Breast Cancer: Wisconsin

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```
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")
```

```
dataBreast <- read.csv("~/GitHub/RISKPLOTS/DATA/wpbc.data", header=FALSE)
table(dataBreast$V2)
```

```
##
##   N   R
## 151  47
```

```
rownames(dataBreast) <- dataBreast$V1
dataBreast$V1 <- NULL
dataBreast$status <- 1*(dataBreast$V2=="R")
dataBreast$V2 <- NULL
dataBreast$time <- dataBreast$V3
dataBreast$V3 <- NULL
dataBreast <- sapply(dataBreast,as.numeric)
```

```
## Warning in lapply(X = X, FUN = FUN, ...): NAs introduced by coercion
```

```
dataBreast <- as.data.frame(dataBreast[complete.cases(dataBreast),])
table(dataBreast$status)
```

```
##
##   0   1
## 148  46
```

Modeling

```
ml <- BSWiMS.model(Surv(time,status)~1,data=dataBreast)
```

[++++++]

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

Table 1: Table continues below

	Estimate	lower	HR	upper	u.Accuracy	r.Accuracy
V24	0.04693	1.015	1.048	1.082	0.5979	0.2371
V26	0.004724	1.001	1.005	1.008	0.5928	0.2371
V27	0.0002419	1	1	1	0.6082	0.2371
V34	0.01194	1.002	1.012	1.022	0.634	0.2371
V7	6.051e-08	1	1	1	0.5876	0.2371
V35	5.064e-06	1	1	1	0.7268	0.2371

Table 2: Table continues below

	full.Accuracy	u.AUC	r.AUC	full.AUC	IDI	NRI	z.IDI
V24	0.5979	0.6091	0.5	0.6091	0.0619	0.4365	2.867
V26	0.5928	0.5983	0.5	0.5983	0.06261	0.3931	2.771
V27	0.6082	0.6084	0.5	0.6084	0.05632	0.4336	2.762
V34	0.634	0.6178	0.5	0.6178	0.03201	0.4712	2.421
V7	0.5876	0.5949	0.5	0.5949	0.04868	0.3796	2.296
V35	0.7268	0.6412	0.5	0.6412	0.02892	0.5646	2.283

	z.NRI	Delta.AUC	Frequency
V24	2.666	0.1091	1
V26	2.381	0.09827	1
V27	2.631	0.1084	1
V34	2.855	0.1178	1
V7	2.298	0.09489	1
V35	3.505	0.1412	1

Cox Model Performance

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

The evaluation of the raw Cox model with RRPlot()

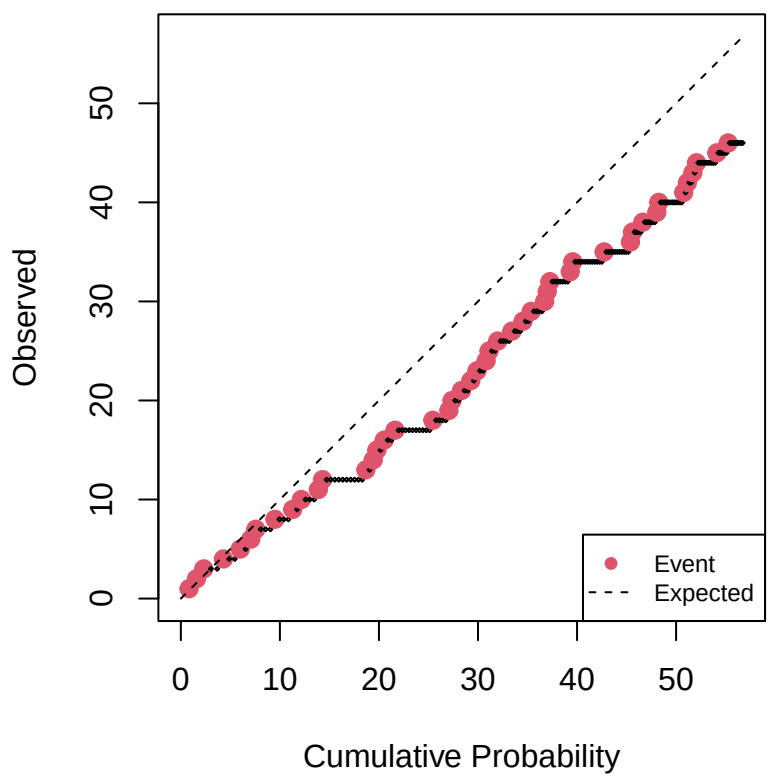
Here we will use the predicted event probability assuming a baseline hazard for events withing 5 years

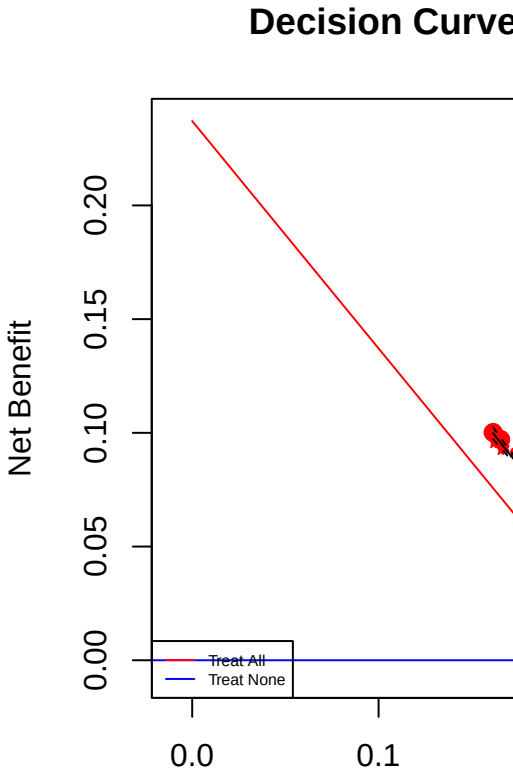
```
index <- predict(ml,dataBreast)
timeinterval <- 2*mean(subset(dataBreast,status==1)$time)

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

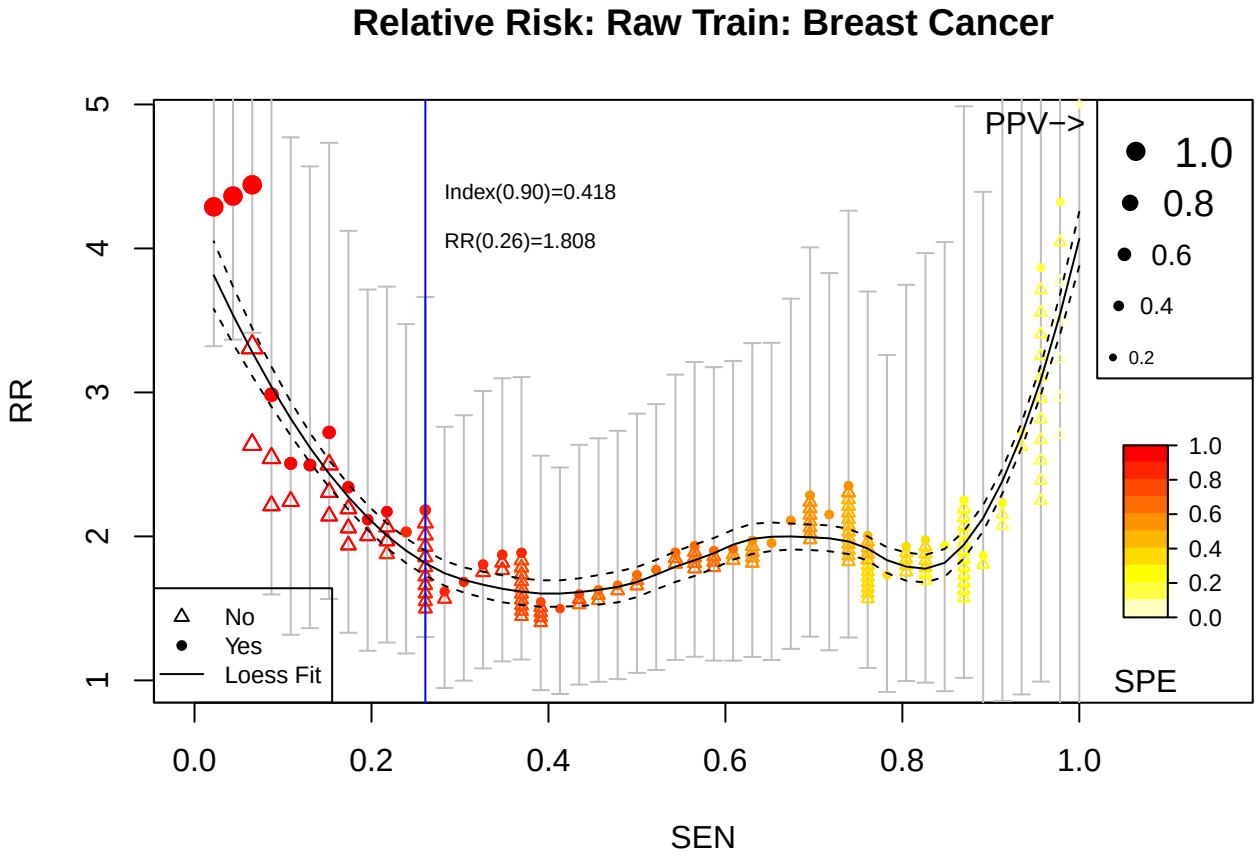
Table 4: Initial Parameters

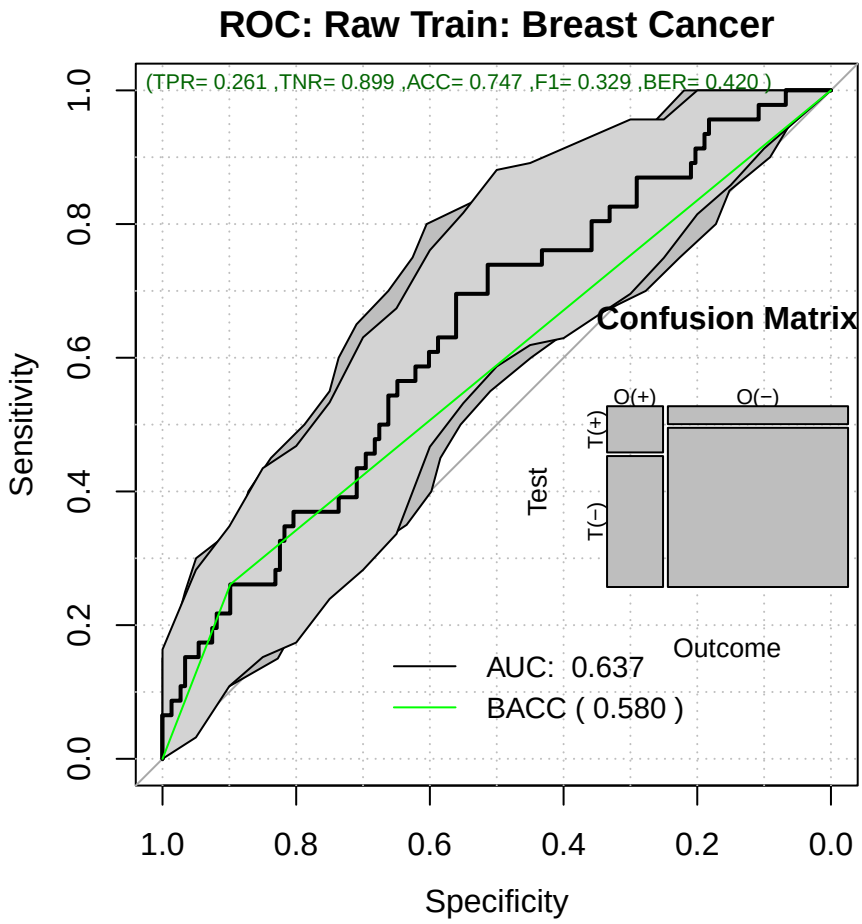
h0	timeinterval
0.3226	51.13

```
rdata <- cbind(dataBreast$status,ppoisGzero(index,h0))
rownames(rdata) <- rownames(dataBreast)

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

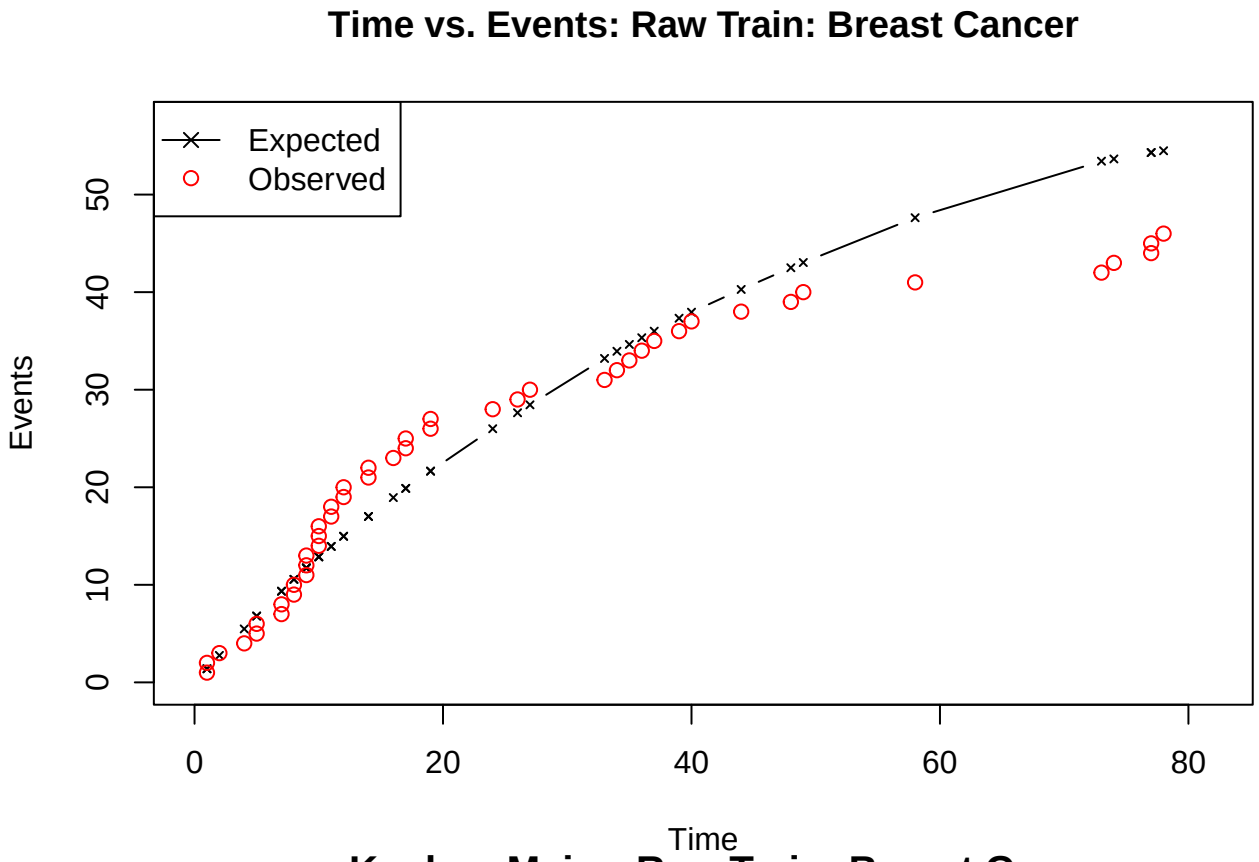


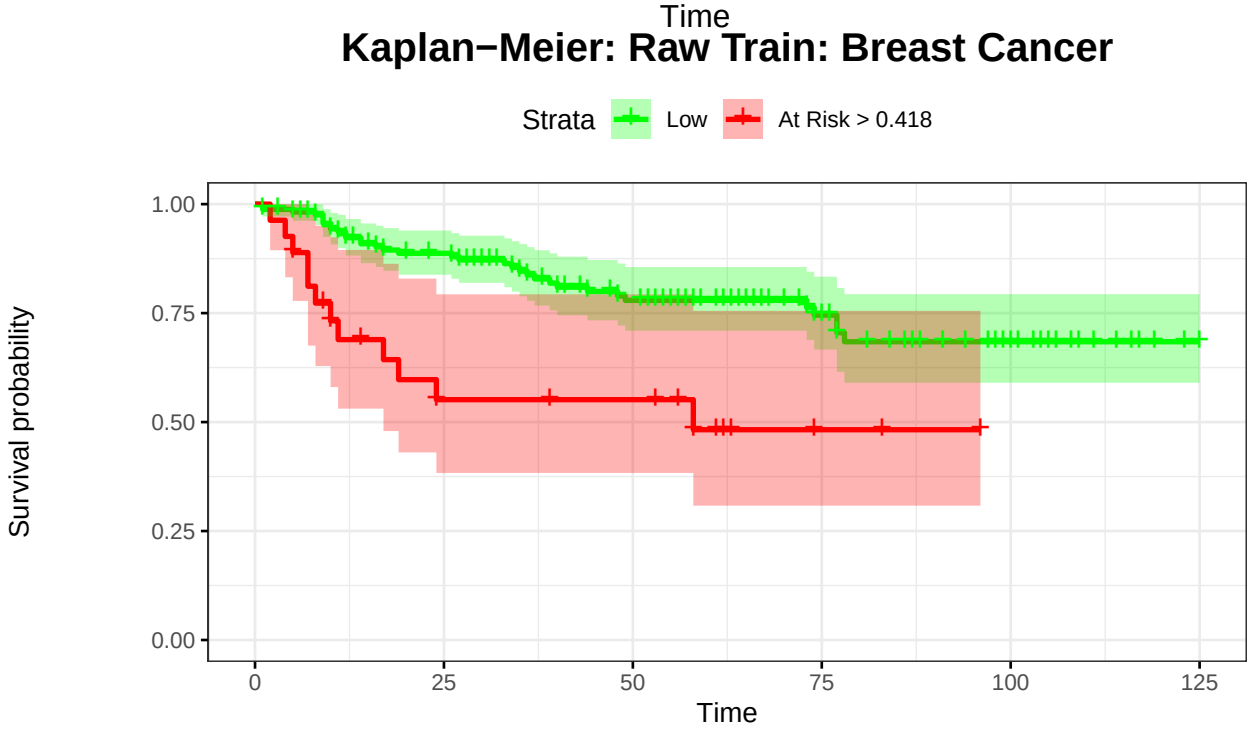



Relative Risk: Raw Train: Breast Cancer
PPV−>
Index(0.90)=0.418
RR(0.26)=1.808
1.0
0.8
0.6
0.4
0.2
1.0
0.8
0.6
0.4
0.2
0.0
SPE
No
Yes
Loess Fit
RR
SEN
1
2
3
4
5
0.0
0.2
0.4
0.6
0.8
1.0



ROC: Raw Train: Breast Cancer





Number at risk

Low	167	116	76	42	20	1
At Risk > 0.418	27	11	10	2	0	0

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

Uncalibrated Performance Report

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

Table 5: O/E Ratio

est	lower	upper
0.8442	0.618	1.126

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

Table 6: O/E Ratio

mean	50%	2.5%	97.5%
1.018	1.018	0.9692	1.065

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

Table 7: O/Acum Ratio

mean	50%	2.5%	97.5%
0.7968	0.7969	0.7893	0.8061

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

mean.C Index	median	lower	upper
0.6799	0.6807	0.5977	0.763

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

Table 9: ROC AUC

est	lower	upper
0.637	0.5458	0.7283

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

Table 10: Sensitivity

est	lower	upper
0.2609	0.1427	0.4113

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

Table 11: Specificity

est	lower	upper
0.8986	0.8383	0.9422

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

Table 12: Probability Thresholds

90%
0.4182

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

Table 13: Risk Ratio

est	lower	upper
1.808	1.059	3.089

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

Table 14: Logrank test Chisq = 11.608565 on 1 degrees of freedom, p = 0.000656

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	167	34	41.1	1.225	11.61
class=1	27	12	4.904	10.27	11.61

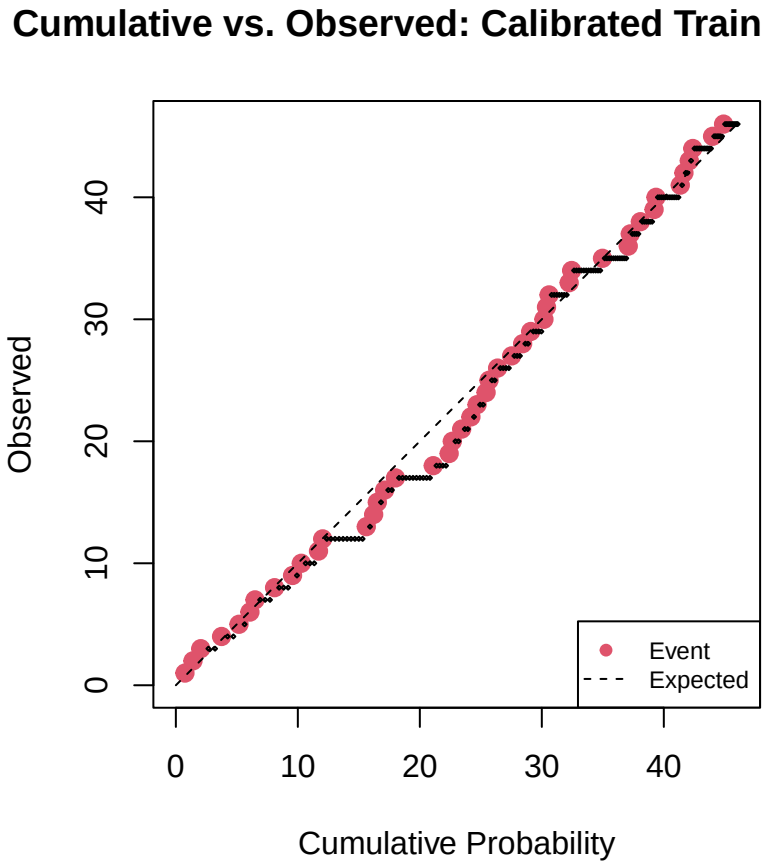
Cox Calibration

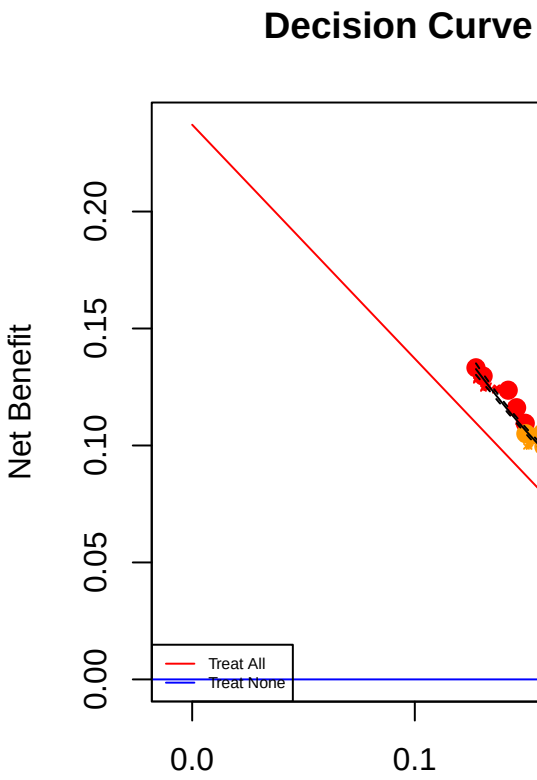
```
op <- par(no.readonly = TRUE)


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

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

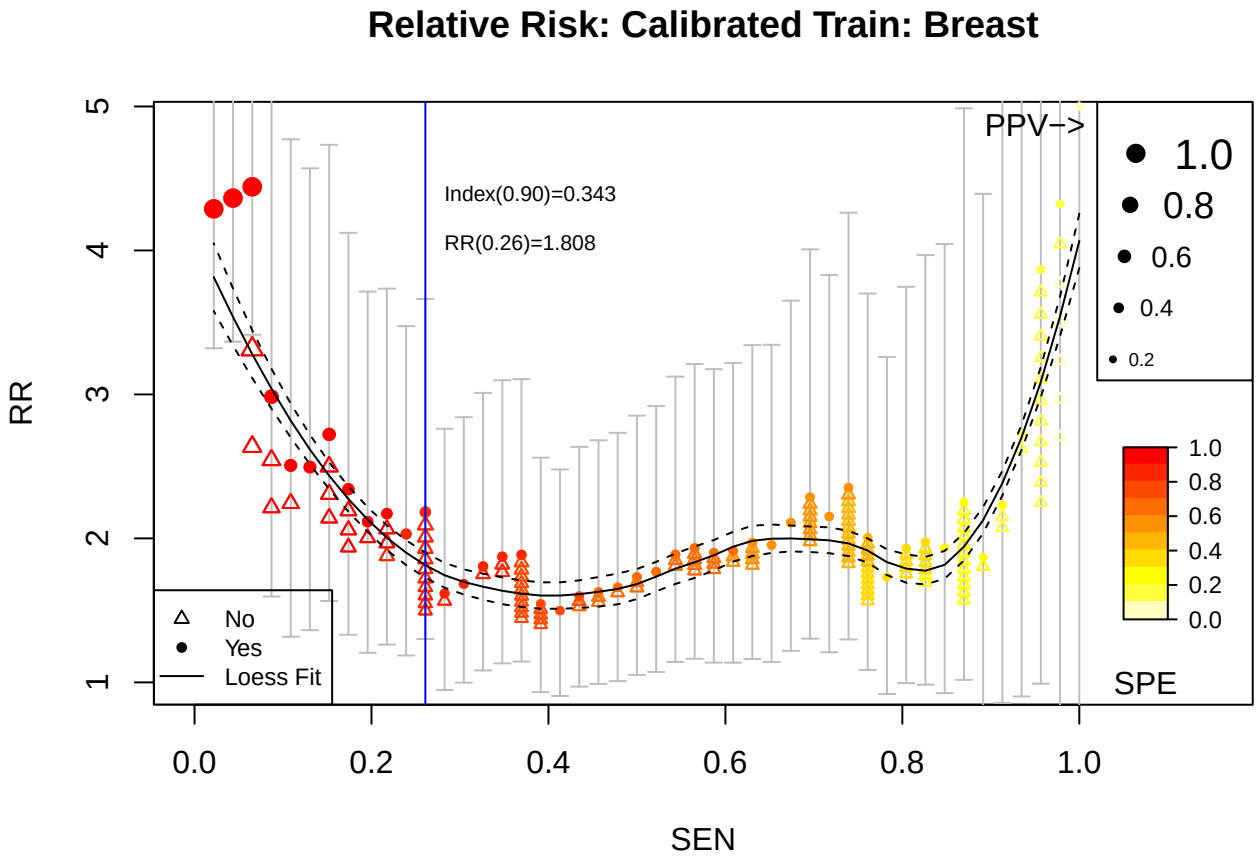
h0	Gain	DeltaTime
0.2498	0.7743	40.88

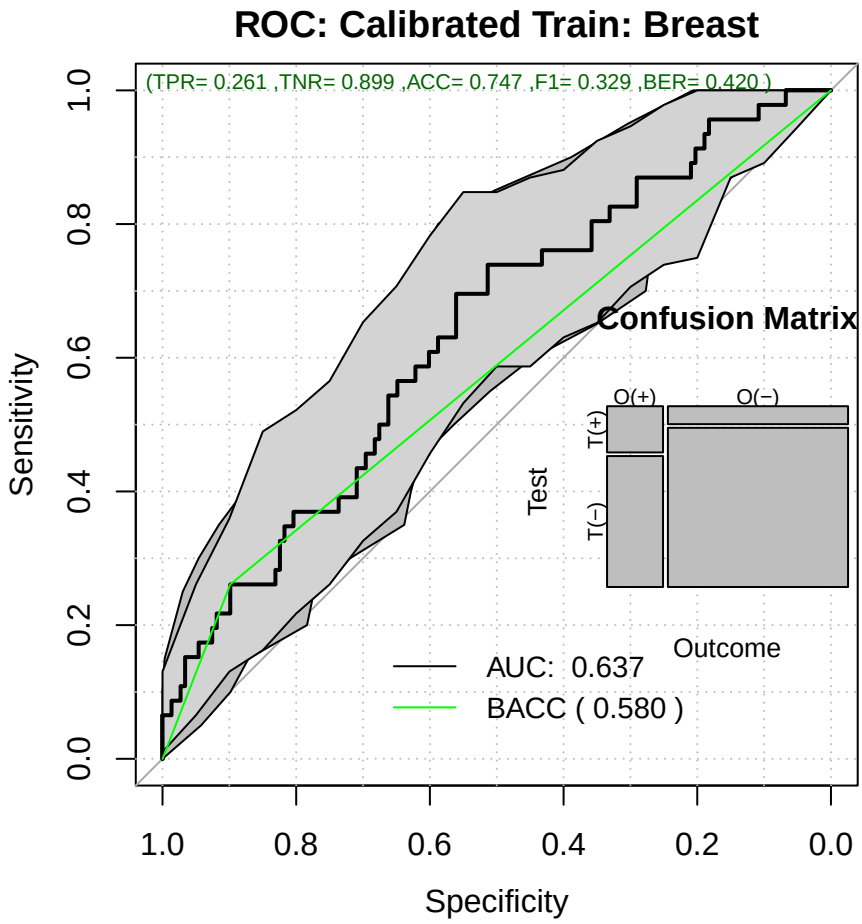
The RRplot() of the calibrated model

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

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


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

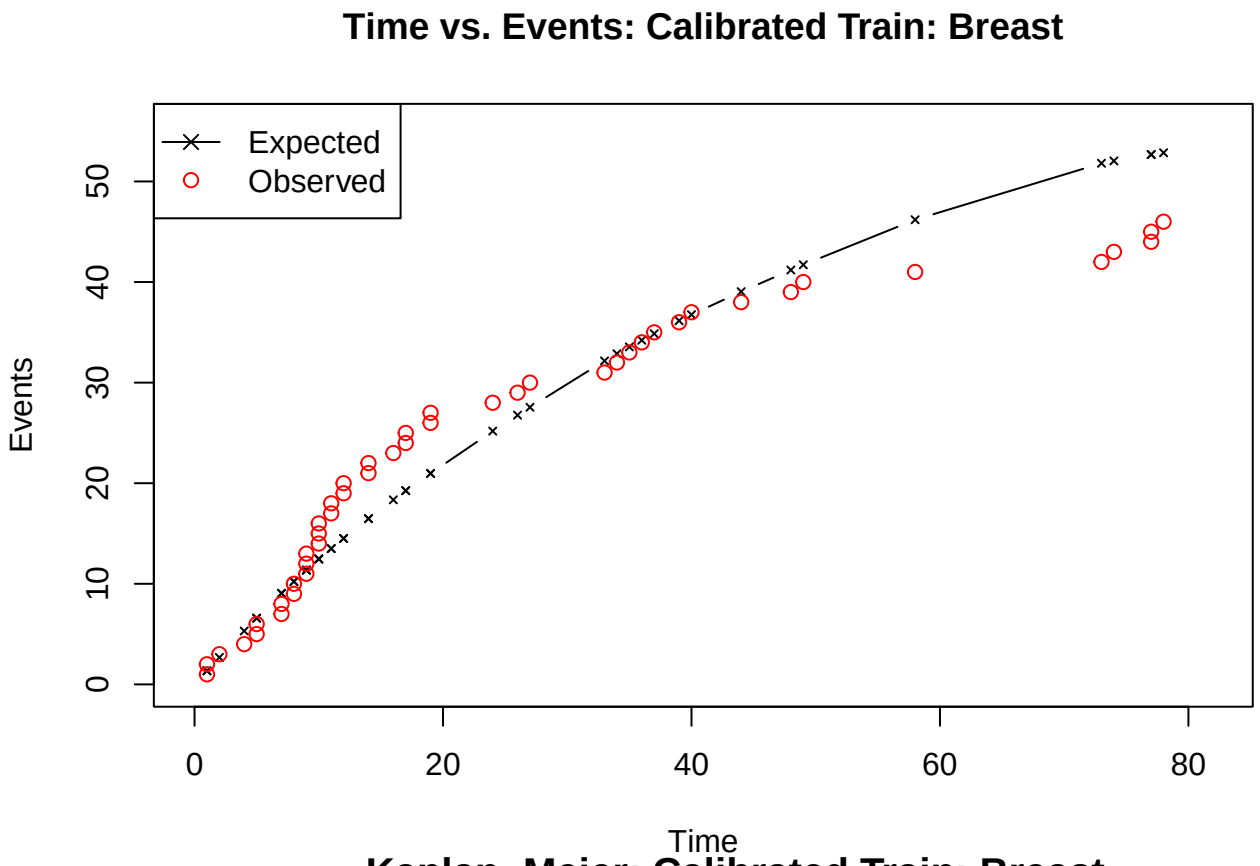


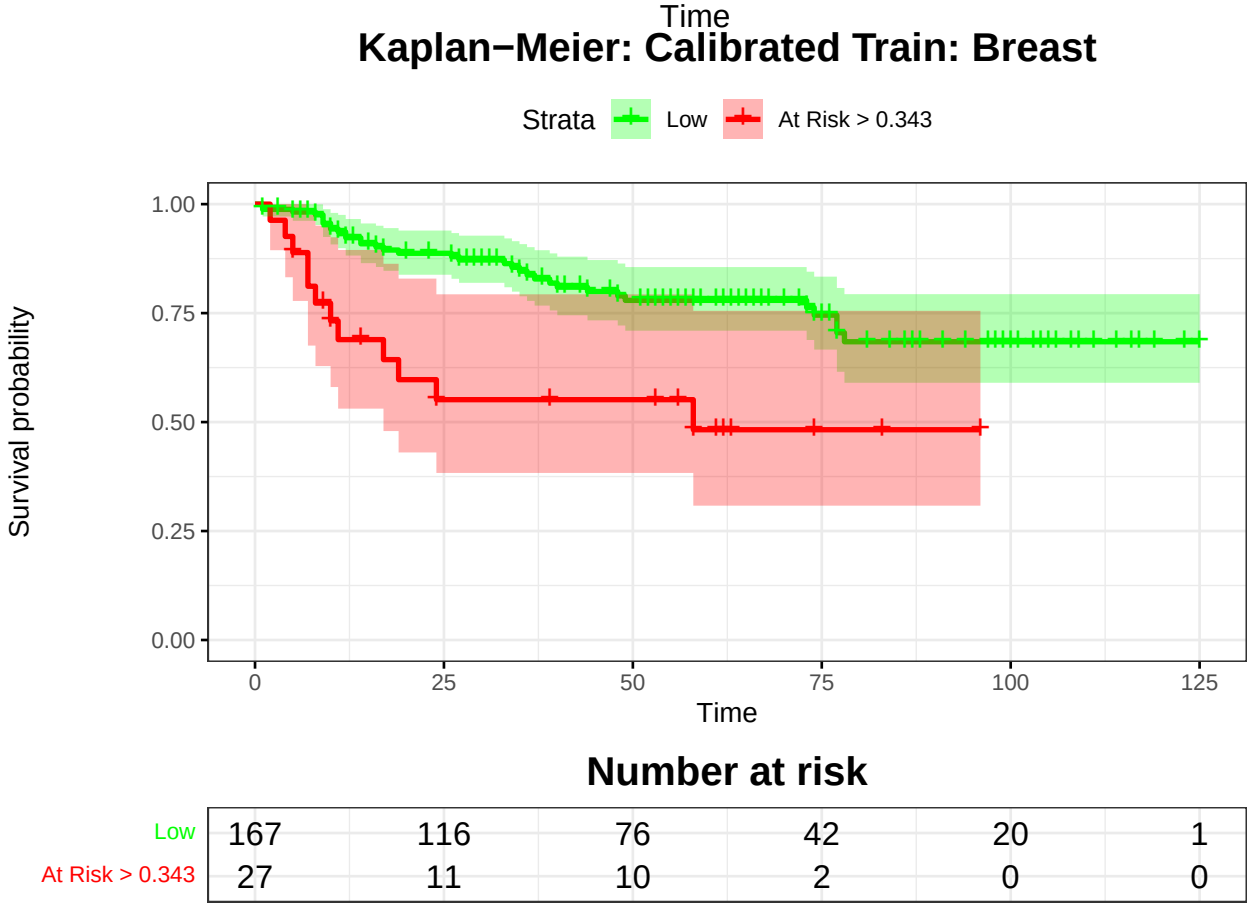



Relative Risk: Calibrated Train: Breast
PPV−>
Index(0.90)=0.343
RR(0.26)=1.808
1.0
0.8
0.6
0.4
0.2
1.0
0.8
0.6
0.4
0.2
0.0
SPE
No
Yes
Loess Fit
RR
SEN
1
2
3
4
5
0.0
0.2
0.4
0.6
0.8
1.0



ROC: Calibrated Train: Breast





Number at risk

Low	167	116	76	42	20	1
At Risk > 0.343	27	11	10	2	0	0

Calibrated Train Performance

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

Table 16: O/E Ratio

est	lower	upper
0.8703	0.6372	1.161

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

Table 17: O/E Ratio

mean	50%	2.5%	97.5%
1.051	1.05	1.001	1.103

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

Table 18: O/Acum Ratio

mean	50%	2.5%	97.5%
0.9624	0.9627	0.954	0.9717

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

Table 19: C. Index

mean.C Index	median	lower	upper
0.6799	0.6798	0.5955	0.7601

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

Table 20: ROC AUC

est	lower	upper
0.637	0.5458	0.7283

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

Table 21: Sensitivity

est	lower	upper
0.2609	0.1427	0.4113

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

Table 22: Specificity

est	lower	upper
0.8986	0.8383	0.9422

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

Table 23: Probability Thresholds

90%
0.3426

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

Table 24: Risk Ratio

est	lower	upper
1.808	1.059	3.089

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

Table 25: Logrank test Chisq = 11.608565 on 1 degrees of freedom, p = 0.000656

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	167	34	41.1	1.225	11.61
class=1	27	12	4.904	10.27	11.61

Cross-Validation

Here we use the estimated h0 and timeinterval from the full set

```
rcv <- randomCV(theData=dataBreast,
                theOutcome = Surv(time,status)~1,
                fittingFunction=BSWiMS.model,
                trainFraction = 0.9,
                repetitions=100,
                classSamplingType = "Pro"
        )
```

```
## .[+++++].[++++].[--]
```

```
## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features
```

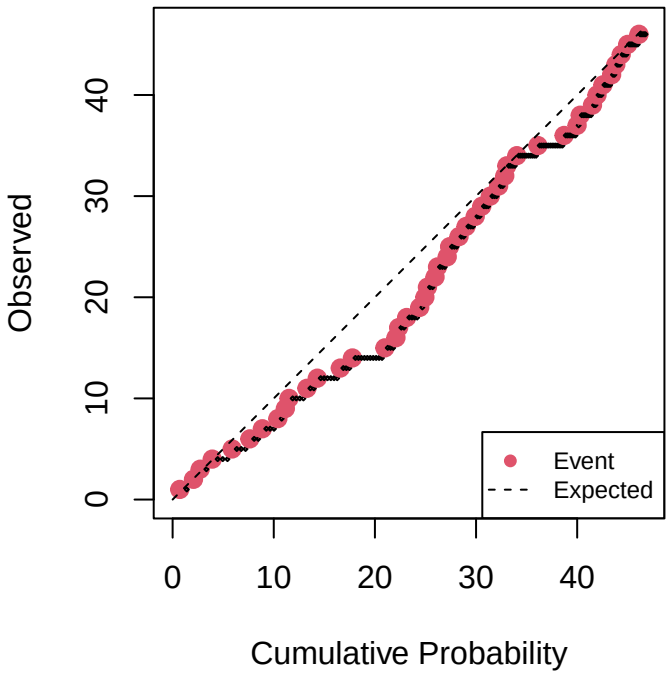
```
## Warning in survpredict(currentModel, trainSet, trainSet,
## selectedFeaturesSet[[rept]]): Method did not select any features
```

```
## .[+].[+].[-+].[+++].[+++++].[++].[+++]10  Tested: 120 Avg. Selected: 2.9 Min Tests: 1 Max Tests: 5 M
## .[+++++].[+].[++++].[+++++++].[++++].[++++].[+++].[++++++].[+++++].[+++++]20  Tested: 171 Avg. Selec
## .[+++++].[+++].[++++++].[+++++++].[+++].[++++].[++++++].[++++++].[+++].[+]30  Tested: 182 Avg. Selec
## .[++].[+++].[++].[+++].[+++].[+++++++].[--]

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## .[+++].[+++].[+++++]40  Tested: 190 Avg. Selected: 4.075 Min Tests: 1 Max Tests: 10 Mean Tests: 4.21
## .[++++].[--]

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## .[+++++++].[+++].[++++].[+++++++].[++++++++].[+++++].[+].[--]

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## 50  Tested: 193 Avg. Selected: 4.06 Min Tests: 1 Max Tests: 12 Mean Tests: 5.181347 . MAD: 0.4811933
## .[+].[++++++].[+].[++++].[-+].[+++].[+++++++].[++++++++].[++++++].[++++]60  Tested: 193 Avg. Selecte
## .[++++++].[++].[+++++].[+++++++].[++].[++++++].[++].[+++++].[+++].[+]70  Tested: 194 Avg. Selected:
## .[++++++].[++++].[++++].[--]

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## Warning in survpredict(currentModel, trainSet, testSet,
## selectedFeaturesSet[[rept]]): Method did not select any features

## .[+++++].[+++].[+++].[++++].[+].[+++++]80  Tested: 194 Avg. Selected: 4.125 Min Tests: 2 Max Tests:
## .[++++++].[++++].[+++].[+++++].[+++++].[++++++].[+++++].[++++++].[++].[++++++++]90  Tested: 194 Avg.
## .[+++].[+++].[++++++].[+++].[++++].[++++].[+++].[++++].[++++].[+++]100  Tested: 194 Avg. Selected: 4
##

## Warning in eval(predvars, data, env): NAs introduced by coercion

## Warning in eval(predvars, data, env): NAs introduced by coercion

## Warning in eval(predvars, data, env): NAs introduced by coercion

## Warning in eval(predvars, data, env): NAs introduced by coercion
```

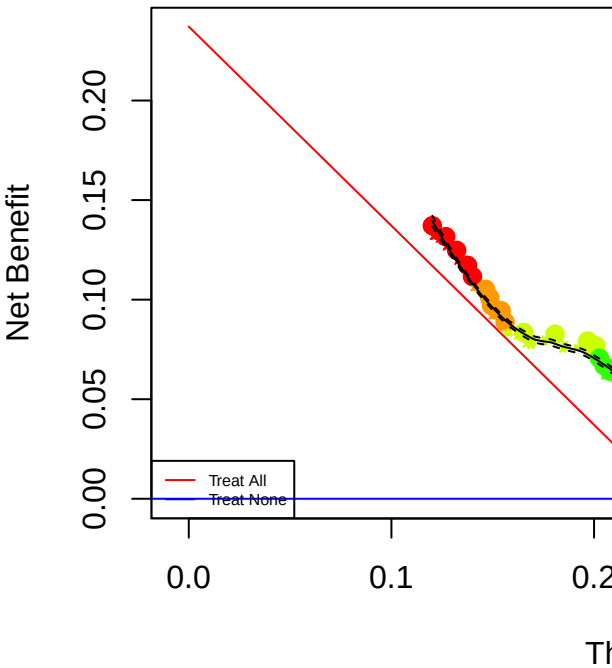
```r
stp <- rcv$survTestPredictions
stp <- stp[!is.na(stp[,4]),]

bbx <- boxplot(unlist(stp[,1])~rownames(stp),plot=FALSE)
times <- bbx$stats[3,]
status <- boxplot(unlist(stp[,2])~rownames(stp),plot=FALSE)$stats[3,]
prob <- ppoisGzero(boxplot(unlist(stp[,4])~rownames(stp),plot=FALSE)$stats[3,],h0)
```

```
rdatacv <- cbind(status,prob)
rownames(rdatacv) <- bbx$names
names(times) <- bbx$names

rrAnalysisTest <- RRPlot(rdatacv,atThr = rrAnalysisTrain$thr_atP,
                      timetoEvent=times,
                      title="Test: Breast Cancer",
                      ysurvlim=c(0.00,1.0),
                      riskTimeInterval=timeinterval)
```

Cumulative vs. Observed: Test: Breast Cancer



Decision Curve Anal




```
## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font metrics unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font metrics unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font metrics unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
## character 0x1

## Warning in plot.xy(xy.coords(x, y), type = type, ...): font metrics unknown for
```

```
## character 0x1
## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
## character 0x1
## Warning in plot.xy(xy.coords(x, y), type = type, ...): font metrics unknown for
## character 0x1
## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
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## character 0x1
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## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
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## character 0x1
## Warning in plot.xy(xy.coords(x, y), type = type, ...): font metrics unknown for
## character 0x1
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## character 0x1
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## character 0x1
## Warning in plot.xy(xy.coords(x, y), type = type, ...): font width unknown for
## character 0x1
```

```
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```
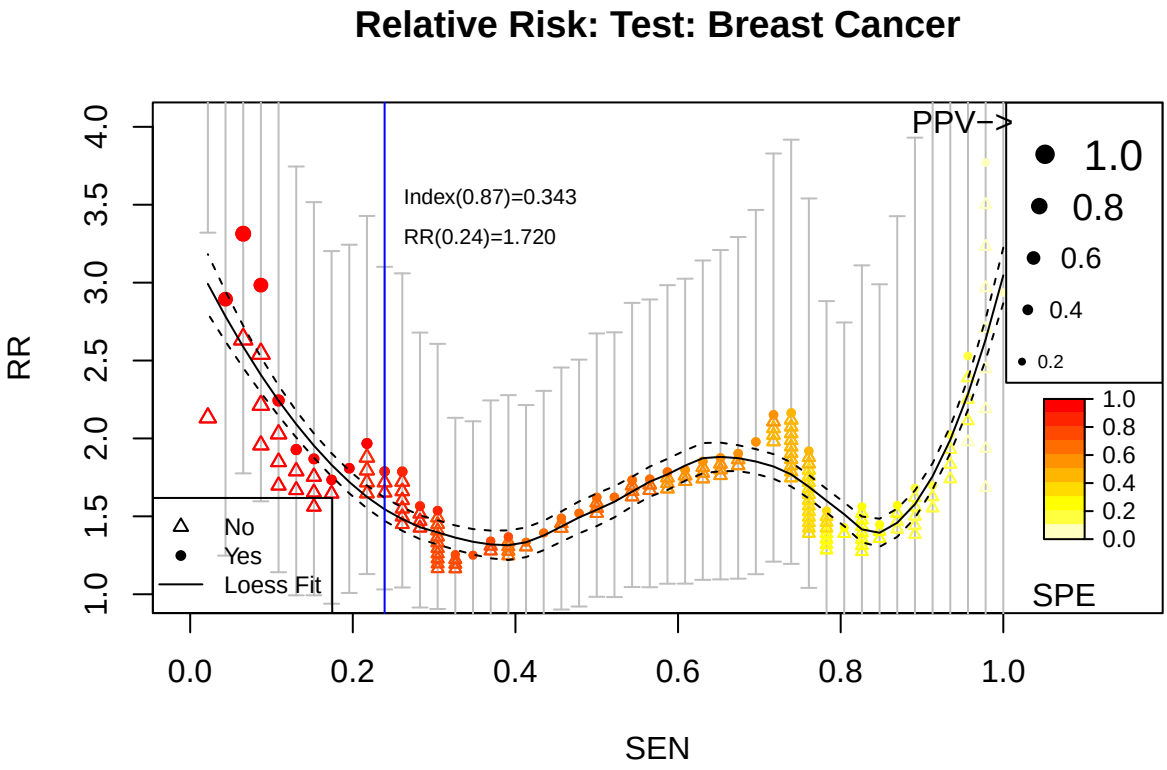
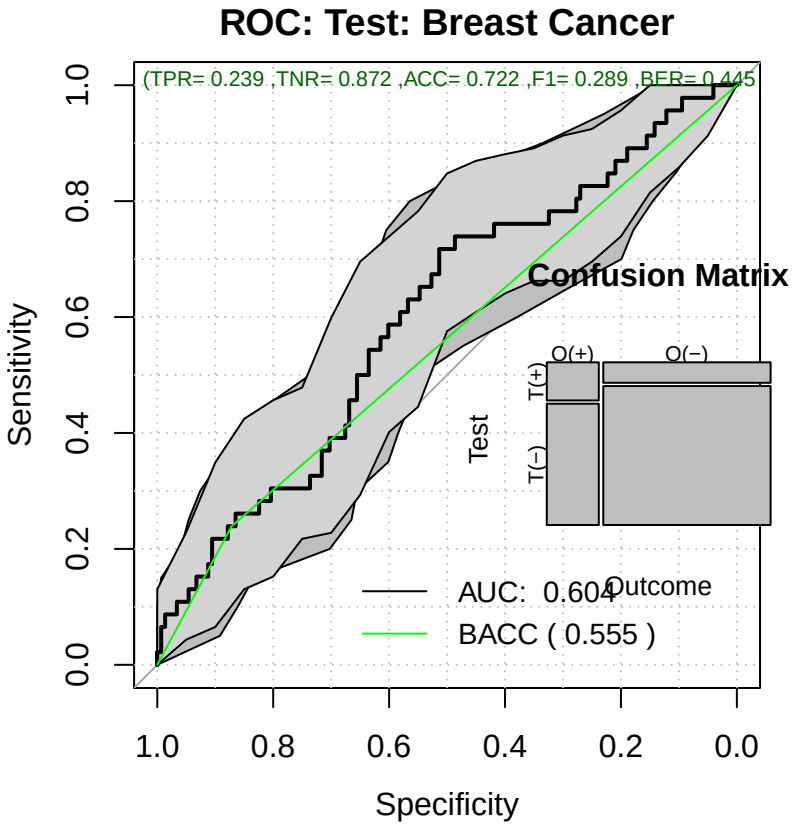
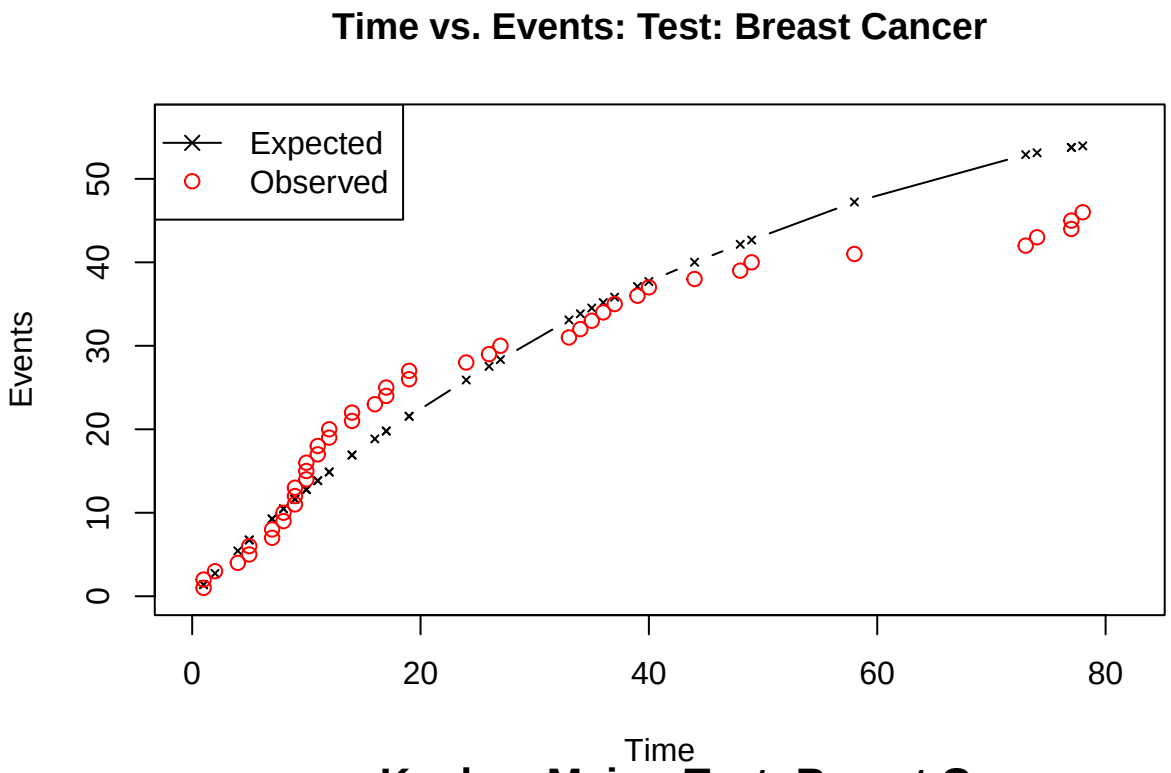
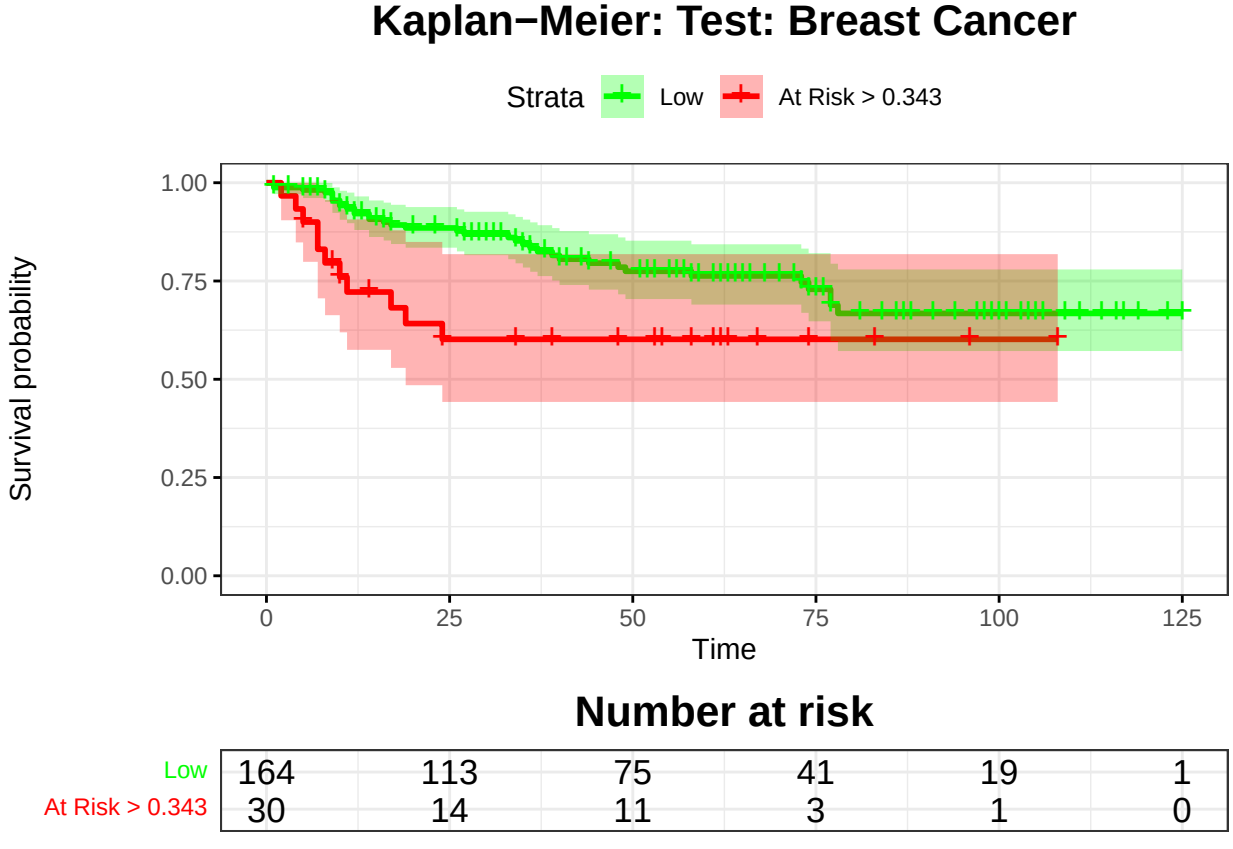




```
## ROC: Test: Breast Cancer
```




```
## Warning in cstat$cstatCI <- cstatCI: Coercing LHS to a list
```





Number at risk

Low	164	113	75	41	19	1
At Risk > 0.343	30	14	11	3	1	0

Cross-Validation Test Performance

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

Table 26: O/E Ratio

est	lower	upper
0.8526	0.6242	1.137

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

Table 27: O/E Ratio

mean	50%	2.5%	97.5%
1.024	1.025	0.9695	1.077

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

Table 28: O/Acum Ratio

mean	50%	2.5%	97.5%
0.8857	0.8856	0.873	0.898

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

mean.C Index	median	lower	upper
0.6549	0.654	0.5626	0.7368

```
pander::pander(t(rrAnalysisTest$ROCAnalysis$aucs),caption="ROC AUC")
```

Table 30: ROC AUC

est	lower	upper
0.6043	0.5105	0.6981

```
pander::pander((rrAnalysisTest$ROCAnalysis$sensitivity),caption="Sensitivity")
```

Table 31: Sensitivity

est	lower	upper
0.2391	0.1259	0.3877

```
pander::pander((rrAnalysisTest$ROCAnalysis$specificity),caption="Specificity")
```

Table 32: Specificity

est	lower	upper
0.8716	0.8068	0.9209

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

Table 33: Probability Thresholds

90%
0.3426

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

Table 34: Risk Ratio

est	lower	upper
1.72	0.9878	2.994

```
pander::pander(rrAnalysisTest$sufdif,caption="Logrank test")
```

Table 35: Logrank test Chisq = 5.352791 on 1 degrees of freedom, p = 0.020689

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	164	35	40.19	0.6704	5.353
class=1	30	11	5.809	4.638	5.353

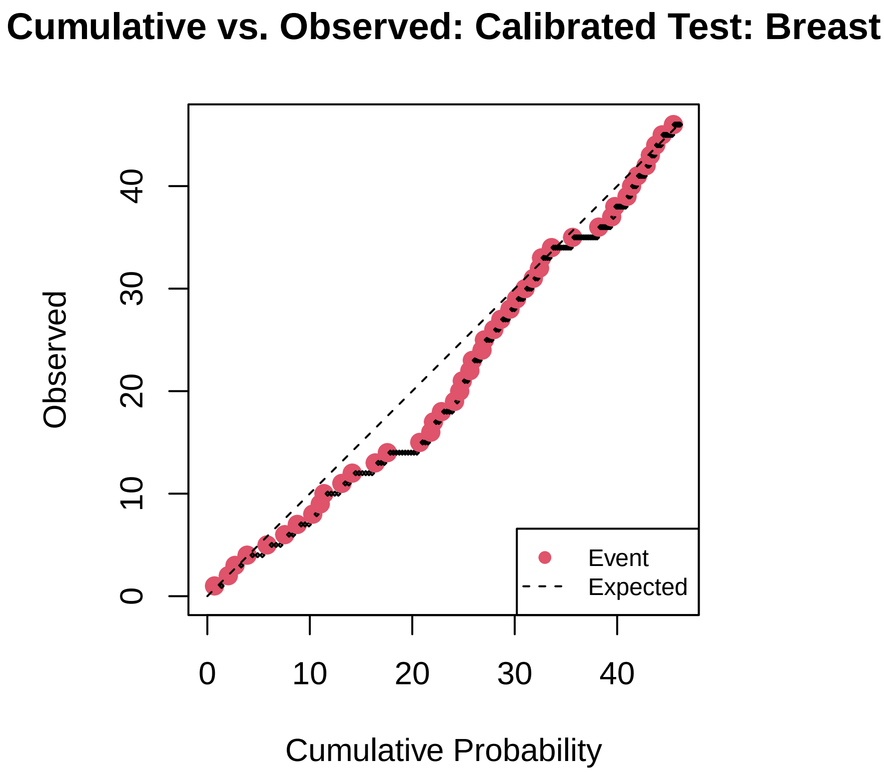
Calibrating the test results

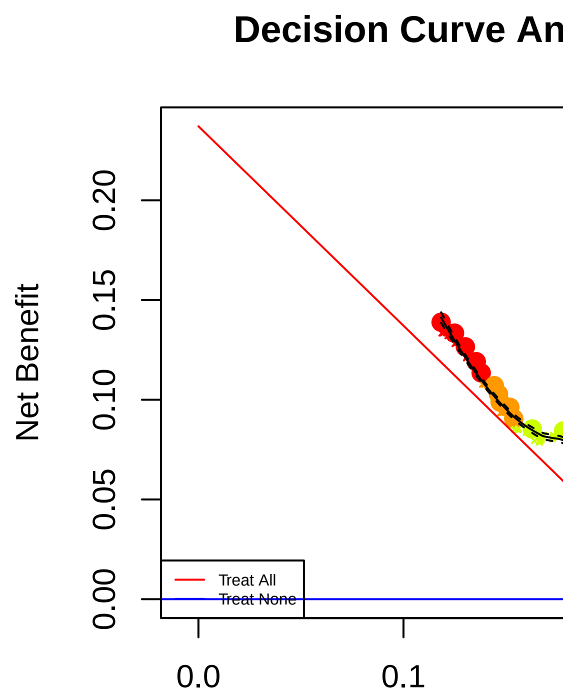
```
rdatacv <- cbind(status,prob,times)
calprob <- CalibrationProbPoissonRisk(rdatacv)

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

h0	Gain	DeltaTime
0.3174	0.9838	41.29

```
timeinterval <- calprob$timeInterval;

rdata <- cbind(status,calprob$prob)


rrAnalysisTest <- RRPlot(rdata,atProb=c(0.90),
```

```
                        timetoEvent=times,
                        title="Calibrated Test: Breast",
                        ysurvlim=c(0.00,1.0),
                        riskTimeInterval=timeinterval)
```



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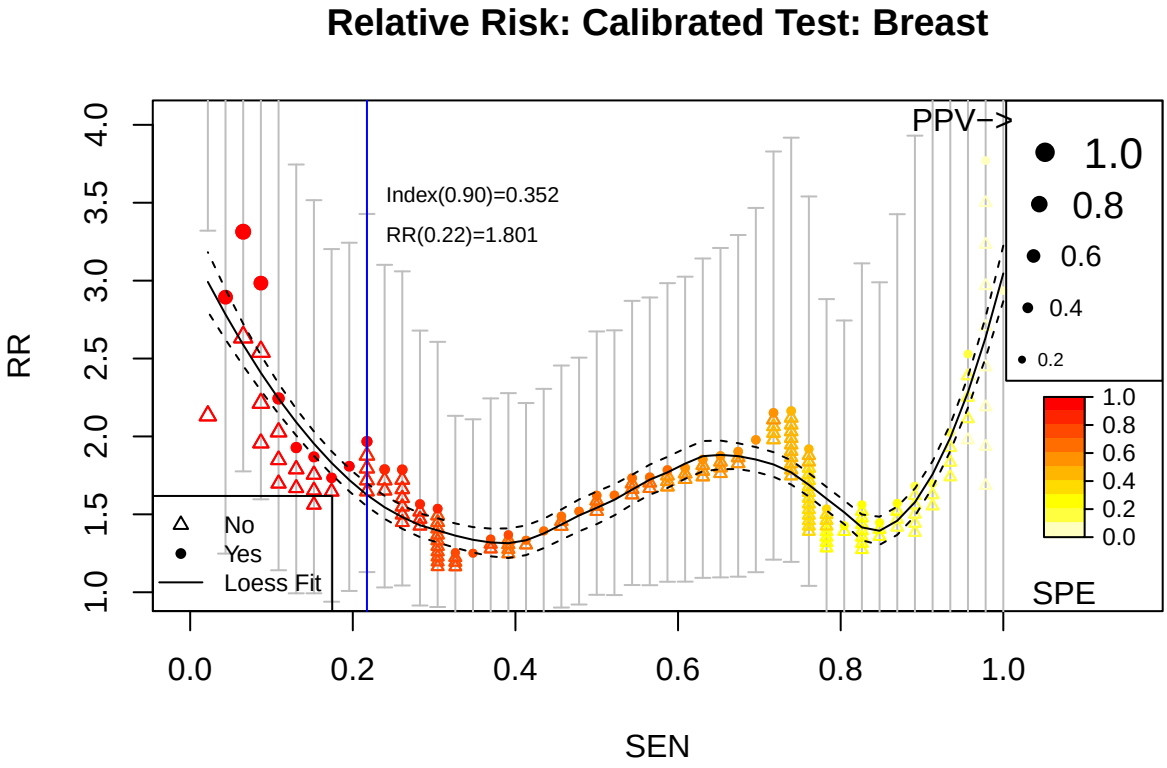
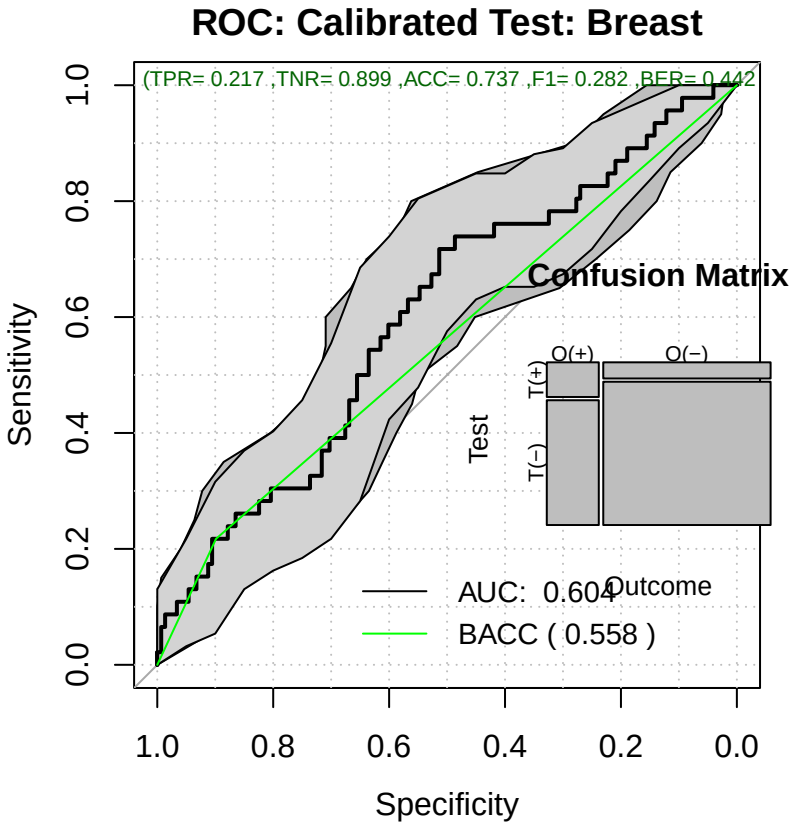
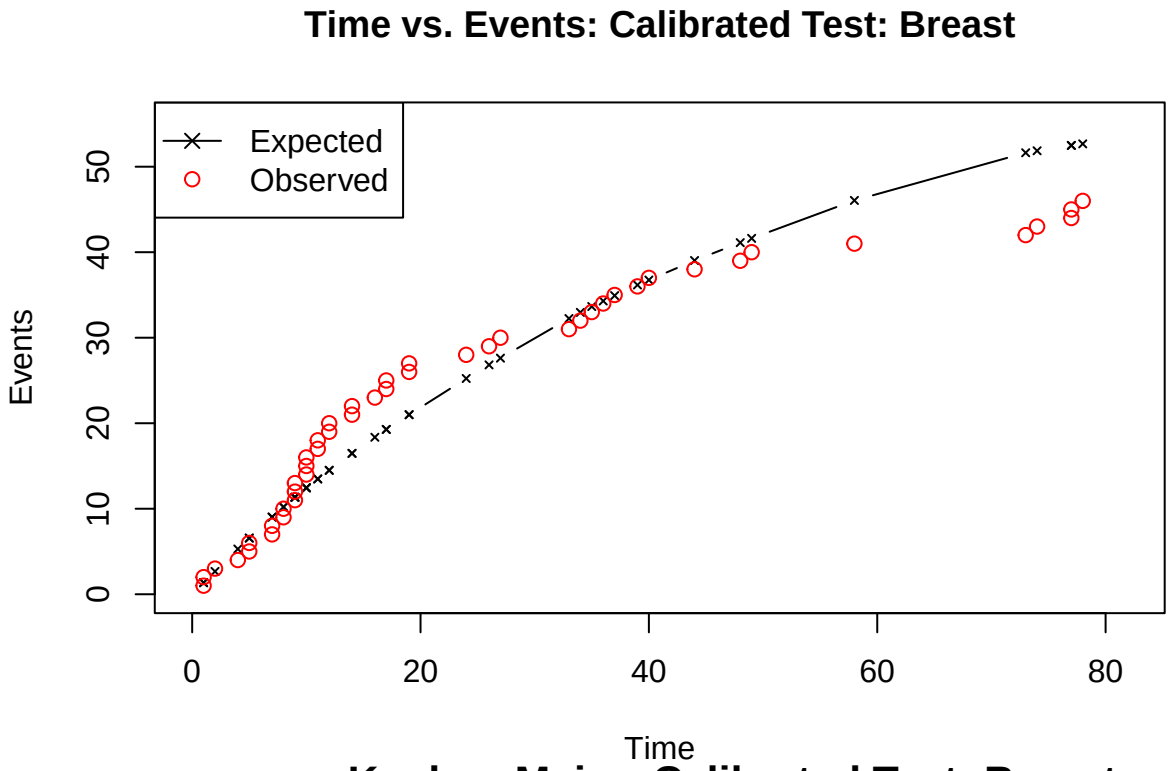
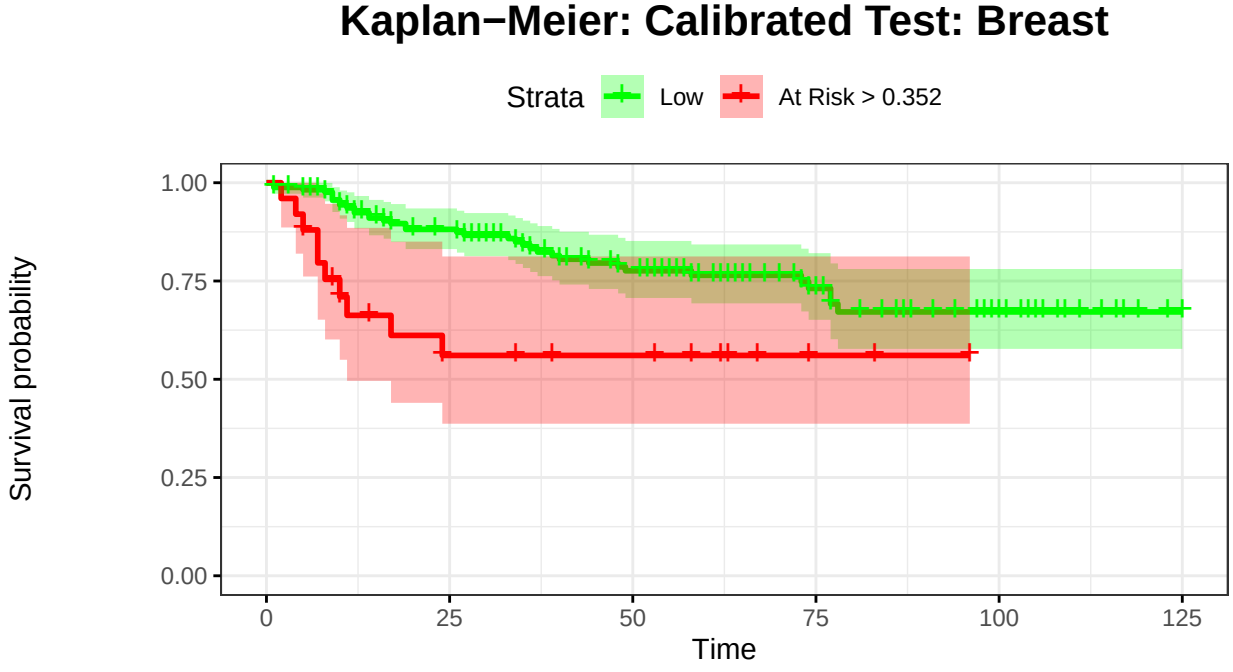



```
## ROC: Calibrated Test: Breast
```




```
## Warning in cstat$cstatCI <- cstatCI: Coercing LHS to a list
```





Number at risk

Low	169	117	78	42	20	1
At Risk > 0.352	25	10	8	2	0	0

Calibrated Test Performance

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

Table 37: O/E Ratio

est	lower	upper
0.8734	0.6394	1.165

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

Table 38: O/E Ratio

mean	50%	2.5%	97.5%
1.051	1.051	0.9966	1.106

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

Table 39: O/Acum Ratio

mean	50%	2.5%	97.5%
0.8969	0.8975	0.8841	0.9119

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

mean.C Index	median	lower	upper
0.6549	0.6549	0.5713	0.7301

```
pander::pander(t(rrAnalysisTest$ROCAnalysis$aucs),caption="ROC AUC")
```

Table 41: ROC AUC

est	lower	upper
0.6043	0.5105	0.6981

```
pander::pander((rrAnalysisTest$ROCAnalysis$sensitivity),caption="Sensitivity")
```

Table 42: Sensitivity

est	lower	upper
0.2174	0.1095	0.3636

```
pander::pander((rrAnalysisTest$ROCAnalysis$specificity),caption="Specificity")
```

Table 43: Specificity

est	lower	upper
0.8986	0.8383	0.9422

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

Table 44: Probability Thresholds

90%
0.3517

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

Table 45: Risk Ratio

est	lower	upper
1.801	1.024	3.169

```
pander::pander(rrAnalysisTest$sufdif,caption="Logrank test")
```

Table 46: Logrank test Chisq = 8.161728 on 1 degrees of freedom, p = 0.004278

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	169	36	41.65	0.7654	8.162
class=1	25	10	4.354	7.32	8.162