

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

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

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

colnames(dataBreastCancerTrain) <- str_replace_all(colnames(dataBreastCancerTrain), ":", "_")
colnames(dataBreastCancerTrain) <- str_replace_all(colnames(dataBreastCancerTrain), " ", "_")
colnames(dataBreastCancerTrain) <- str_replace_all(colnames(dataBreastCancerTrain), "\\.", "_")
colnames(dataBreastCancerTrain) <- str_replace_all(colnames(dataBreastCancerTrain), "-", "_")
colnames(dataBreastCancerTrain) <- str_replace_all(colnames(dataBreastCancerTrain), ">", "_")
dataBreastCancerTrain$time <- dataBreastCancerTrain$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)
```

	Estimate	lower	HR	upper	ru.Accuracy	Accuracy	fact.Accuracy	AUC	AUC	Full.AUC	IDI	NRI	z.IDI	z.NRI	Delta.AUC	Frequency
age_nodes	0.00716	0.001	1.001	1.001	0.626	0.600	0.632	0.630	0.601	0.634	0.0304	0.459	12.81	14.37	0.0330	561
size_grade	0.05649	0.005	1.006	1.006	0.598	0.623	0.632	0.599	0.626	0.634	0.0186	0.391	149.82	11.29	0.0079	471
nodes	0.08658	0.082	1.090	1.099	0.637	0.642	0.643	0.640	0.643	0.644	0.0074	0.056	48.33	1.66	0.0001	1481
size	0.00688	0.005	1.007	1.009	0.595	0.641	0.643	0.595	0.642	0.644	0.0144	0.358	78.05	9.97	0.0013	221
size_nodes	1.000	1.000	1.000	1.000	0.624	0.643	0.643	0.629	0.644	0.644	0.0034	0.343	07.25	9.57	-	1
	0.000378														0.000377	
age_size	-	1.000	1.000	1.000	0.567	0.627	0.632	0.568	0.630	0.634	0.0063	0.193	55.95	5.36	0.0040	781
	0.000149															
grade	0.20493	0.146	1.227	1.314	0.565	0.637	0.643	0.561	0.638	0.644	0.0092	0.206	95.88	6.31	0.0053	441

	Estimate	lower HR	upper HR	u.Accuracy	l.Accuracy	full.Accuracy	AUC	CAUC	Full.AUC	IDI	NRI	z.IDI	z.NRI	Delta.AUC	Frequency
age	-	0.996	0.997	0.998	0.513	0.628	0.643	0.513	0.628	0.644	0.00416	0.09175	2.7	2.51	0.0154651
	0.003113														
grade_nodes	0.981	0.986	0.992	0.635	0.645	0.643	0.639	0.646	0.644	0.00207	-	5.03	-	-	1
	0.013784										0.0910		2.55	0.002609	

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")
```

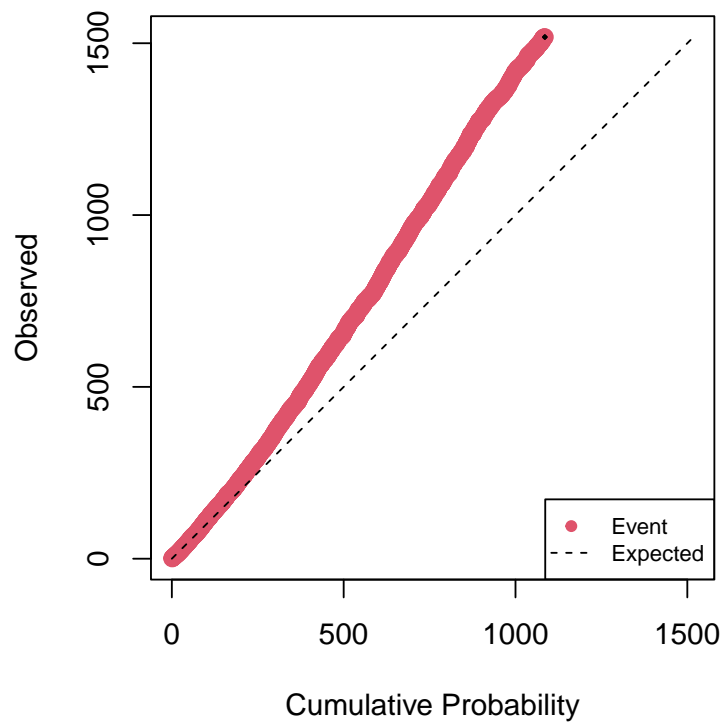
Table 4: Initial Parameters

h0	timeinterval
0.429	5

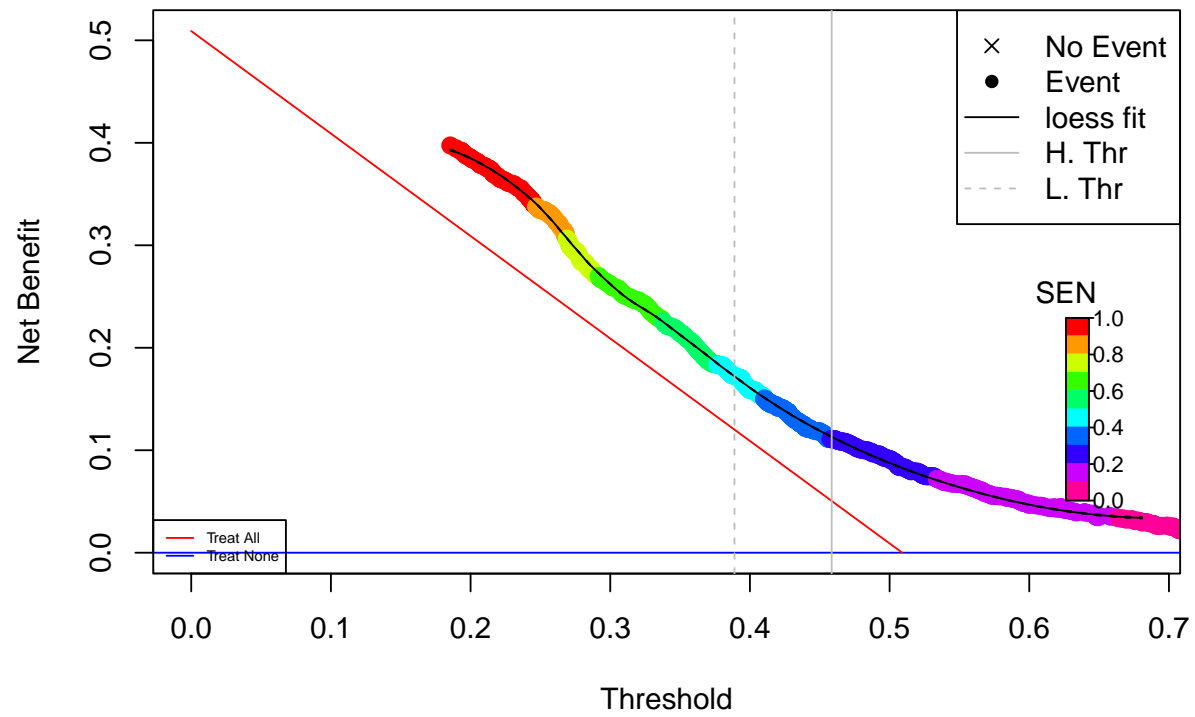
```
index <- predict(ml,dataBrestCancerTrain)
rdata <- cbind(dataBrestCancerTrain$status,ppoisGzero(index,h0))

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

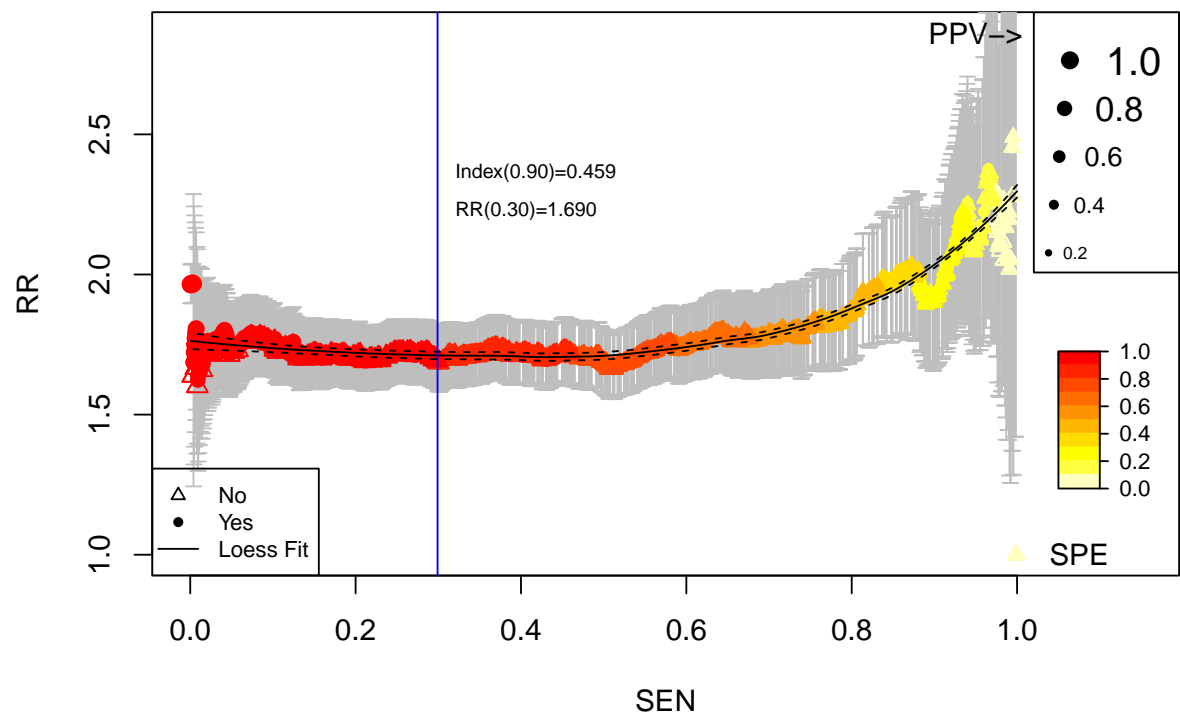
Cumulative vs. Observed: Train: Breast Cancer

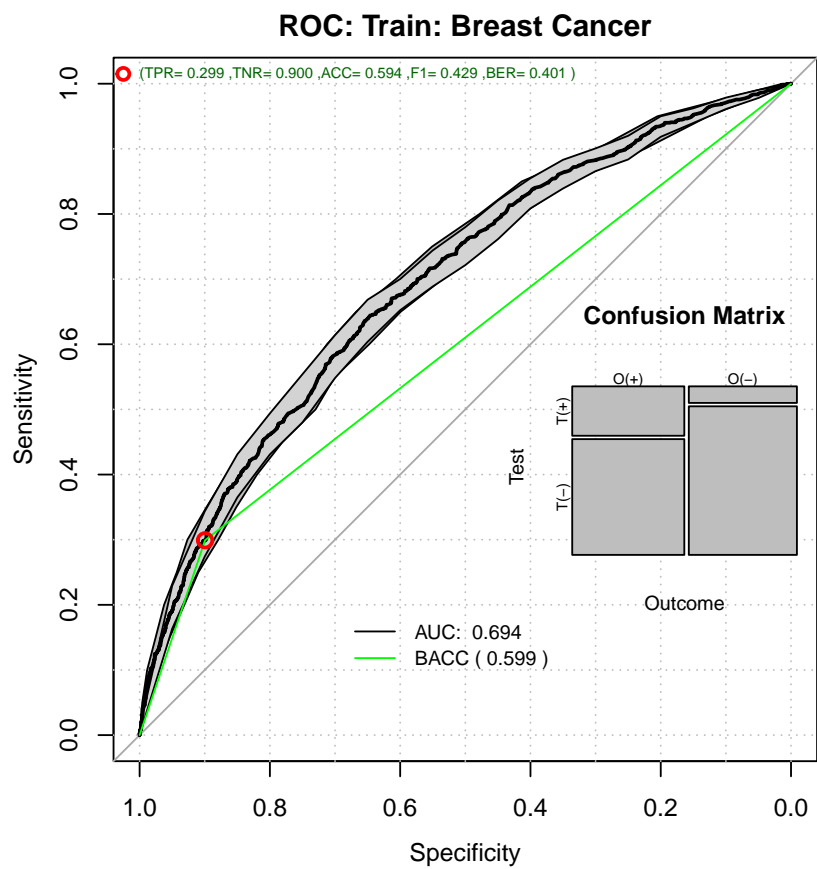


Decision Curve Analysis: Train: Breast Cancer

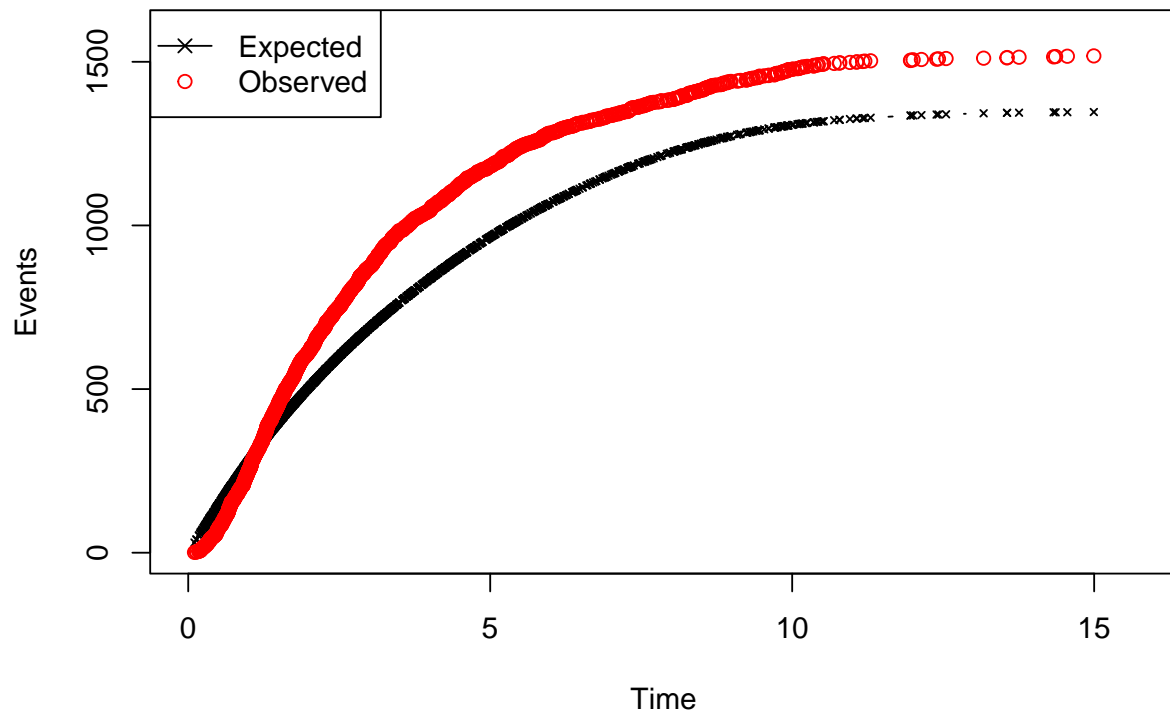


Relative Risk: Train: Breast Cancer

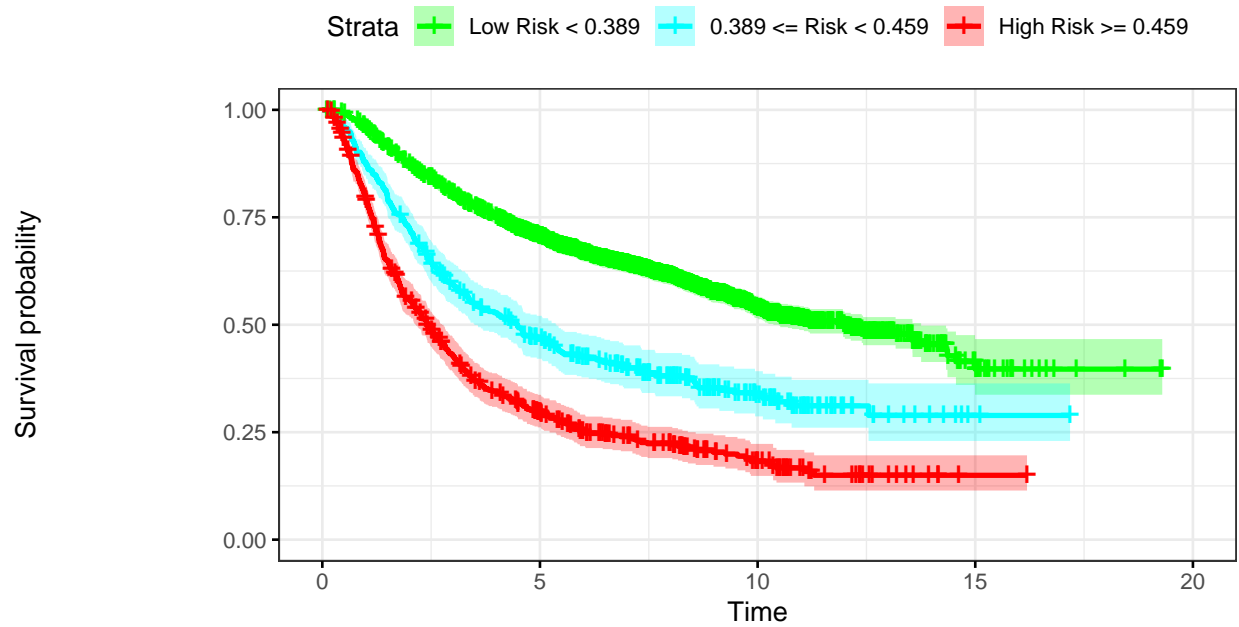




Time vs. Events: Train: Breast Cancer



Kaplan–Meier: Train: Breast Cancer



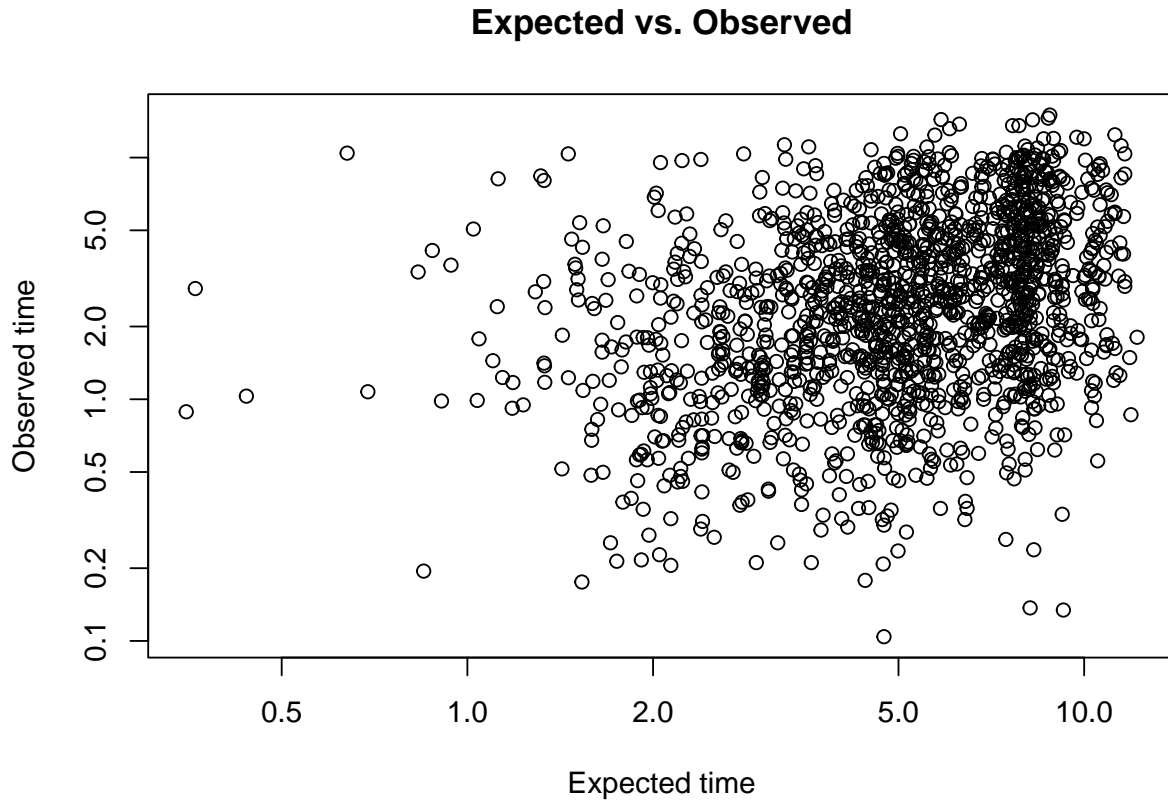
Number at risk

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

```
timetoEvent <- meanTimeToEvent(rdata[rdata[,1]==1,2],timeinterval)
obstime <- dataBreStCancerTrain[rdata[,1]==1,"time"]

plot(timetoEvent,obstime,xlab="Expected time",ylab="Observed time",main="Expected vs. Observed",log="xy")
```



```
pander::pander(cor.test(timetoEvent,obstime,method="spearman"))
```

Table 5: Spearman's rank correlation rho: `timetoEvent` and `obstime`

Test statistic	P value	Alternative hypothesis	rho
3.95e+08	5.22e-38 * * *	two.sided	0.322

```
MADerror <- mean(abs(timetoEvent-obstime))
pander::pander(MADerror)
```

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 6: 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

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
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
SEN	0.299	0.462	0.644	0.965	1.00000	0.2464
SPE	0.900	0.798	0.646	0.125	0.00137	0.9310
BACC	0.599	0.630	0.645	0.545	0.50068	0.5887
NetBenefit	0.110	0.172	0.246	0.374	0.39742	0.0916

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

Table 7: O/E Ratio

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

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

Table 8: O/E Mean

mean	50%	2.5%	97.5%
1.16	1.16	1.15	1.17

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

Table 9: 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	0.677	0.663	0.69

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

Table 11: ROC AUC

est	lower	upper
0.694	0.675	0.713

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

Table 12: Sensitivity

est	lower	upper
0.299	0.276	0.323

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

Table 13: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 14: Probability Thresholds

90%	80%
0.459	0.389

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

Table 15: 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

```
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

1.4.5 The RRplot() of the calibrated model

```

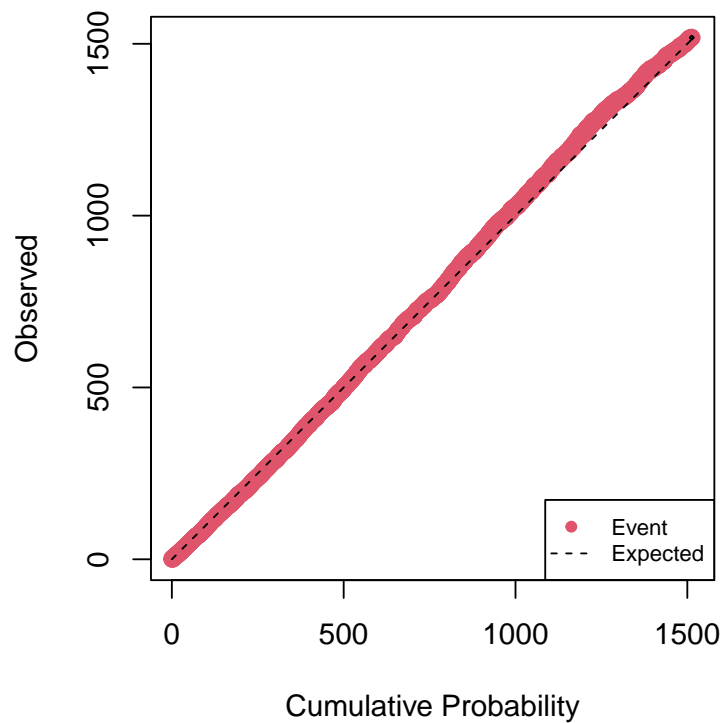
h0 <- calprob$h0
timeinterval <- calprob$timeInterval;

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

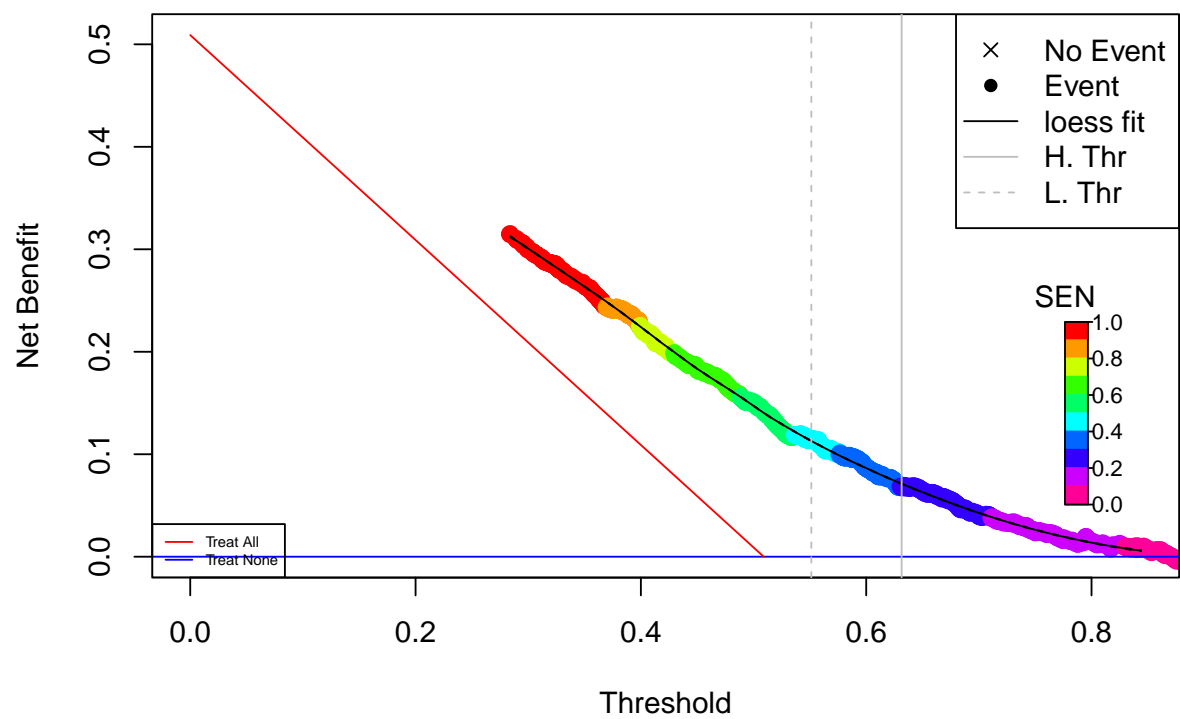
rrAnalysisTrain <- RRPlot(rdata,atRate=c(0.90,0.80),
                           timetoEvent=dataBrestCancerTrain$time,
                           title="Cal. Train: Breast Cancer",
                           ysurvlim=c(0.00,1.0),
                           riskTimeInterval=timeinterval)

```

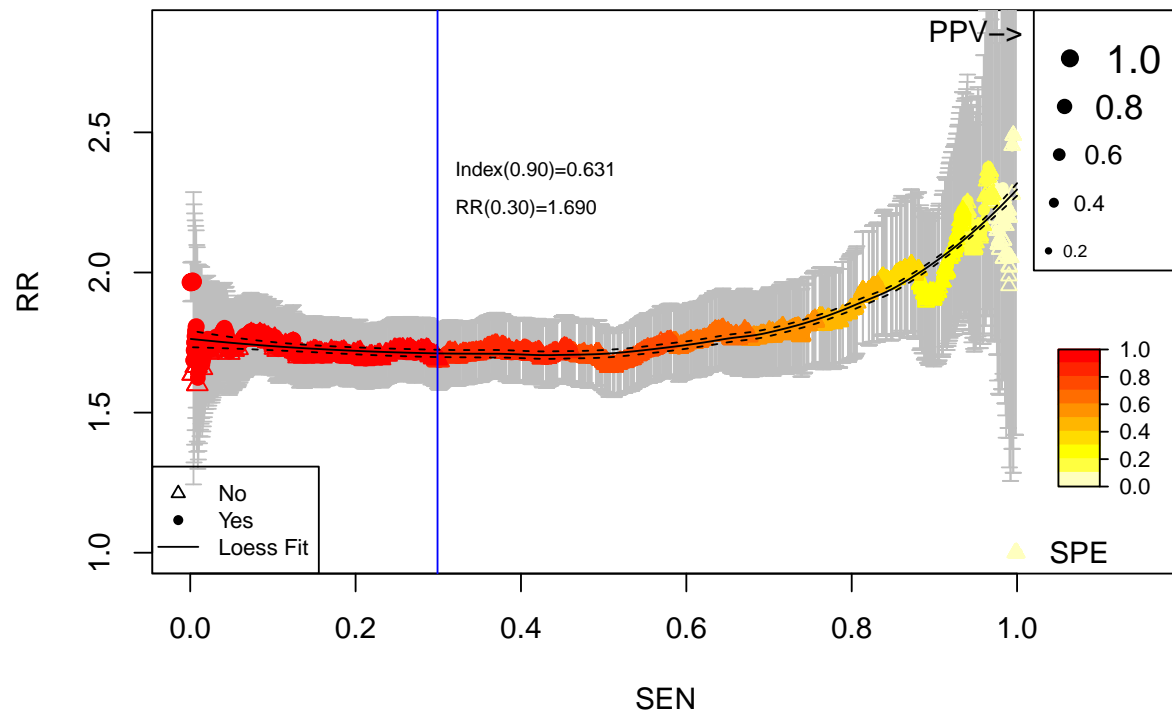
Cumulative vs. Observed: Cal. Train: Breast Cancer

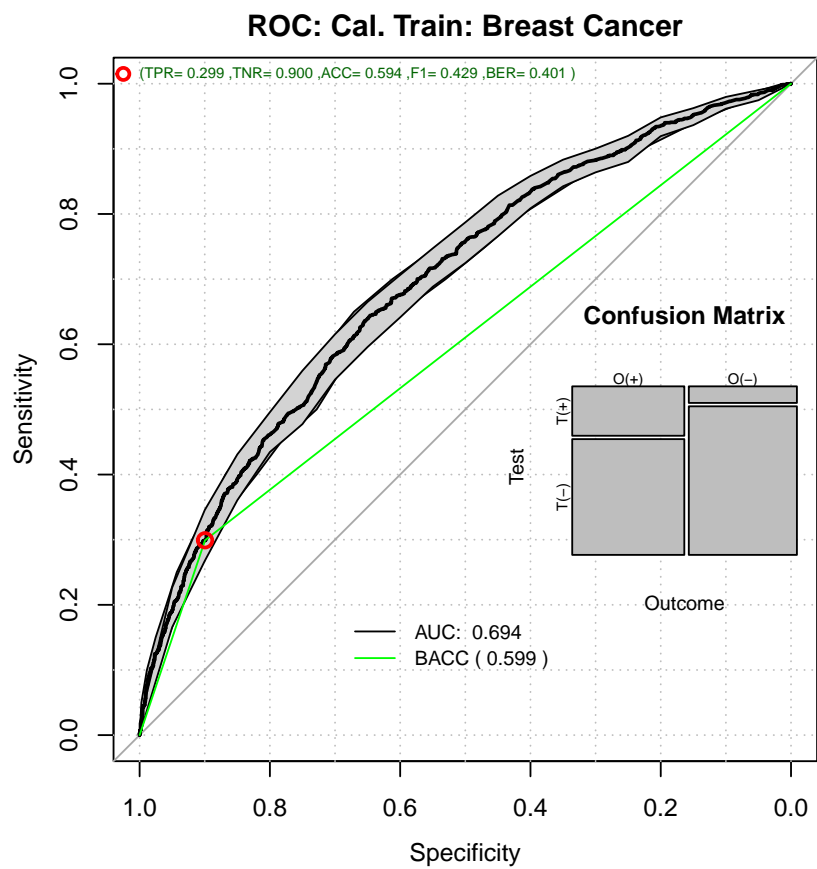


Decision Curve Analysis: Cal. Train: Breast Cancer

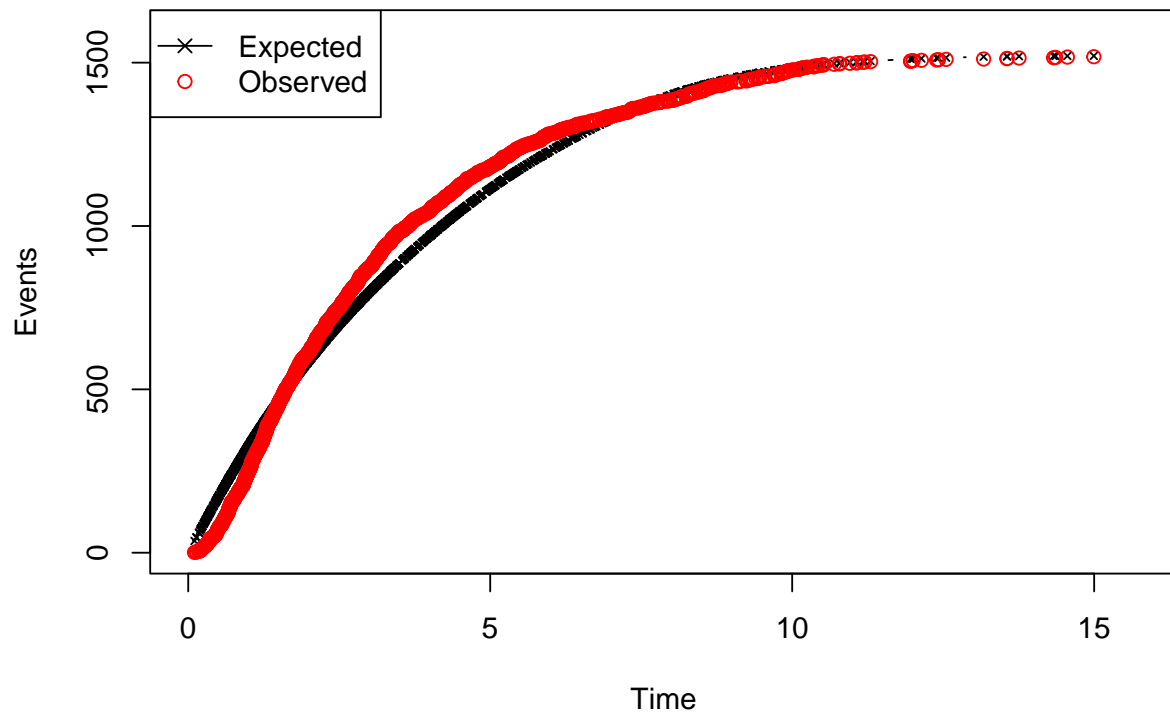


Relative Risk: Cal. Train: Breast Cancer

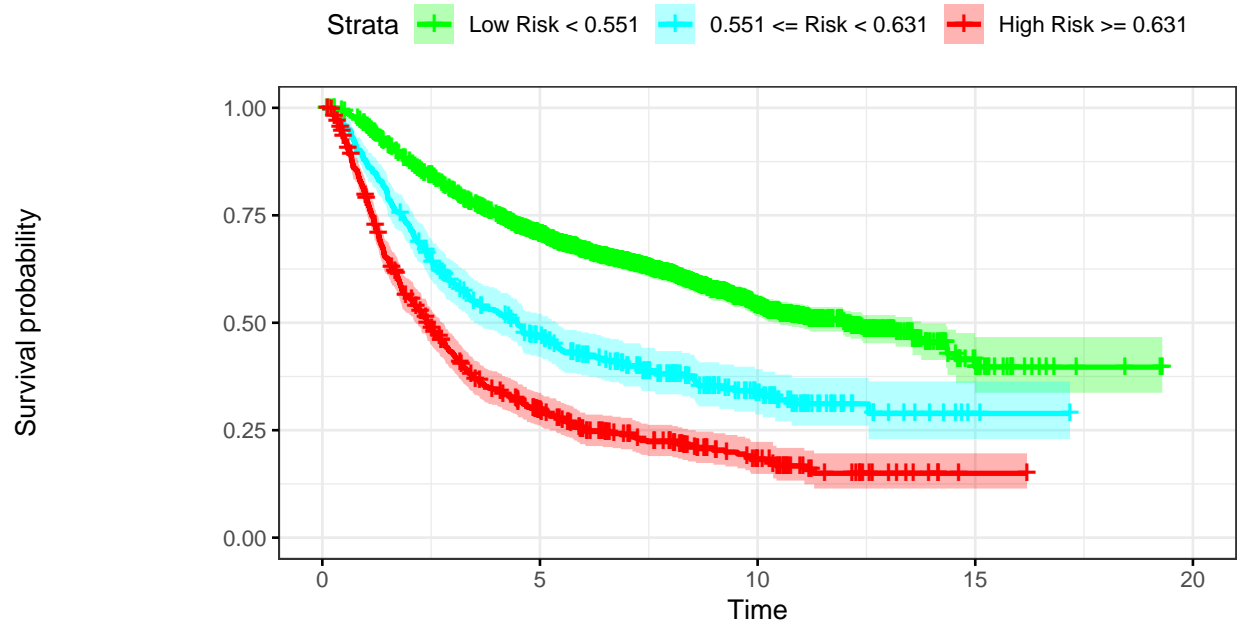




Time vs. Events: Cal. Train: Breast Cancer



Kaplan–Meier: Cal. Train: Breast Cancer



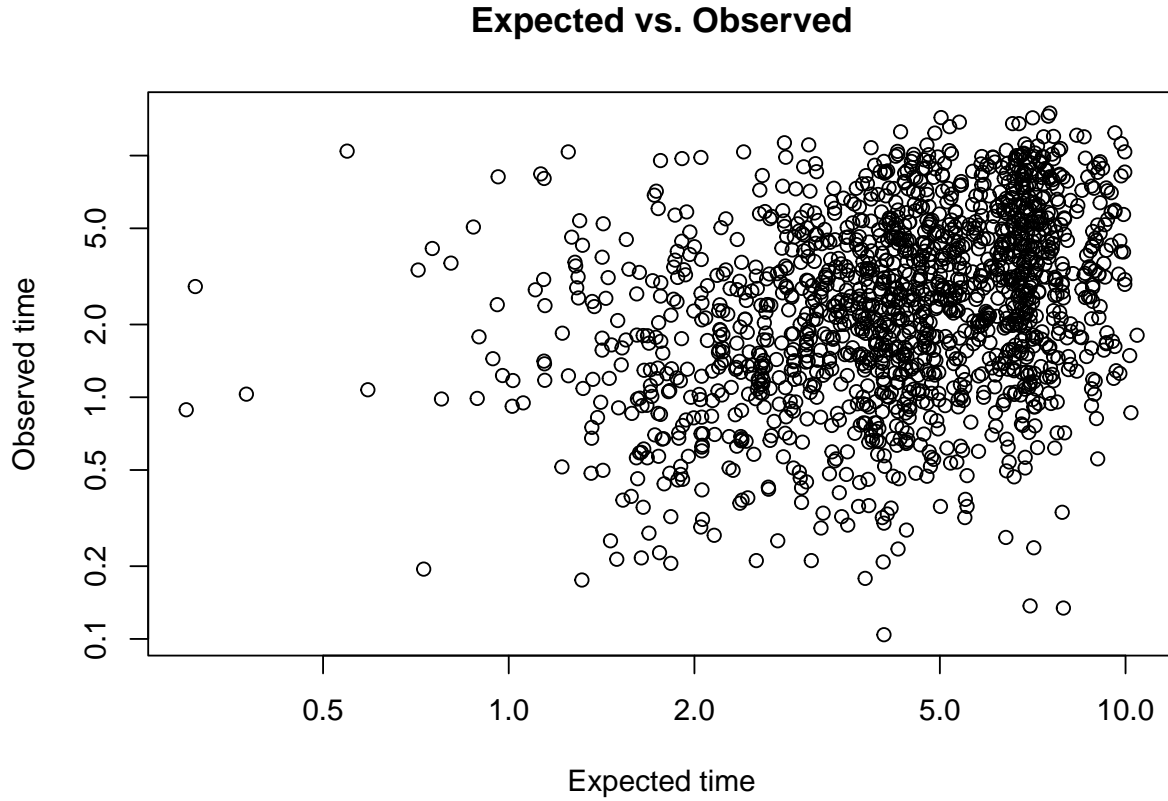
Number at risk

Low Risk < 0.551	1985	1260	393	23	0
0.551 <= Risk < 0.631	396	166	51	2	0
High Risk >= 0.631	601	145	39	1	0

1.4.6 Time to event after calibration

```
timetoEvent <- meanTimeToEvent(rdata[rdata[,1]==1,2],timeinterval)
obstime <- dataBrestCancerTrain[rdata[,1]==1,"time"]

plot(timetoEvent,obstime,xlab="Expected time",ylab="Observed time",main="Expected vs. Observed",log="xy")
```



```
pander::pander(cor.test(timetoEvent,obstime,method="spearman"))
```

Table 17: Spearman's rank correlation rho: timetoEvent and obstime

Test statistic	P value	Alternative hypothesis	rho
3.95e+08	5.22e-38 * * *	two.sided	0.322

```
MADerror <- mean(abs(timetoEvent-obstime))
pander::pander(MADerror)
```

2.63

1.4.7 Calibrated Train Performance

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

Table 18: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.6318	0.551	0.466	0.324	0.28381	0.500
RR	1.6904	1.713	1.799	2.376	1.00000	1.758
RR_LCI	1.5860	1.603	1.666	1.869	0.00000	1.636

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
RR_UCI	1.8018	1.830	1.942	3.019	0.00000	1.889
SEN	0.2991	0.462	0.644	0.965	1.00000	0.580
SPE	0.8996	0.798	0.646	0.125	0.00137	0.706
BACC	0.5993	0.630	0.645	0.545	0.50068	0.643
NetBenefit	0.0677	0.114	0.176	0.286	0.31480	0.150

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

Table 19: O/E Ratio

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

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

Table 20: O/E Mean

mean	50%	2.5%	97.5%
1	1	0.996	1.01

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

Table 21: 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	0.69

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

Table 23: ROC AUC

est	lower	upper
0.694	0.675	0.713

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

Table 24: Sensitivity

est	lower	upper
0.299	0.276	0.323

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

Table 25: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 26: Probability Thresholds

90%	80%
0.631	0.551

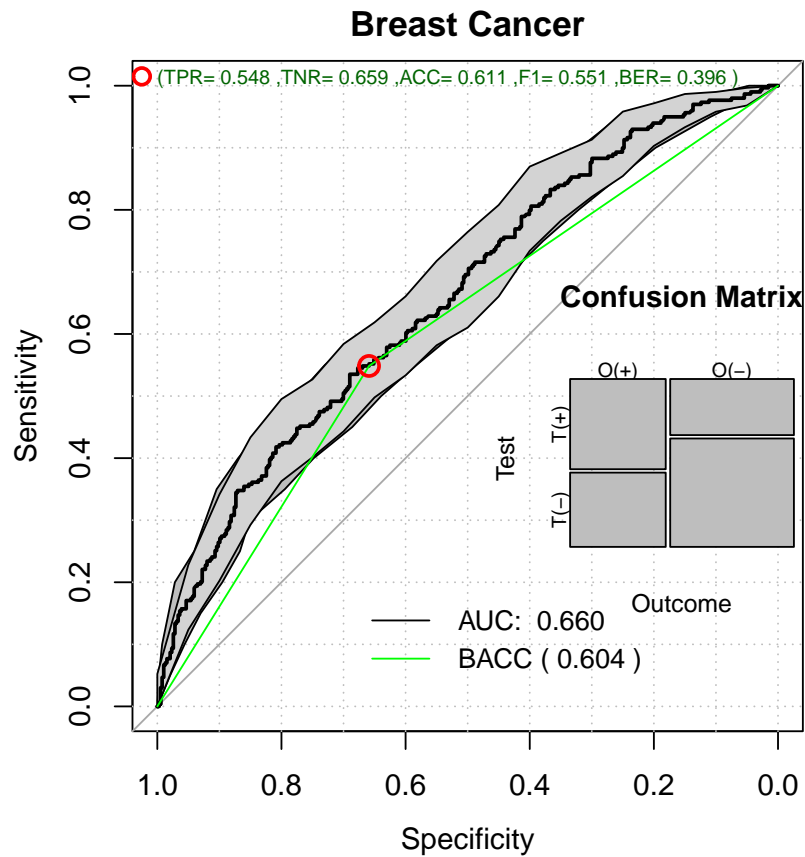
```
pander::pander(rrAnalysisTrain$surdif,caption="Logrank test")
```

Table 27: 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

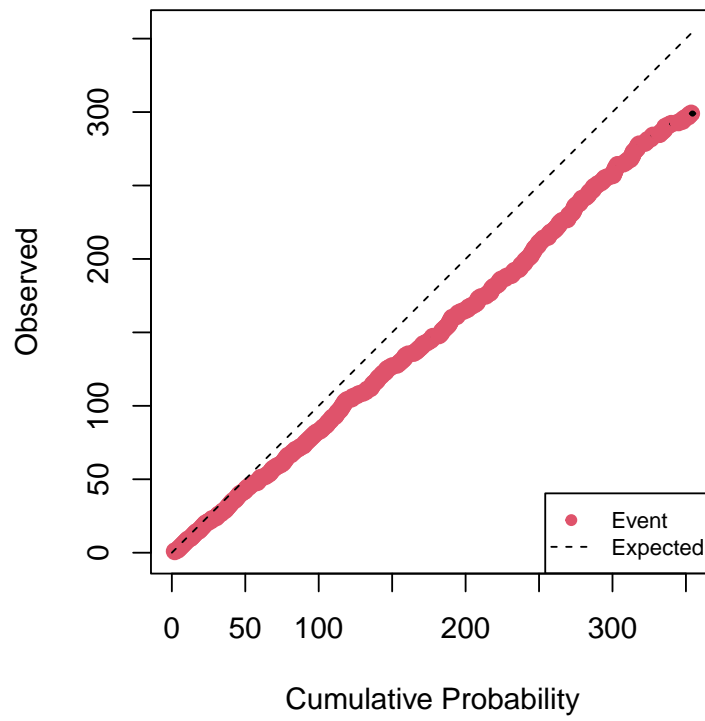
```
index <- predict(ml,dataBrestCancerTest)
pp <- predictionStats_binary(cbind(dataBrestCancerTest$status,index),plotname="Breast Cancer")
```



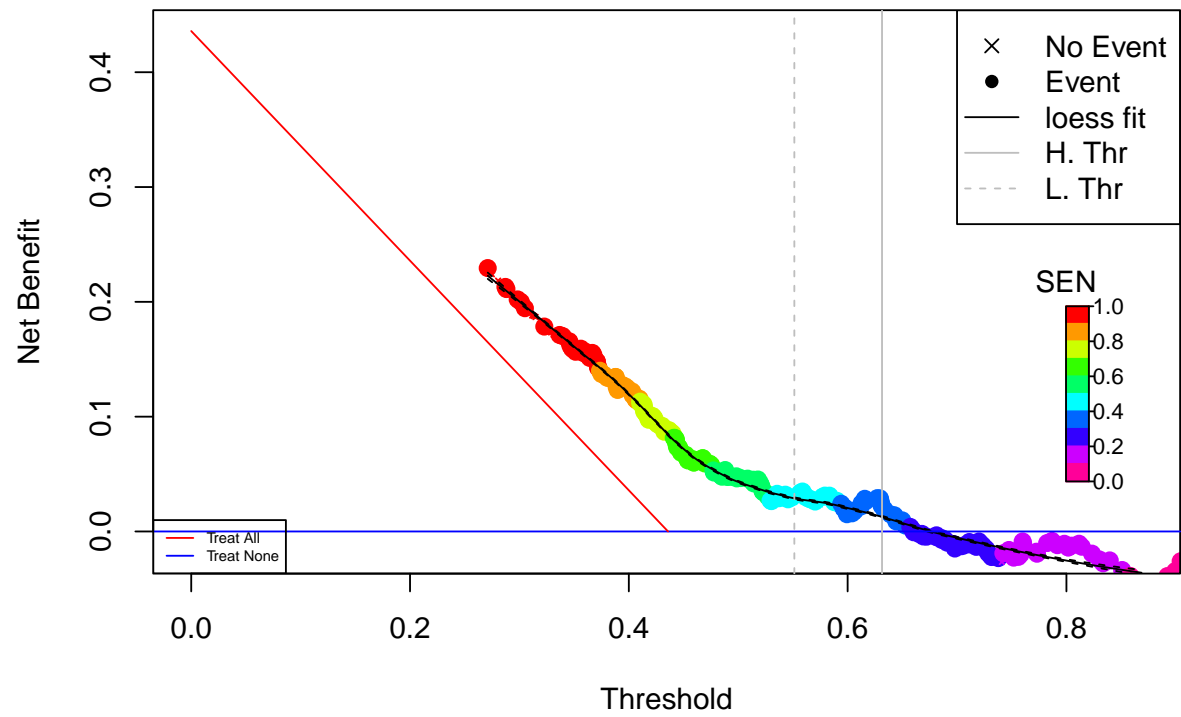
```
par(op)
```

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

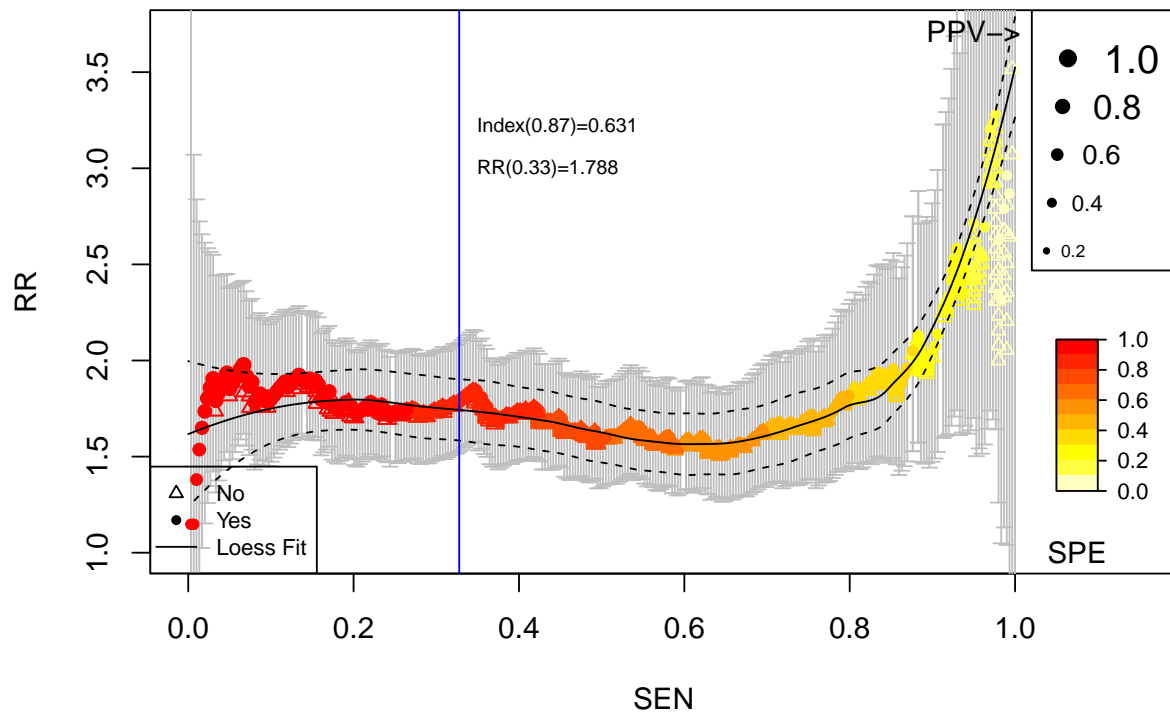
Cumulative vs. Observed: Test: Breast Cancer

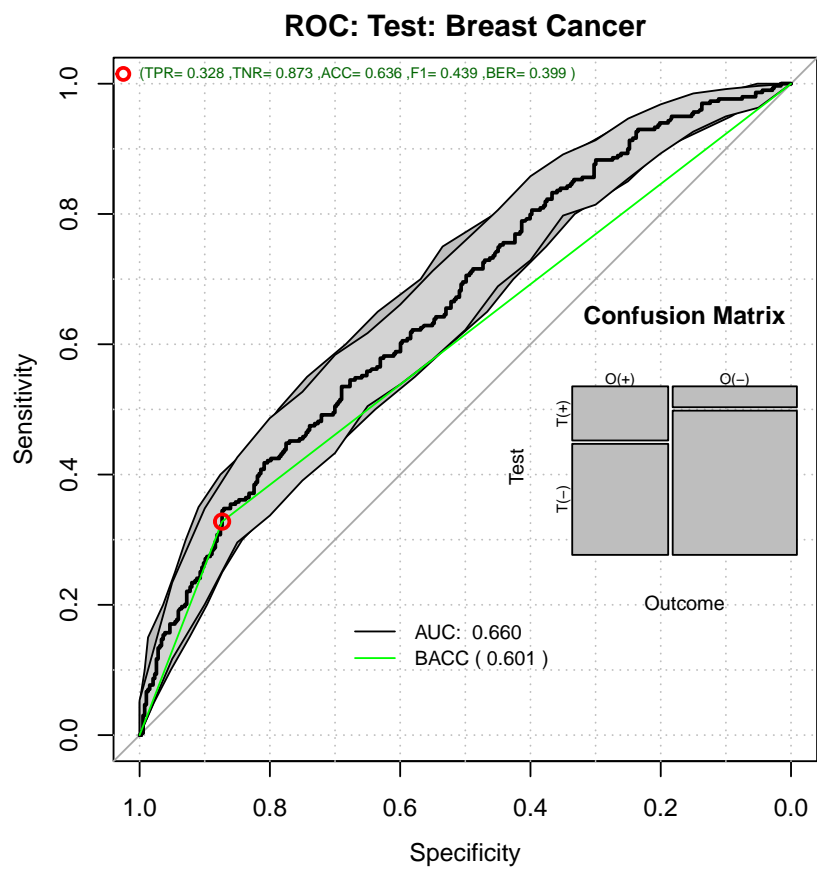


Decision Curve Analysis: Test: Breast Cancer

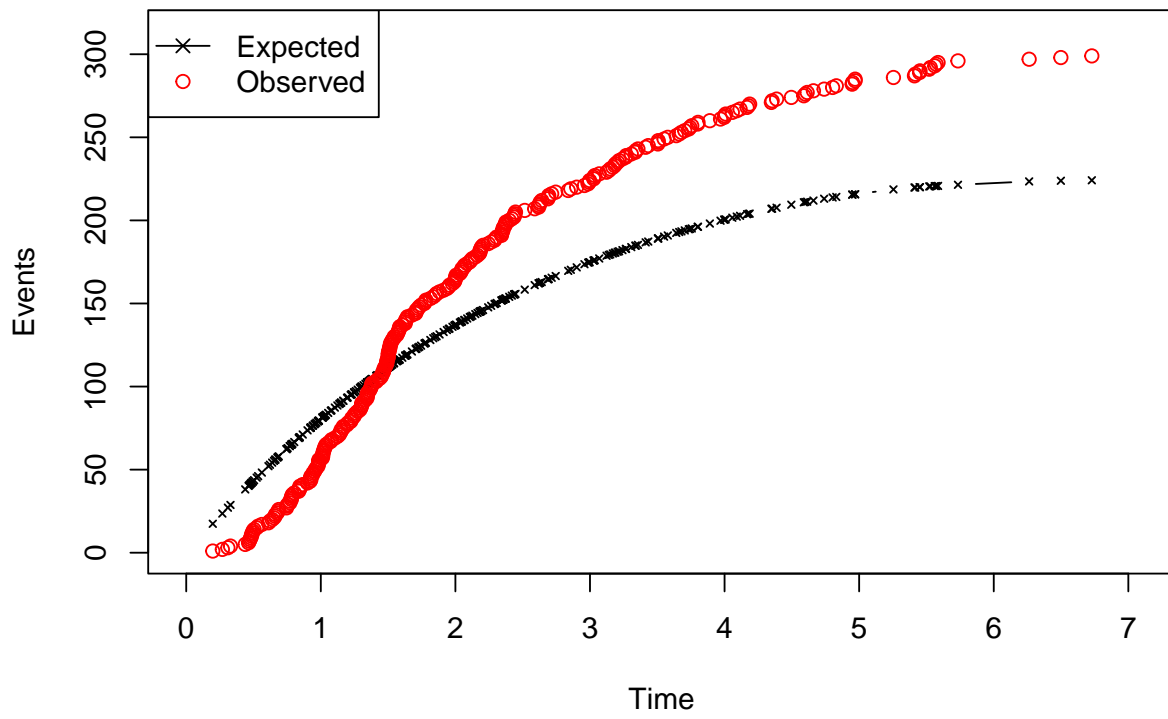


Relative Risk: Test: Breast Cancer

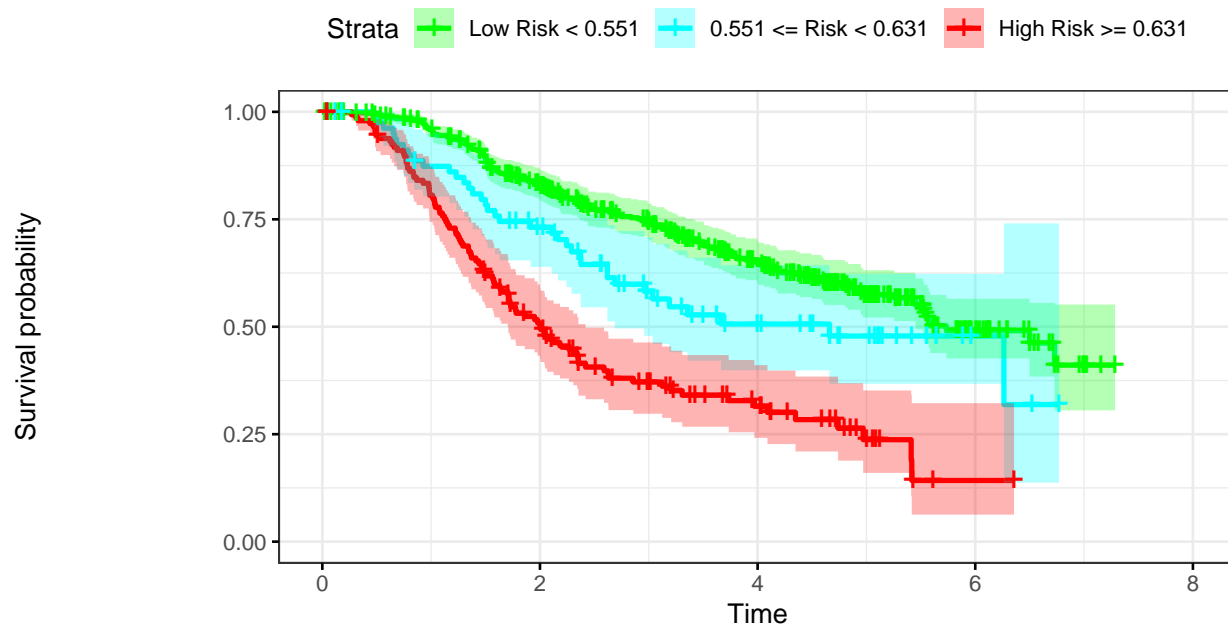




Time vs. Events: Test: Breast Cancer



Kaplan–Meier: Test: Breast Cancer



Number at risk

Low Risk < 0.551

0.551 <= Risk < 0.631

High Risk >= 0.631

457	338	183	32	0
82	53	22	3	0
147	68	24	1	0

```
par(op)
```

1.5.1 External Data Report

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

Table 28: Threshold values

	@:0.631	@:0.551	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.6312	0.5516	0.5834	0.337	2.71e-01	0.4996
RR	1.7994	1.6427	1.7581	3.279	2.64e+01	1.5937
RR_LCI	1.5366	1.3951	1.4980	1.641	5.65e-02	1.3435
RR_UCI	2.1071	1.9343	2.0632	6.552	1.23e+04	1.8906
SEN	0.3311	0.4515	0.4181	0.977	1.00e+00	0.5518
SPE	0.8734	0.7571	0.8088	0.111	1.55e-02	0.6537
BACC	0.6022	0.6043	0.6134	0.544	5.08e-01	0.6028
NetBenefit	0.0221	0.0283	0.0312	0.171	2.29e-01	0.0455

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

Table 29: O/E Ratio

O/E	Low	Upper	p.value
1.33	1.19	1.49	1.74e-06

```
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	0.663	0.632	0.692

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

Table 31: ROC AUC

est	lower	upper
0.66	0.619	0.7

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

Table 32: Sensitivity

est	lower	upper
0.328	0.275	0.384

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

Table 33: Specificity

est	lower	upper
0.873	0.836	0.905

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

Table 34: Probability Thresholds

90%	80%
0.631	0.551

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

Table 35: 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")
```

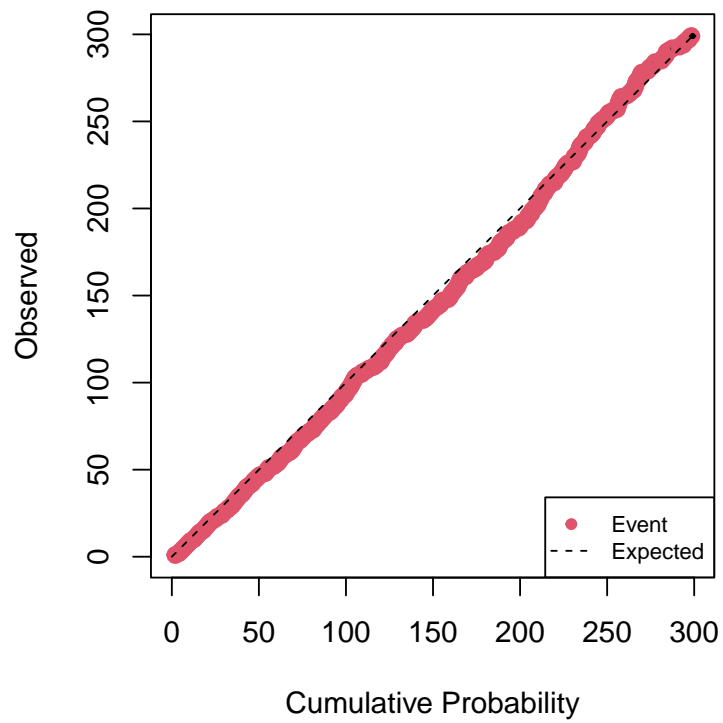
```
pander::pander(c(h0=calprob$h0,
  Gain=calprob$hazardGain,
  DeltaTime=calprob$timeInterval),
  caption="Cox Calibration Parameters")
```

h0	Gain	DeltaTime
0.535	0.925	4.87

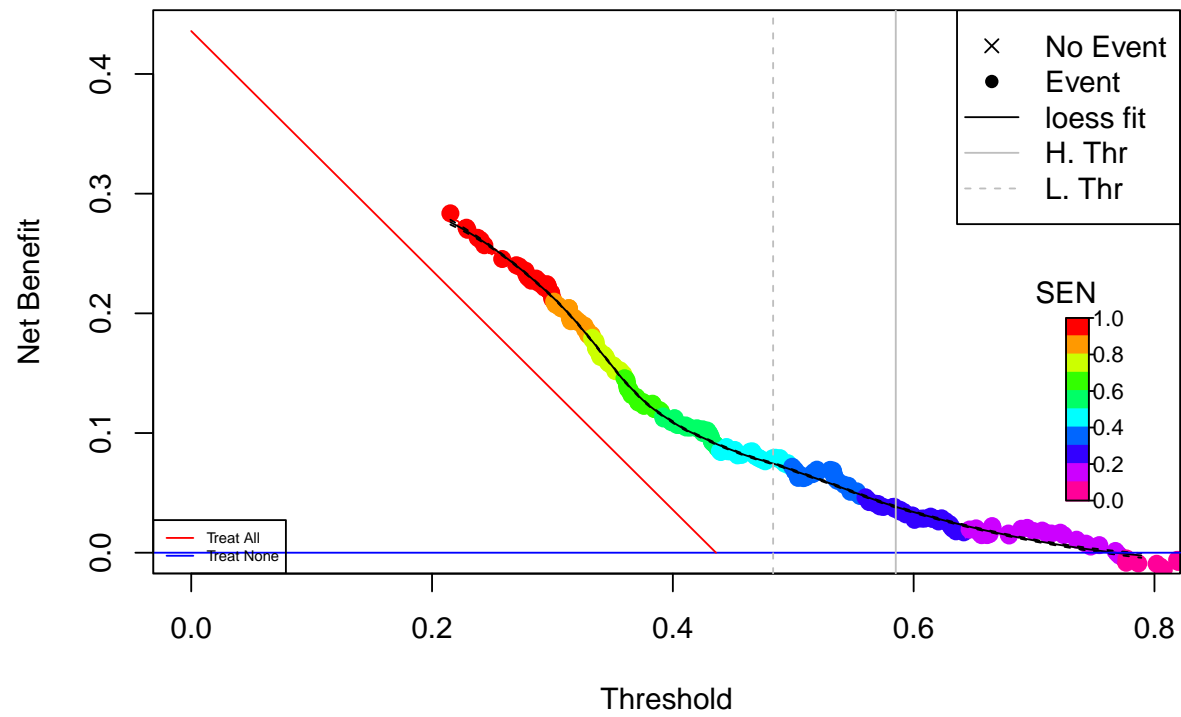
```
rdata <- cbind(dataBrestCancerTest$status,calprob$prob)
```

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

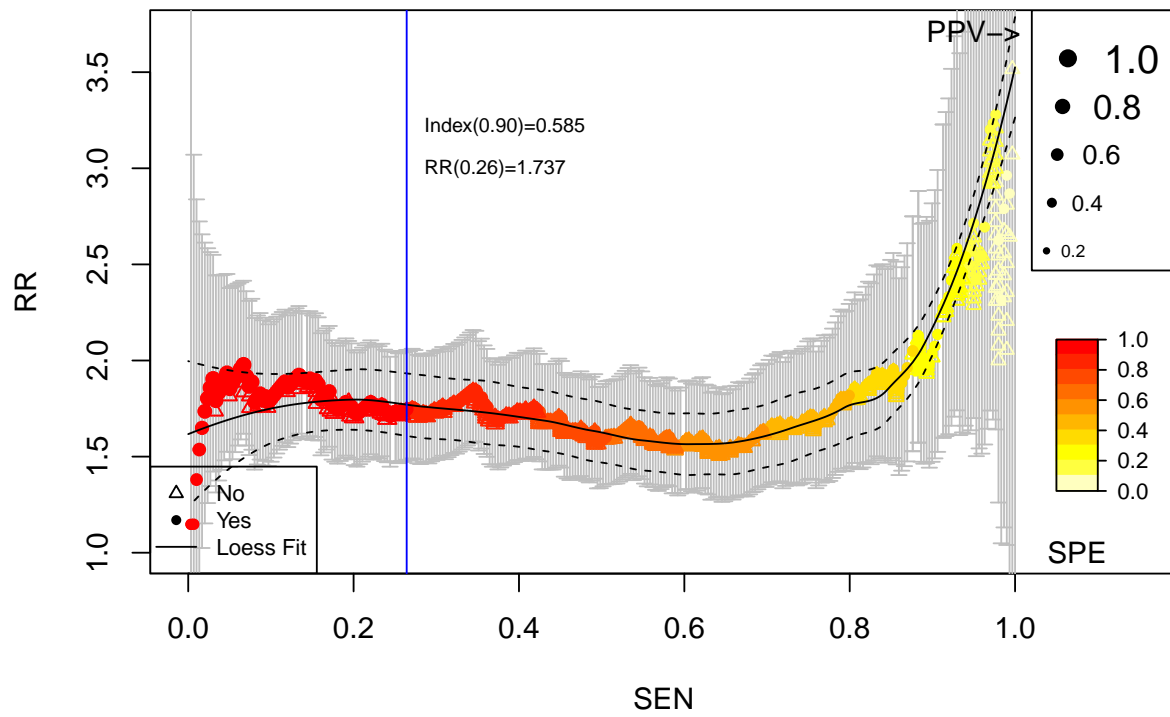
Cumulative vs. Observed: Cal. Test: Breast Cancer

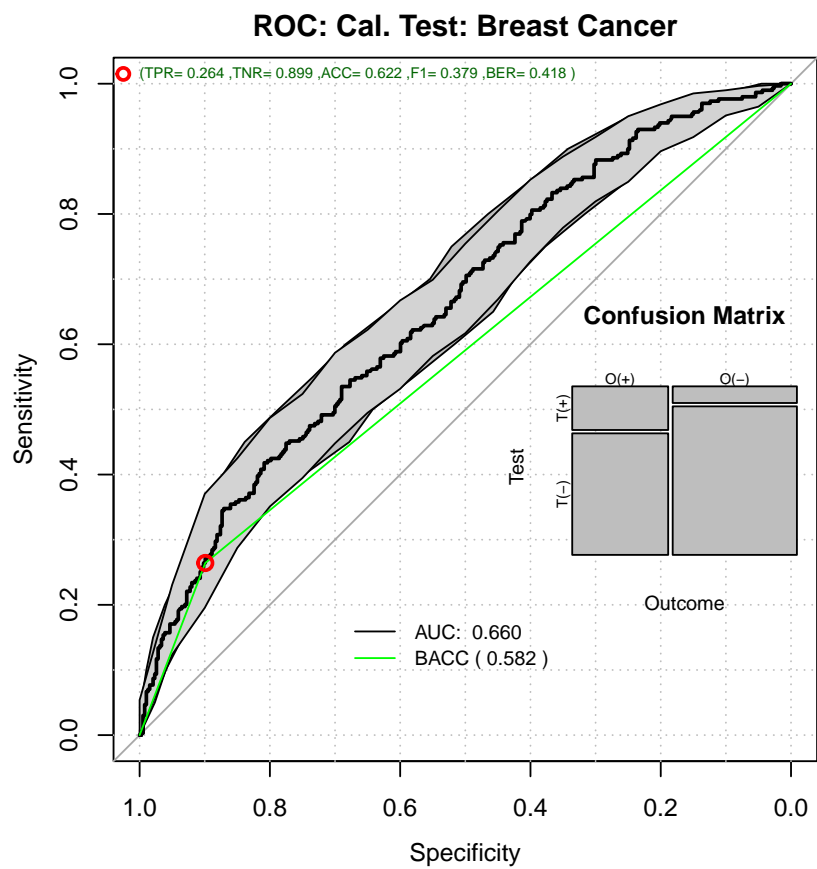


Decision Curve Analysis: Cal. Test: Breast Cancer

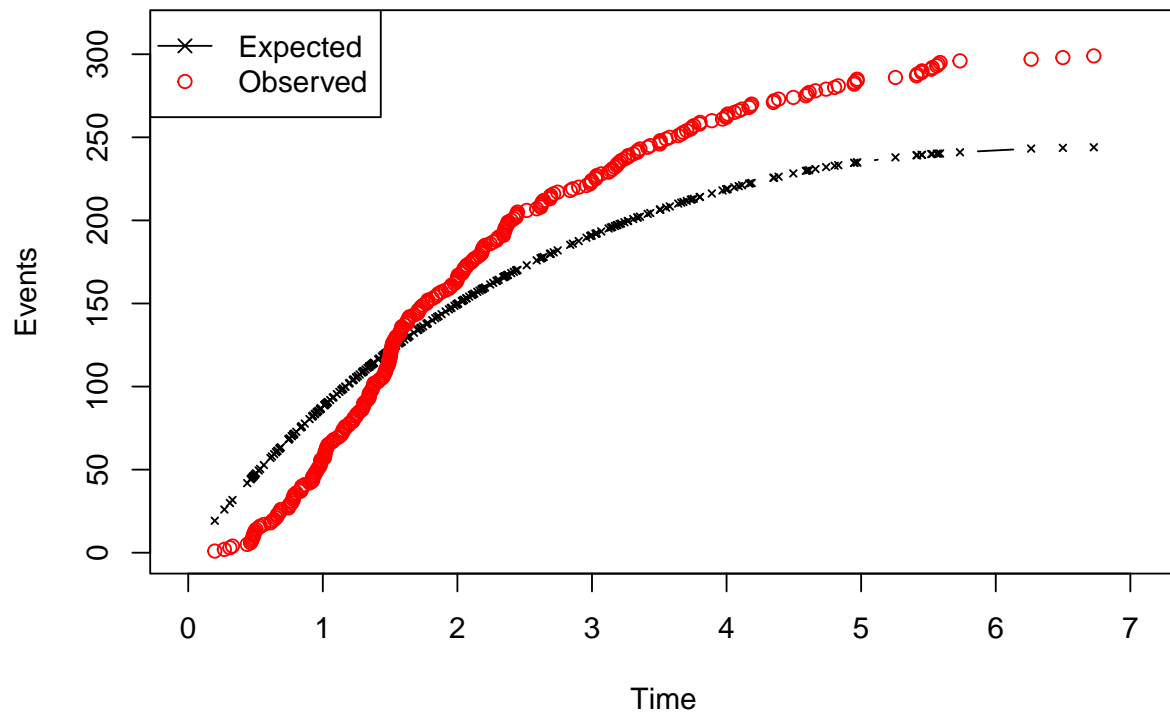


Relative Risk: Cal. Test: Breast Cancer

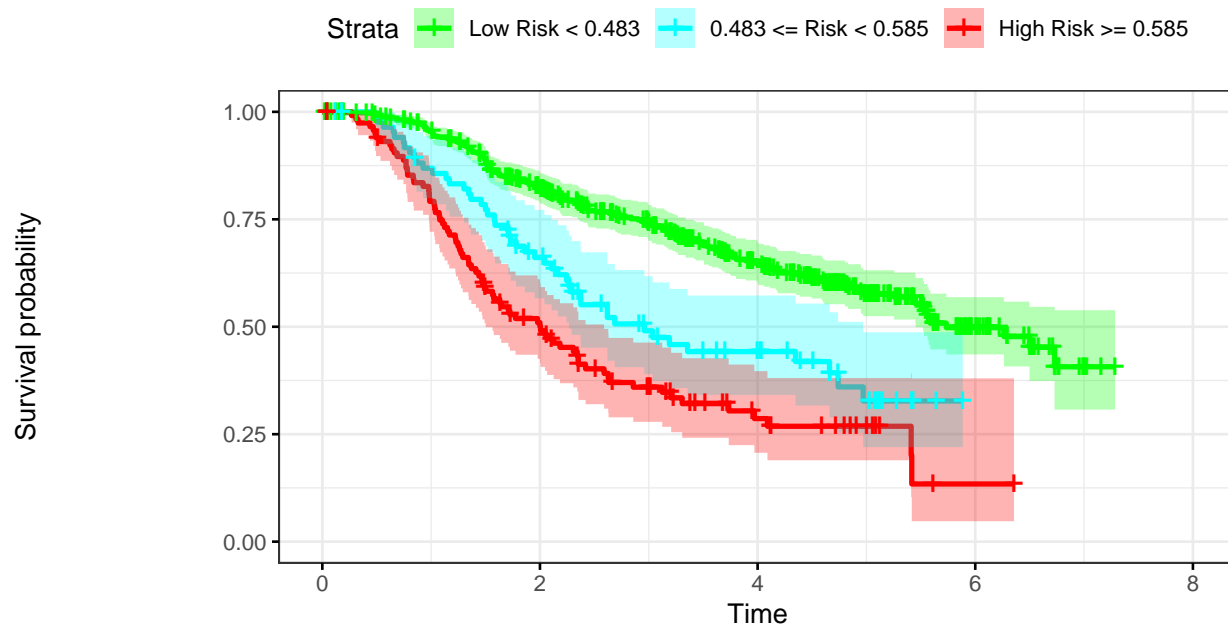




Time vs. Events: Cal. Test: Breast Cancer



Kaplan–Meier: Cal. Test: Breast Cancer



Number at risk

Low Risk < 0.483	482	354	190	35	0
0.483 <= 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 37: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.5843	0.483	0.489	0.270	2.15e-01	0.4991
RR	1.7405	1.732	1.758	3.279	2.64e+01	1.7385
RR_LCI	1.4790	1.475	1.498	1.641	5.65e-02	1.4816
RR_UCI	2.0483	2.035	2.063	6.552	1.23e+04	2.0399
SEN	0.2676	0.425	0.418	0.977	1.00e+00	0.3980
SPE	0.8992	0.798	0.809	0.111	1.55e-02	0.8191
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="O/E Ratio")
```

Table 38: O/E Ratio

O/E	Low	Upper	p.value
1.23	1.09	1.37	0.00061

```
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	0.663	0.634	0.694

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

Table 40: ROC AUC

est	lower	upper
0.66	0.619	0.7

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

Table 41: Sensitivity

est	lower	upper
0.264	0.215	0.318

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

Table 42: Specificity

est	lower	upper
0.899	0.865	0.927

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

Table 43: Probability Thresholds

90%	80%
0.585	0.483

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

Table 44: 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)
```

```
—..
```

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

	Estimate	lower OR	upper	u.Accuracy	Accuracy	Accuracy	AUC	Full AUC	AUC	NRI	z.IDI	z.NRI	Delta AUC	Frequency		
size_nodes	4.5e-03	1.001	1.001	1.001	0.669	0.571	0.668	0.627	0.500	0.628	0.1123	0.6365	17.86	18.87	0.1284	901
nodes	4.33e-02	1.040	1.044	1.048	0.676	0.634	0.690	0.639	0.621	0.662	0.0711	0.5710	14.13	16.17	0.0404	941
grade_nodes	1.01e-02	1.014	1.015	1.016	0.682	0.637	0.686	0.649	0.624	0.655	0.0658	0.5486	13.66	15.65	0.0310	871
age_nodes	1.06e-03	1.001	1.001	1.001	0.678	0.653	0.686	0.642	0.621	0.657	0.0334	0.2131	2.39	5.71	0.0358	961
size_grade	1.75e-03	1.001	1.002	1.002	0.632	0.682	0.686	0.626	0.646	0.655	0.0178	0.2941	6.74	7.72	0.0086	481
age_size	8.73e-05	1.000	1.000	1.000	0.608	0.682	0.686	0.577	0.649	0.657	0.0153	0.2915	3.41	7.65	0.0076	001
grade	2.27e-01	1.168	1.254	1.347	0.571	0.683	0.690	0.500	0.653	0.662	0.0134	0.1903	6.20	4.98	0.0084	611
age_meno	6.04e-03	0.992	0.994	0.996	0.571	0.676	0.686	0.500	0.645	0.657	0.0078	0.0805	1.76	2.33	0.0120	651

	Estimate	lower OR	upper	u.Accuracy	Accuracy	Accuracy	AUC	AUC	AUC	Full.AUC	DI	NRI	z.IDI	z.NRI	Delta.AUC	Frequency
age_pgr -	1.000	1.000	1.000	0.571	0.686	0.686	0.500	0.656	0.657	0.0051	0.0074	1.11	0.194	0.0004	171	
5.42e-06																
age_grade	0.997	0.998	0.999	0.574	0.690	0.690	0.507	0.661	0.662	0.0045	0.1137	3.60	2.960	0.0003	151	
1.65e-03																
meno_grade	1.045	1.107	1.173	0.571	0.683	0.686	0.500	0.652	0.657	0.0042	0.2042	3.47	5.343	0.0044	11	
0.01																
nodes_hormon	0.979	0.986	0.994	0.587	0.688	0.686	0.526	0.658	0.655	0.0028	0.4552	3.44	12.150	-	1	
1.38e-02															0.0028	53
size	3.94e-03	1.002	1.004	1.006	0.611	0.693	0.690	0.618	0.663	0.662	0.0050	0.2105	3.42	5.600	-	1
															0.0010	75
meno_pgr	1.000	1.000	1.001	0.571	0.687	0.686	0.500	0.657	0.657	0.0031	0.0597	3.35	1.558	-	1	
0.04															0.0004	29
pgr	1.000	1.000	1.000	0.571	0.689	0.686	0.500	0.659	0.655	0.0025	0.1975	2.64	5.745	-	1	
1.07e-04															0.0041	23
meno_nodes	0.955	0.974	0.994	0.640	0.686	0.686	0.595	0.656	0.657	0.0026	-	2.59	-	0.0006	311	
2.60e-02											0.0632	9	1.645			
grade_pgr	1.000	1.000	1.000	0.571	0.669	0.668	0.500	0.627	0.628	0.0024	0.1747	2.55	5.058	0.0012	521	
3.51e-05																
meno_size	1.000	1.002	1.004	0.604	0.691	0.690	0.578	0.663	0.662	0.0018	0.1022	2.43	2.662	-	1	
1.28e-03															0.0013	78

1.7 Logistic Model Performance

```

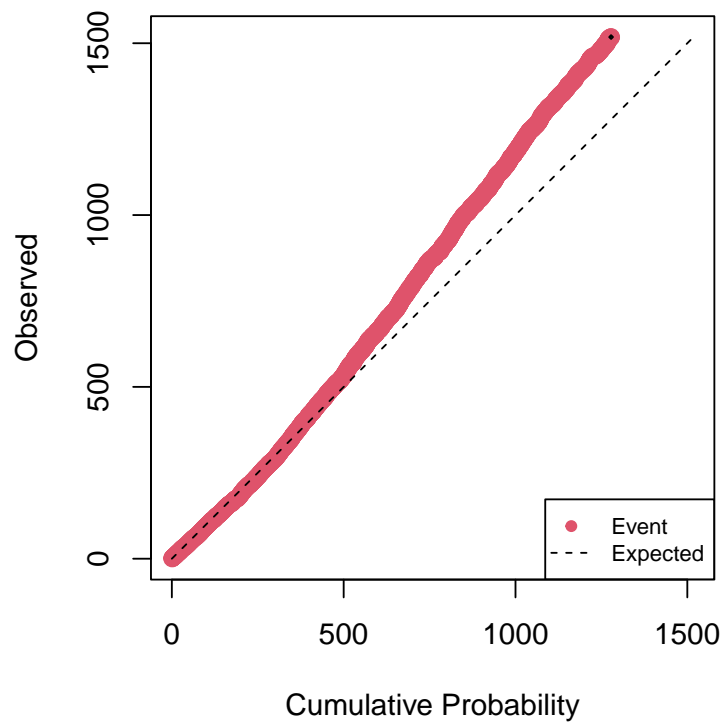
op <- par(no.readonly = TRUE)

cprob <- predict(mlog,dataBrestCancerTrain)

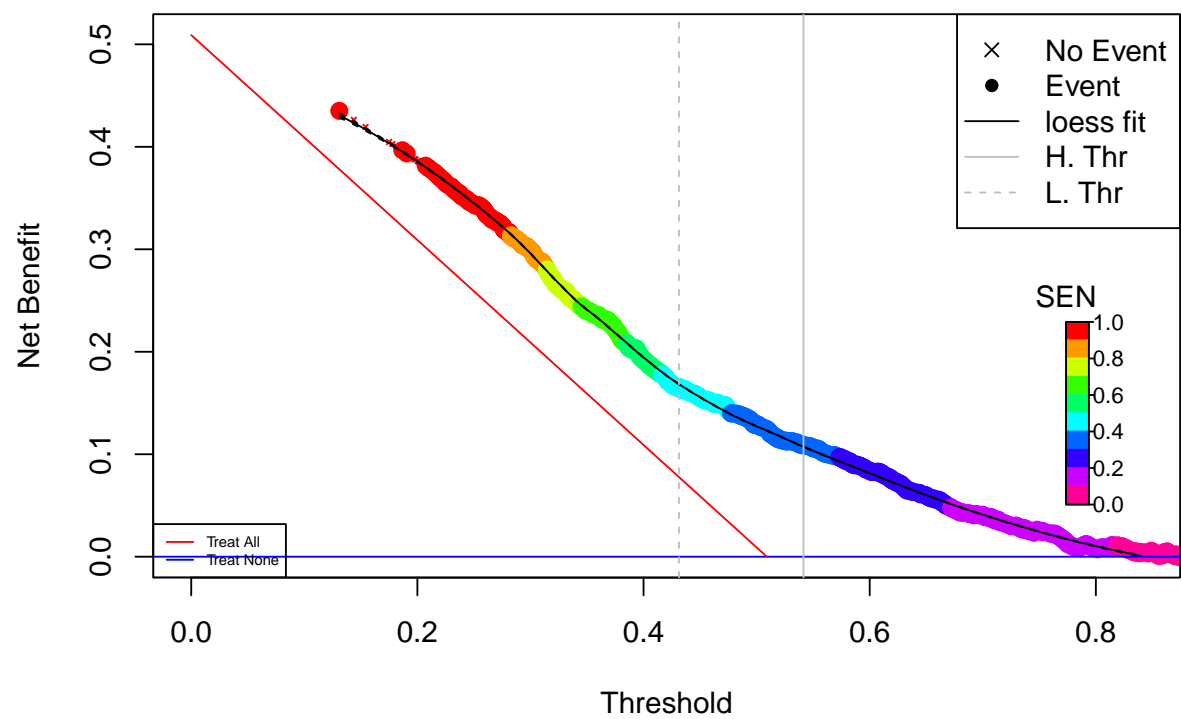
rdata <- cbind(dataBrestCancerTrain$status,cprob)
rrAnalysisTrain <- RRPlot(rdata,atRate=c(0.90,0.80),
                           timetoEvent=dataBrestCancerTrain$time,
                           title="Logistic Train: Breast Cancer",
                           ysurvlim=c(0.00,1.0),
                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

```

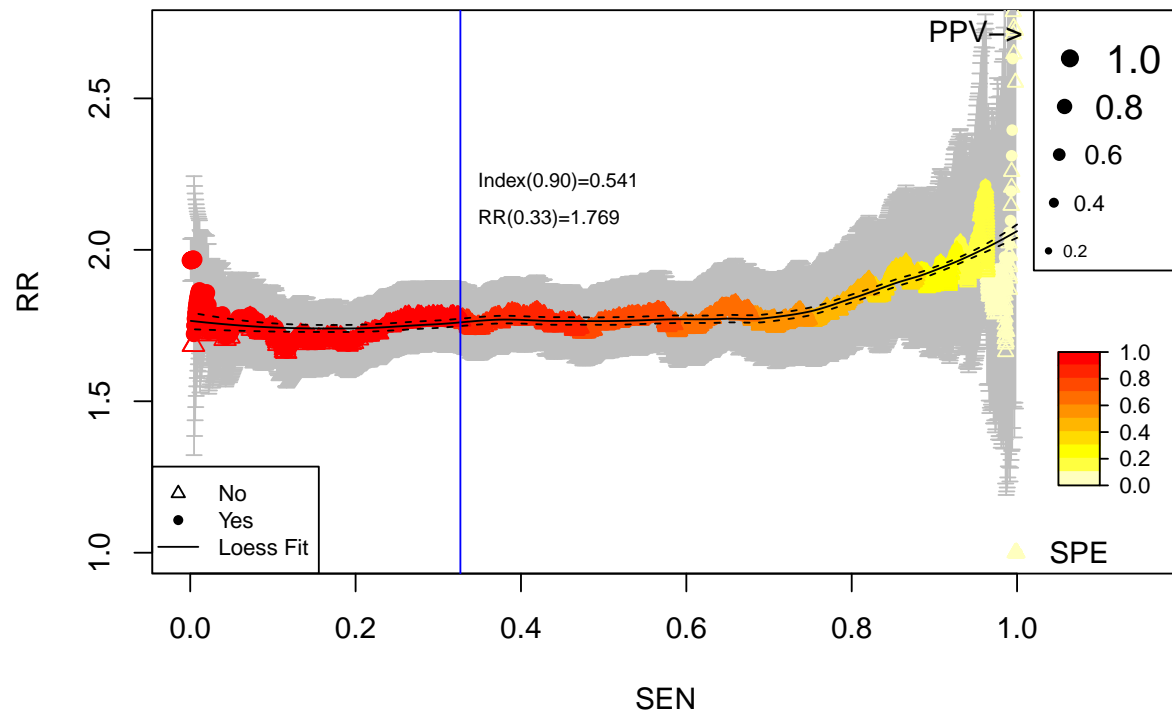

Cumulative vs. Observed: Logistic Train: Breast Cancer

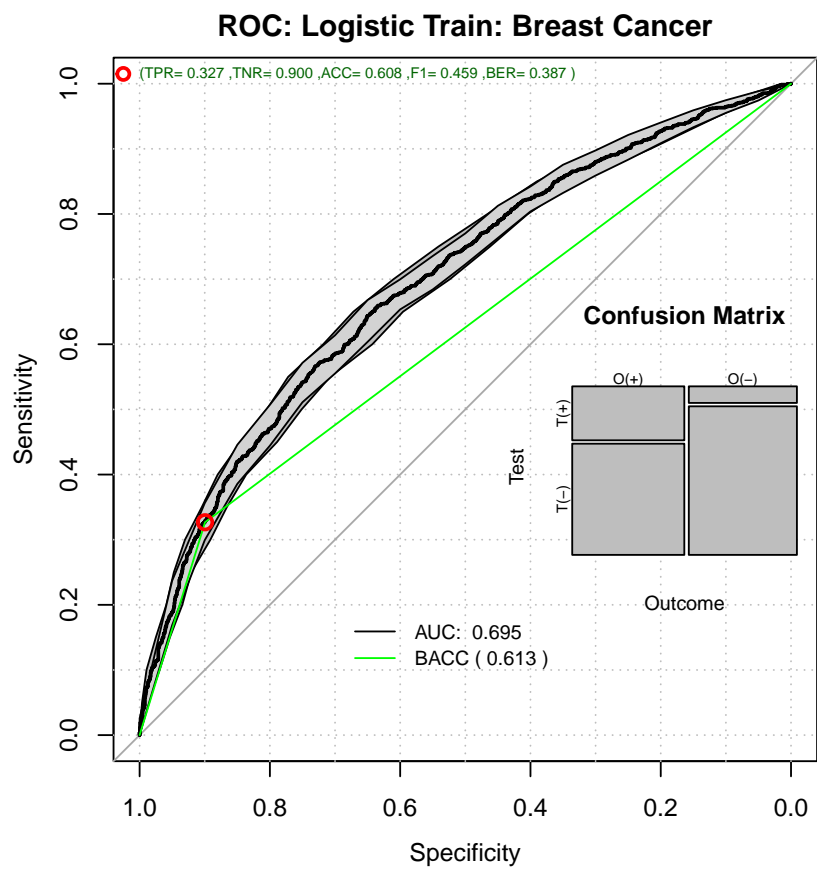


Decision Curve Analysis: Logistic Train: Breast Cancer

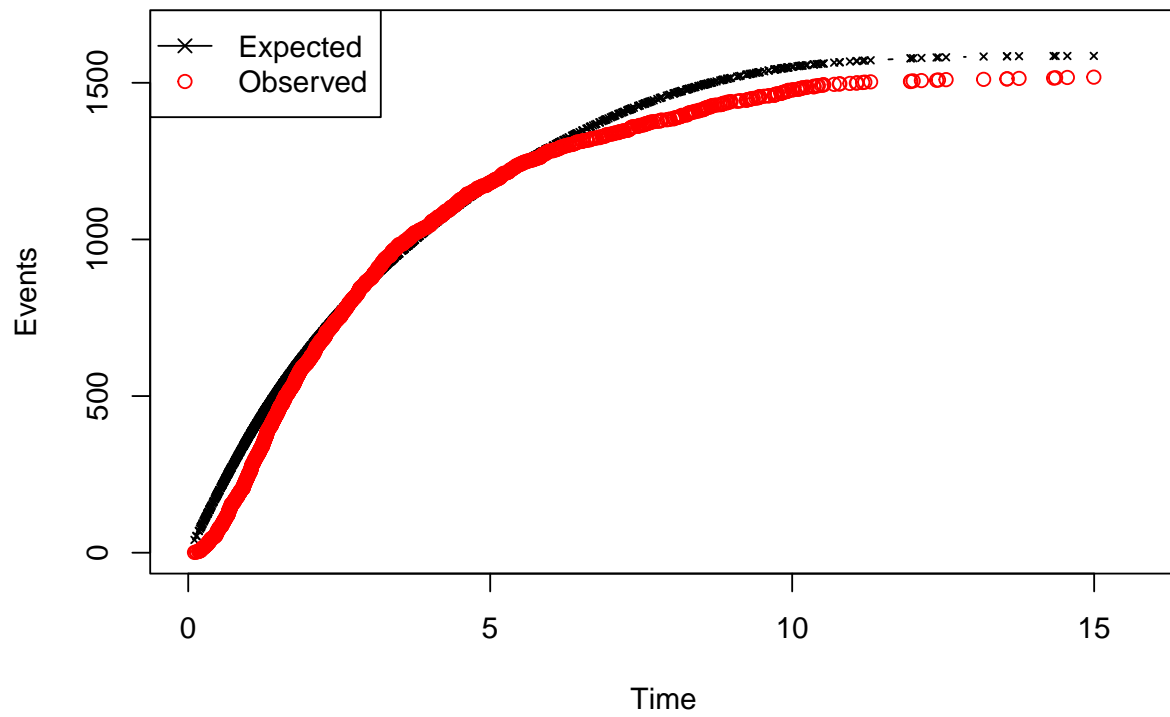


Relative Risk: Logistic Train: Breast Cancer

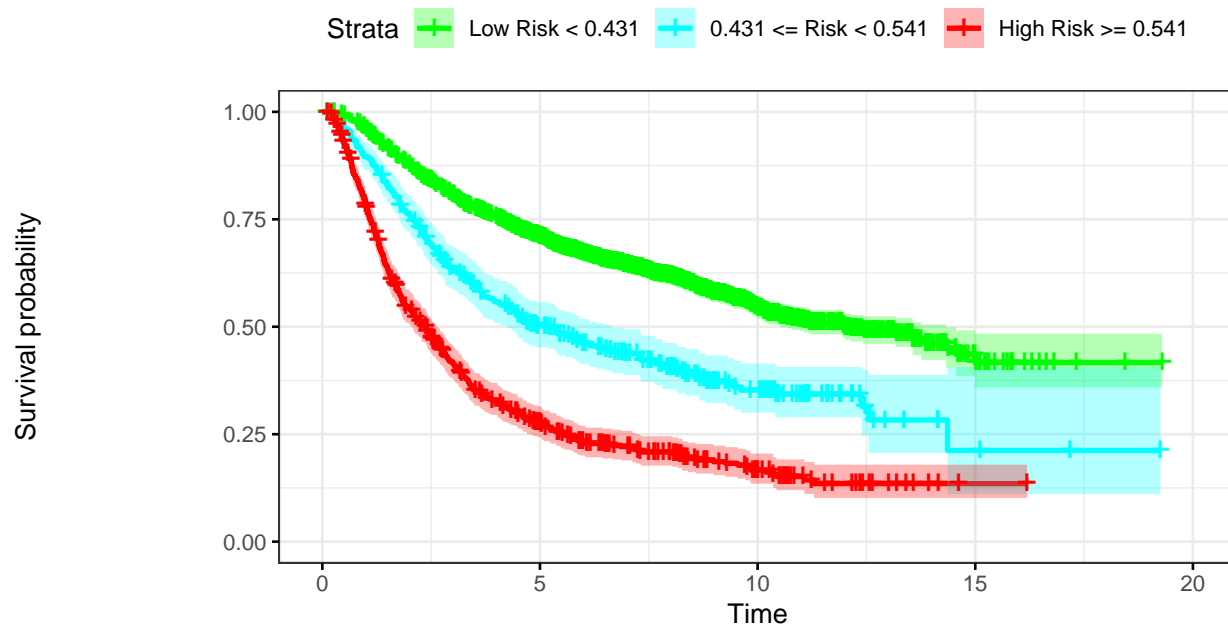




Time vs. Events: Logistic Train: Breast Cancer



Kaplan–Meier: Logistic Train: Breast Cancer



Number at risk

Low Risk < 0.431	1974	1267	398	22	0
0.431 <= Risk < 0.541	365	161	48	3	0
High Risk >= 0.541	643	143	37	1	0

```
par(op)
```

1.7.1 Training Report

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

Table 46: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.542	0.431	0.394	0.255	0.130969	0.500
RR	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
SEN	0.327	0.470	0.566	0.962	1.000000	0.374
SPE	0.900	0.799	0.731	0.125	0.000683	0.874
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$OERatio$estimate),caption="O/E Ratio")
```

Table 47: 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:** *0.36*
- **S.D.:** *0.014*
- **n:** *2982*
- **missing:** *0*
- **uncensored:** *1518*
- **Relevant Pairs:** *6184528*
- **Concordant:** *4206584*
- **Uncertain:** *2703838*
- **cstatCI:**

mean.C Index	median	lower	upper
0.68	0.681	0.667	0.695

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

Table 49: ROC AUC

est	lower	upper
0.695	0.677	0.714

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

Table 50: Sensitivity

est	lower	upper
0.327	0.303	0.351

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

Table 51: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 52: Probability Thresholds

90%	80%
0.541	0.431

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

Table 53: Logrank test Chisq = 541.976716 on 2 degrees of freedom,
p = 0.000000

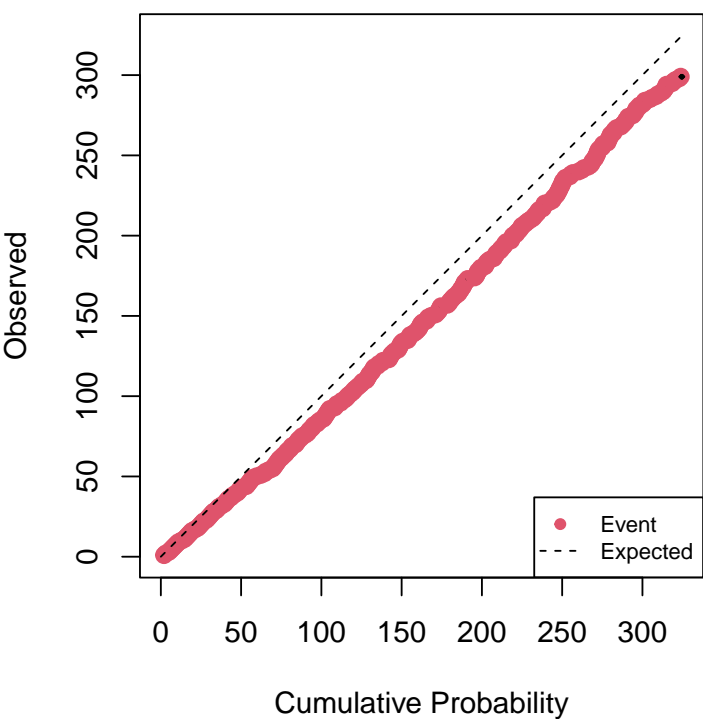
	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1974	804	1144	100.9	415.3
class=1	365	218	170	13.4	15.1
class=2	643	496	204	418.2	490.7

1.7.2 Results on the validation set using Logistic model

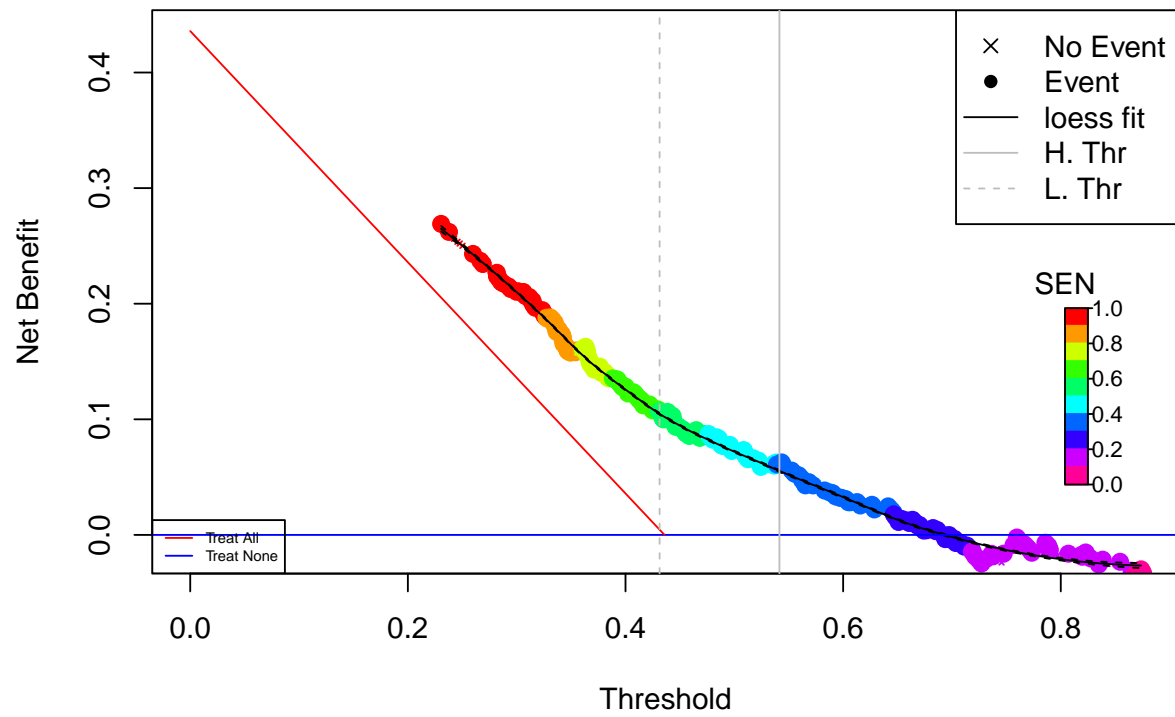
```
pre <- predict(mlog,dataBrestCancerTest)
rdata <- cbind(dataBrestCancerTest$status,pre)

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

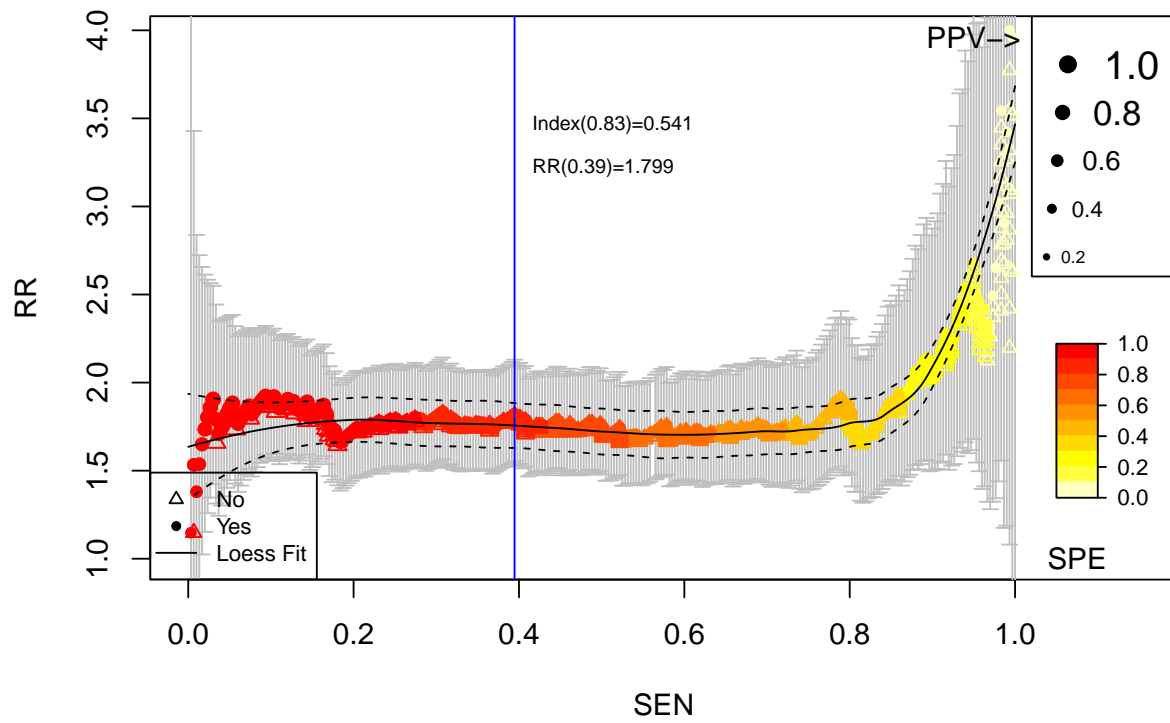

Cumulative vs. Observed: Logistic Test: Breast Cancer

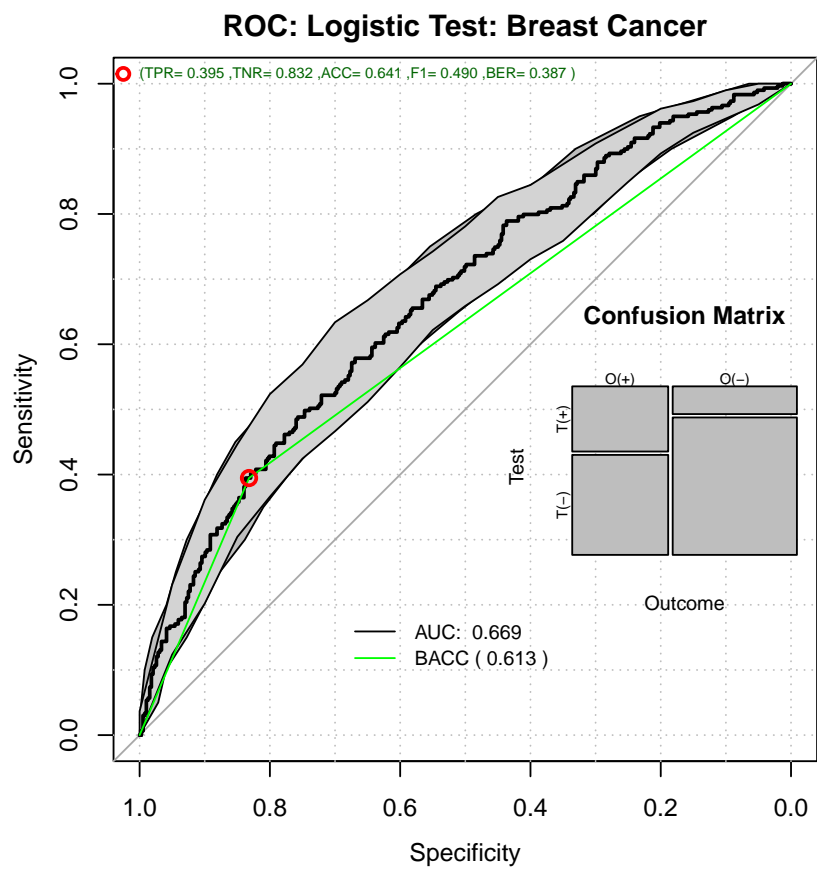


Decision Curve Analysis: Logistic Test: Breast Cancer

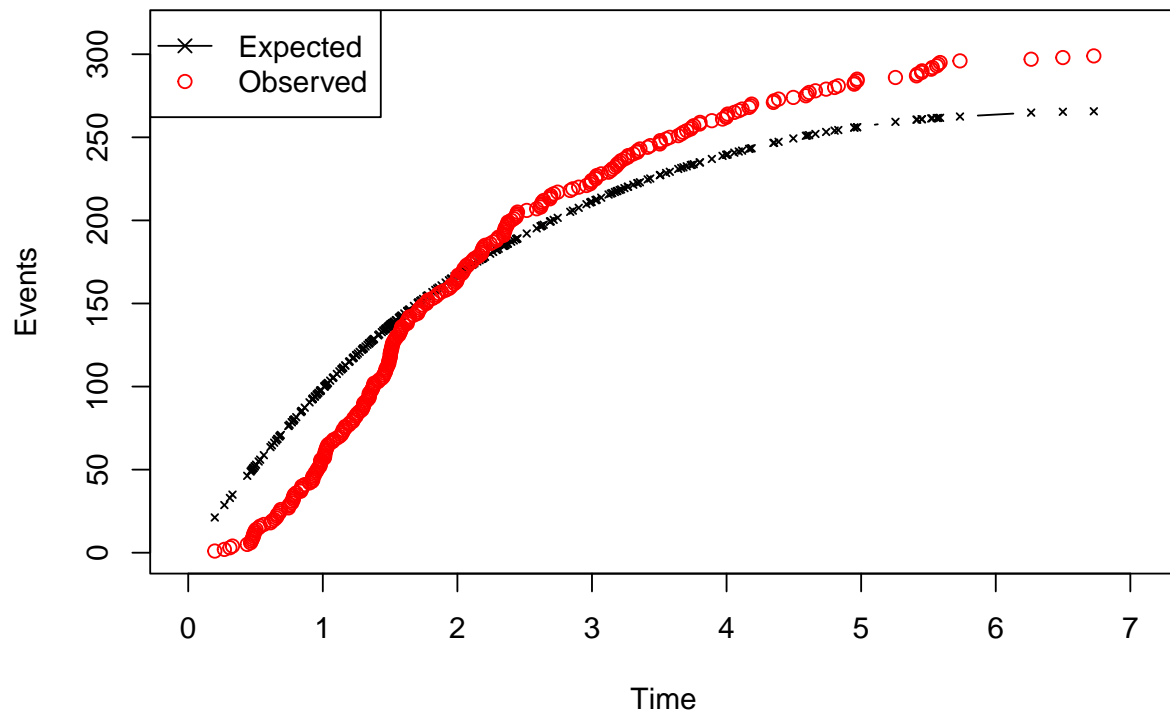


Relative Risk: Logistic Test: Breast Cancer

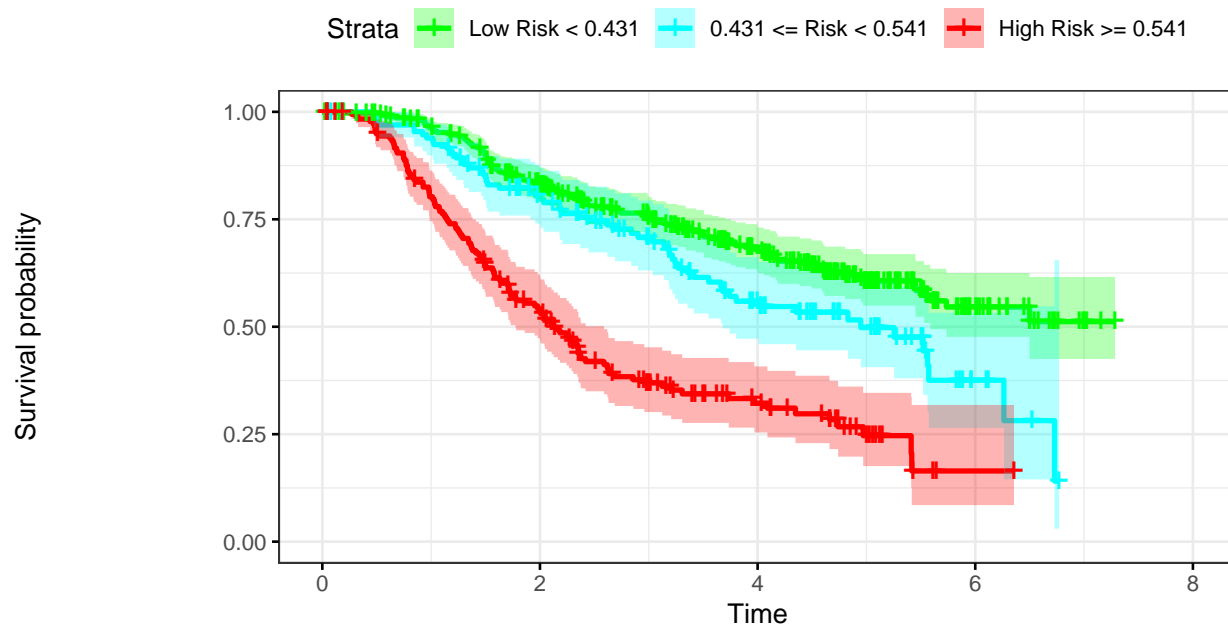




Time vs. Events: Logistic Test: Breast Cancer



Kaplan–Meier: Logistic Test: Breast Cancer



Number at risk

Low Risk < 0.431	369	274	154	29	0
0.431 <= Risk < 0.541	134	96	46	6	0
High Risk >= 0.541	183	89	29	1	0

```
par(op)
```

1.7.3 Validation Report

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

Table 54: 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
RR	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
SEN	0.395	0.595	0.579	0.950	1.00e+00	0.4482
SPE	0.832	0.638	0.669	0.181	1.29e-02	0.7804
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="O/E Ratio")
```

Table 55: 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:** *0.338*
- **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	0.64	0.7

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

Table 57: ROC AUC

est	lower	upper
0.669	0.628	0.709

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

Table 58: Sensitivity

est	lower	upper
0.395	0.339	0.453

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

Table 59: Specificity

est	lower	upper
0.832	0.791	0.868

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

Table 60: Probability Thresholds

90%	80%
0.541	0.431

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

Table 61: 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")
```

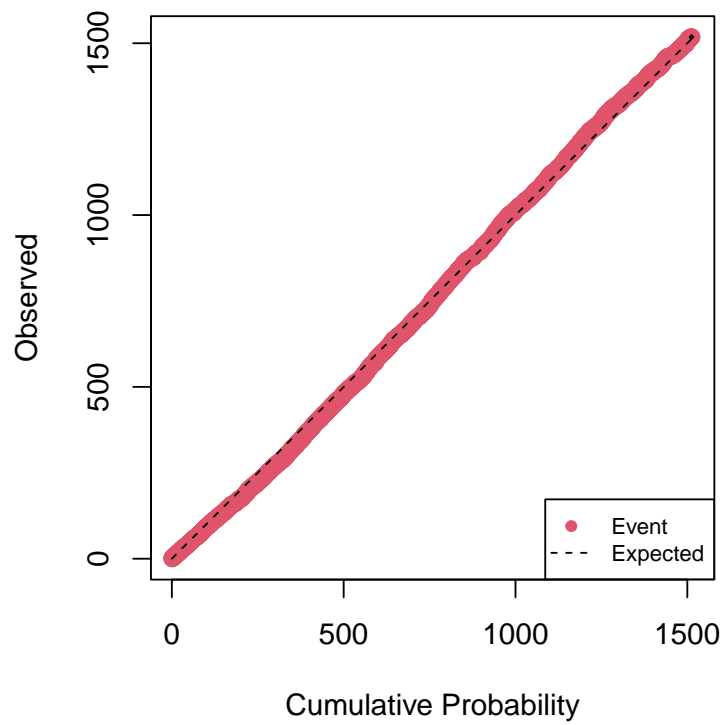
h0	Gain	DeltaTime
0.676	1.31	7.14

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

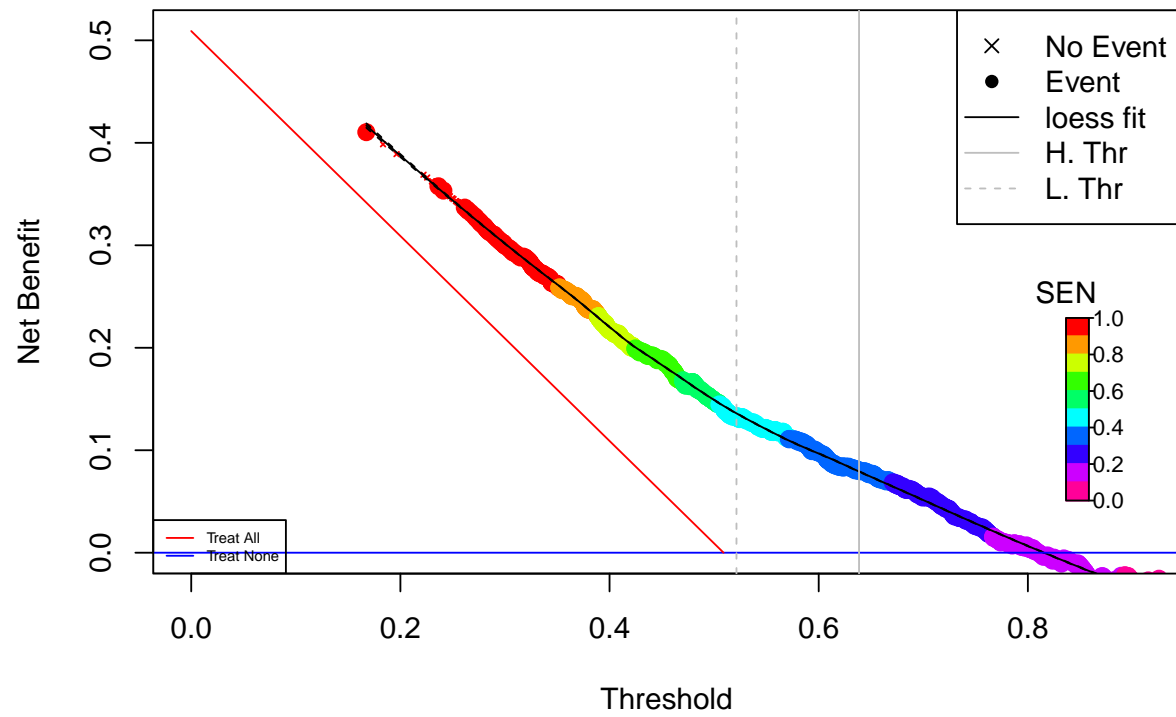
```
rdata <- cbind(dataBrestCancerTrain$status,calprob$prob)
```

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

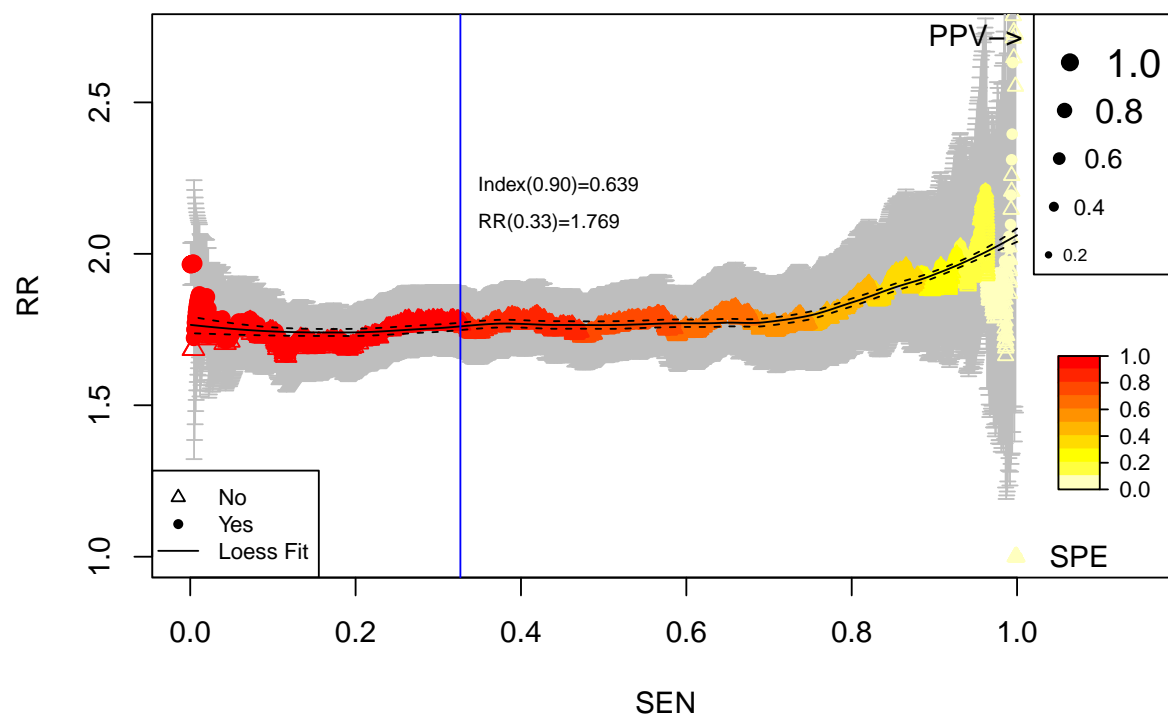

Cumulative vs. Observed: Cal. Logistic Train: Breast Cancer

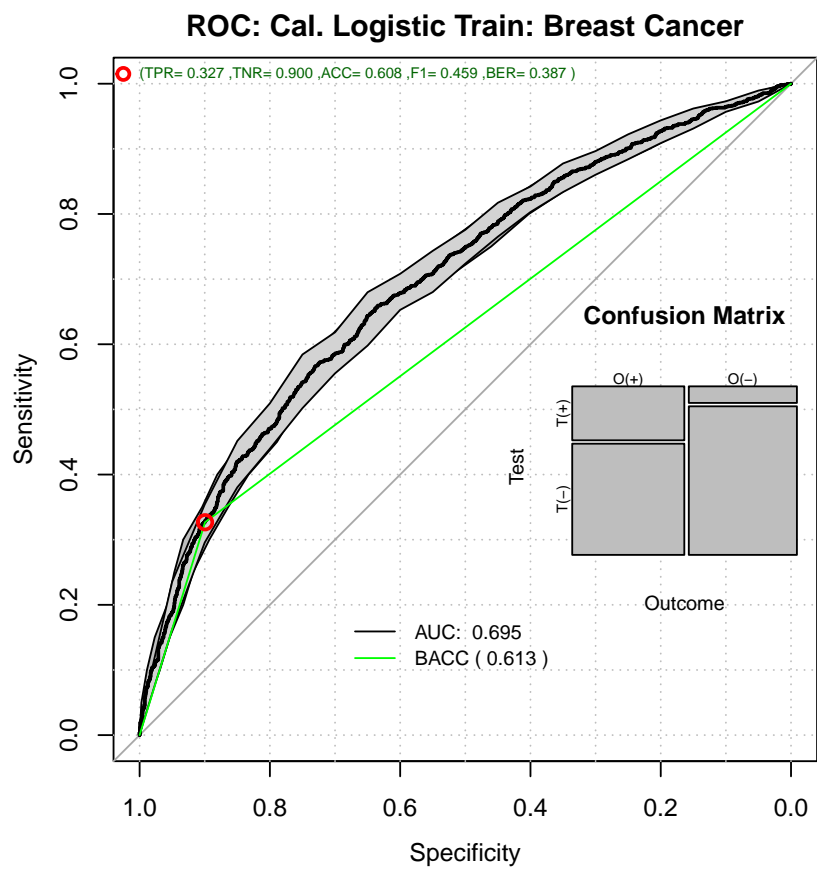


Decision Curve Analysis: Cal. Logistic Train: Breast Cancer

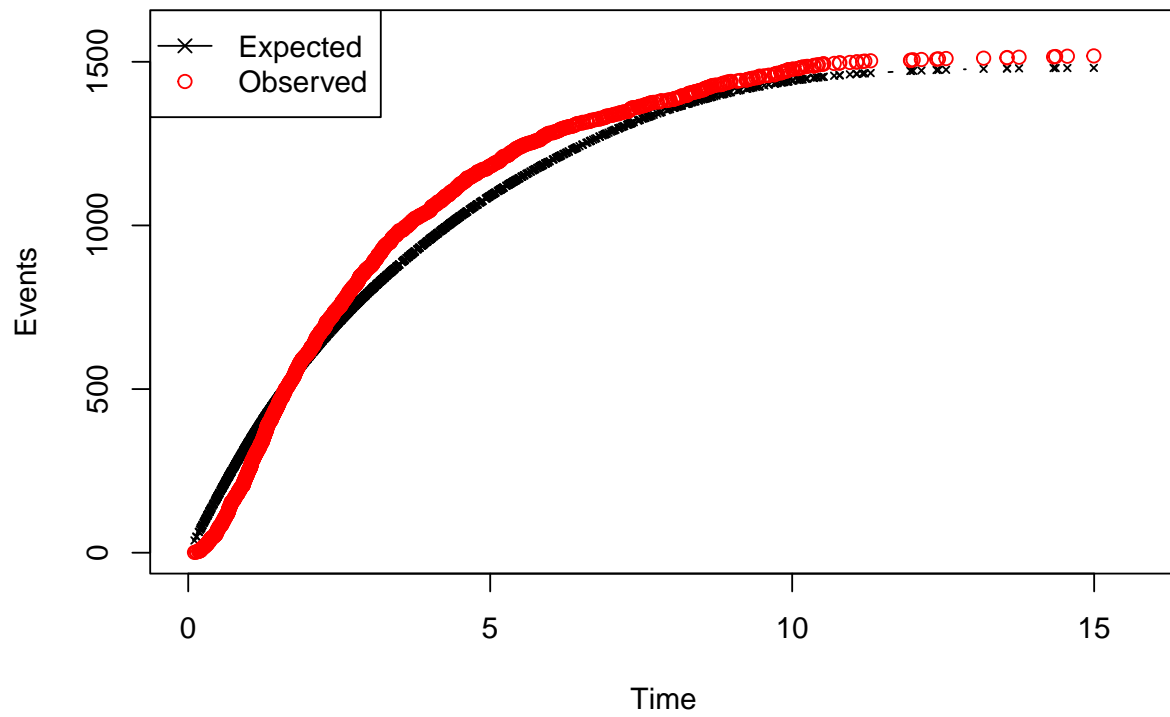


Relative Risk: Cal. Logistic Train: Breast Cancer

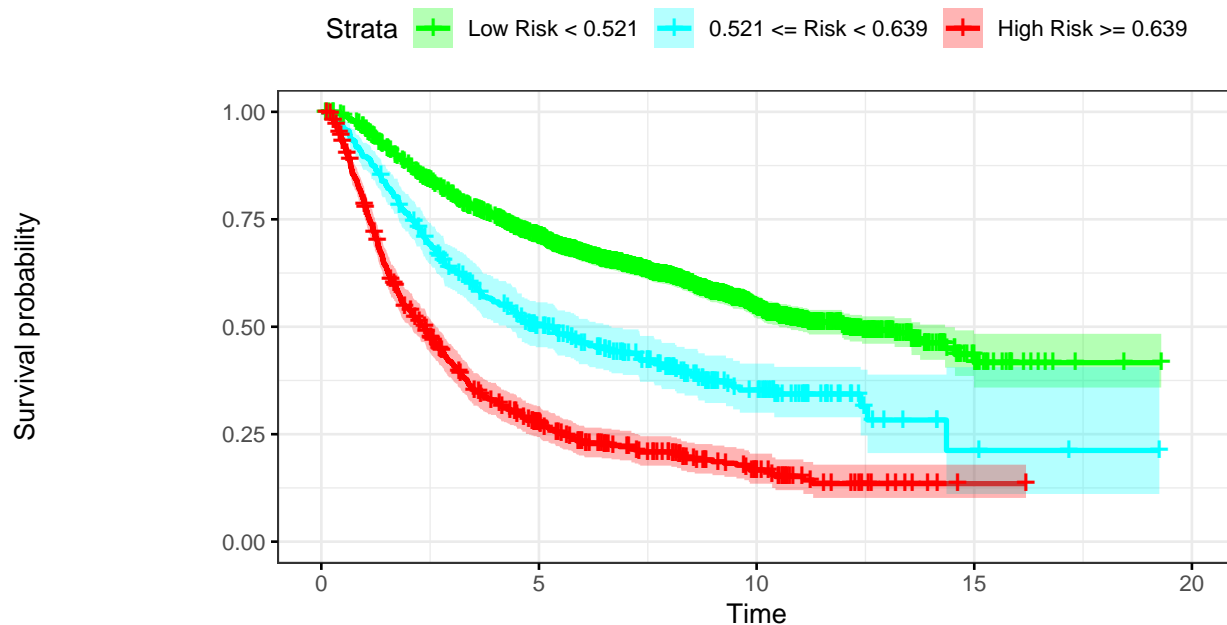




Time vs. Events: Cal. Logistic Train: Breast Cancer



Kaplan–Meier: Cal. Logistic Train: Breast Cancer



Number at risk

Low Risk < 0.521	1974	1267	398	22	0
0.521 <= Risk < 0.639	365	161	48	3	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 63: Threshold values

	@:0.9	@:0.8	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.6395	0.521	0.480	0.319	0.167426	0.500
RR	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
SEN	0.3267	0.470	0.566	0.962	1.000000	0.507
SPE	0.8996	0.799	0.731	0.125	0.000683	0.774
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$OERatio$estimate),caption="O/E Ratio")
```

Table 64: O/E Ratio

O/E	Low	Upper	p.value
1.02	0.974	1.08	0.343

```
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	0.693

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

Table 66: ROC AUC

est	lower	upper
0.695	0.677	0.714

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

Table 67: Sensitivity

est	lower	upper
0.327	0.303	0.351

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

Table 68: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 69: Probability Thresholds

90%	80%
0.639	0.521

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

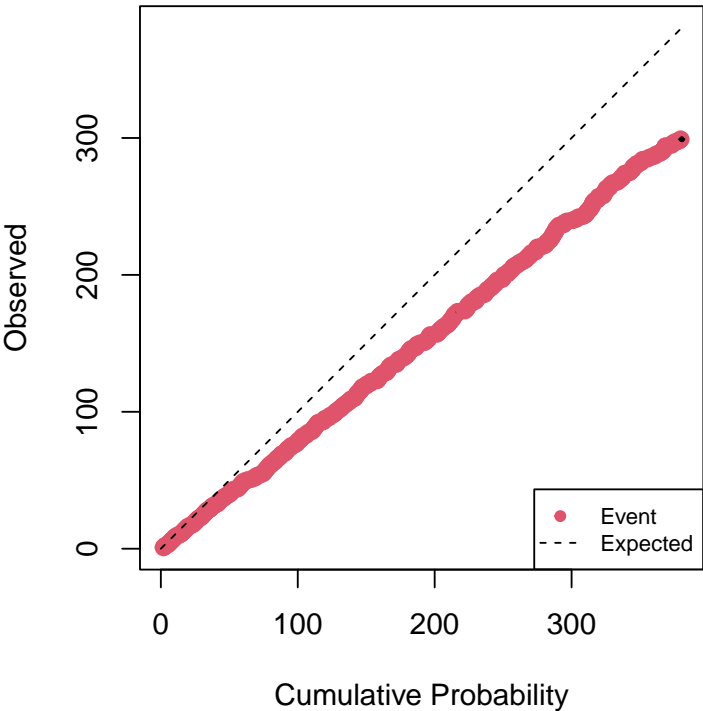
Table 70: Logrank test Chisq = 541.976716 on 2 degrees of freedom,
p = 0.000000

	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

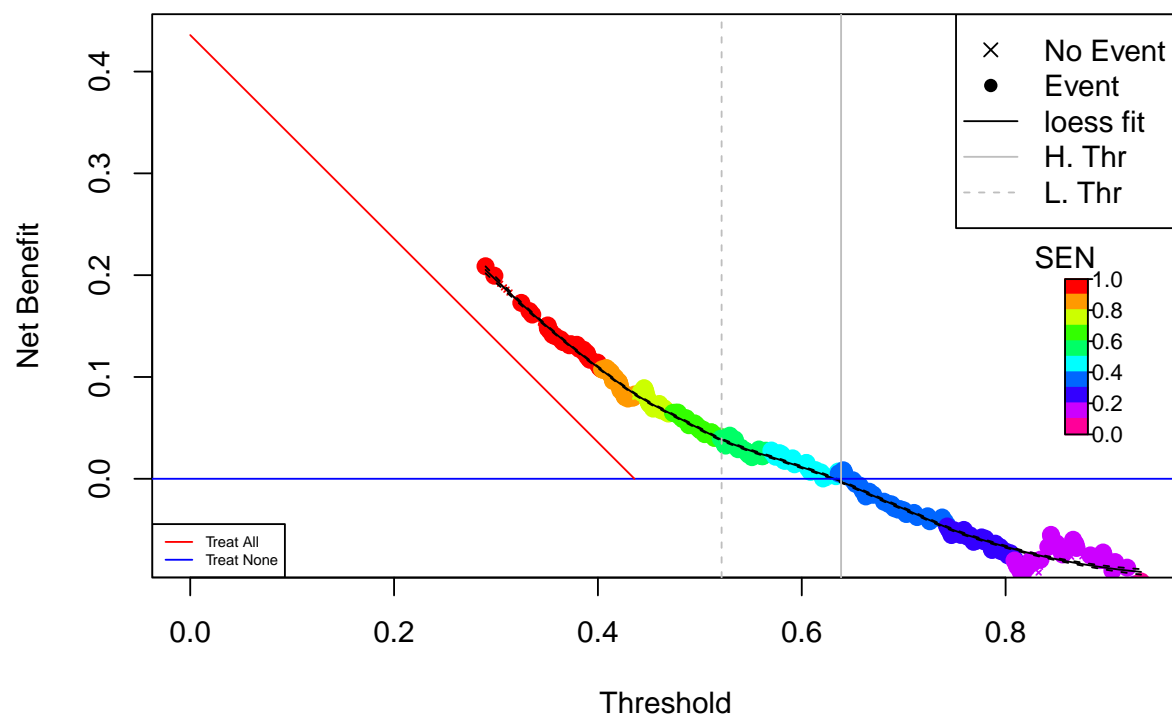
```
probLog <- predict(mlog,dataBrestCancerTest)
aprof <- adjustProb(probLog,gain)

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

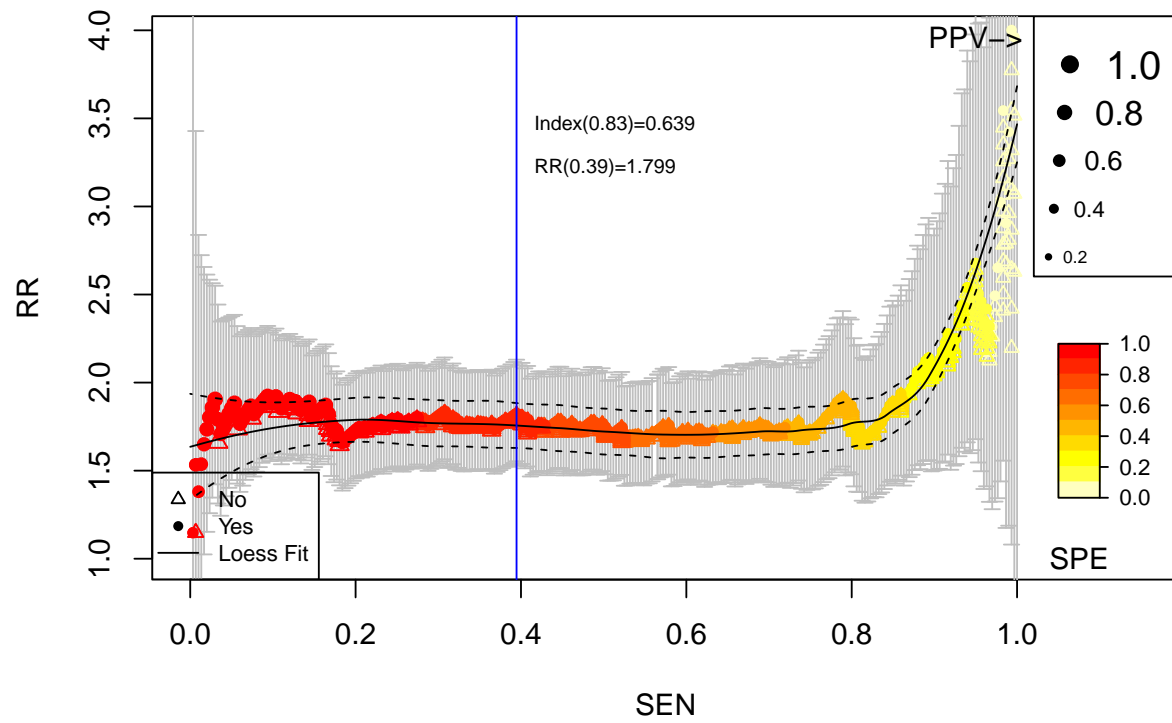

Cumulative vs. Observed: Cal. Logistic Test: Breast Cancer

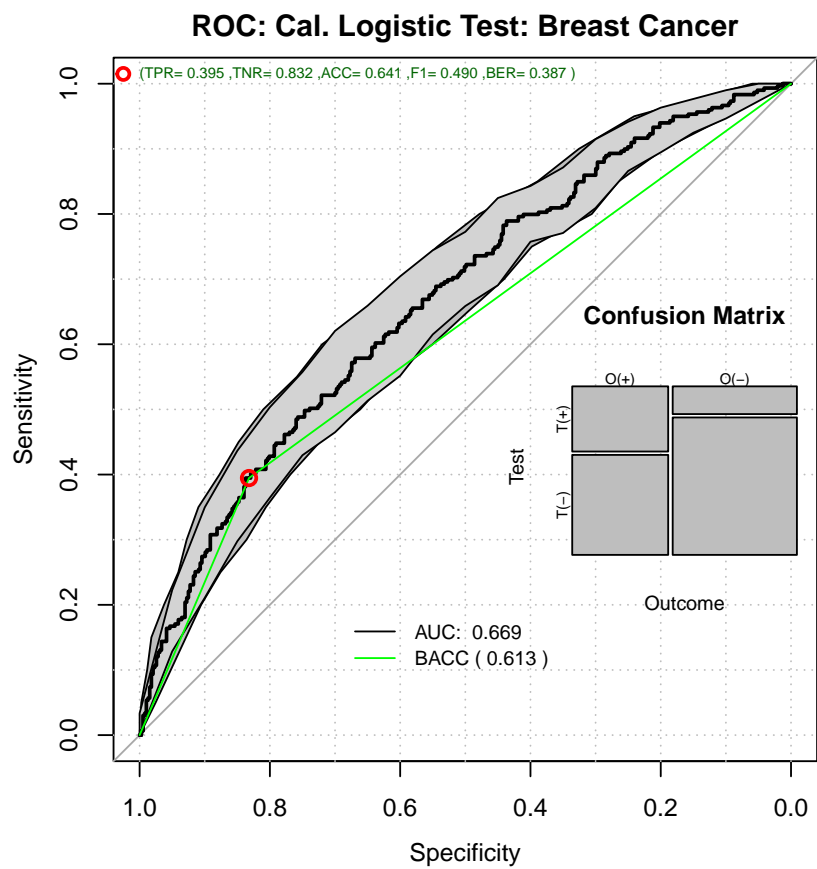


Decision Curve Analysis: Cal. Logistic Test: Breast Cancer

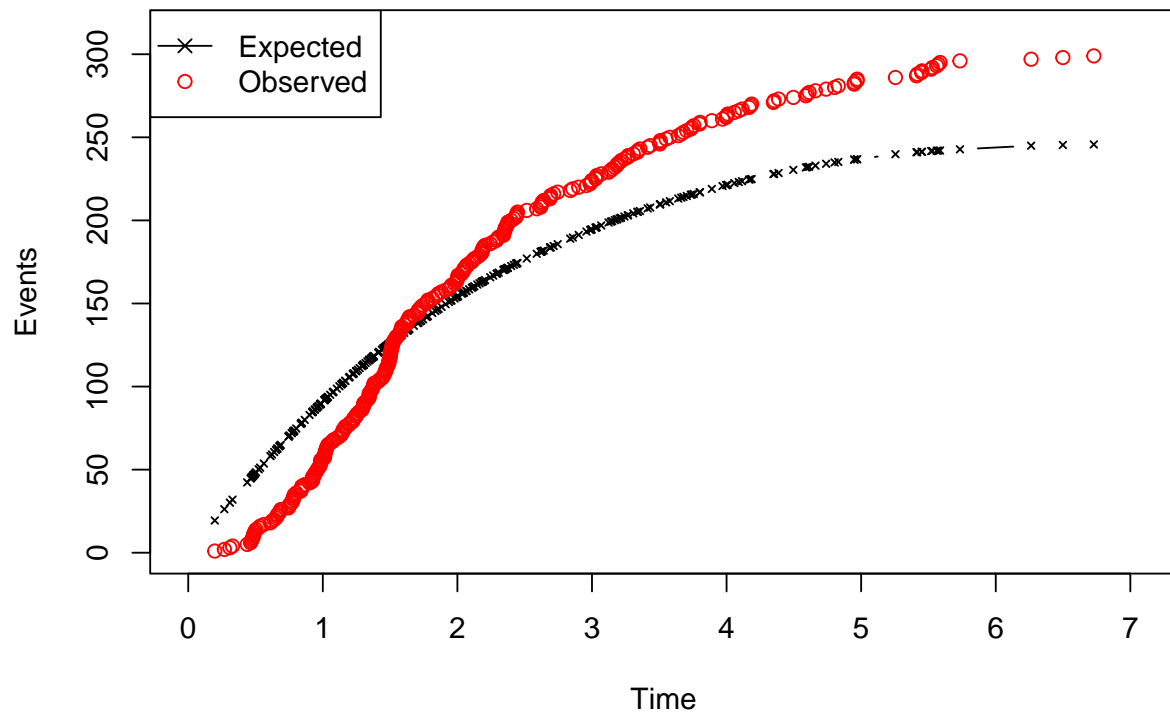


Relative Risk: Cal. Logistic Test: Breast Cancer

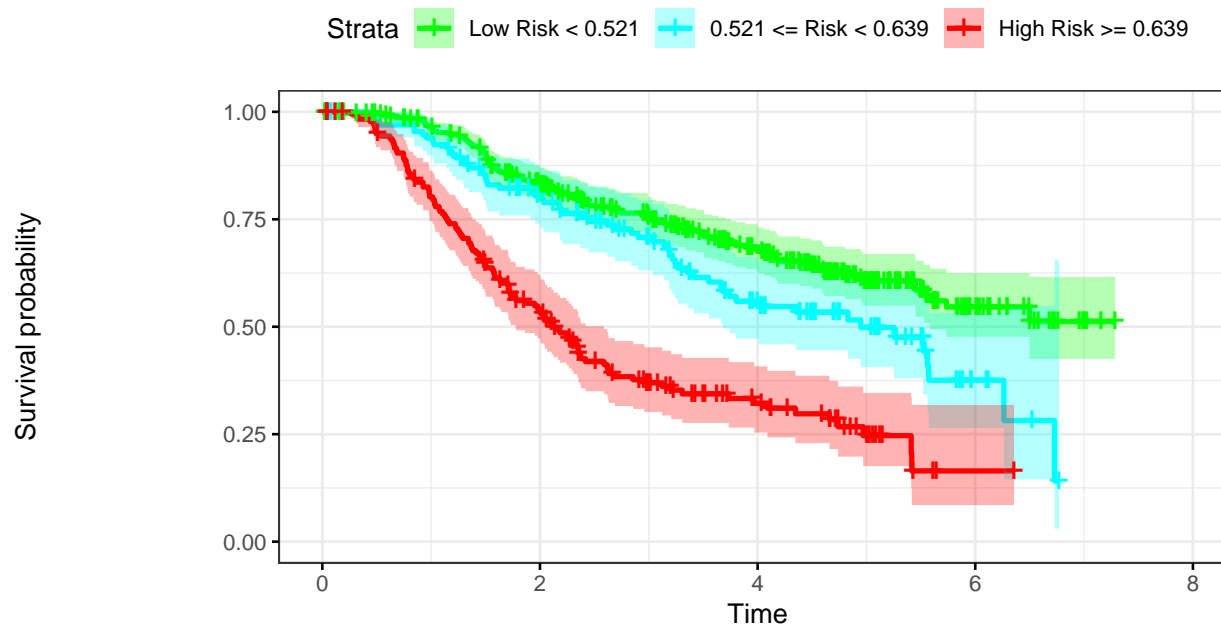




Time vs. Events: Cal. Logistic Test: Breast Cancer



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 71: 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
SEN	0.39465	0.5953	0.5786	0.950	1.00e+00	0.6421
SPE	0.83204	0.6382	0.6693	0.181	1.29e-02	0.5866
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$OERatio$estimate),caption="O/E Ratio")
```

Table 72: O/E Ratio

O/E	Low	Upper	p.value
1.22	1.08	1.36	0.00101

```
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	0.638	0.699

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

Table 74: ROC AUC

est	lower	upper
0.669	0.628	0.709

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

Table 75: Sensitivity

est	lower	upper
0.395	0.339	0.453

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

Table 76: Specificity

est	lower	upper
0.832	0.791	0.868

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

Table 77: Probability Thresholds

90%	80%
0.639	0.521

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

Table 78: 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	0.84	0.843

```
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%
1.11	1.11	1.08	1.13

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

mean	50%	2.5%	97.5%
0.989	0.989	0.962	1.01

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

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

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

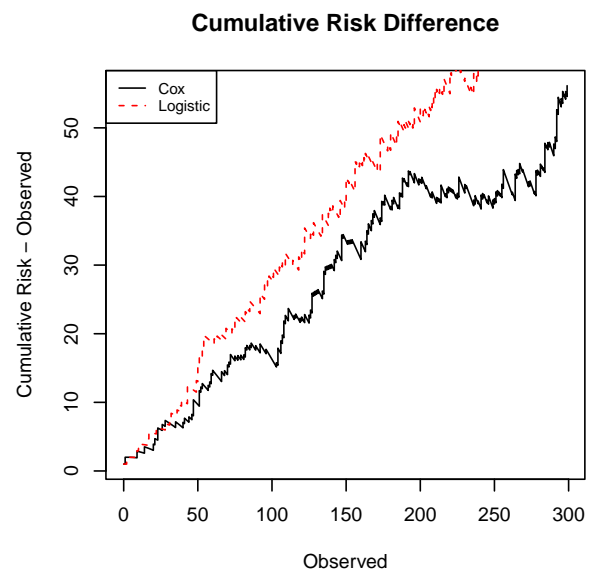
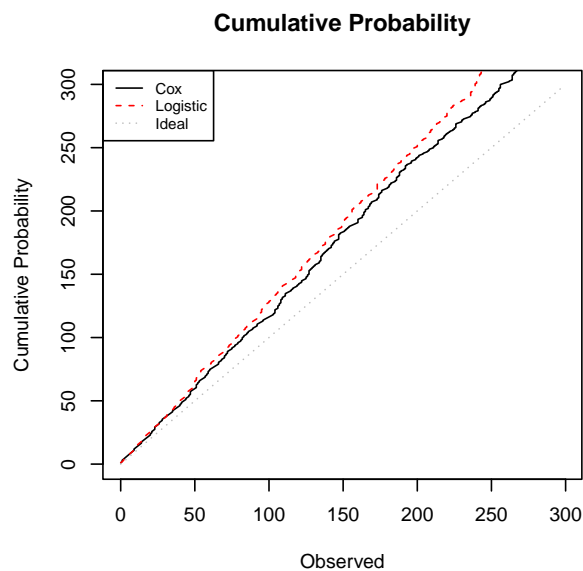


```

    main="Cumulative Probability",
    xlab="Observed",
    ylab="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="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
)

```



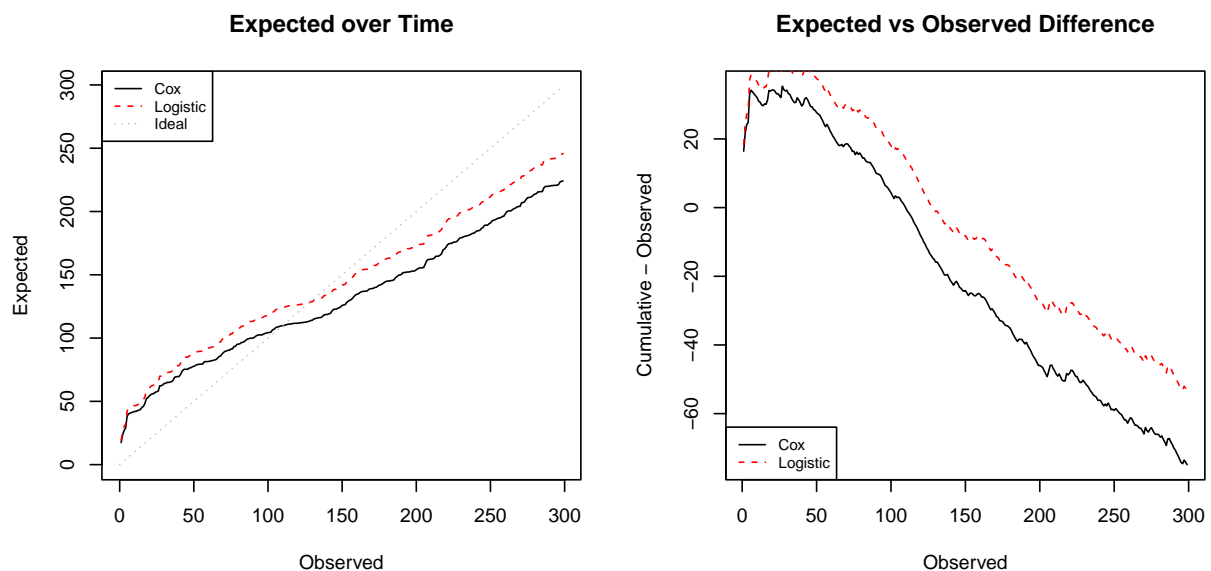
```

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

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

```



`par(op)`