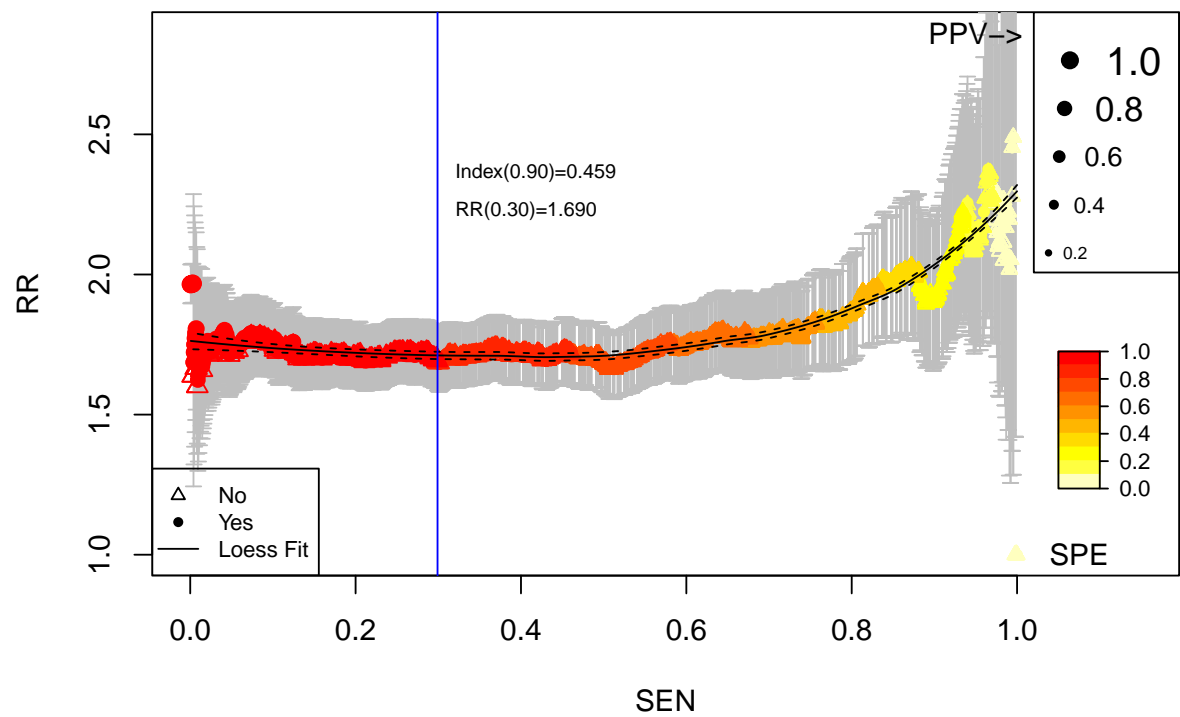
Cumulative vs. Observed: Train: Breast Cancer

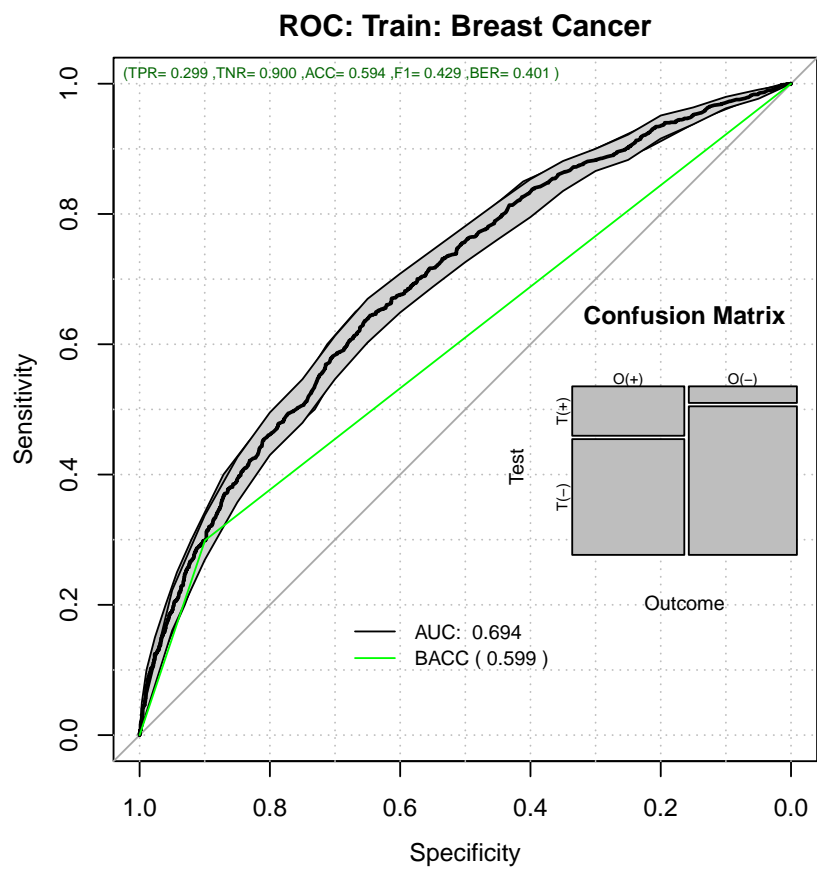


Decision Curve Analysis: Train: Breast Cancer

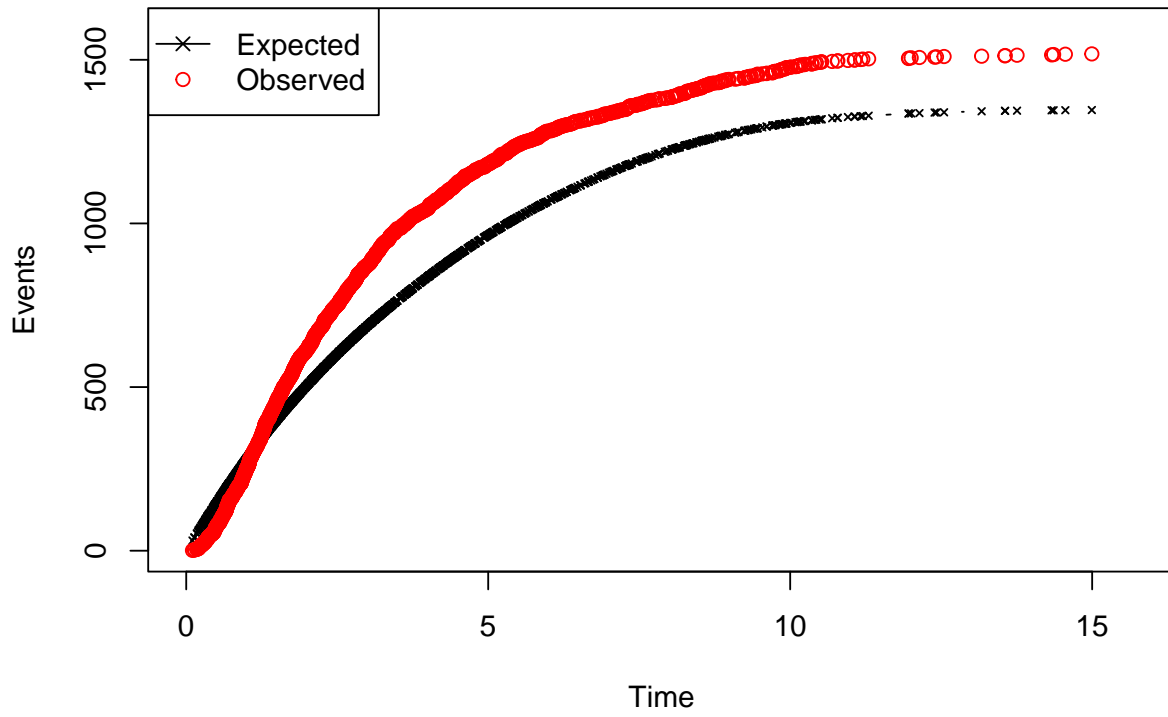


Relative Risk: Train: Breast Cancer

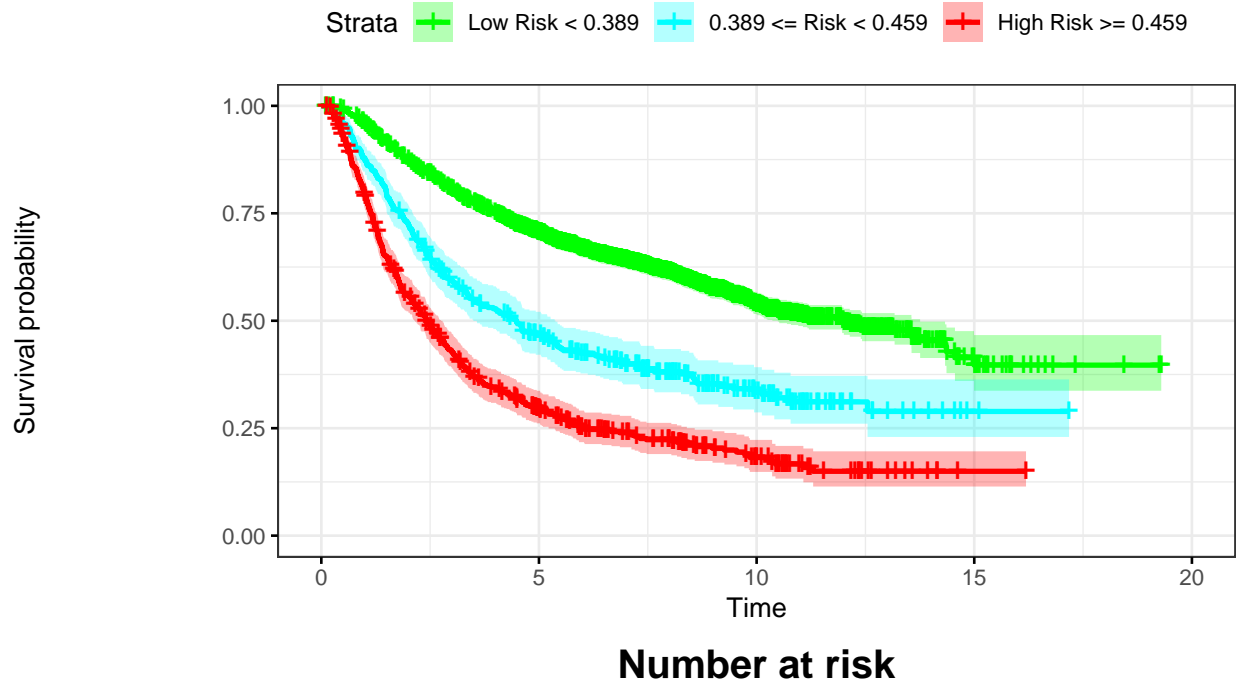




Time vs. Events: Train: Breast Cancer



Kaplan–Meier: Train: Breast Cancer



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

As we can see the Observed probability as well as the Time vs. Events are not calibrated.

1.4.2 Uncalibrated Performance Report

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

Table 7: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.459	0.389	0.320	0.214	0.18549
RR	1.690	1.713	1.799	2.376	1.00000
SEN	0.299	0.462	0.644	0.965	1.00000
SPE	0.900	0.798	0.646	0.125	0.00137
BACC	0.599	0.630	0.645	0.545	0.50068

```
pander::pander(t(rrAnalysisTrain$OERatio),caption="O/E Ratio")
```

Table 8: O/E Ratio

est	lower	upper
1.13	1.07	1.19

```
pander::pander(t(rrAnalysisTrain$OE95ci),caption="O/E Ratio")
```

Table 9: O/E Ratio

mean	50%	2.5%	97.5%
1.13	1.13	1.12	1.14

```
pander::pander(t(rrAnalysisTrain$OAcum95ci),caption="O/Acum Ratio")
```

Table 10: O/Acum Ratio

mean	50%	2.5%	97.5%
1.34	1.34	1.34	1.34

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

mean.C Index	median	lower	upper
0.676	0.677	0.662	0.69

```
pander::pander(t(rrAnalysisTrain$ROCAAnalysis$aucs),caption="ROC AUC")
```

Table 12: ROC AUC

est	lower	upper
0.694	0.675	0.713

```
pander::pander((rrAnalysisTrain$ROCAAnalysis$sensitivity),caption="Sensitivity")
```

Table 13: Sensitivity

est	lower	upper
0.299	0.276	0.323

```
pander::pander((rrAnalysisTrain$ROCAAnalysis$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%	at_max_BACC	at_max_RR	atSPE100
0.459	0.389	0.32	0.214	0.185

```
pander::pander(t(rrAnalysisTrain$RR_atP),caption="Risk Ratio")
```

Table 16: Risk Ratio

est	lower	upper
1.69	1.59	1.8

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

Table 17: 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

1.4.3 Cox Calibration

```
op <- par(no.readonly = TRUE)

calprob <- CoxRiskCalibration(ml,dataBrestCancerTrain,"status","time")

pander::pander(c(h0=calprob$h0,
  Gain=calprob$hazardGain,
  DeltaTime=calprob$timeInterval),
  caption="Cox Calibration Parameters")
```

h0	Gain	DeltaTime
0.698	1.35	6.97

1.4.4 The RRplot() of the calibrated model

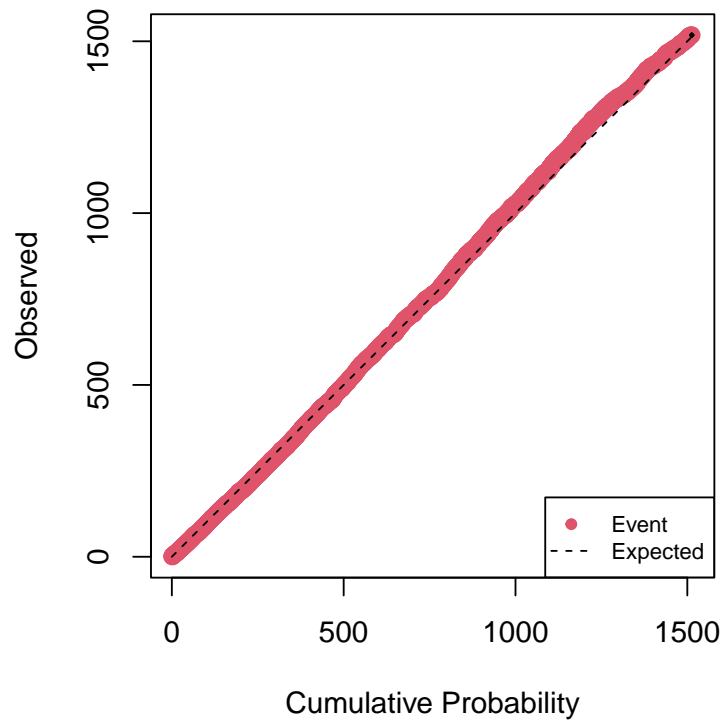
```
h0 <- calprob$h0
timeinterval <- calprob$timeInterval;

rdata <- cbind(dataBrestCancerTrain$status,calprob$prob)

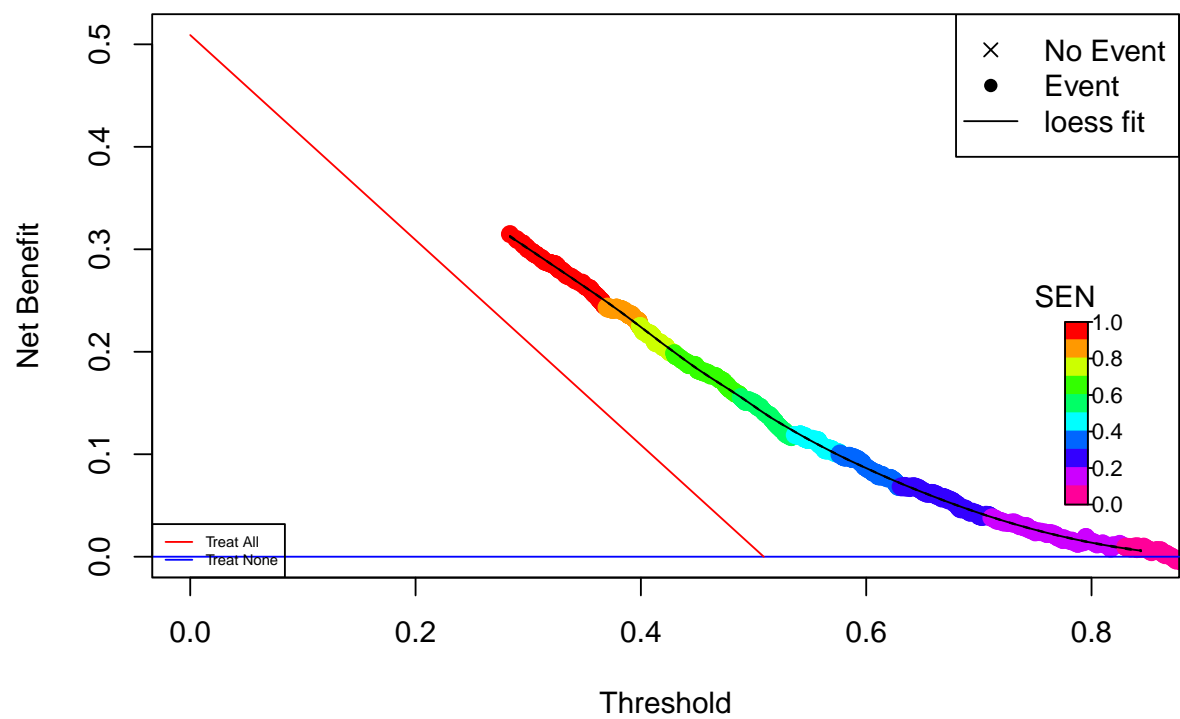
rrAnalysisTrain <- RRPlot(rdata,atProb=c(0.90,0.80),
  timetoEvent=dataBrestCancerTrain$time,
```

```
title="Cal. Train: Breast Cancer",  
ysurvlim=c(0.00,1.0),  
riskTimeInterval=timeinterval)
```

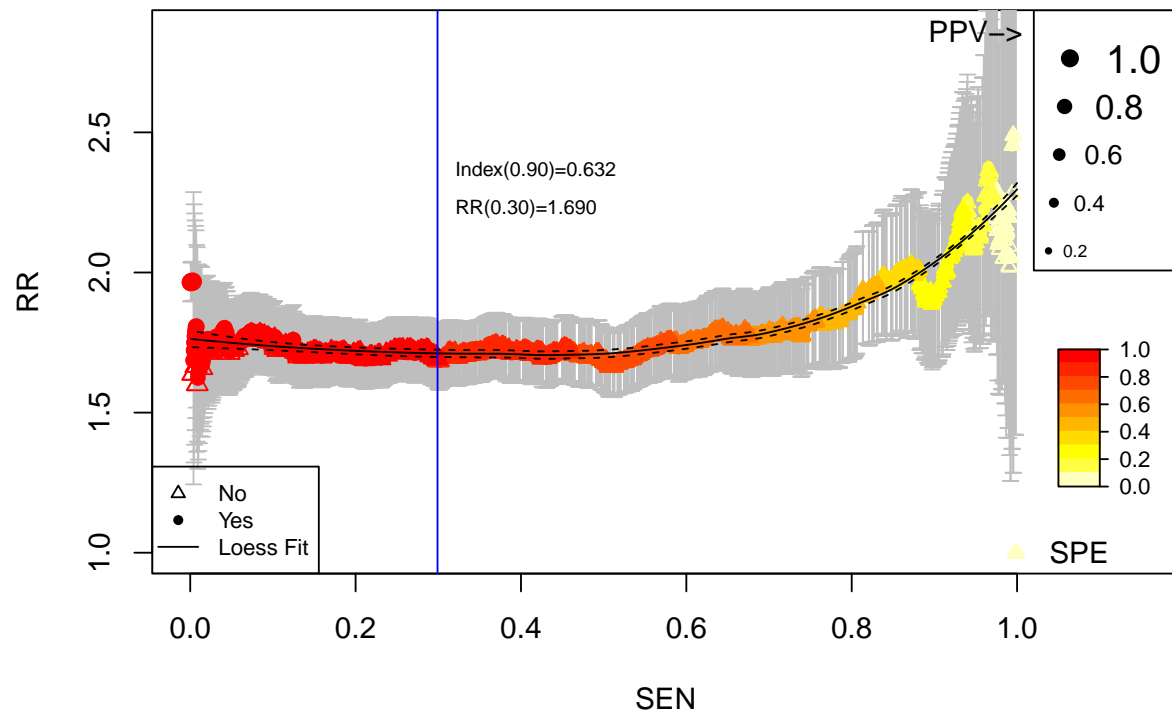
Cumulative vs. Observed: Cal. Train: Breast Cancer

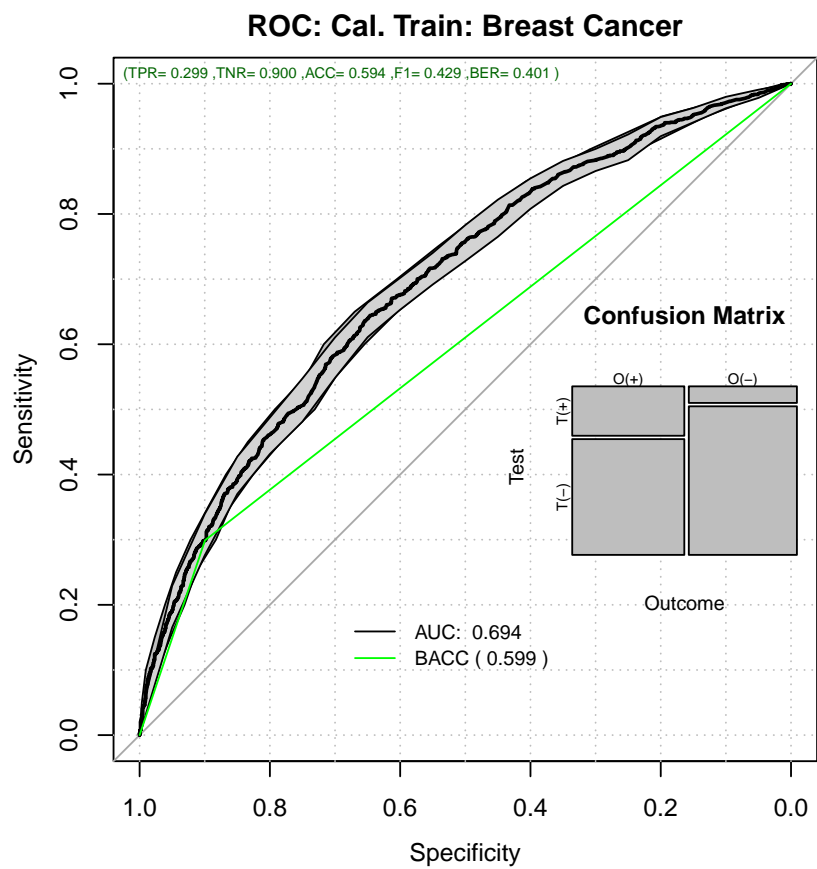


Decision Curve Analysis: Cal. Train: Breast Cancer

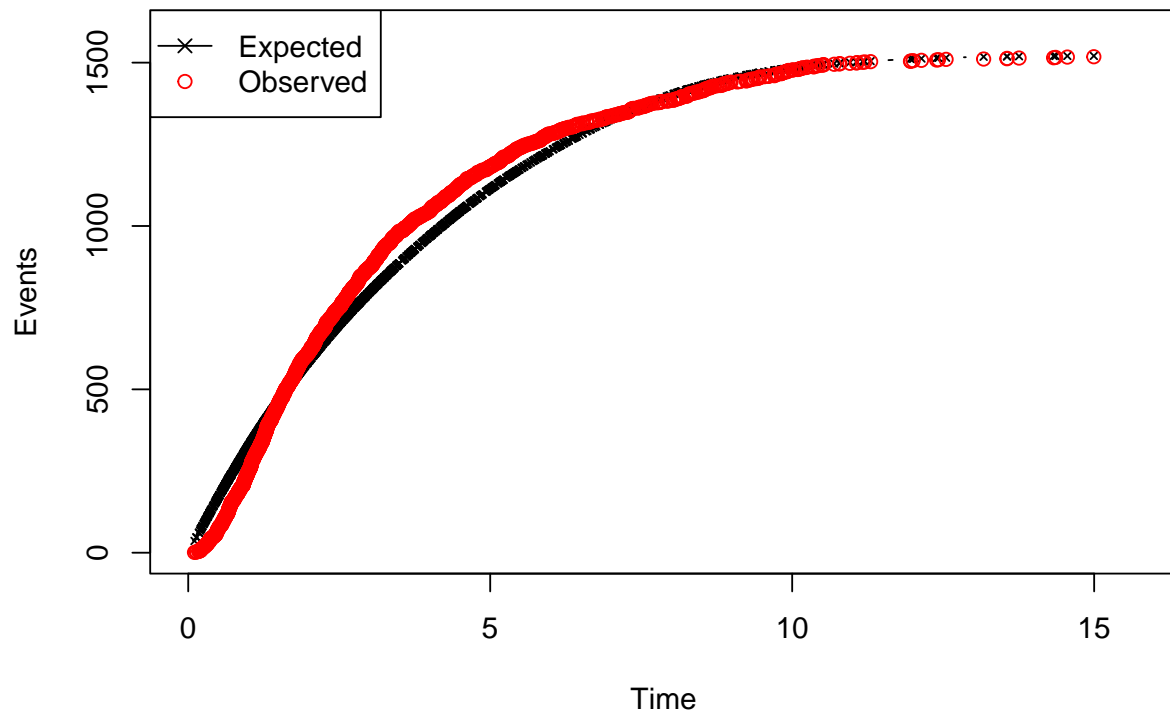


Relative Risk: Cal. Train: Breast Cancer

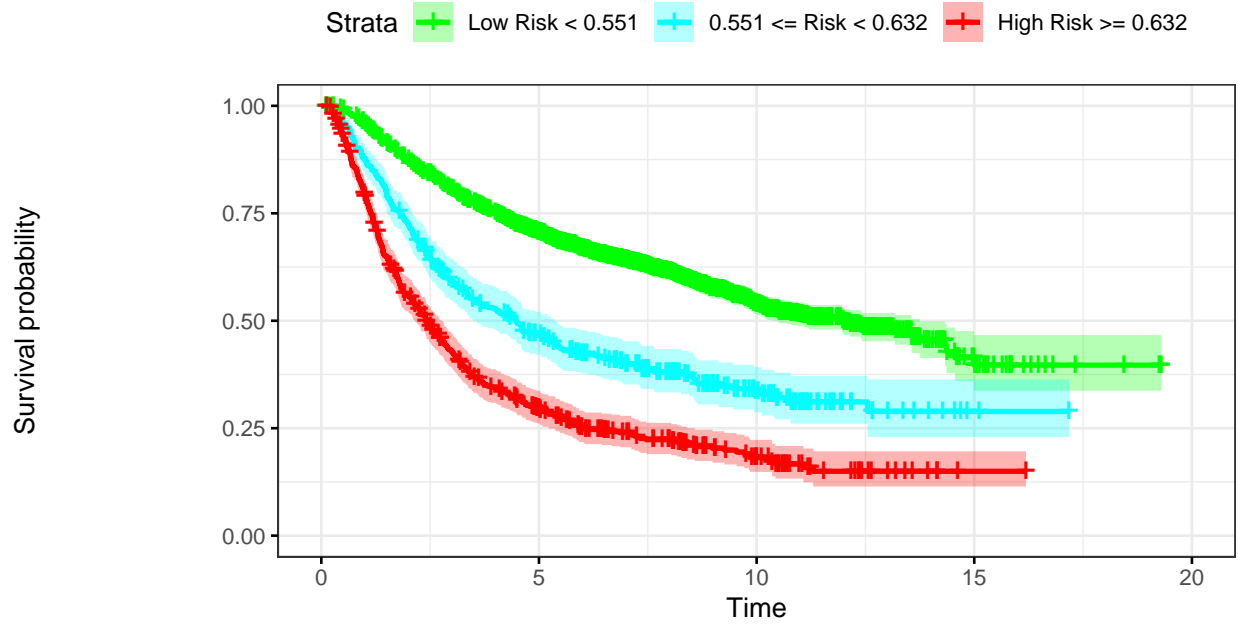




Time vs. Events: Cal. Train: Breast Cancer



Kaplan–Meier: Cal. Train: Breast Cancer



Number at risk

Low Risk < 0.551	1985	1260	393	23	0
0.551 <= Risk < 0.632	396	166	51	2	0
High Risk >= 0.632	601	145	39	1	0

1.4.5 Calibrated Train Performance

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

Table 19: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.632	0.551	0.466	0.324	0.28381
RR	1.690	1.713	1.799	2.376	1.00000
SEN	0.299	0.462	0.644	0.965	1.00000
SPE	0.900	0.798	0.646	0.125	0.00137
BACC	0.599	0.630	0.645	0.545	0.50068

```
pander::pander(t(rrAnalysisTrain$OERatio),caption="O/E Ratio")
```

Table 20: O/E Ratio

est	lower	upper
0.998	0.949	1.05

```
pander::pander(t(rrAnalysisTrain$OE95ci),caption="O/E Ratio")
```

Table 21: O/E Ratio

mean	50%	2.5%	97.5%
0.977	0.977	0.969	0.985

```
pander::pander(t(rrAnalysisTrain$OAcum95ci),caption="O/Acum Ratio")
```

Table 22: O/Acum Ratio

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	0.663	0.69

```
pander::pander(t(rrAnalysisTrain$ROCAAnalysis$aucs),caption="ROC AUC")
```

Table 24: ROC AUC

est	lower	upper
0.694	0.675	0.713

```
pander::pander((rrAnalysisTrain$ROCAAnalysis$sensitivity),caption="Sensitivity")
```

Table 25: Sensitivity

est	lower	upper
0.299	0.276	0.323

```
pander::pander((rrAnalysisTrain$ROCAAnalysis$specificity),caption="Specificity")
```

Table 26: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 27: Probability Thresholds

90%	80%	at_max_BACC	at_max_RR	atSPE100
0.632	0.551	0.466	0.324	0.284

```
pander::pander(t(rrAnalysisTrain$RR_atP),caption="Risk Ratio")
```

Table 28: Risk Ratio

est	lower	upper
1.69	1.59	1.8

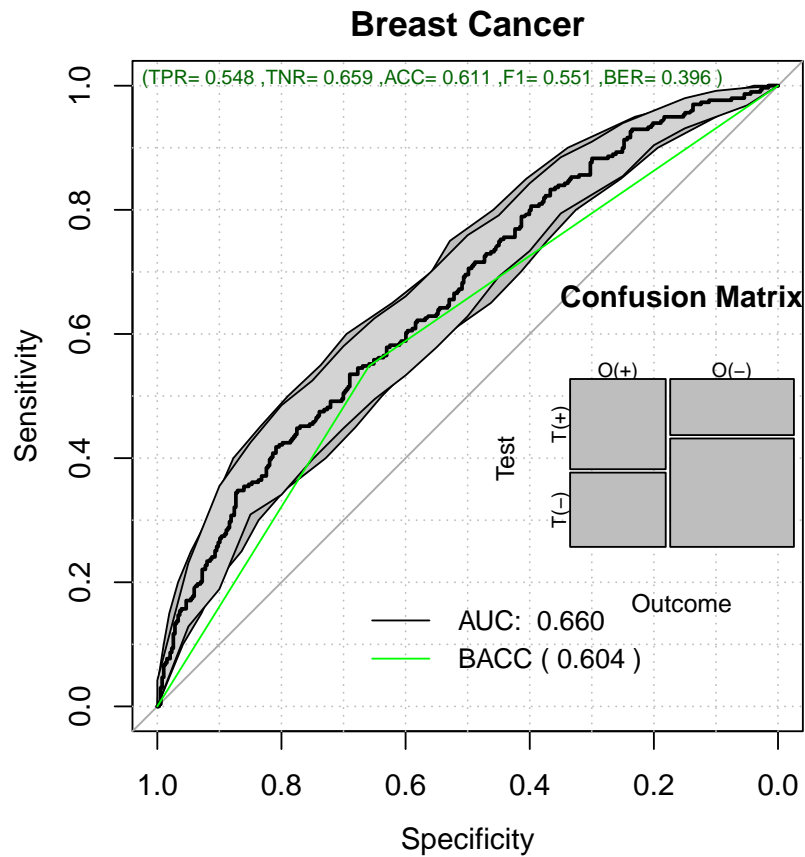
```
pander::pander(rrAnalysisTrain$surdif,caption="Logrank test")
```

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

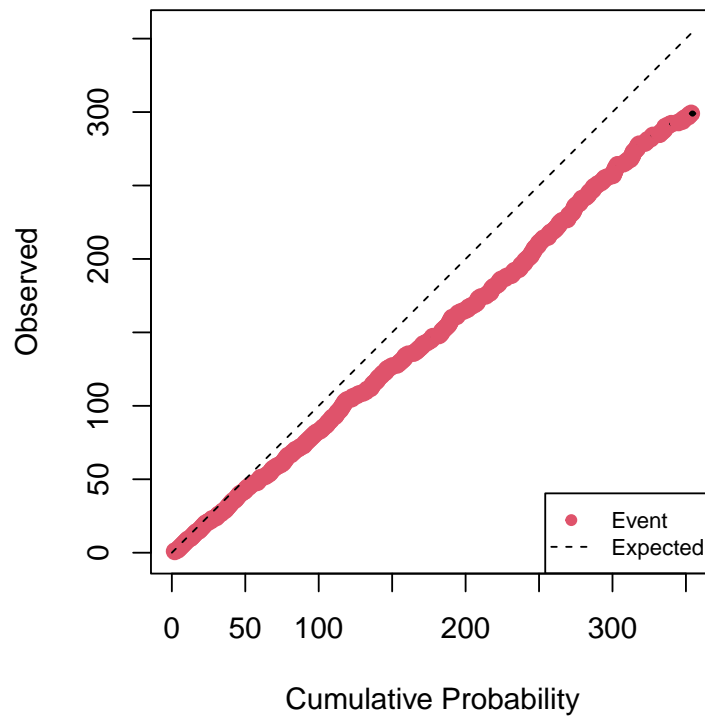
```
index <- predict(ml,dataBrestCancerTest)
pp <- predictionStats_binary(cbind(dataBrestCancerTest$status,index),plotname="Breast Cancer")
```



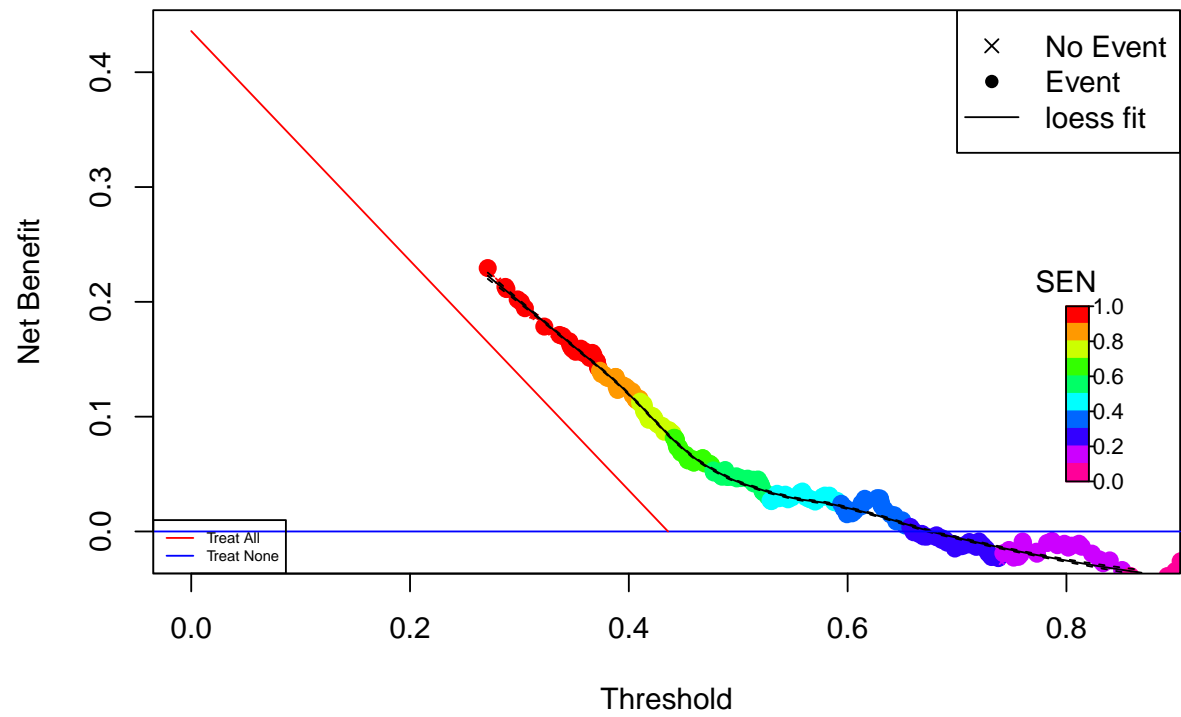
```
par(op)

prob <- ppoisGzero(index,h0)
rdata <- cbind(dataBrestCancerTest$status,prob)
rrCoxTestAnalysis <- RRPlot(rdata,atThr=rrAnalysisTrain$thr_atP,
                             timetoEvent=dataBrestCancerTest$time,
                             title="Test: Breast Cancer",
                             ysurvlim=c(0.00,1.0),
                             riskTimeInterval=timeinterval)
```

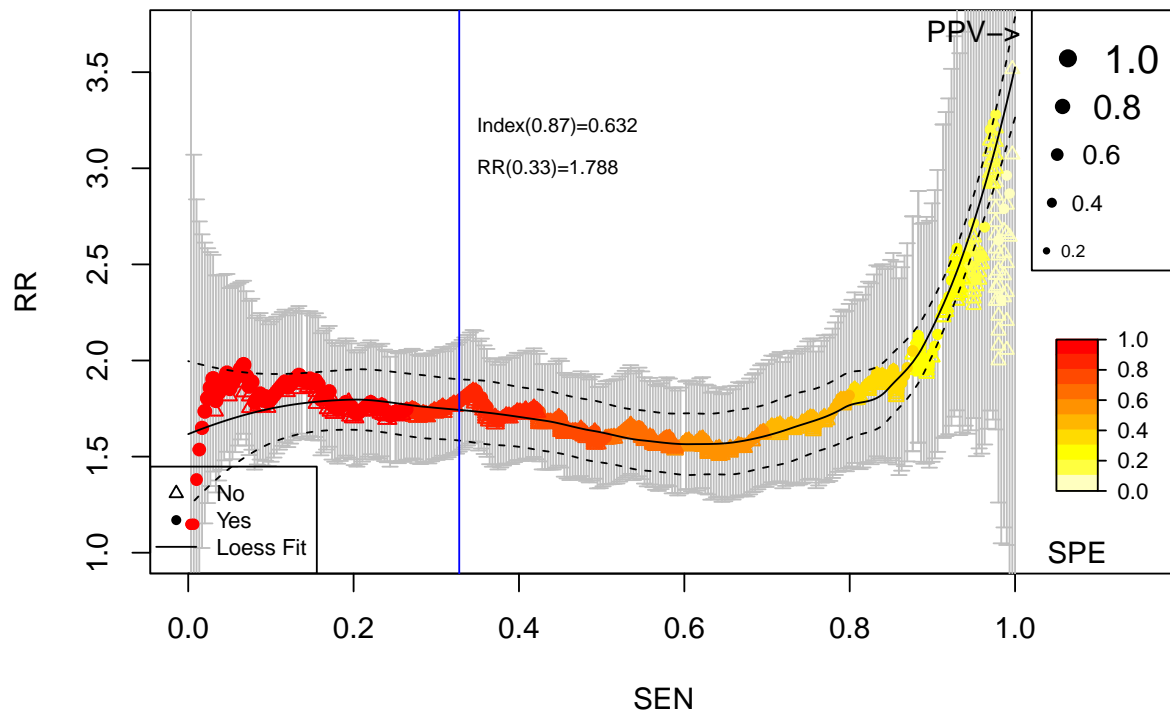
Cumulative vs. Observed: Test: Breast Cancer

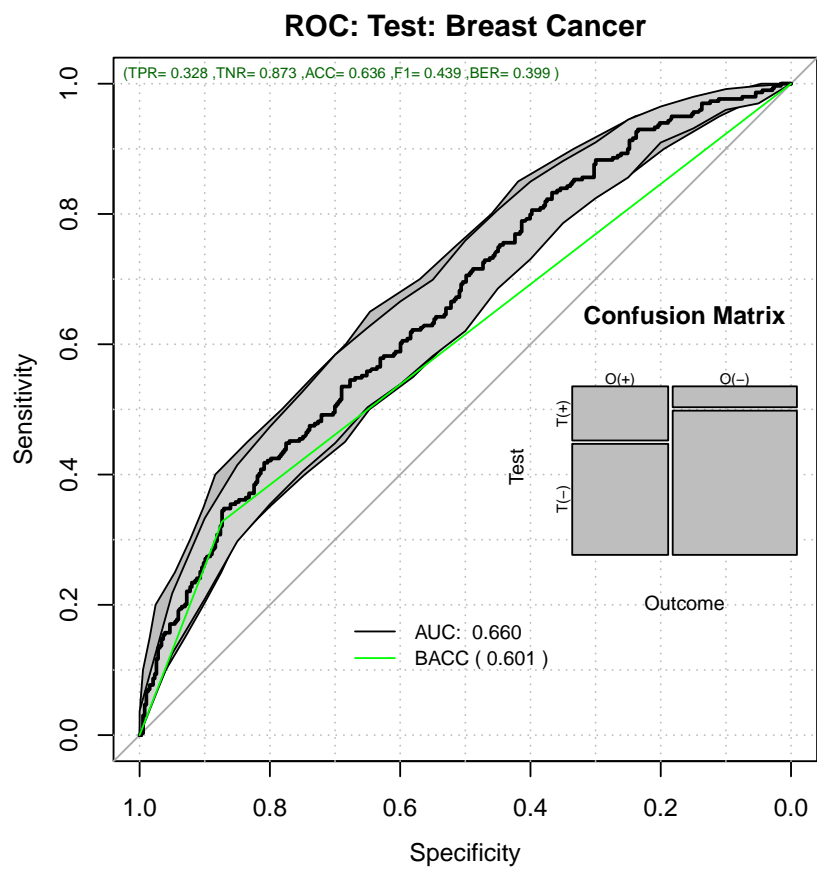


Decision Curve Analysis: Test: Breast Cancer

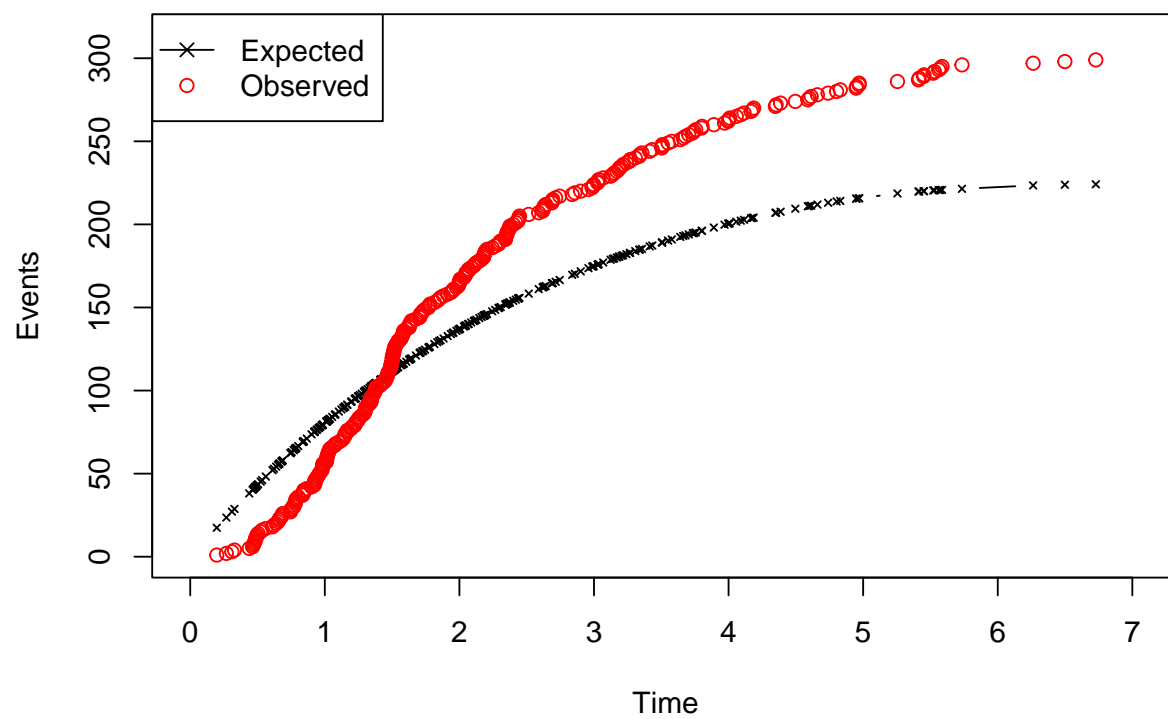


Relative Risk: Test: Breast Cancer

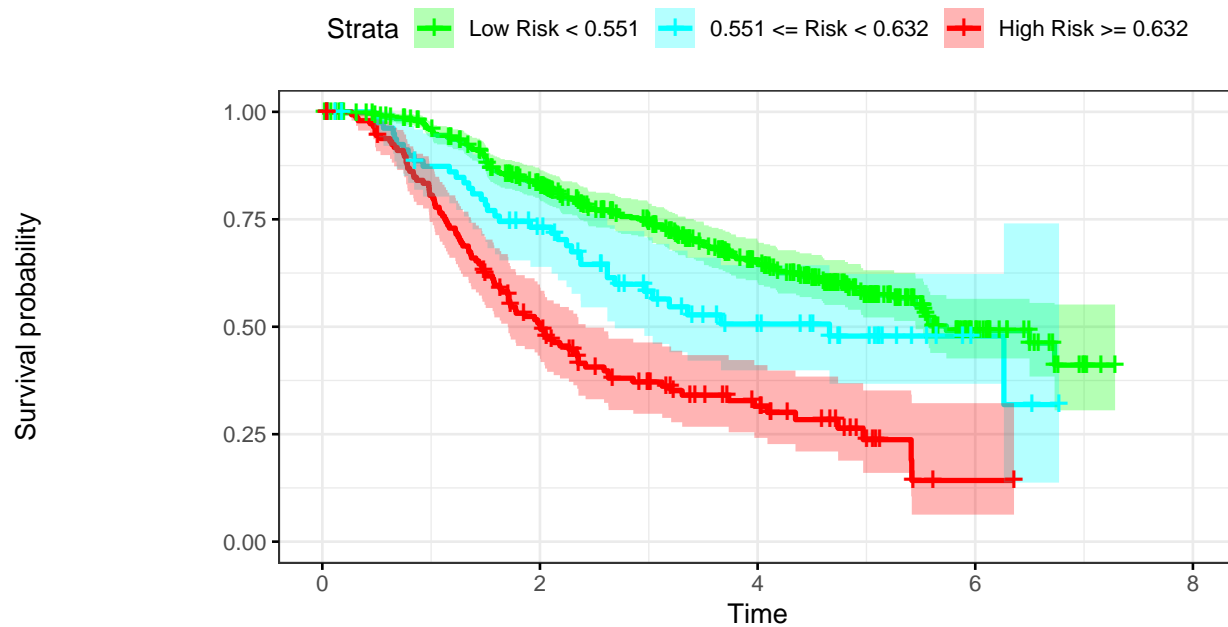




Time vs. Events: Test: Breast Cancer



Kaplan–Meier: Test: Breast Cancer



Number at risk

Low Risk < 0.551	457	338	183	32	0
0.551 <= Risk < 0.632	82	53	22	3	0
High Risk >= 0.632	147	68	24	1	0

```
par(op)
```

1.5.1 External Data Report

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

Table 30: Threshold values (continued below)

	@:0.631504143125695	@:0.551358546734404	@:0.466097007699806
Thr	0.631	0.552	0.466
RR	1.799	1.643	1.589
SEN	0.331	0.452	0.622
SPE	0.873	0.757	0.579
BACC	0.602	0.604	0.600

Table 31: Table continues below

	@:0.323887654054491	@:0.283809391129424	@MAX_BACC	@MAX_RR
Thr	0.3227	0.2846	0.583	0.337
RR	2.6254	4.4083	1.758	3.279
SEN	0.9799	0.9967	0.418	0.977
SPE	0.0749	0.0233	0.809	0.111

	@:0.323887654054491	@:0.283809391129424	@MAX_BACC	@MAX_RR
BACC	0.5274	0.5100	0.613	0.544

	@SPE100
Thr	0.2710
RR	26.3824
SEN	1.0000
SPE	0.0155
BACC	0.5078

```
pander::pander(t(rrCoxTestAnalysis$OERatio),caption="O/E Ratio")
```

Table 33: O/E Ratio

est	lower	upper
1.33	1.19	1.49

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

- **C Index:** *0.664*
- **Dxy:** *0.328*
- **S.D.:** *0.0311*
- **n:** *686*
- **missing:** *0*
- **uncensored:** *299*
- **Relevant Pairs:** *266144*
- **Concordant:** *176737*
- **Uncertain:** *203702*
- **cstatCI:**

mean.C Index	median	lower	upper
0.664	0.664	0.632	0.698

```
pander::pander(t(rrCoxTestAnalysis$ROCAalysis$aucs),caption="ROC AUC")
```

Table 35: ROC AUC

est	lower	upper
0.66	0.619	0.7

```
pander::pander((rrCoxTestAnalysis$ROCAalysis$sensitivity),caption="Sensitivity")
```

Table 36: Sensitivity

est	lower	upper
0.328	0.275	0.384

```
pander::pander((rrCoxTestAnalysis$ROCAAnalysis$specificity),caption="Specificity")
```

Table 37: Specificity

est	lower	upper
0.873	0.836	0.905

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

Table 38: Probability Thresholds (continued below)

90%	80%	at_max_BACC	at_max_RR	atSPE100	at_max_BACC	at_max_RR
0.632	0.551	0.466	0.324	0.284	0.583	0.337

atSPE100
0.271

```
pander::pander(t(rrCoxTestAnalysis$RR_atP),caption="Risk Ratio")
```

Table 40: Risk Ratio

est	lower	upper
1.79	1.53	2.09

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

Table 41: 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

```
calprob <- CoxRiskCalibration(ml,dataBrestCancerTest,"status","time")

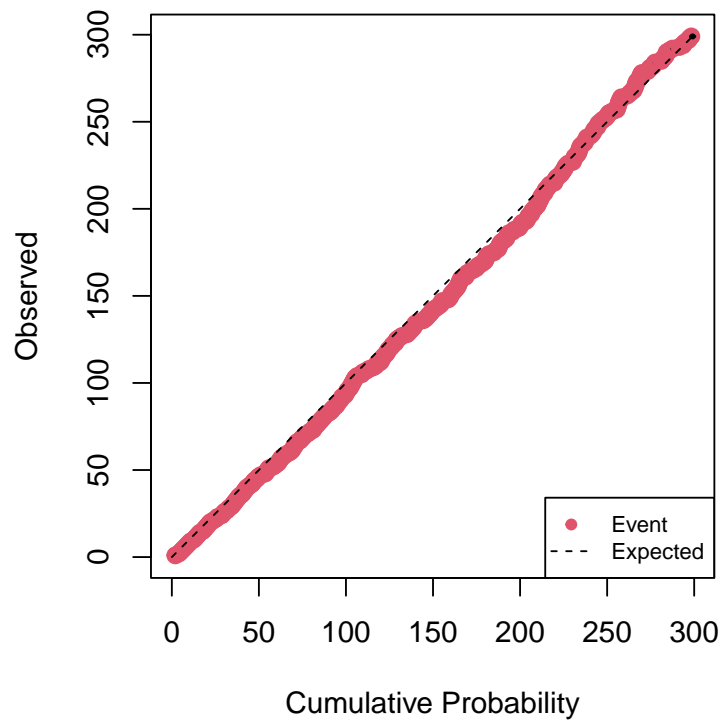
pander::pander(c(h0=calprob$h0,
  Gain=calprob$hazardGain,
  DeltaTime=calprob$timeInterval),
  caption="Cox Calibration Parameters")
```

h0	Gain	DeltaTime
0.535	0.925	4.87

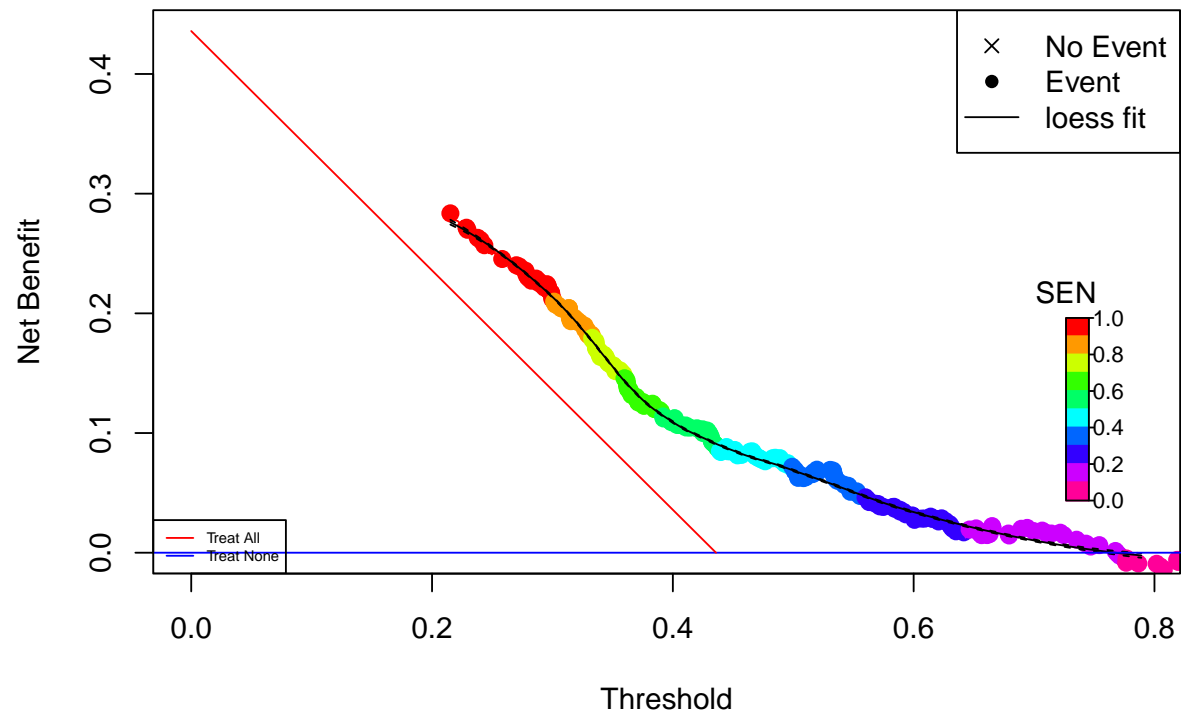
```
rdata <- cbind(dataBrestCancerTest$status,calprob$prob)

rrAnalysis <- RRPPlot(rdata,atProb=c(0.90,0.80),
                      timetoEvent=dataBrestCancerTest$time,
                      title="Cal. Test: Breast Cancer",
                      ysurvlim=c(0.00,1.0),
                      riskTimeInterval=calprob$timeInterval)
```

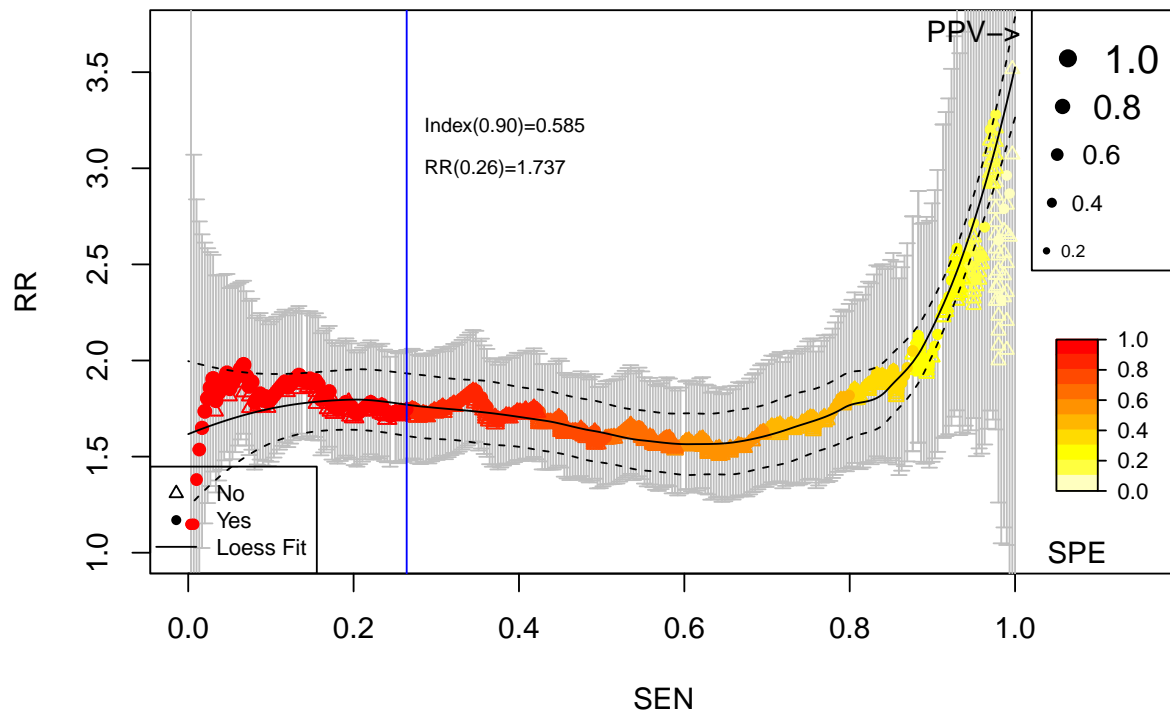
Cumulative vs. Observed: Cal. Test: Breast Cancer

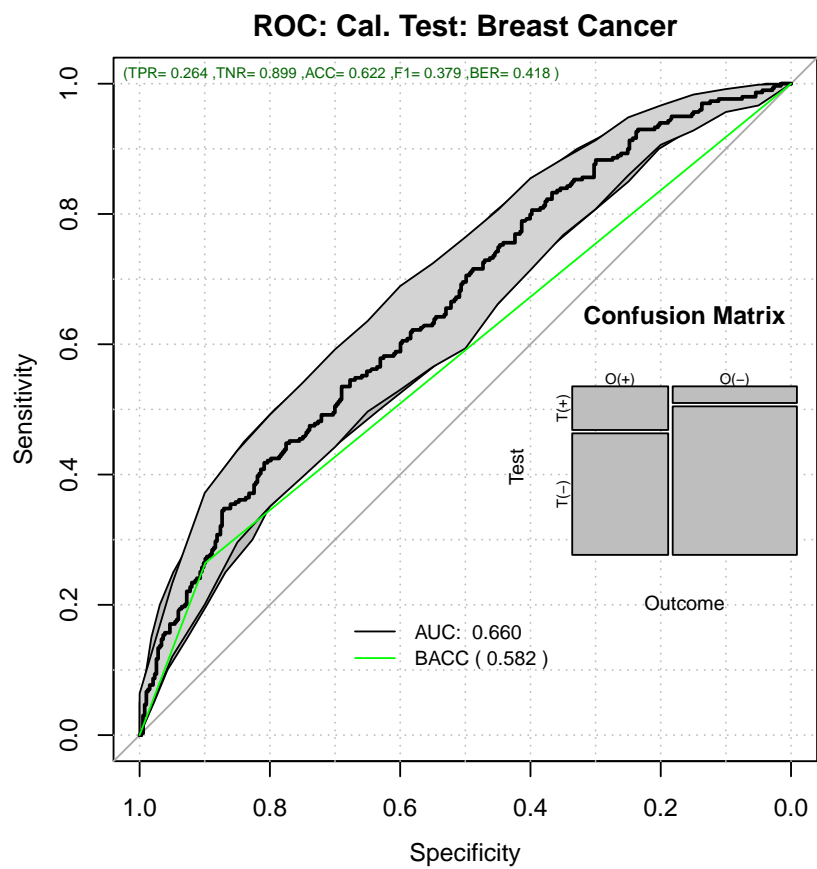


Decision Curve Analysis: Cal. Test: Breast Cancer

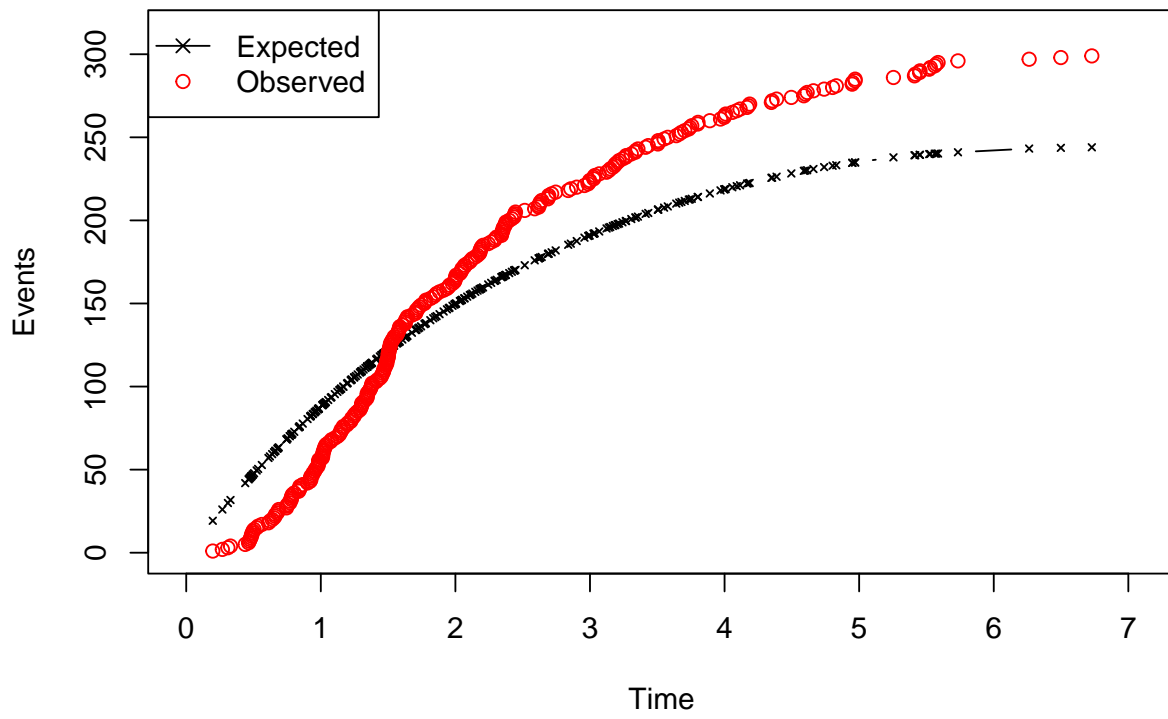


Relative Risk: Cal. Test: Breast Cancer

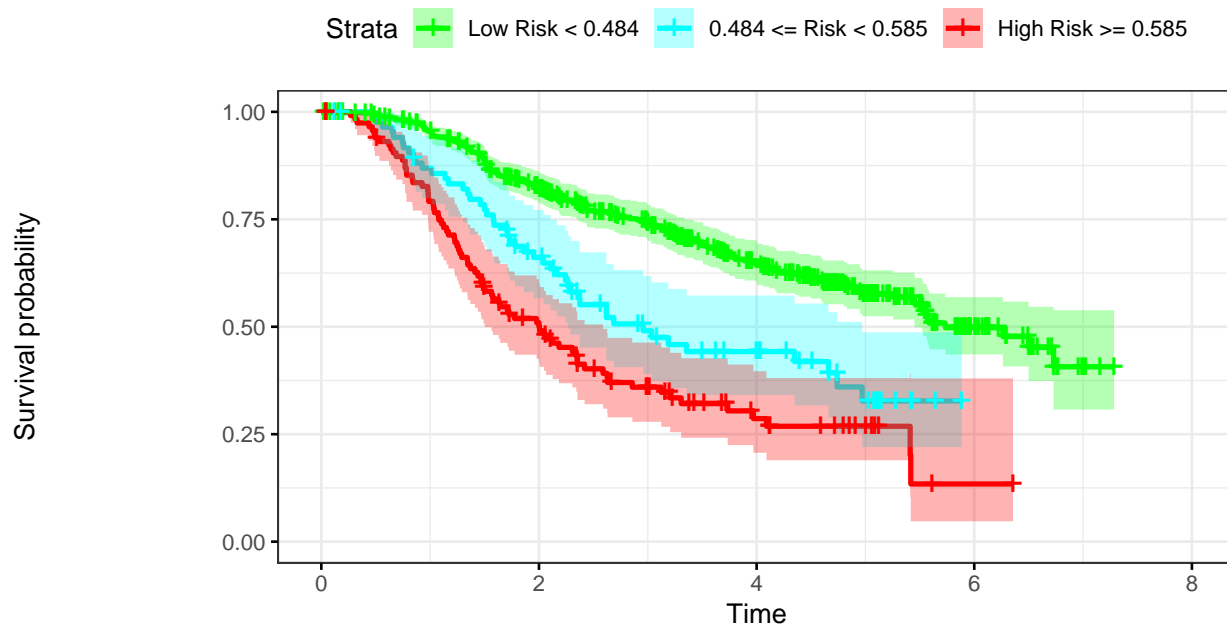




Time vs. Events: Cal. Test: Breast Cancer



Kaplan–Meier: Cal. Test: Breast Cancer



Number at risk

Low Risk < 0.484	482	354	190	35	0
0.484 <= Risk < 0.585	86	51	23	0	0
High Risk >= 0.585	118	54	16	1	0

1.5.3 After Calibration Report

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

Table 43: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.584	0.484	0.489	0.270	0.2152
RR	1.741	1.721	1.758	3.279	26.3824
SEN	0.268	0.421	0.418	0.977	1.0000
SPE	0.899	0.798	0.809	0.111	0.0155
BACC	0.583	0.610	0.613	0.544	0.5078

```
pander::pander(t(rrAnalysis$OERatio),caption="O/E Ratio")
```

Table 44: O/E Ratio

est	lower	upper
1.23	1.09	1.37

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

- **C Index:** *0.664*
- **Dxy:** *0.328*
- **S.D.:** *0.0311*
- **n:** *686*
- **missing:** *0*
- **uncensored:** *299*
- **Relevant Pairs:** *266144*
- **Concordant:** *176737*
- **Uncertain:** *203702*
- **cstatCI:**

mean.C Index	median	lower	upper
0.664	0.664	0.634	0.692

```
pander::pander(t(rrAnalysis$ROCAAnalysis$aucs),caption="ROC AUC")
```

Table 46: ROC AUC

est	lower	upper
0.66	0.619	0.7

```
pander::pander((rrAnalysis$ROCAAnalysis$sensitivity),caption="Sensitivity")
```

Table 47: Sensitivity

est	lower	upper
0.264	0.215	0.318

```
pander::pander((rrAnalysis$ROCAAnalysis$specificity),caption="Specificity")
```

Table 48: Specificity

est	lower	upper
0.899	0.865	0.927

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

Table 49: Probability Thresholds

90%	80%	at_max_BACC	at_max_RR	atSPE100
0.585	0.484	0.489	0.27	0.215

```
pander::pander(t(rrAnalysis$RR_atP),caption="Risk Ratio")
```

Table 50: Risk Ratio

est	lower	upper
1.74	1.48	2.05

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

Table 51: 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
```

```
dataBreastCancerR <- subset(dataBreastCancerTrain, time>=5 | status==1)
dataBreastCancerR$status <- dataBreastCancerR$status * (dataBreastCancerR$time < 5)
dataBreastCancerR$time <- NULL
```

```
#ml <- BSWiMS.model(status~1,data=dataBreastCancerR,loops=20,NumberOfRepeats = 5)
mlog <- BSWiMS.model(status~1,data=dataBreastCancerR,loops=1,NumberOfRepeats = 5)
```

—..

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

Table 52: Table continues below

	Estimate	lower	OR	upper	u.Accuracy	r.Accuracy
size_nodes	1.05e-03	1.001	1.001	1.001	0.669	0.571
nodes	4.33e-02	1.040	1.044	1.048	0.676	0.634
grade_nodes	1.50e-02	1.014	1.015	1.016	0.682	0.637
age_nodes	1.06e-03	1.001	1.001	1.001	0.678	0.653
size_grade	1.75e-03	1.001	1.002	1.002	0.632	0.682
age_size	8.73e-05	1.000	1.000	1.000	0.608	0.682
grade	2.27e-01	1.168	1.254	1.347	0.571	0.683
age_meno	-6.04e-03	0.992	0.994	0.996	0.571	0.676
age_pgr	-5.42e-06	1.000	1.000	1.000	0.571	0.686
age_grade	-1.65e-03	0.997	0.998	0.999	0.574	0.690
meno_grade	1.02e-01	1.045	1.107	1.173	0.571	0.683
nodes_hormon	-1.38e-02	0.979	0.986	0.994	0.587	0.688
size	3.94e-03	1.002	1.004	1.006	0.611	0.693
meno_pgr	3.19e-04	1.000	1.000	1.001	0.571	0.687

	Estimate	lower	OR	upper	u.Accuracy	r.Accuracy
pgr	-1.07e-04	1.000	1.000	1.000	0.571	0.689
meno_nodes	-2.60e-02	0.955	0.974	0.994	0.640	0.686
grade_pgr	-3.51e-05	1.000	1.000	1.000	0.571	0.669
meno_size	2.34e-03	1.000	1.002	1.004	0.604	0.691

Table 53: Table continues below

	full.Accuracy	u.AUC	r.AUC	full.AUC	IDI
size_nodes	0.668	0.627	0.500	0.628	0.11233
nodes	0.690	0.639	0.621	0.662	0.07110
grade_nodes	0.686	0.649	0.624	0.655	0.06580
age_nodes	0.686	0.642	0.621	0.657	0.03346
size_grade	0.686	0.626	0.646	0.655	0.01787
age_size	0.686	0.577	0.649	0.657	0.01534
grade	0.690	0.500	0.653	0.662	0.01340
age_meno	0.686	0.500	0.645	0.657	0.00782
age_pgr	0.686	0.500	0.656	0.657	0.00512
age_grade	0.690	0.507	0.661	0.662	0.00454
meno_grade	0.686	0.500	0.652	0.657	0.00425
nodes_hormon	0.686	0.526	0.658	0.655	0.00280
size	0.690	0.618	0.663	0.662	0.00507
meno_pgr	0.686	0.500	0.657	0.657	0.00316
pgr	0.686	0.500	0.659	0.655	0.00257
meno_nodes	0.686	0.595	0.656	0.657	0.00264
grade_pgr	0.668	0.500	0.627	0.628	0.00241
meno_size	0.690	0.578	0.663	0.662	0.00185

	NRI	z.IDI	z.NRI	Delta.AUC	Frequency
size_nodes	0.63654	17.86	18.870	0.128490	1
nodes	0.57106	14.13	16.179	0.040494	1
grade_nodes	0.54866	13.66	15.650	0.031087	1
age_nodes	0.21312	9.39	5.710	0.035896	1
size_grade	0.29411	6.74	7.728	0.008648	1
age_size	0.29152	6.41	7.652	0.007600	1
grade	0.19036	6.20	4.983	0.008461	1
age_meno	0.08057	4.76	2.337	0.012065	1
age_pgr	0.00745	4.11	0.194	0.000417	1
age_grade	0.11372	3.60	2.960	0.000315	1
meno_grade	0.20428	3.47	5.343	0.004441	1
nodes_hormon	0.45522	3.44	12.150	-0.002853	1
size	0.21050	3.42	5.600	-0.001075	1
meno_pgr	0.05977	3.35	1.558	-0.000429	1
pgr	0.19759	2.64	5.745	-0.004123	1
meno_nodes	-0.06329	2.59	-1.645	0.000631	1
grade_pgr	0.17471	2.55	5.058	0.001252	1
meno_size	0.10227	2.43	2.662	-0.001378	1

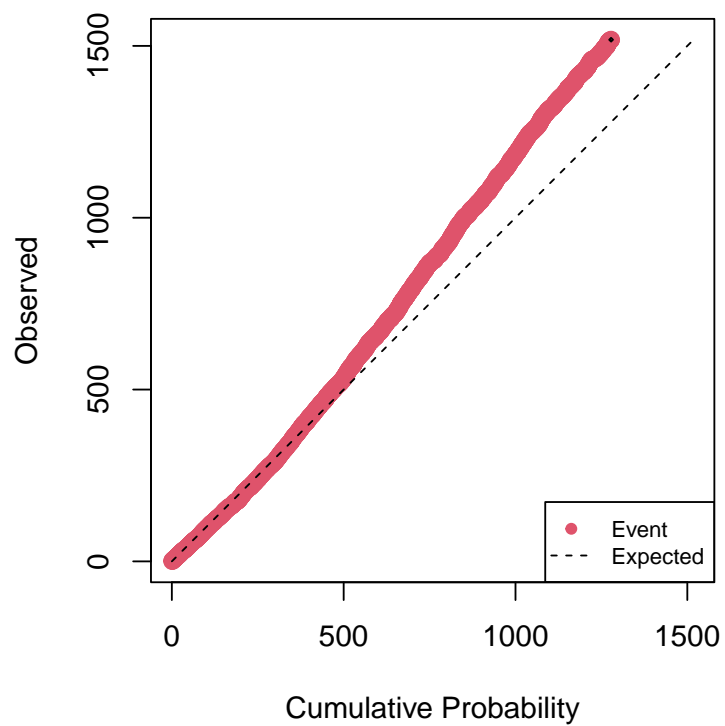
1.7 Logistic Model Performance

```
op <- par(no.readonly = TRUE)

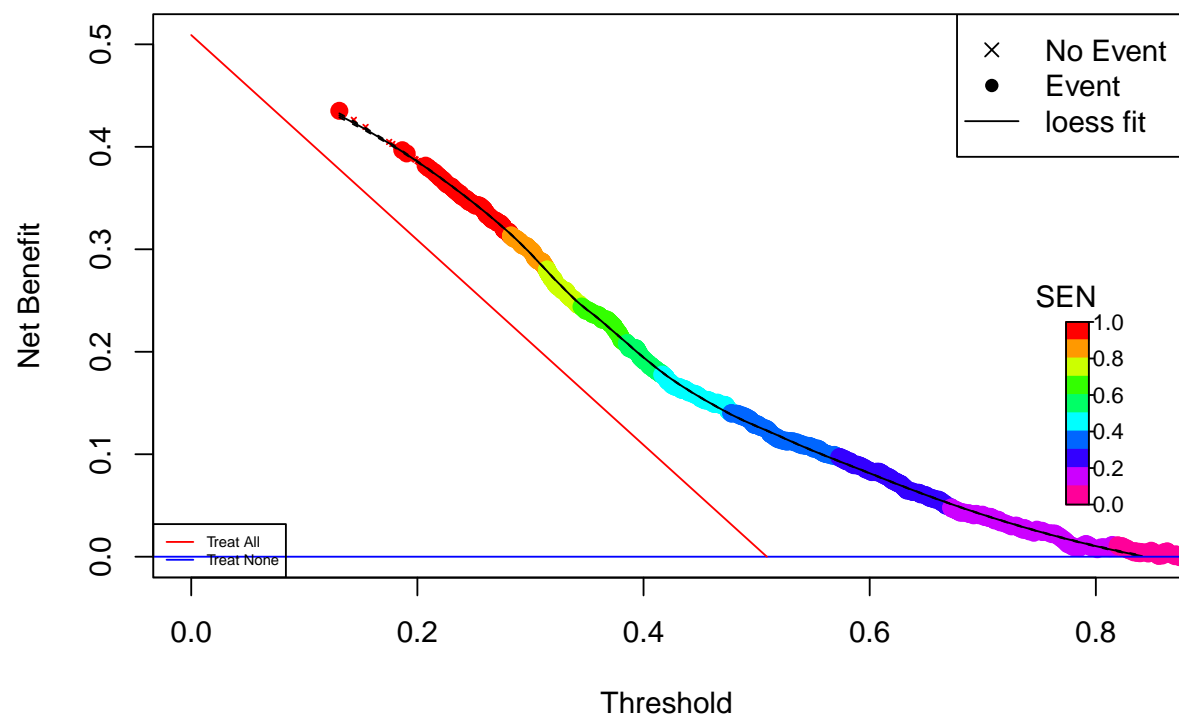
cprob <- predict(mlog,dataBrestCancerTrain)

rdata <- cbind(dataBrestCancerTrain$status,cprob)
rrAnalysisTrain <- RRPlot(rdata,atProb=c(0.90,0.80),
  timetoEvent=dataBrestCancerTrain$time,
  title="Logistic Train: Breast Cancer",
  ysurvlim=c(0.00,1.0),
  riskTimeInterval=5.0)
```

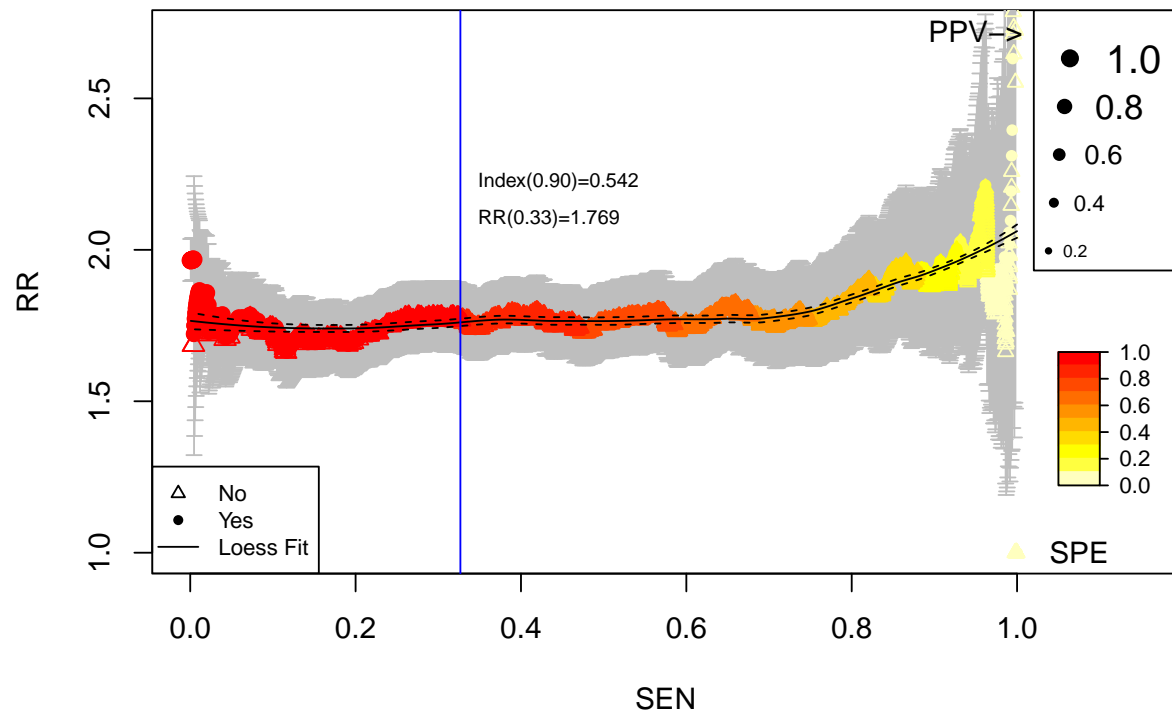
Cumulative vs. Observed: Logistic Train: Breast Cancer

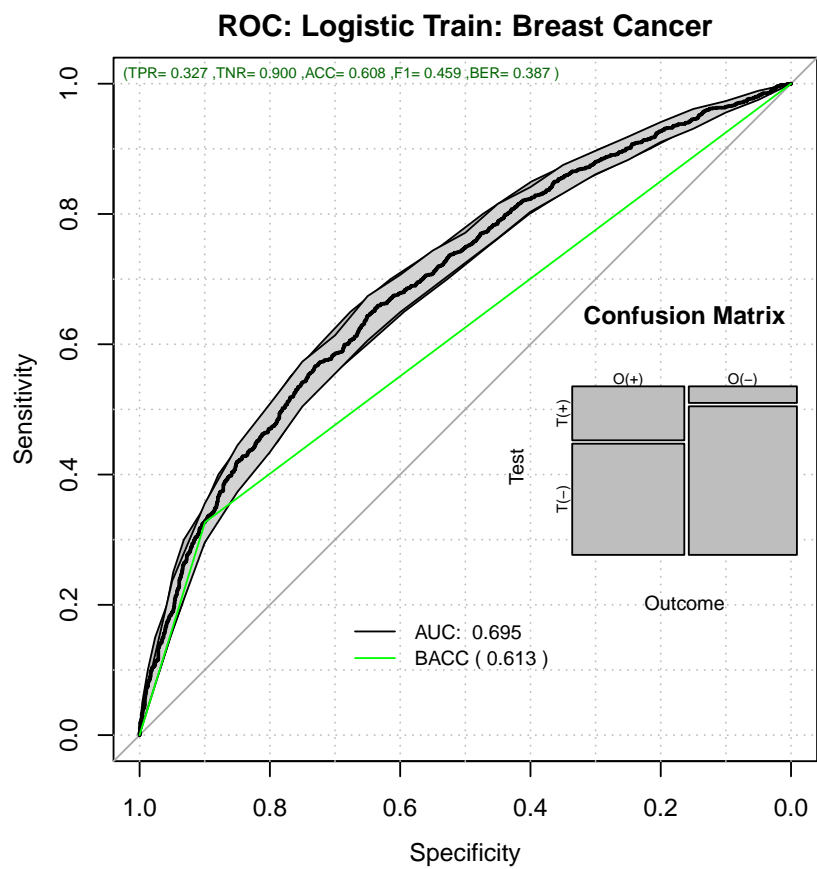


Decision Curve Analysis: Logistic Train: Breast Cancer

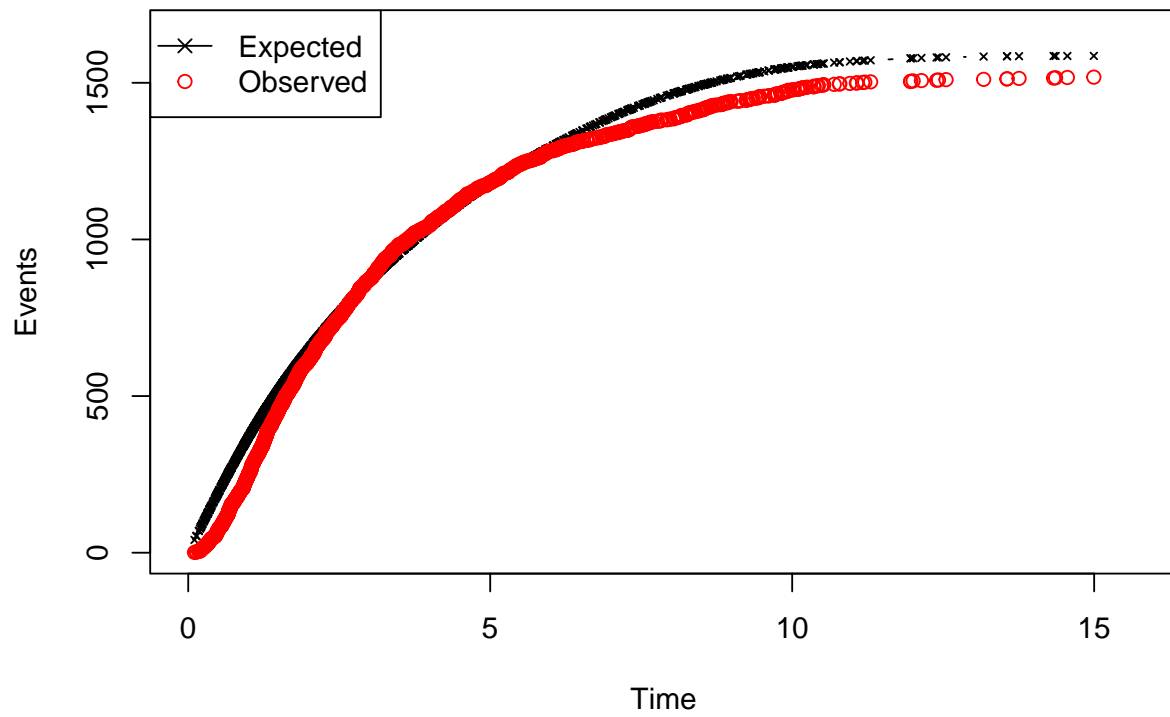


Relative Risk: Logistic Train: Breast Cancer

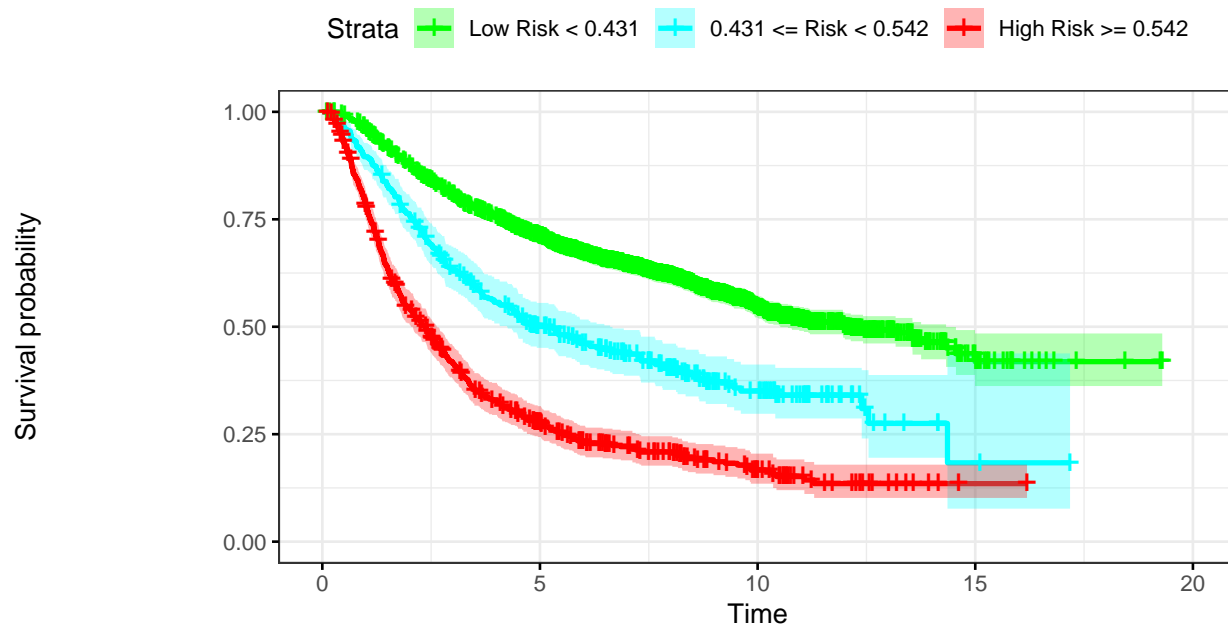




Time vs. Events: Logistic Train: Breast Cancer



Kaplan–Meier: Logistic Train: Breast Cancer



Number at risk

Low Risk < 0.431	1975	1268	399	23	0
0.431 <= Risk < 0.542	364	160	47	2	0
High Risk >= 0.542	643	143	37	1	0

```
par(op)
```

1.7.1 Training Report

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

Table 55: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.542	0.431	0.394	0.255	0.130969
RR	1.765	1.739	1.799	2.213	1.000000
SEN	0.327	0.470	0.566	0.962	1.000000
SPE	0.900	0.799	0.731	0.125	0.000683
BACC	0.613	0.635	0.648	0.543	0.500342

```
pander::pander(t(rrAnalysisTrain$OERatio),caption="O/E Ratio")
```

Table 56: O/E Ratio

est	lower	upper
0.957	0.91	1.01

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

- **C Index:** *0.68*
- **Dxy:** *0.36*
- **S.D.:** *0.014*
- **n:** *2982*
- **missing:** *0*
- **uncensored:** *1518*
- **Relevant Pairs:** *6184528*
- **Concordant:** *4206590*
- **Uncertain:** *2703838*
- **cstatCI:**

mean.C Index	median	lower	upper
0.68	0.68	0.667	0.694

```
pander::pander(t(rrAnalysisTrain$ROCAalysis$aucs),caption="ROC AUC")
```

Table 58: ROC AUC

est	lower	upper
0.695	0.677	0.714

```
pander::pander((rrAnalysisTrain$ROCAalysis$sensitivity),caption="Sensitivity")
```

Table 59: Sensitivity

est	lower	upper
0.327	0.303	0.351

```
pander::pander((rrAnalysisTrain$ROCAalysis$specificity),caption="Specificity")
```

Table 60: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 61: Probability Thresholds

90%	80%	at_max_BACC	at_max_RR	atSPE100
0.542	0.431	0.394	0.255	0.131

```
pander::pander(t(rrAnalysisTrain$RR_atP),caption="Risk Ratio")
```

Table 62: Risk Ratio

est	lower	upper
1.77	1.66	1.88

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

Table 63: Logrank test Chisq = 543.347175 on 2 degrees of freedom,
p = 0.000000

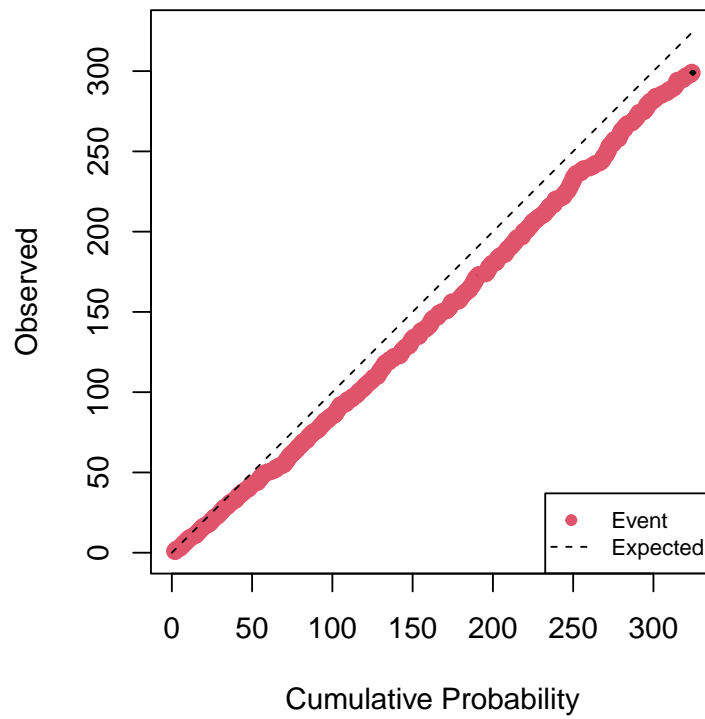
	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1975	804	1145	101.5	418.9
class=1	364	218	169	14.1	15.9
class=2	643	496	204	418.2	490.7

1.7.2 Results on the validation set using Logistic model

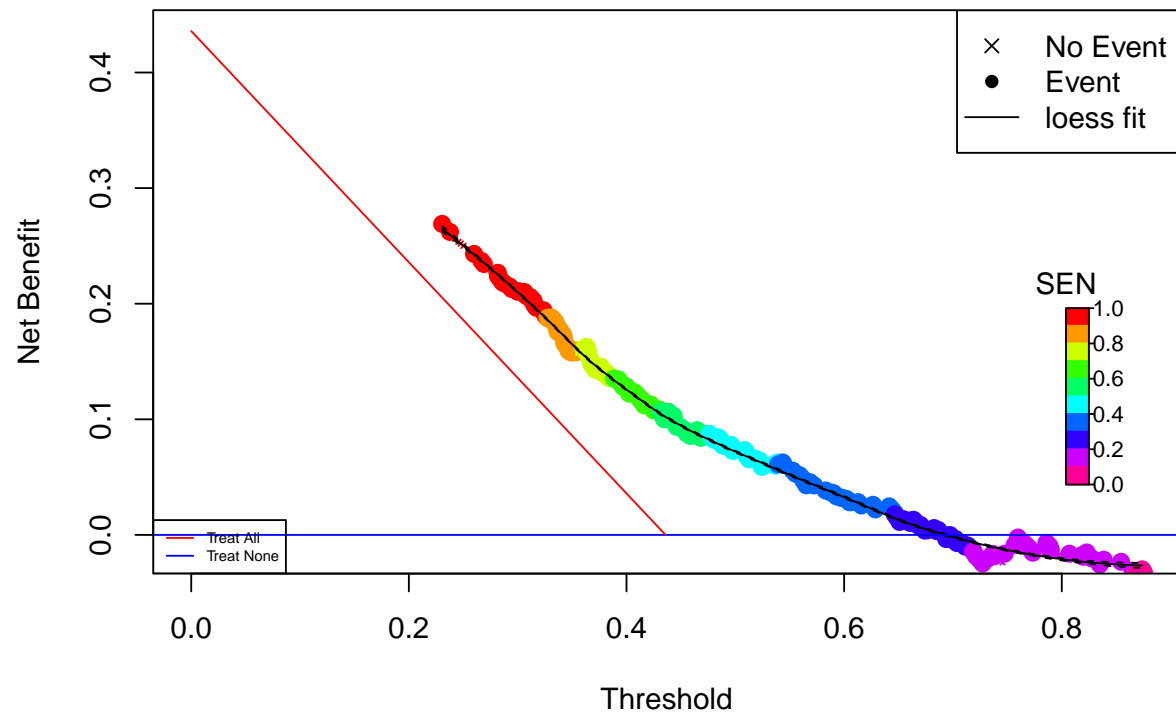
```
pre <- predict(mlog,dataBrestCancerTest)
rdata <- cbind(dataBrestCancerTest$status,pre)

rrAnalysis <- RRPlot(rdata,atThr=rrAnalysisTrain$thr_atP,
                     timetoEvent=dataBrestCancerTest$time,
                     title="Logistic Test: Breast Cancer",
                     ysurvlim=c(0.00,1.0),
                     riskTimeInterval=5)
```

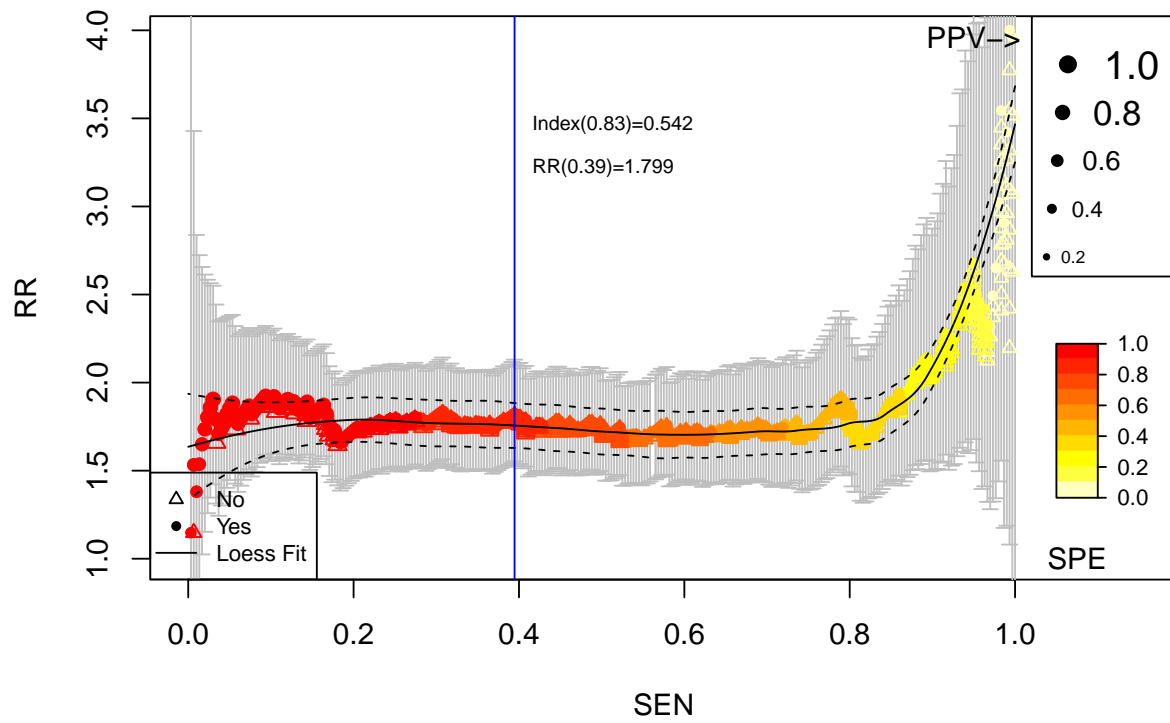
Cumulative vs. Observed: Logistic Test: Breast Cancer

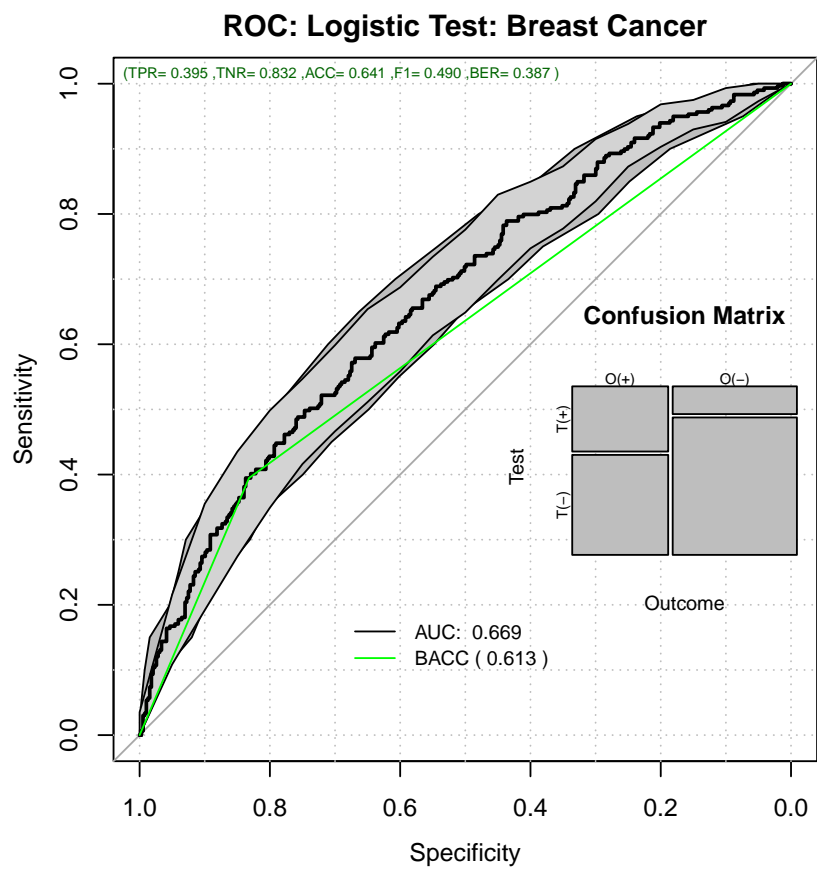


Decision Curve Analysis: Logistic Test: Breast Cancer

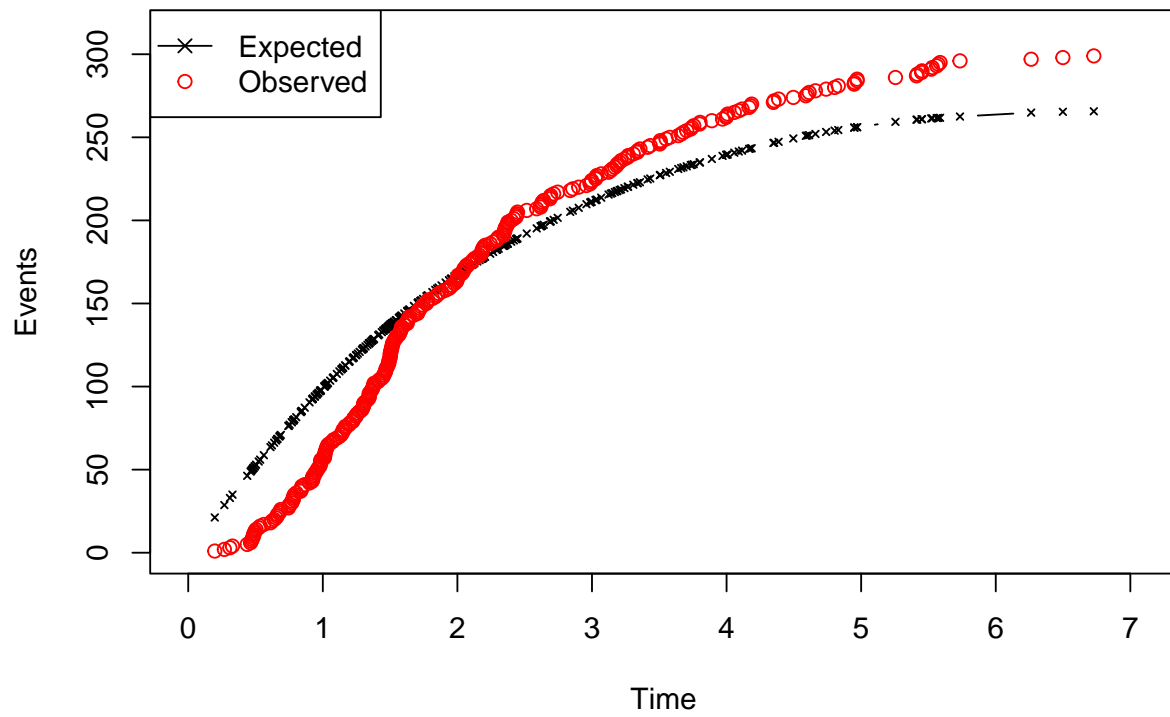


Relative Risk: Logistic Test: Breast Cancer

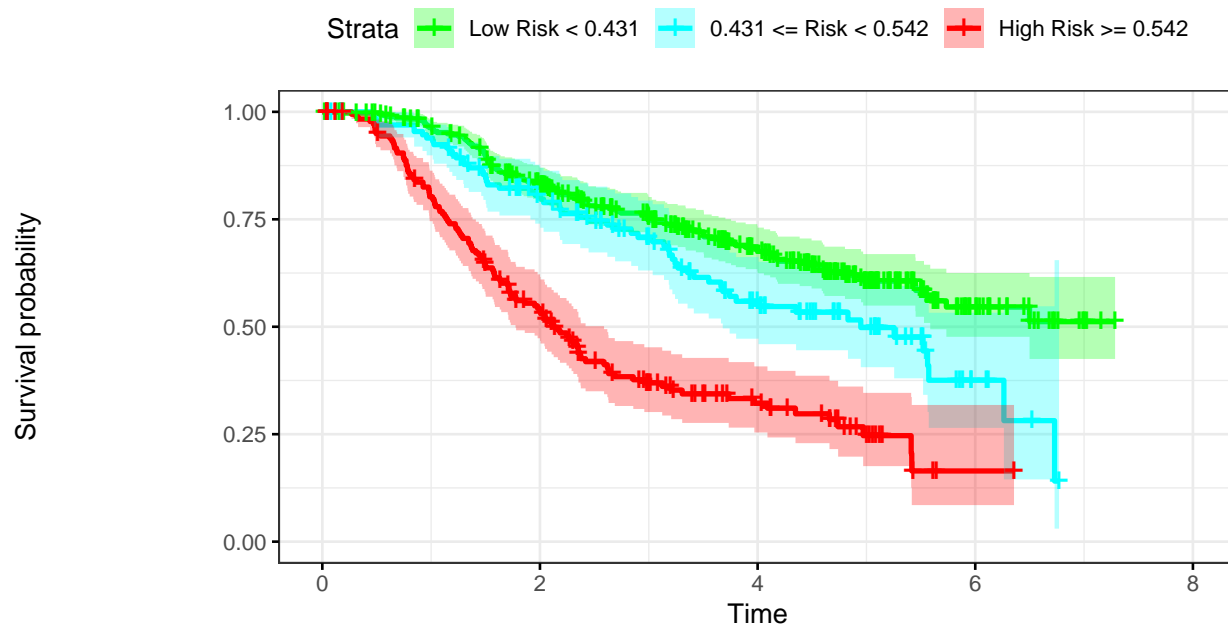




Time vs. Events: Logistic Test: Breast Cancer



Kaplan–Meier: Logistic Test: Breast Cancer



Number at risk

Low Risk < 0.431	369	274	154	29	0
0.431 <= Risk < 0.542	134	96	46	6	0
High Risk >= 0.542	183	89	29	1	0

```
par(op)
```

1.7.3 Validation Report

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

Table 64: Threshold values (continued below)

	@:0.541514635560692	@:0.431407973270606	@:0.394073801020846
Thr	0.542	0.431	0.394
RR	1.792	1.702	1.746
SEN	0.395	0.595	0.686
SPE	0.832	0.638	0.545
BACC	0.613	0.617	0.615

Table 65: Table continues below

	@:0.255194040798287	@:0.130968771182643	@MAX_BACC	@MAX_RR
Thr	0.255	0.2306	0.439	0.306
RR	3.094	21.9530	1.756	2.678
SEN	0.993	1.0000	0.579	0.950
SPE	0.031	0.0129	0.669	0.181

	@:0.255194040798287	@:0.130968771182643	@MAX_BACC	@MAX_RR
BACC	0.512	0.5065	0.624	0.565

	@SPE100
Thr	0.2306
RR	21.9530
SEN	1.0000
SPE	0.0129
BACC	0.5065

```
pander::pander(t(rrAnalysis$OERatio),caption="O/E Ratio")
```

Table 67: O/E Ratio

est	lower	upper
1.13	1	1.26

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

- **C Index:** *0.669*
- **Dxy:** *0.338*
- **S.D.:** *0.0309*
- **n:** *686*
- **missing:** *0*
- **uncensored:** *299*
- **Relevant Pairs:** *266144*
- **Concordant:** *178115*
- **Uncertain:** *203702*
- **cstatCI:**

mean.C Index	median	lower	upper
0.669	0.67	0.639	0.699

```
pander::pander(t(rrAnalysis$ROCAAnalysis$aucs),caption="ROC AUC")
```

Table 69: ROC AUC

est	lower	upper
0.669	0.628	0.709

```
pander::pander((rrAnalysis$ROCAAnalysis$sensitivity),caption="Sensitivity")
```

Table 70: Sensitivity

est	lower	upper
0.395	0.339	0.453

```
pander::pander((rrAnalysis$ROCAAnalysis$specificity),caption="Specificity")
```

Table 71: Specificity

est	lower	upper
0.832	0.791	0.868

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

Table 72: Probability Thresholds (continued below)

90%	80%	at_max_BACC	at_max_RR	atSPE100	at_max_BACC	at_max_RR
0.542	0.431	0.394	0.255	0.131	0.439	0.306

atSPE100
0.231

```
pander::pander(t(rrAnalysis$RR_atP),caption="Risk Ratio")
```

Table 74: Risk Ratio

est	lower	upper
1.8	1.54	2.11

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

Table 75: 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

```
riskdata <- cbind(dataBrestCancerTrain$status,predict(mlog,dataBrestCancerTrain,type="prob"),dataBrestC  
calprob <- CalibrationProbPoissonRisk(riskdata)
```

```
pander::pander(c(h0=calprob$h0,
```

```
Gain=calprob$hazardGain,
DeltaTime=calprob$timeInterval),
caption="Logistic Calibration Parameters")
```

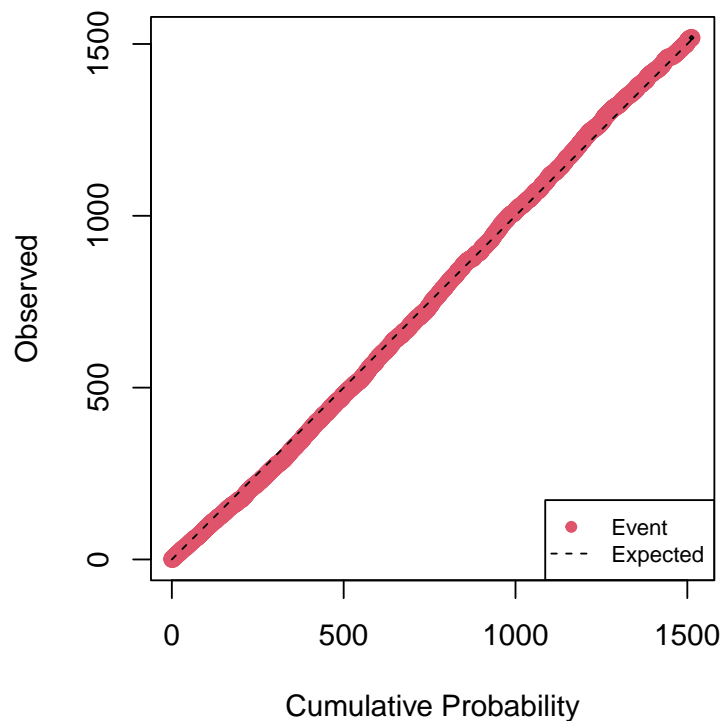
h0	Gain	DeltaTime
0.676	1.31	7.14

```
timeinterval <- calprob$timeInterval;
gain <- calprob$hazardGain

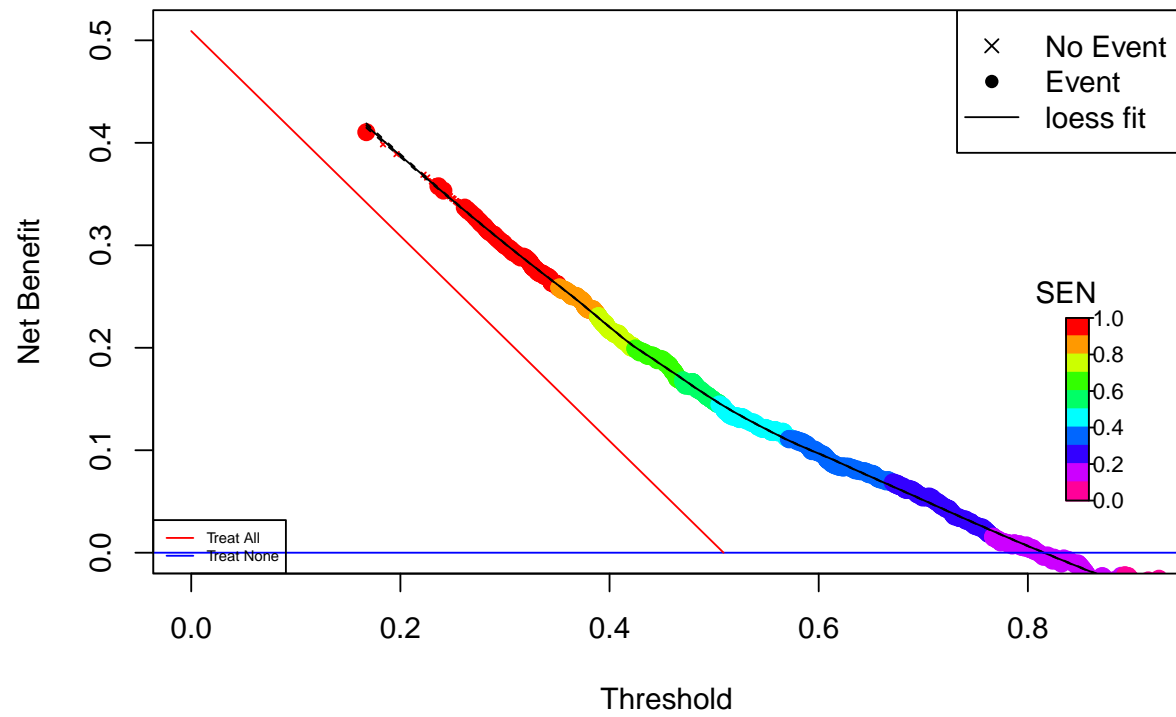
rdata <- cbind(dataBrestCancerTrain$status,calprob$prob)

rrAnalysisTrain <- RRPlot(rdata,atProb=c(0.90,0.80),
  timetoEvent=dataBrestCancerTrain$time,
  title="Cal. Logistic Train: Breast Cancer",
  ysurvlim=c(0.00,1.0),
  riskTimeInterval=timeinterval)
```

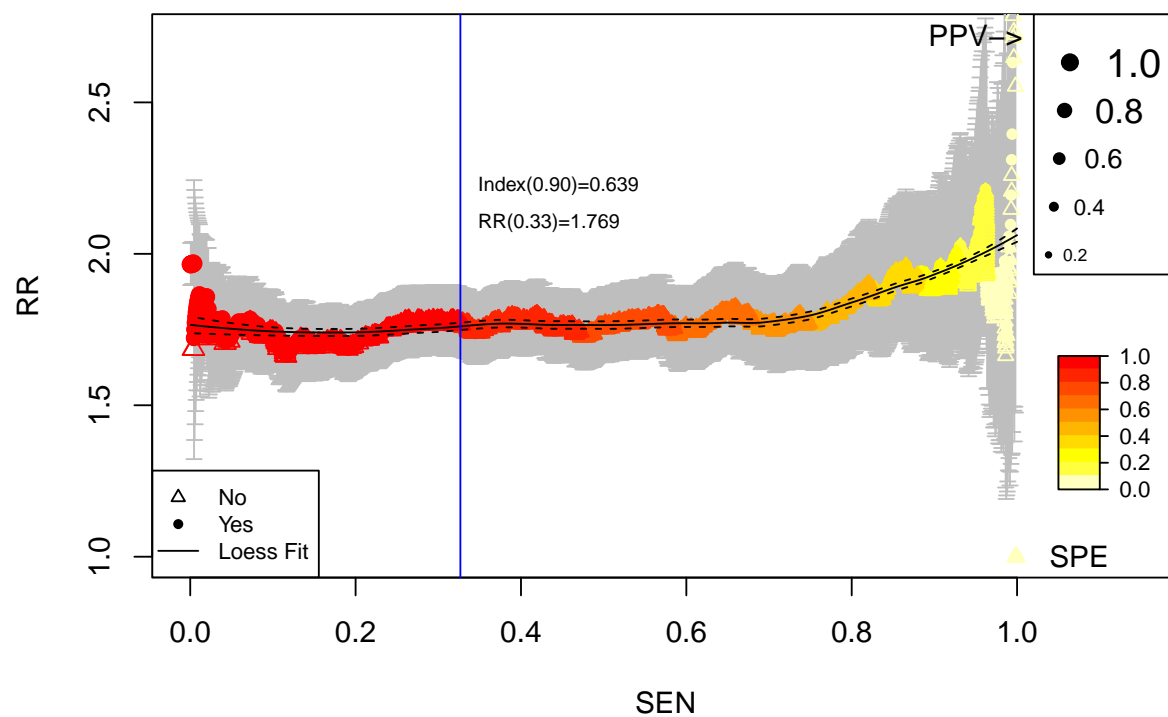
Cumulative vs. Observed: Cal. Logistic Train: Breast Cancer

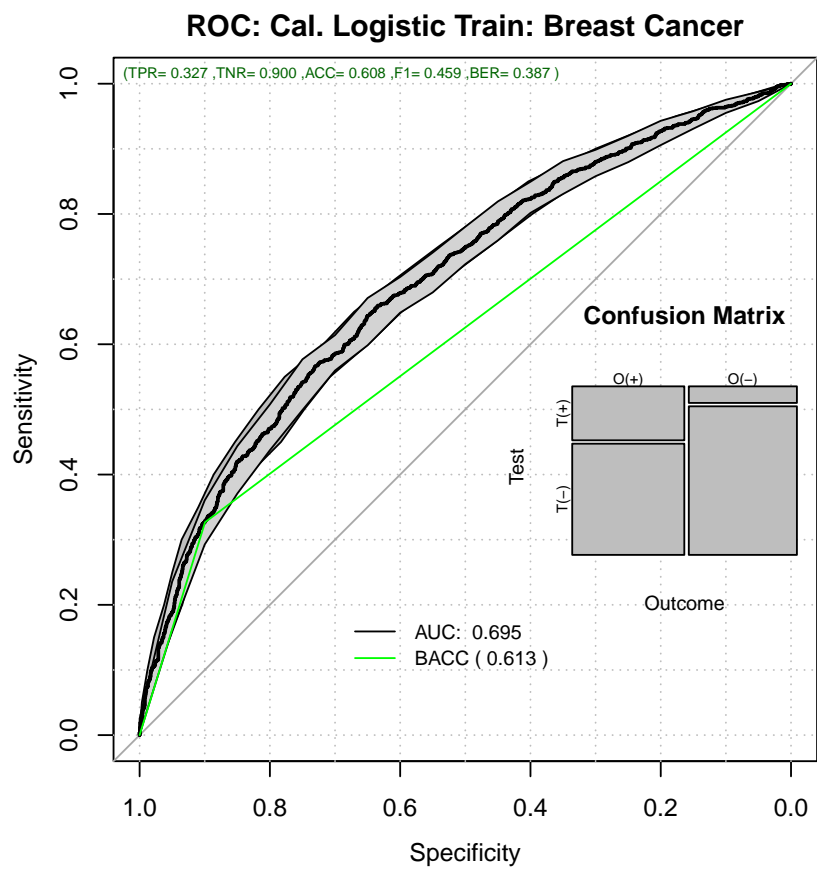


Decision Curve Analysis: Cal. Logistic Train: Breast Cancer

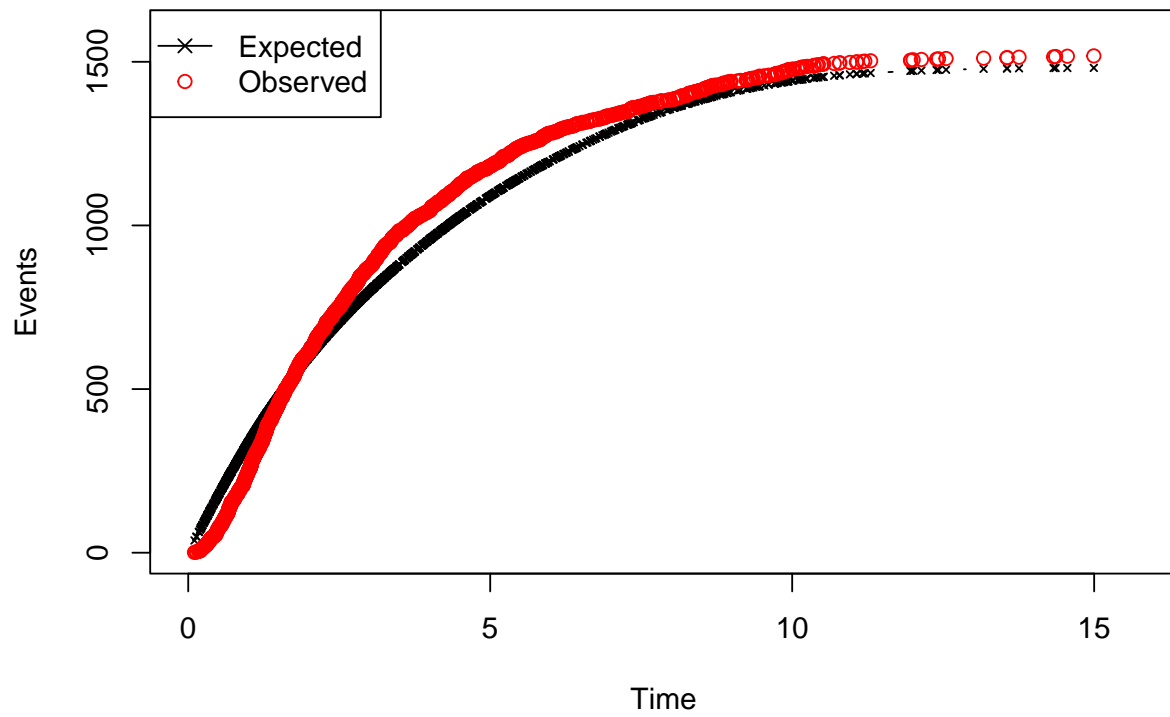


Relative Risk: Cal. Logistic Train: Breast Cancer

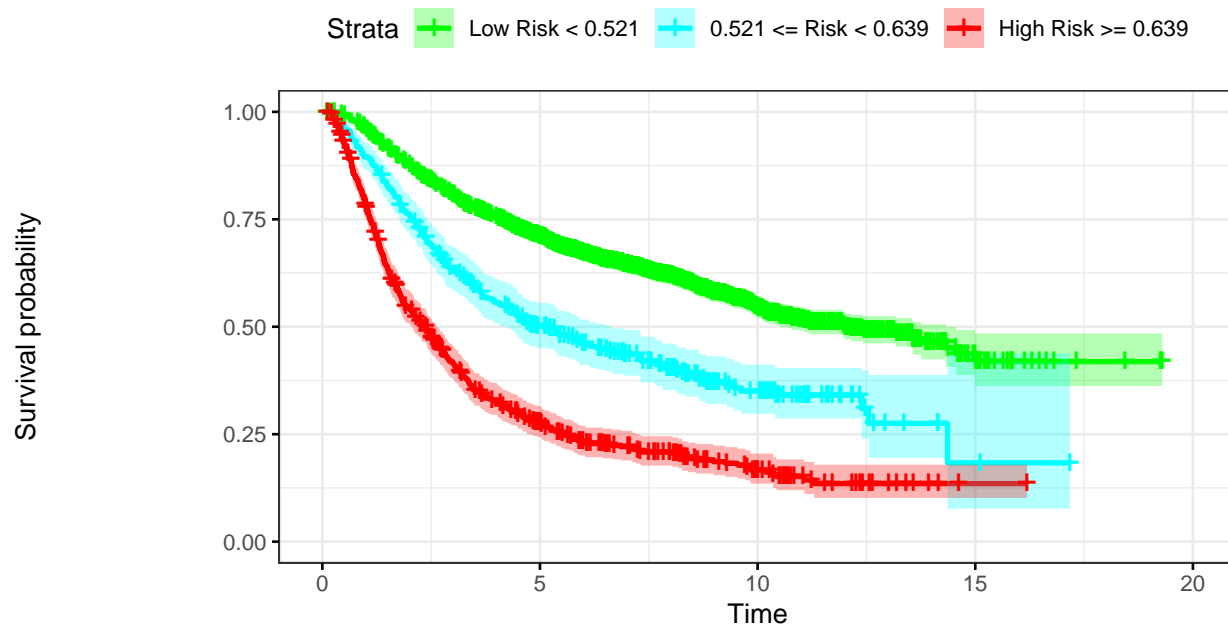




Time vs. Events: Cal. Logistic Train: Breast Cancer



Kaplan–Meier: Cal. Logistic Train: Breast Cancer



Number at risk

Low Risk < 0.521	1975	1268	399	23	0
0.521 <= Risk < 0.639	364	160	47	2	0
High Risk >= 0.639	643	143	37	1	0

```
par(op)
```

1.8.1 Report of the calibrated logistic: training

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

Table 77: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.639	0.521	0.480	0.319	0.167426
RR	1.765	1.739	1.799	2.213	1.000000
SEN	0.327	0.470	0.566	0.962	1.000000
SPE	0.900	0.799	0.731	0.125	0.000683
BACC	0.613	0.635	0.648	0.543	0.500342

```
pander::pander(t(rrAnalysisTrain$OERatio),caption="O/E Ratio")
```

Table 78: O/E Ratio

est	lower	upper
1.02	0.974	1.08

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

- **C Index:** *0.68*
- **Dxy:** *0.36*
- **S.D.:** *0.014*
- **n:** *2982*
- **missing:** *0*
- **uncensored:** *1518*
- **Relevant Pairs:** *6184528*
- **Concordant:** *4206588*
- **Uncertain:** *2703838*
- **cstatCI:**

mean.C Index	median	lower	upper
0.68	0.68	0.666	0.693

```
pander::pander(t(rrAnalysisTrain$ROCAalysis$aucs),caption="ROC AUC")
```

Table 80: ROC AUC

est	lower	upper
0.695	0.677	0.714

```
pander::pander((rrAnalysisTrain$ROCAalysis$sensitivity),caption="Sensitivity")
```

Table 81: Sensitivity

est	lower	upper
0.327	0.303	0.351

```
pander::pander((rrAnalysisTrain$ROCAalysis$specificity),caption="Specificity")
```

Table 82: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 83: Probability Thresholds

90%	80%	at_max_BACC	at_max_RR	atSPE100
0.639	0.521	0.48	0.319	0.167

```
pander::pander(t(rrAnalysisTrain$RR_atP),caption="Risk Ratio")
```

Table 84: Risk Ratio

est	lower	upper
1.77	1.66	1.88

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

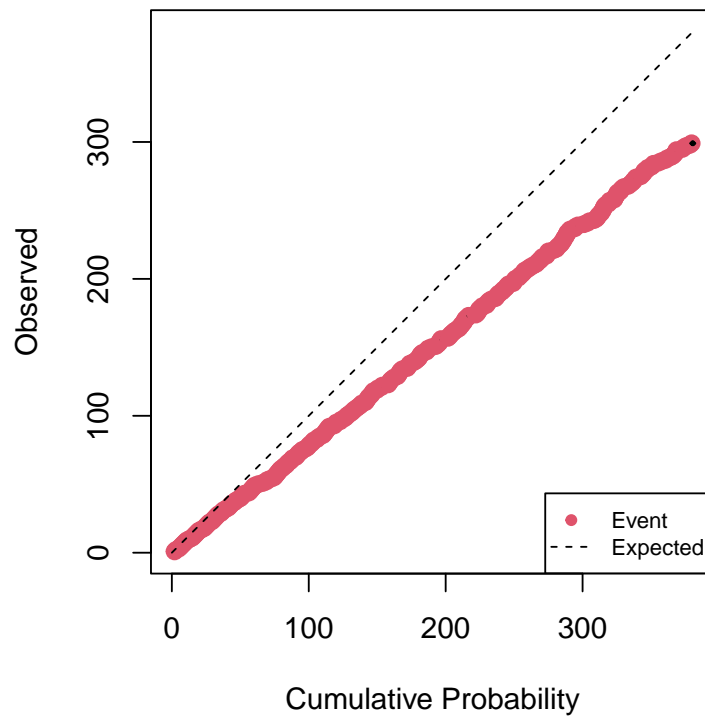
Table 85: Logrank test Chisq = 543.347175 on 2 degrees of freedom,
p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1975	804	1145	101.5	418.9
class=1	364	218	169	14.1	15.9
class=2	643	496	204	418.2	490.7

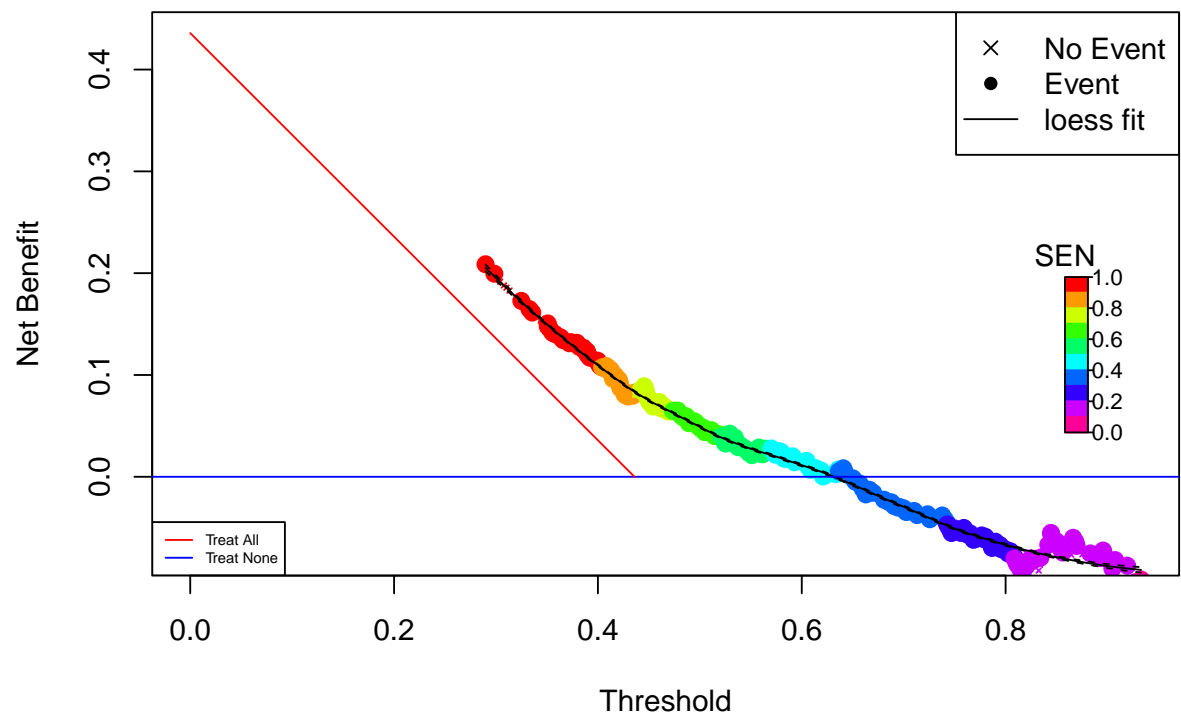
```
probLog <- predict(mlog,dataBrestCancerTest)
aproba <- adjustProb(probLog,gain)

rdata <- cbind(dataBrestCancerTest$status,aproba)
rrAnalysisTestLogistic <- RRPlot(rdata,atThr=rrAnalysisTrain$thr_atP,
  timetoEvent=dataBrestCancerTest$time,
  title="Cal. Logistic Test: Breast Cancer",
  ysurvlim=c(0.00,1.0),
  riskTimeInterval=timeinterval)
```

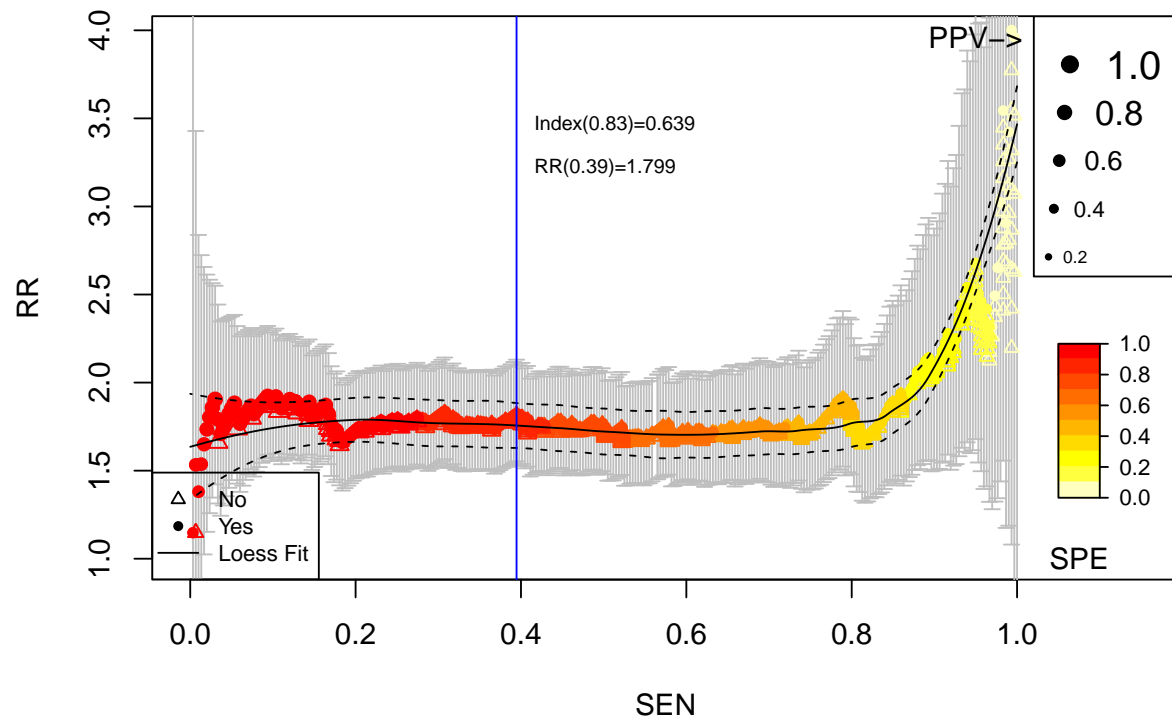
Cumulative vs. Observed: Cal. Logistic Test: Breast Cancer

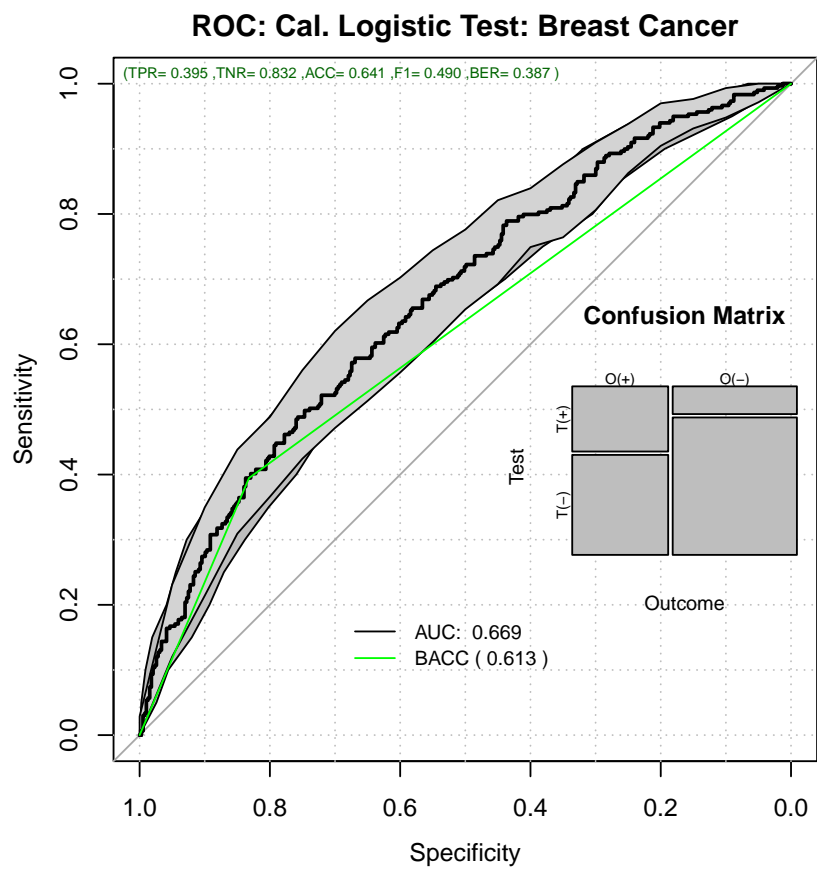


Decision Curve Analysis: Cal. Logistic Test: Breast Cancer

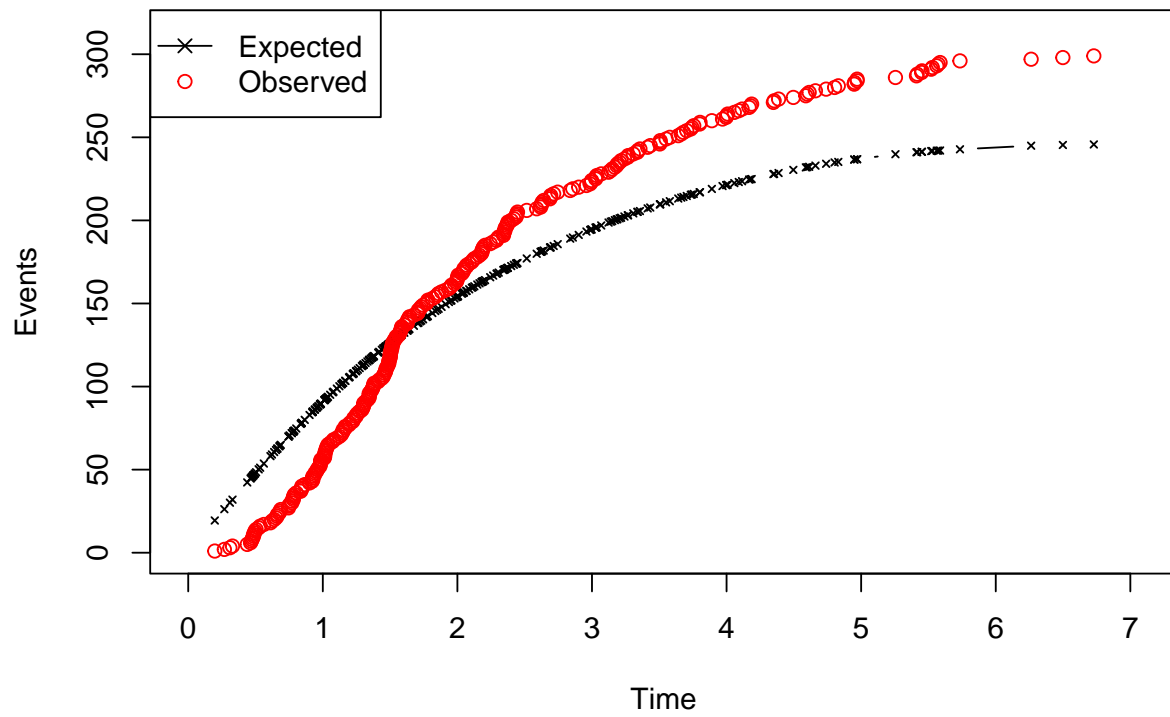


Relative Risk: Cal. Logistic Test: Breast Cancer

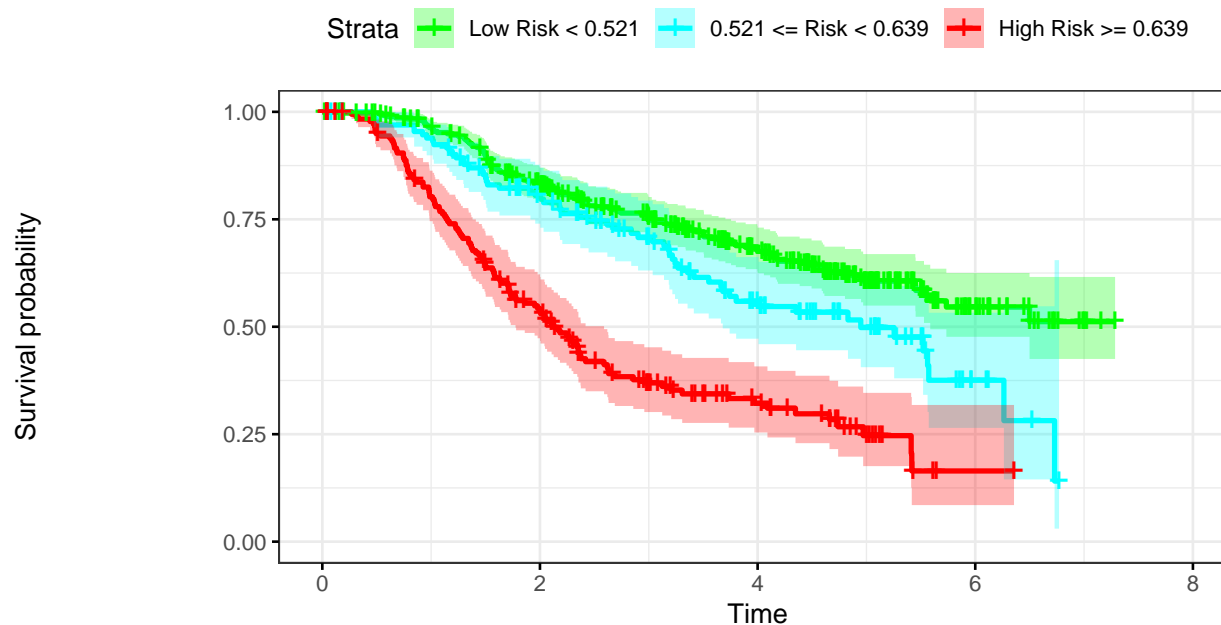




Time vs. Events: Cal. Logistic Test: Breast Cancer



Kaplan–Meier: Cal. Logistic Test: Breast Cancer



Number at risk

Low Risk < 0.521	369	274	154	29	0
0.521 <= Risk < 0.639	134	96	46	6	0
High Risk >= 0.639	183	89	29	1	0

```
par(op)
```

1.8.2 Report of the calibrated validation

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

Table 86: Threshold values (continued below)

	@:0.63864953482035	@:0.521434578375582	@:0.480013144733203
Thr	0.639	0.521	0.480
RR	1.792	1.702	1.746
SEN	0.395	0.595	0.686
SPE	0.832	0.638	0.545
BACC	0.613	0.617	0.615

Table 87: Table continues below

	@:0.319265361359366	@:0.167425979697821	@MAX_BACC	@MAX_RR
Thr	0.320	0.2897	0.529	0.379
RR	3.094	21.9530	1.756	2.678
SEN	0.993	1.0000	0.579	0.950
SPE	0.031	0.0129	0.669	0.181

	@:0.319265361359366	@:0.167425979697821	@MAX_BACC	@MAX_RR
BACC	0.512	0.5065	0.624	0.565

	@SPE100
Thr	0.2897
RR	21.9530
SEN	1.0000
SPE	0.0129
BACC	0.5065

```
pander::pander(t(rrAnalysisTestLogistic$OERatio),caption="O/E Ratio")
```

Table 89: O/E Ratio

est	lower	upper
1.22	1.08	1.36

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

- **C Index:** *0.669*
- **Dxy:** *0.338*
- **S.D.:** *0.0309*
- **n:** *686*
- **missing:** *0*
- **uncensored:** *299*
- **Relevant Pairs:** *266144*
- **Concordant:** *178115*
- **Uncertain:** *203702*
- **cstatCI:**

mean.C Index	median	lower	upper
0.669	0.67	0.639	0.701

```
pander::pander(t(rrAnalysisTestLogistic$ROCAAnalysis$aucs),caption="ROC AUC")
```

Table 91: ROC AUC

est	lower	upper
0.669	0.628	0.709

```
pander::pander((rrAnalysisTestLogistic$ROCAAnalysis$sensitivity),caption="Sensitivity")
```

Table 92: Sensitivity

est	lower	upper
0.395	0.339	0.453

```
pander::pander((rrAnalysisTestLogistic$ROCAAnalysis$specificity),caption="Specificity")
```

Table 93: Specificity

est	lower	upper
0.832	0.791	0.868

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

Table 94: Probability Thresholds (continued below)

90%	80%	at_max_BACC	at_max_RR	atSPE100	at_max_BACC	at_max_RR
0.639	0.521	0.48	0.319	0.167	0.529	0.379

atSPE100
0.29

```
pander::pander(t(rrAnalysisTestLogistic$RR_atP),caption="Risk Ratio")
```

Table 96: Risk Ratio

est	lower	upper
1.8	1.54	2.11

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

Table 97: 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%
0.841	0.841	0.839	0.842

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

mean	50%	2.5%	97.5%
0.791	0.791	0.791	0.792

```
pander::pander(t(rrCoxTestAnalysis$OE95ci))
```

mean	50%	2.5%	97.5%
1.07	1.07	1.03	1.1

```
pander::pander(t(rrAnalysisTestLogistic$OE95ci))
```

mean	50%	2.5%	97.5%
0.955	0.955	0.926	0.984

```
maxobs <- sum(dataBrestCancerTest$status)

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

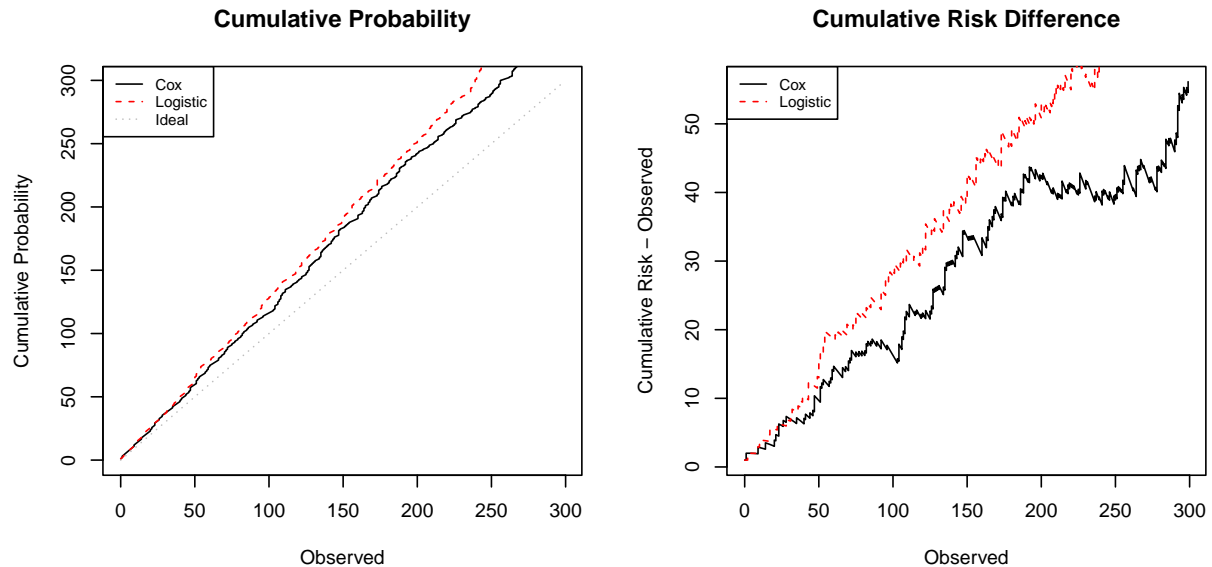
plot(rrCoxTestAnalysis$CumulativeOvs,type="l",lty=1,
     main="Cumulative Probability",
     xlab="Observed",
     ylab="Cumulative Probability",
     ylim=c(0,maxobs),
     xlim=c(0,maxobs))
lines(rrAnalysisTestLogistic$CumulativeOvs,lty=2,col="red")
lines(x=c(0,maxobs),y=c(0,maxobs),lty=3,col="gray")
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="l",
     lty=1)
lines(rrAnalysisTestLogistic$CumulativeOvs$Observed,
     rrAnalysisTestLogistic$CumulativeOvs$Cumulative-
     rrAnalysisTestLogistic$CumulativeOvs$Observed,
```

```

    lty=2,
    col="red")
legend("topleft", legend = c("Cox", "Logistic"),
      col=c("black", "red"),
      lty=c(1,2),
      cex=0.75
)

```



```

plot(rrCoxTestAnalysis$OEData[,2:3], type="l", lty=1,
     main="Expected over Time",
     xlab="Observed",
     ylab="Expected",
     ylim=c(0,maxobs),
     xlim=c(0,maxobs))
lines(rrAnalysisTestLogistic$OEData[,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$OEData$Observed,
     rrCoxTestAnalysis$OEData$Expected-
     rrCoxTestAnalysis$OEData$Observed,
     main="Expected vs Observed Difference",
     xlab="Observed",
     ylab="Cumulative - Observed",
     type="l",
     lty=1)
lines(rrAnalysisTestLogistic$OEData$Observed,
     rrAnalysisTestLogistic$OEData$Expected-
     rrAnalysisTestLogistic$OEData$Observed,
     lty=2, col="red")

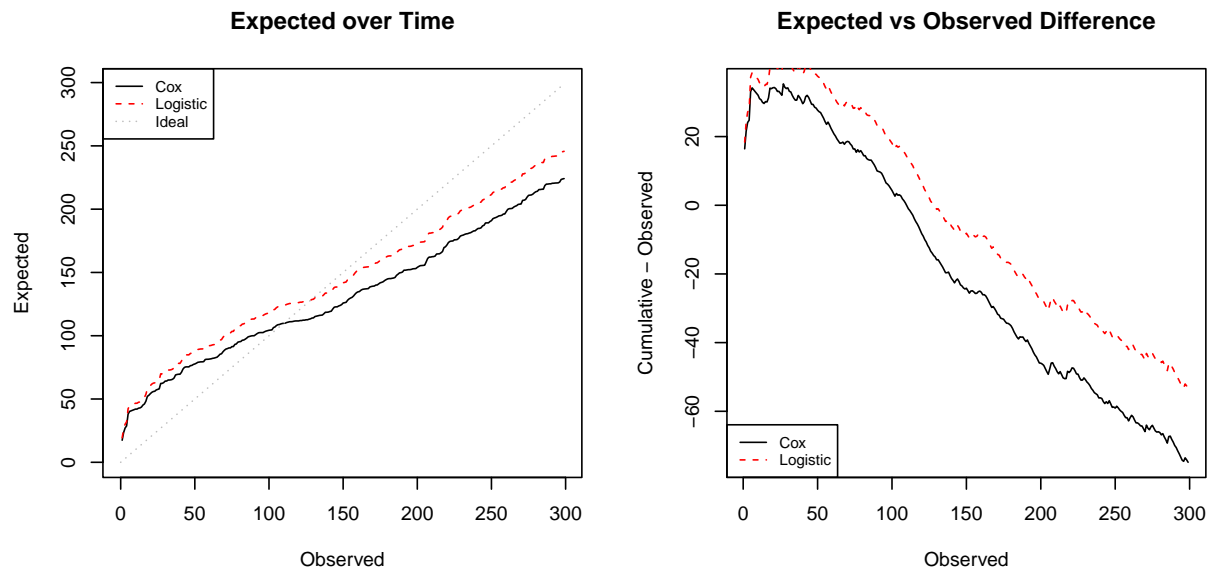
```



```

legend("bottomleft", legend = c("Cox", "Logistic"),
      col=c("black", "red"),
      lty=c(1, 2),
      cex=0.75
)

```



```

par(op)

```