

NIK Recurrence

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Contents

NIK and RRPlots	1
The libraries	1
Getting the clinical data	3
ROC Plots	3
RR Plot Signature correlation	4
Node positive data	7
RR Plot Signature correlation	7
Node Negative data	10
RR Plot Signature correlation	10
RRPlot Cox Model	13
Expected time to event	17
RRPlot Cox Adjusted Model	21
Expected time to event	24
Calibrating the index	28
Expected time to event	31
Comparing Risks	35
Compare the ROC AUC	38

NIK and RRPlots

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
library(Biobase)

## Loading required package: BiocGenerics
##
## Attaching package: 'BiocGenerics'
## The following object is masked from 'package:pROC':
##
##      var
## The following objects are masked from 'package:stats':
##
##      IQR, mad, sd, var, xtabs
## The following objects are masked from 'package:base':
##
##      anyDuplicated, append, as.data.frame, basename, cbind, colnames,
##      dirname, do.call, duplicated, eval, evalq, Filter, Find, get, grep,
##      grepl, intersect, is.unsorted, lapply, Map, mapply, match, mget,
##      order, paste, pmax, pmax.int, pmin, pmin.int, Position, rank,
##      rbind, Reduce, rownames, sapply, setdiff, sort, table, tapply,
##      union, unique, unsplit, which.max, which.min
## Welcome to Bioconductor
##
##      Vignettes contain introductory material; view with
##      'browseVignettes()'. To cite Bioconductor, see
##      'citation("Biobase")', and for packages 'citation("pkgname)".

##
## Attaching package: 'Biobase'

## The following object is masked from 'package:Hmisc':
##
##      contents
## The following object is masked from 'package:miscTools':
##
##      rowMedians
op <- par(no.readonly = TRUE)
pander::panderOptions('digits', 3)
pander::panderOptions('table.split.table', 400)
pander::panderOptions('keep.trailing.zeros', TRUE)

if (!require("BiocManager", quietly = TRUE))
  install.packages("BiocManager")

## Bioconductor version '3.15' is out-of-date; the current release version '3.17'
## is available with R version '4.3'; see https://bioconductor.org/install

```

```
BiocManager::install("seventyGeneData")
```

```
## Bioconductor version 3.15 (BiocManager 1.30.20), R 4.2.3 (2023-03-15 ucrt)
```

```
## Warning: package(s) not installed when version(s) same as or greater than current; use  
##   `force = TRUE` to re-install: 'seventyGeneData'
```

```
## Installation paths not writeable, unable to update packages
```

```
##   path: C:/Program Files/R/R-4.2.3/library
```

```
##   packages:
```

```
##     class, KernSmooth, lattice, MASS, Matrix, nnet, survival
```

```
library(seventyGeneData)
```

```
data(vanDeVijver)
```

```
class(vanDeVijver)
```

```
## [1] "ExpressionSet"
```

```
## attr(,"package")
```

```
## [1] "Biobase"
```

Getting the clinical data

```
pdata <- pData(vanDeVijver)
```

ROC Plots

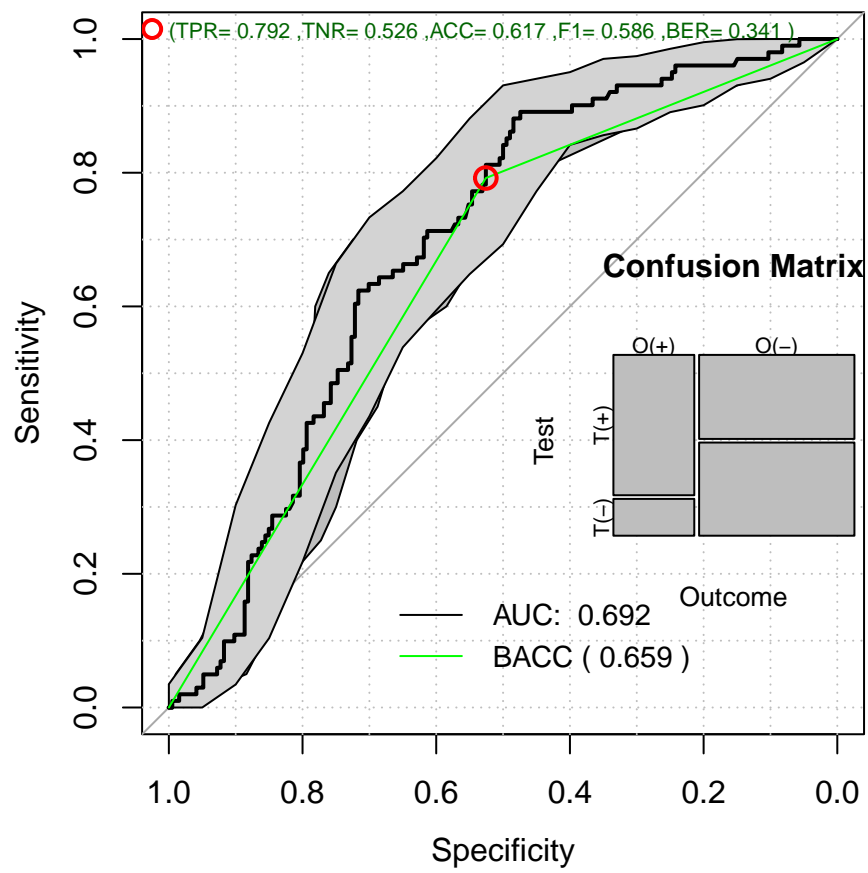
```
table(pdata$Posnodes)
```

```
n y 151 144
```

```
pander::pander(table(pdata$TTMevent))
```

0	1
194	101

```
pmroc <- plotModels.ROC(cbind(pdata$TTMevent,-pdata$C1used),name="NIK",thr= -0.4) ## Using paper thresh
```



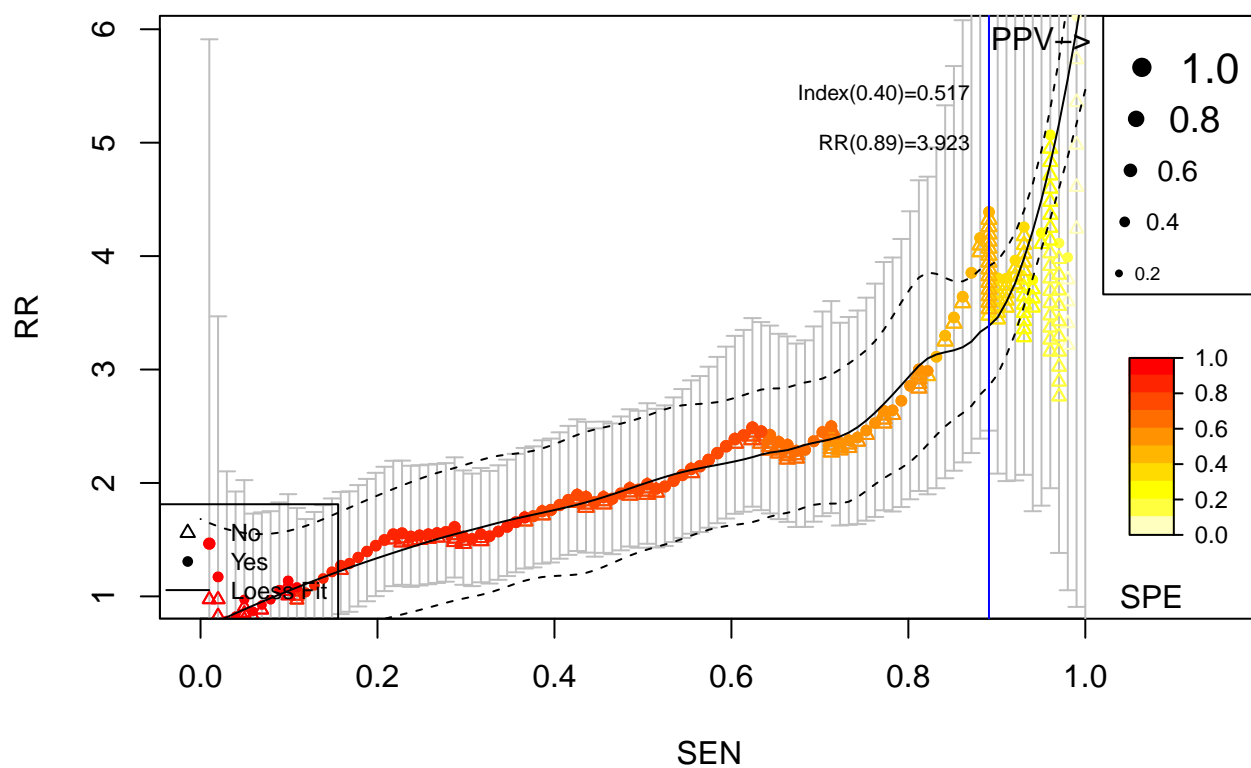
```
par(op)
```

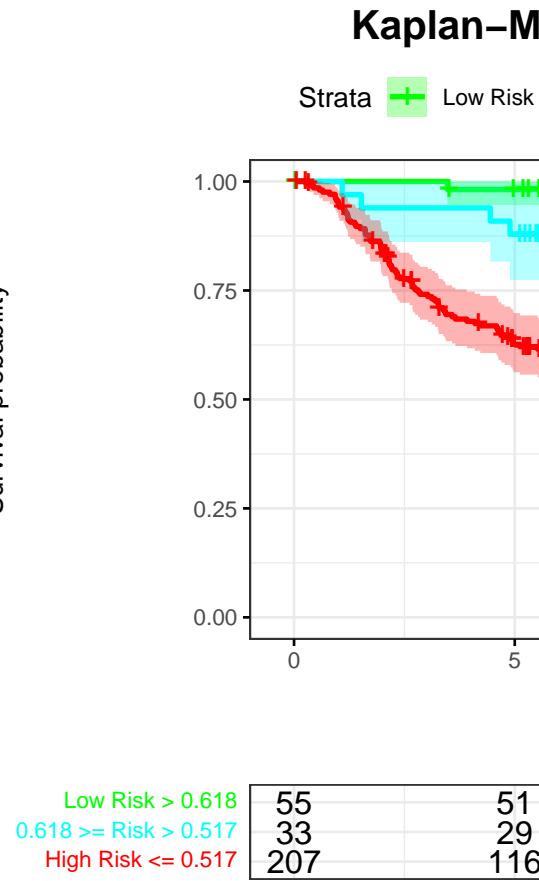
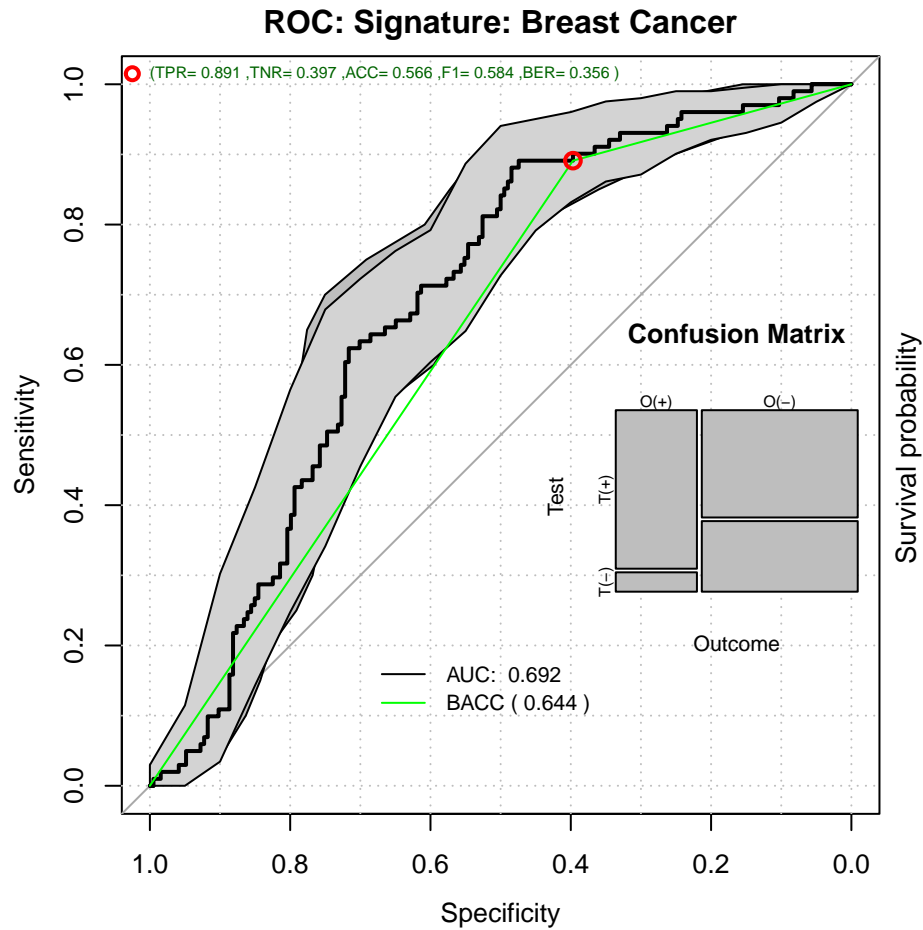
RR Plot Signature correlation

```
rdata <- cbind(pdata$TTMevent,pdata$C1used)

RRAnalysisCI <- RRPlot(rdata,atRate=c(0.10,0.05),
  timetoEvent=pdata$RFS,
  title="Signature: Breast Cancer",
  ysurvlim=c(0.00,1.0))
```

Relative Risk: Signature: Breast Cancer





```
par(op)
```

CI Performance all data

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

Table 2: Threshold values

	@:0.1	@:0.05	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.519	0.619	0.465	0.623	7.56e-01
RR	3.806	3.548	4.160	5.069	3.91e+01
RR_LCI	2.082	1.642	2.391	1.954	8.17e-02
RR_UCI	6.957	7.666	7.237	13.150	1.87e+04
SEN	0.901	0.941	0.881	0.960	1.00e+00
SPE	0.397	0.247	0.485	0.242	5.67e-02
BACC	0.649	0.594	0.683	0.601	5.28e-01

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

mean.C Index	median	lower	upper
0.698	0.698	0.648	0.745

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

Table 4: ROC AUC

est	lower	upper
0.692	0.631	0.752

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

Table 5: Sensitivity

est	lower	upper
0.891	0.813	0.944

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

Table 6: Specificity

est	lower	upper
0.397	0.328	0.469

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

Table 7: Probability Thresholds

10%	5%
0.517	0.618

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

Table 8: Logrank test Chisq = 28.085735 on 2 degrees of freedom,
p = 0.000001

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	55	6	23.5	13.01	17.1
class=1	33	5	12.9	4.87	5.6
class=2	207	90	64.6	10.00	27.9

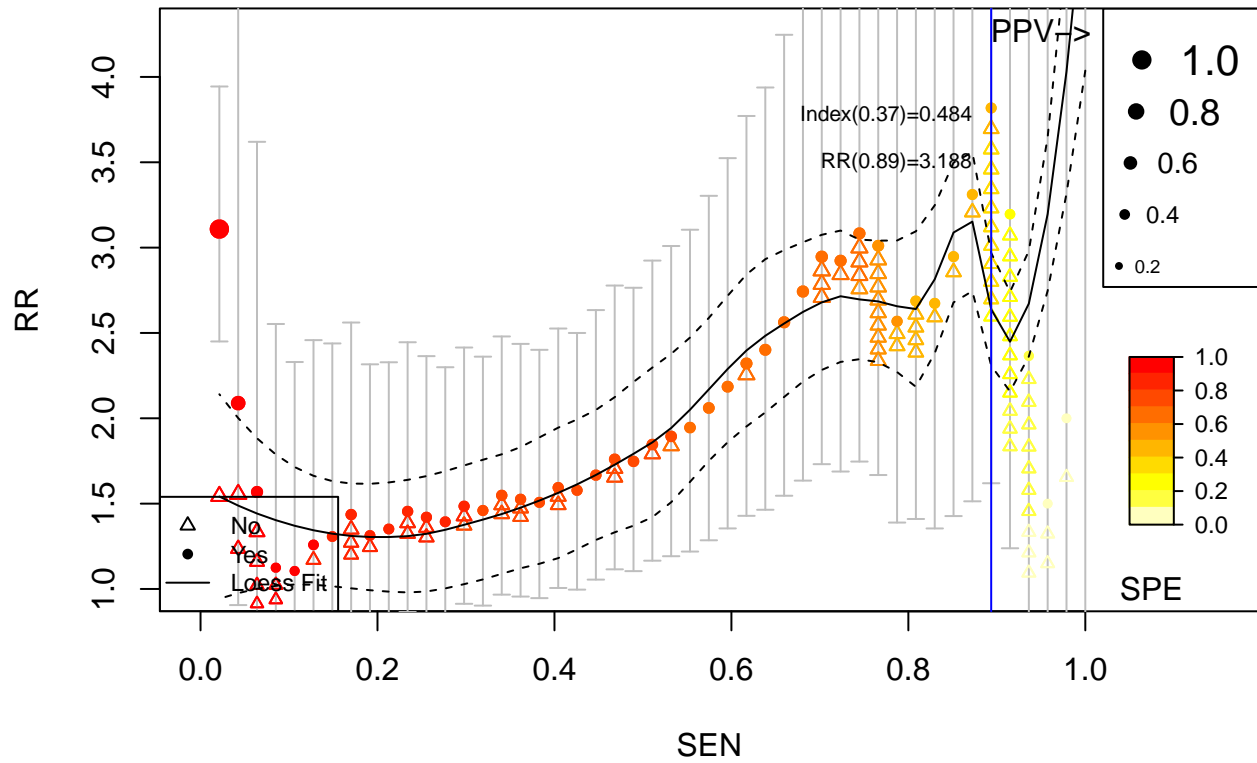
Node positive data

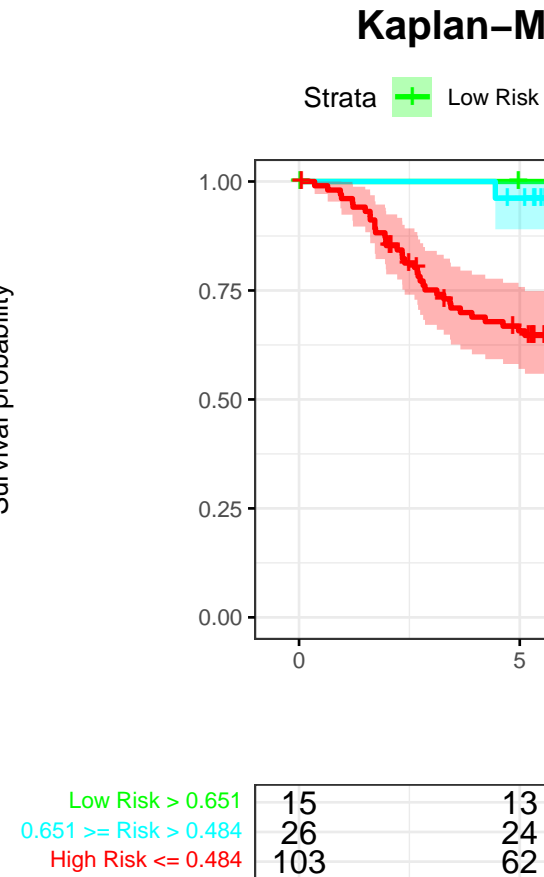
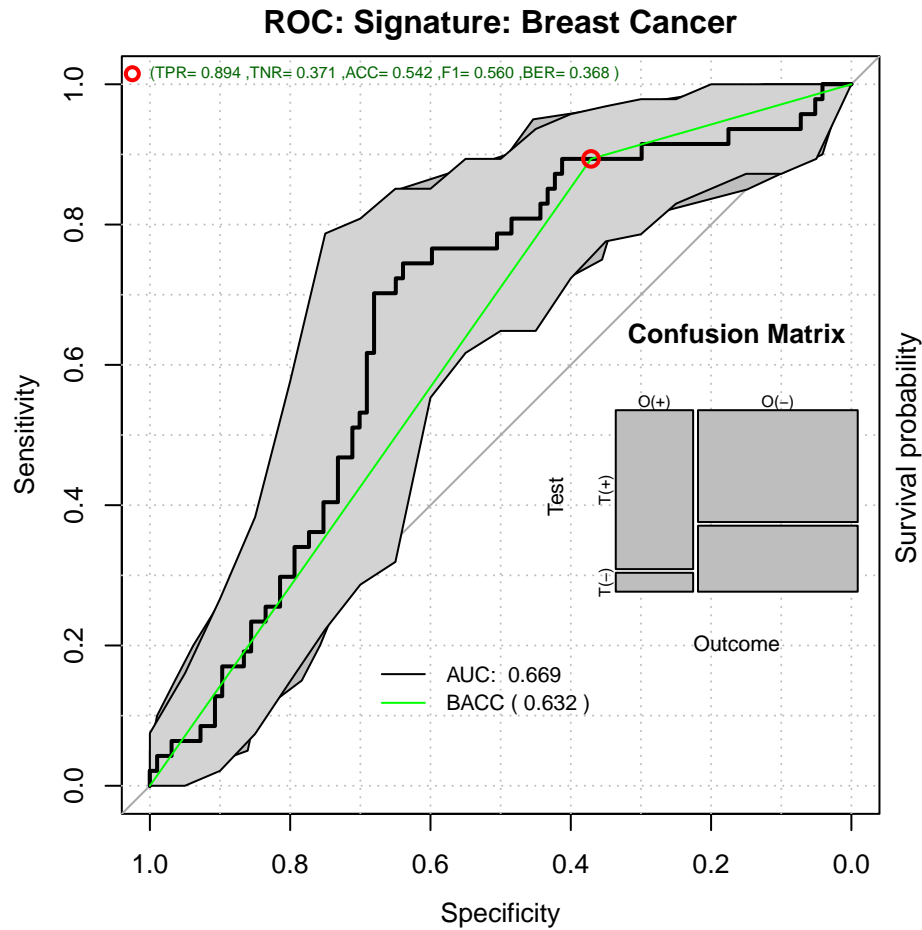
RR Plot Signature correlation

```
NodePdata <- subset(pdata,Posnodes=="y")
rdata <- cbind(NodePdata$TTMevent,NodePdata$Clused)
```

```
RRAnalysisPos <- RRPlot(rdata,atRate=c(0.90,0.95),
  timetoEvent=NodePdata$RFS,
  title="Signature: Breast Cancer",
  ysurvlim=c(0.00,1.0))
```

Relative Risk: Signature: Breast Cancer





```
par(op)
```

CI Performance positive data

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

Table 9: Threshold values

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.486	0.655	0.267	0.486	7.17e-01
RR	3.231	1.579	3.083	3.231	1.34e+01
RR_LCI	1.377	0.563	1.746	1.377	2.94e-02
RR_UCI	7.578	4.431	5.444	7.578	6.14e+03
SEN	0.894	0.936	0.745	0.894	1.00e+00
SPE	0.361	0.113	0.639	0.361	4.12e-02
BACC	0.627	0.525	0.692	0.627	5.21e-01

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

mean.C Index	median	lower	upper
0.7	0.7	0.634	0.771

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

Table 11: ROC AUC

est	lower	upper
0.669	0.576	0.761

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

Table 12: Sensitivity

est	lower	upper
0.894	0.769	0.965

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

Table 13: Specificity

est	lower	upper
0.371	0.275	0.475

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

Table 14: Probability Thresholds

10%	5%
0.484	0.651

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

Table 15: Logrank test Chisq = 11.060876 on 2 degrees of freedom,
p = 0.003964

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	15	3	5.80	1.35	1.55
class=1	26	2	9.73	6.14	7.77
class=2	103	42	31.47	3.52	10.71

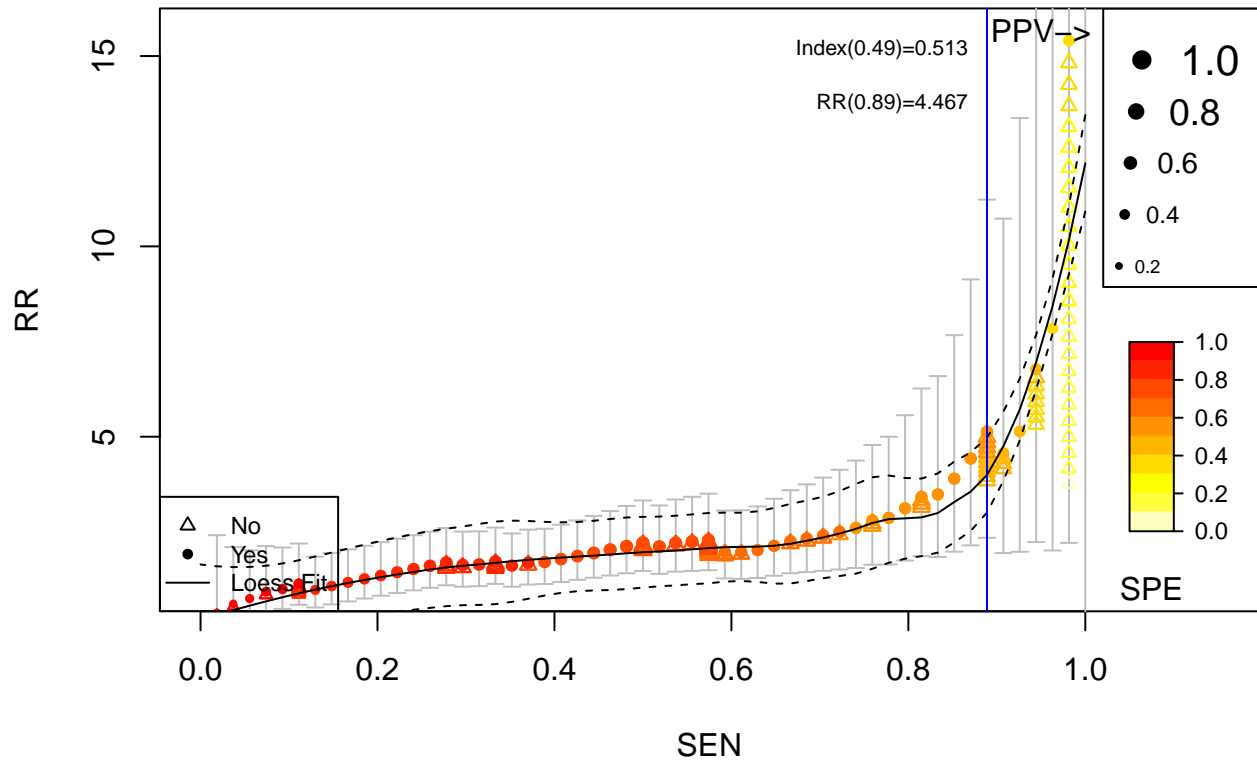
Node Negative data

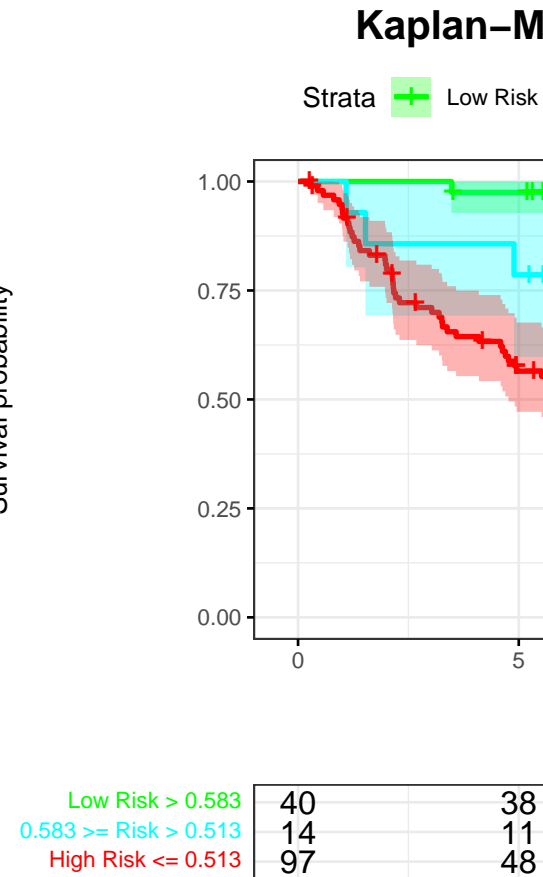
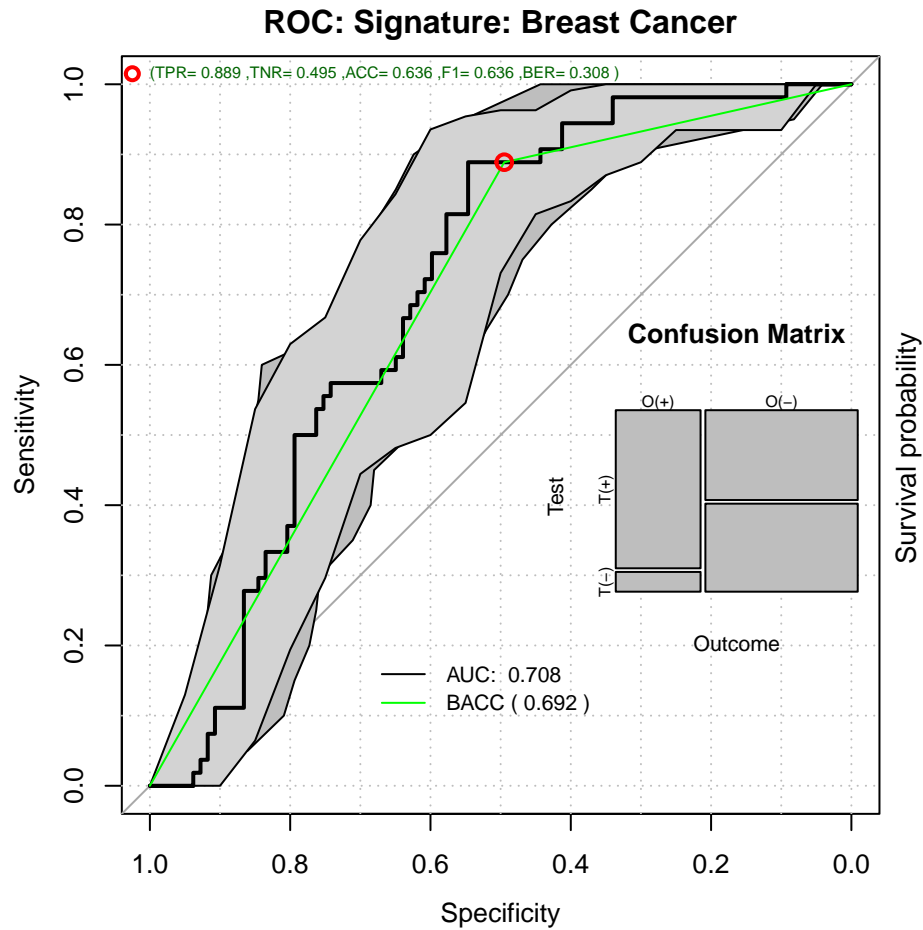
RR Plot Signature correlation

```
NodeNdata <- subset(pdata,Posnodes=="n")
rdata <- cbind(NodeNdata$TTMevent,NodeNdata$C1used)
```

```
RRAnalysisNeg <- RRPlot(rdata,atRate=c(0.90,0.95),
  timetoEvent=NodeNdata$RFS,
  title="Signature: Breast Cancer",
  ysurvlim=c(0.00,1.0))
```

Relative Risk: Signature: Breast Cancer





```
par(op)
```

CI Performance negative data

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

Table 16: Threshold values

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100
Thr	0.507	0.585	0.465	0.623	7.56e-01
RR	4.454	5.920	5.130	15.402	3.42e+01
RR_LCI	2.040	1.959	2.344	2.211	7.18e-02
RR_UCI	9.723	17.889	11.228	107.305	1.63e+04
SEN	0.889	0.944	0.889	0.981	1.00e+00
SPE	0.495	0.371	0.546	0.340	9.28e-02
BACC	0.692	0.658	0.718	0.661	5.46e-01

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

mean.C Index	median	lower	upper
0.696	0.695	0.63	0.759

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

Table 18: ROC AUC

est	lower	upper
0.708	0.627	0.79

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

Table 19: Sensitivity

est	lower	upper
0.889	0.774	0.958

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

Table 20: Specificity

est	lower	upper
0.495	0.392	0.598

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

Table 21: Probability Thresholds

10%	5%
0.513	0.583

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

Table 22: Logrank test Chisq = 24.223875 on 2 degrees of freedom,
p = 0.000005

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	40	3	18.18	12.67	19.29
class=1	14	3	5.43	1.09	1.21
class=2	97	48	30.39	10.21	23.58

RRPlot Cox Model

```
timeinterval <- 5 # Five years
```

```
h0 <- sum(pdata$TTMevent & pdata$RFS <= timeinterval)
h0 <- h0/sum((pdata$RFS > timeinterval) | (pdata$TTMevent==1))
```

```
mcox <- coxph(Surv(RFS,TTMevent)~Clused,pdata)
pander::pander(summary(mcox)$coefficients)
```

	coef	exp(coef)	se(coef)	z	Pr(> z)
C1used	-1.5	0.224	0.263	-5.69	1.3e-08

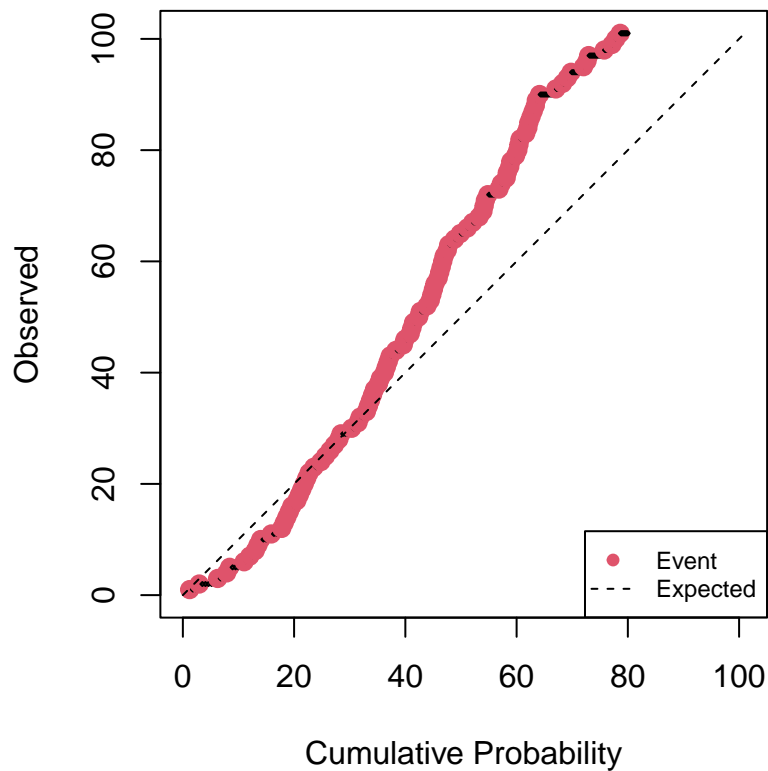
```

index <- predict(mcox,pdata)
rdata <- cbind(pdata$TTEvent,ppoisGzero(index,h0))

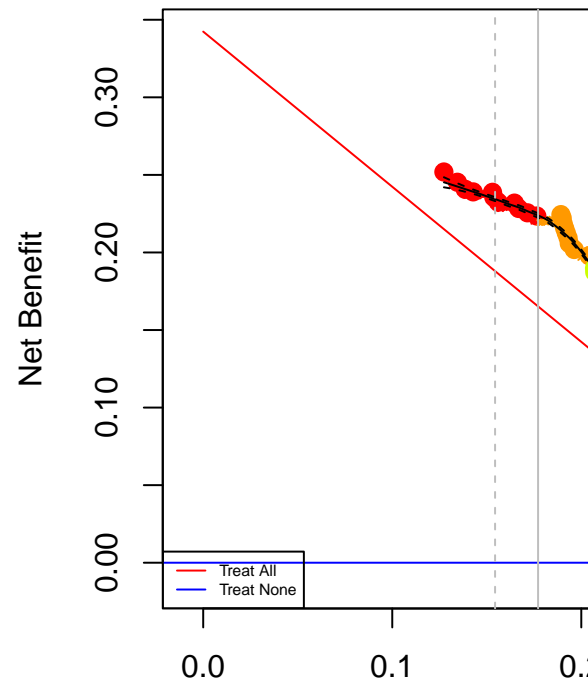
RRAnalysisCox <- RRPlot(rdata,atRate=c(0.90,0.95),
                        timetoEvent=pdata$RFS,
                        title="NIK: Breast Cancer",
                        ysurvlim=c(0.00,1.0),
                        riskTimeInterval=timeinterval)

```

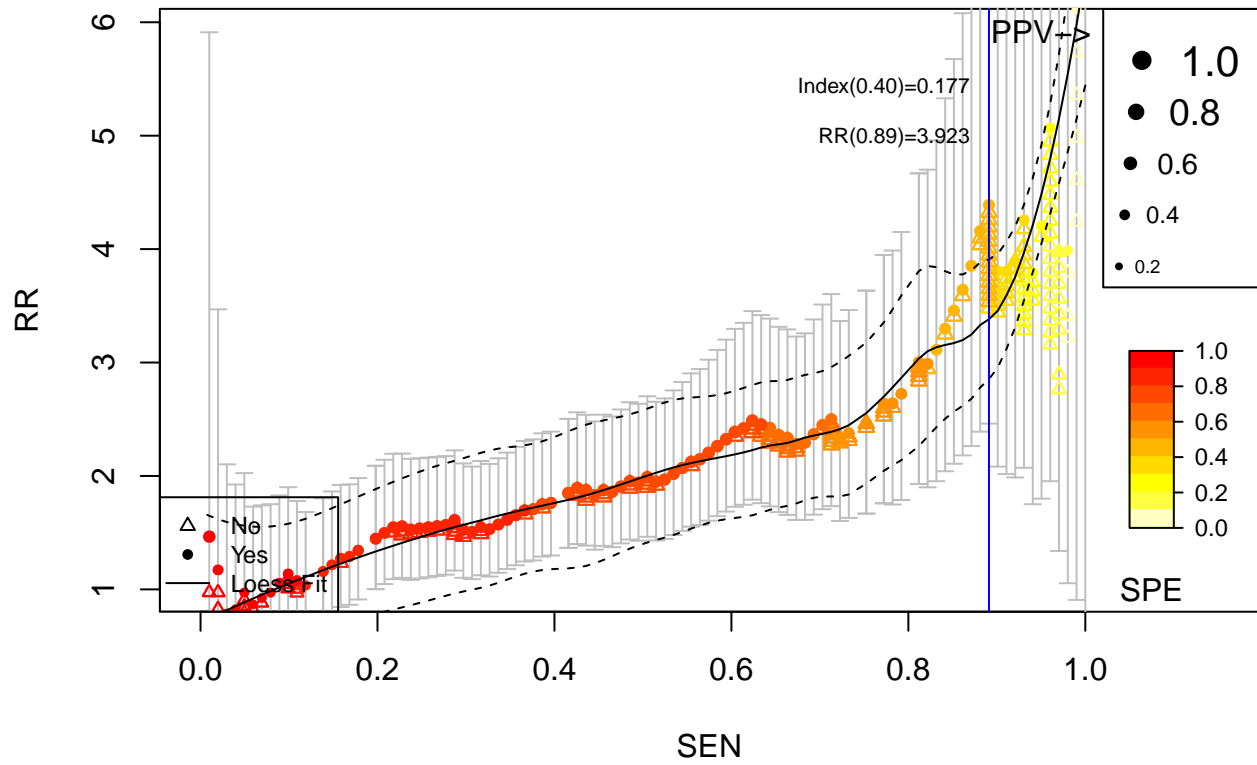
Cumulative vs. Observed: NIK: Breast Cancer

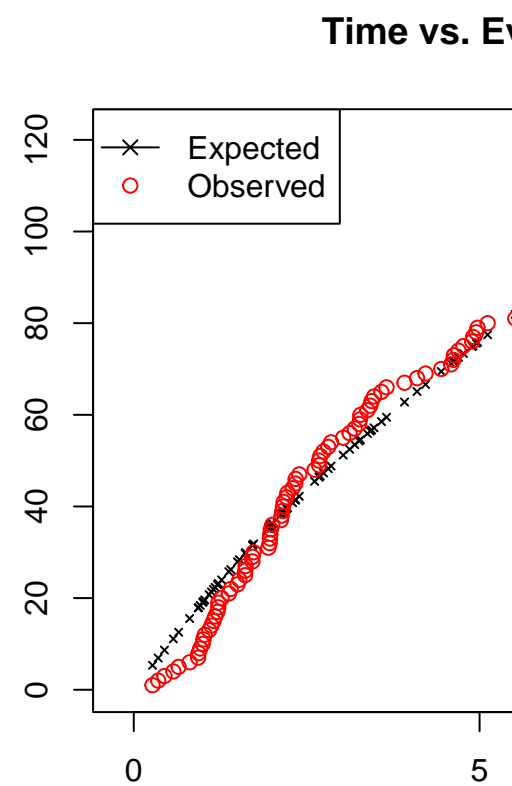
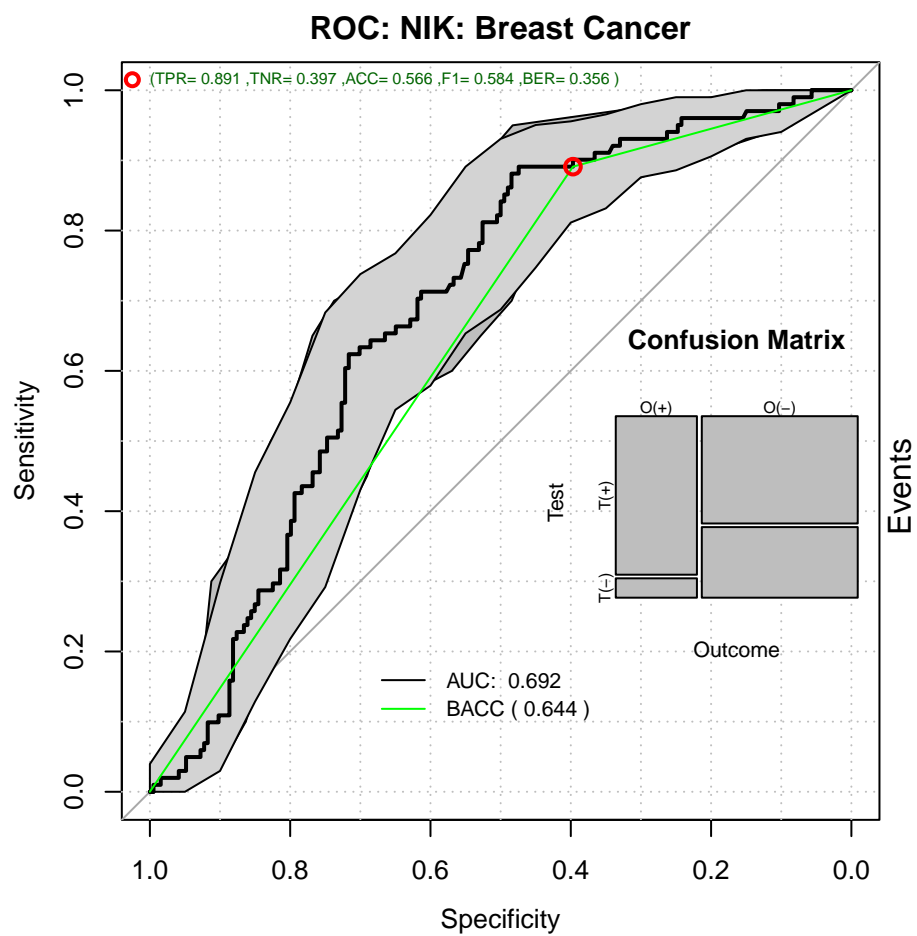


Decision Curve

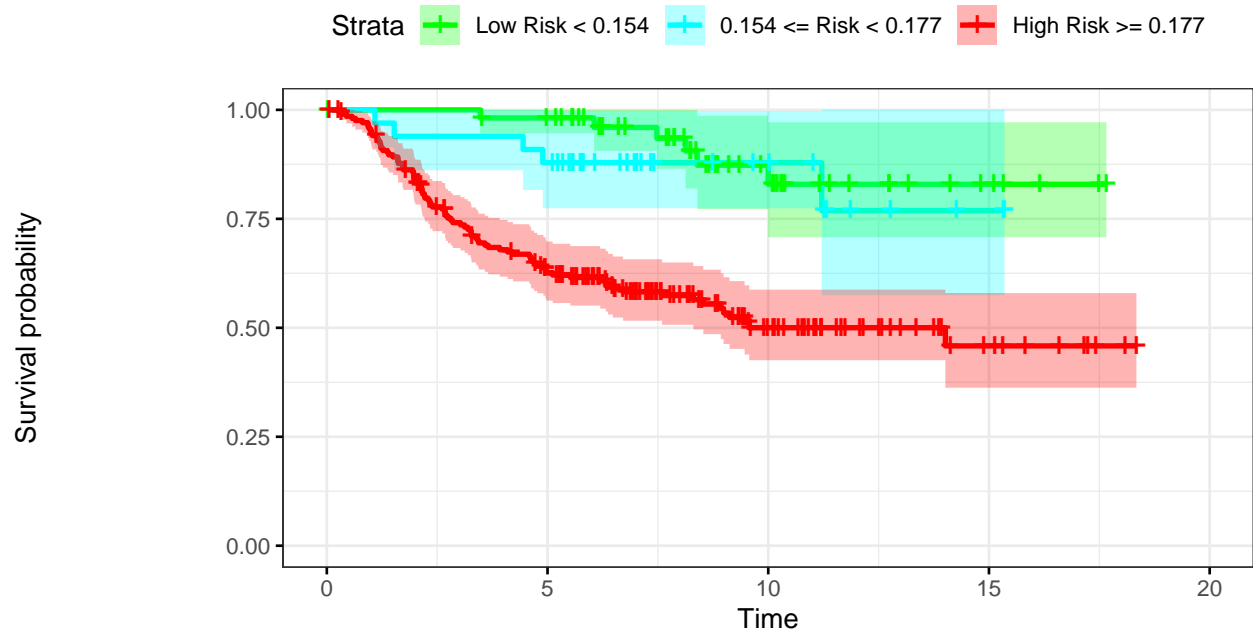


Relative Risk: NIK: Breast Cancer





Kaplan–Meier: NIK: Breast Cancer



Number at risk

Low Risk < 0.154	55	51	19	5	0
0.154 <= Risk < 0.177	33	29	10	2	0
High Risk >= 0.177	207	116	39	9	0

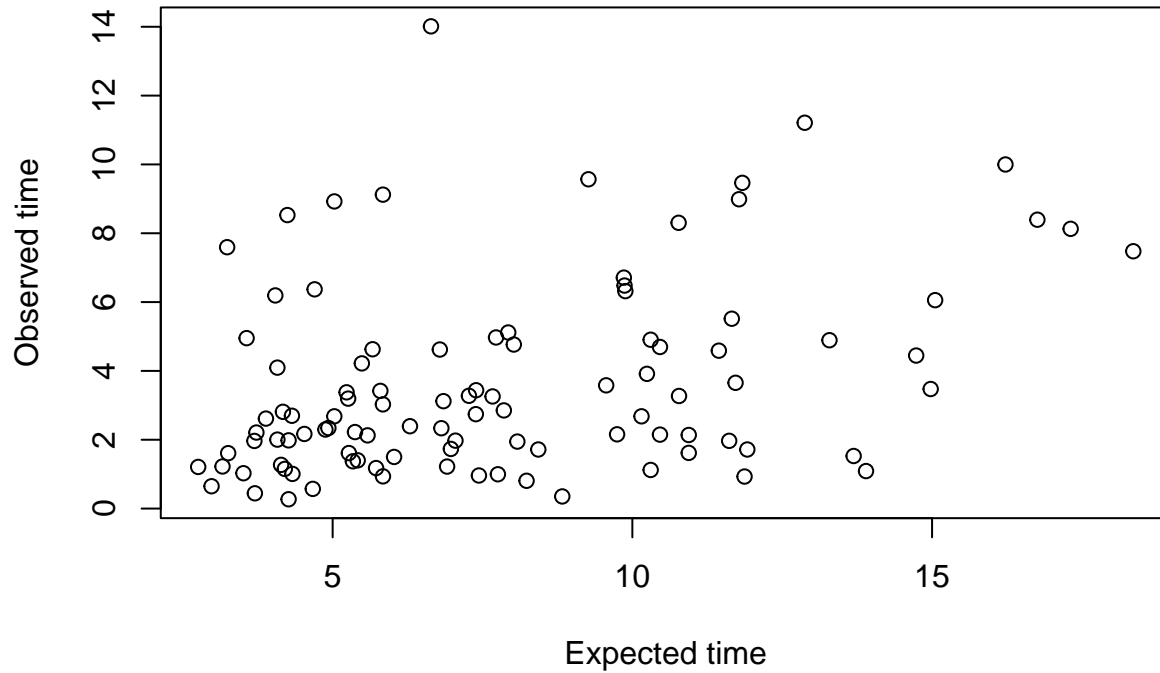
```
par(op)
```

Expected time to event

```
timetoEvent <- meanTimeToEvent(rdata[rdata[,1]==1,2],timeinterval)
```

```
plot(timetoEvent,pdata[rdata[,1]==1,"RFS"],xlab="Expected time",ylab="Observed time",main="Expected vs.
```

Expected vs. Observed



```
pander::pander(cor.test(timetoEvent,pdata[rdata[,1]==1,"RFS"],method="spearman"))
```

```
## Warning in cor.test.default(timetoEvent, pdata[rdata[, 1] == 1, "RFS"], :  
## Cannot compute exact p-value with ties
```

Table 24: Spearman's rank correlation rho: timetoEvent and
pdata[rdata[, 1] == 1, "RFS"]

Test statistic	P value	Alternative hypothesis	rho
115797	0.000892 * * *	two.sided	0.326

```
MADerror <- mean(abs(timetoEvent-pdata[rdata[,1]==1,"RFS"]))  
pander::pander(MADerror)
```

```
4.75
```

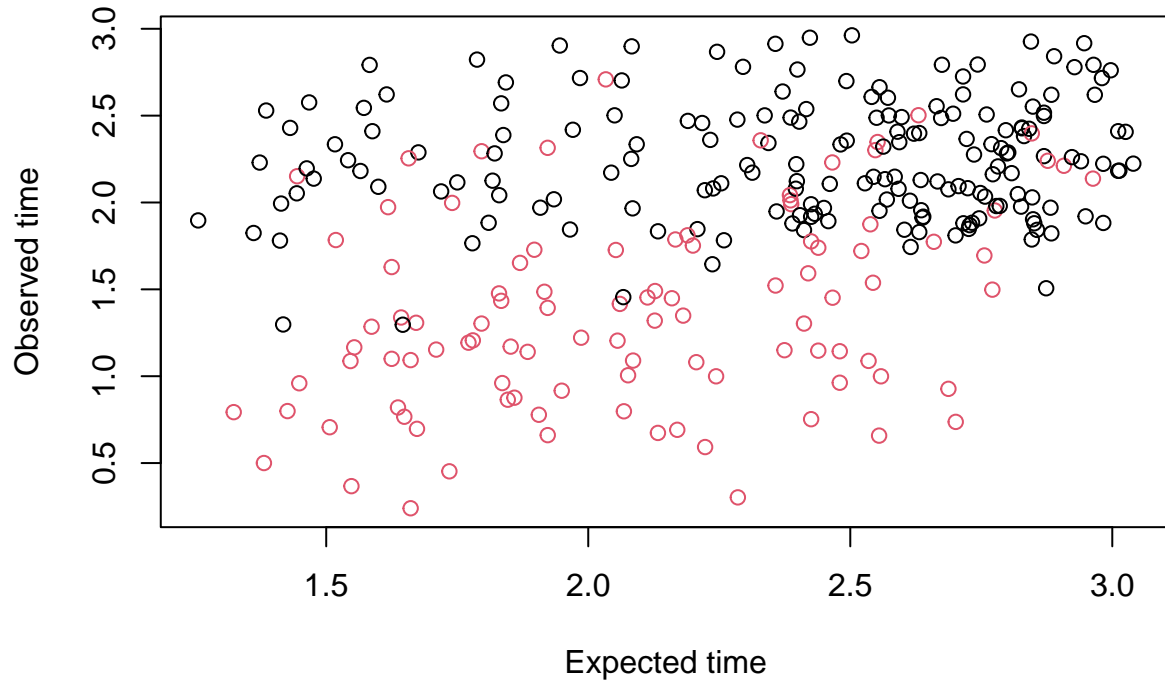
```
toinclude <- rdata[,1]==1 | pdata$RFS > 0.5*timeinterval  
sum(toinclude)
```

```
## [1] 285
```

```
timetoEvent <- log(1.0+meanTimeToEvent(rdata[toinclude,2],timeinterval))  
obstiemToEvent <- log(1.0+pdata[toinclude,"RFS"])
```

```
plot(timetoEvent,obstiemToEvent,  
     col=1+rdata[toinclude,1],  
     xlab="Expected time",  
     ylab="Observed time",main="Expected vs. Observed")
```

Expected vs. Observed



```
pander::pander(cor.test(timetoEvent,obstiemToEvent,method="kendall"))
```

Table 25: Kendall's rank correlation tau: `timetoEvent` and `obstiemToEvent`

Test statistic	P value	Alternative hypothesis	tau
5.7	1.18e-08 * * *	two.sided	0.227

```
MADerror2 <- mean(abs(timetoEvent-obstiemToEvent))
pander::pander(MADerror2)
```

0.595

Unadjusted Cox Performance

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

Table 26: Threshold values

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.176	0.154	0.190	0.153	1.27e-01	0.5041
RR	3.806	3.548	4.160	5.069	3.91e+01	0.9241
RR_LCI	2.082	1.642	2.391	1.954	8.17e-02	0.4906
RR_UCI	6.957	7.666	7.237	13.150	1.87e+04	1.7407
SEN	0.901	0.941	0.881	0.960	1.00e+00	0.0693
SPE	0.397	0.247	0.485	0.242	5.67e-02	0.9227
BACC	0.649	0.594	0.683	0.601	5.28e-01	0.4960

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
NetBenefit	0.223	0.232	0.222	0.239	2.52e-01	-0.0279

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

Table 27: O/E Ratio

O/E	Low	Upper	p.value
0.871	0.709	1.06	0.178

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

Table 28: O/E Mean

mean	50%	2.5%	97.5%
0.958	0.957	0.932	0.982

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

Table 29: O/Acum Mean

mean	50%	2.5%	97.5%
1.22	1.22	1.2	1.24

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

mean.C Index	median	lower	upper
0.698	0.698	0.653	0.745

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

Table 31: ROC AUC

est	lower	upper
0.692	0.631	0.752

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

Table 32: Sensitivity

est	lower	upper
0.891	0.813	0.944

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

Table 33: Specificity

est	lower	upper
0.397	0.328	0.469

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

Table 34: Probability Thresholds

10%	5%
0.177	0.154

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

Table 35: Logrank test Chisq = 28.085735 on 2 degrees of freedom,
p = 0.000001

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	55	6	23.5	13.01	17.1
class=1	33	5	12.9	4.87	5.6
class=2	207	90	64.6	10.00	27.9

RRPlot Cox Adjusted Model

This time we will include Lymph node status from pathology report and Estrogen receptor alpha expression measurement from microarray

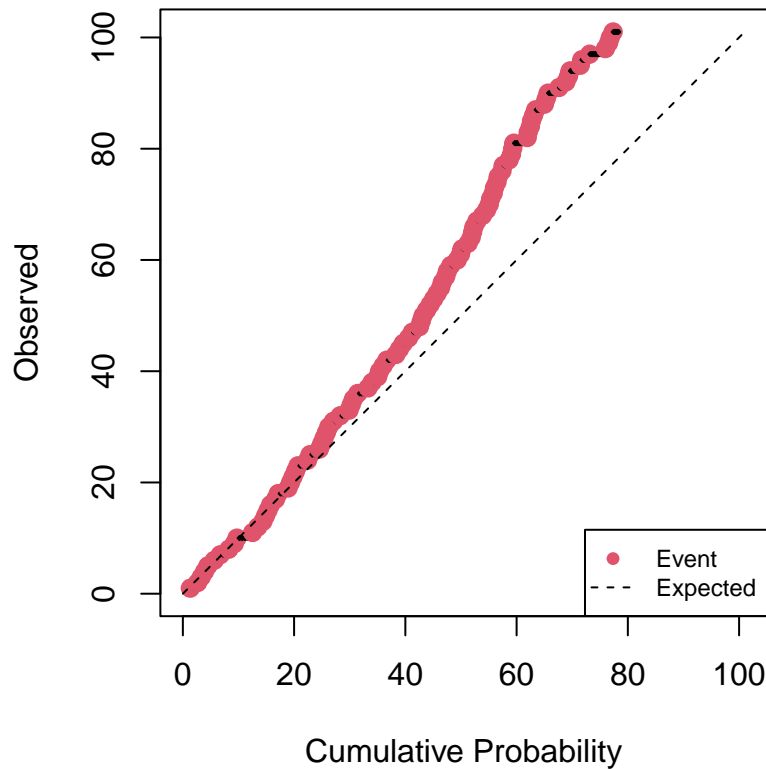
```
mcox <- coxph(Surv(RFS,TTMevent)~C1used*(ESR1 + Posnodes),pdata)
pander::pander(summary(mcox)$coefficients)
```

	coef	exp(coef)	se(coef)	z	Pr(> z)
C1used	-0.403	0.668	0.629	-0.640	0.52186
ESR1	0.123	1.131	0.255	0.481	0.63079
Posnodesy	-0.305	0.737	0.217	-1.401	0.16112
C1used:ESR1	-1.913	0.148	0.739	-2.588	0.00966
C1used:Posnodesy	0.378	1.460	0.583	0.649	0.51661

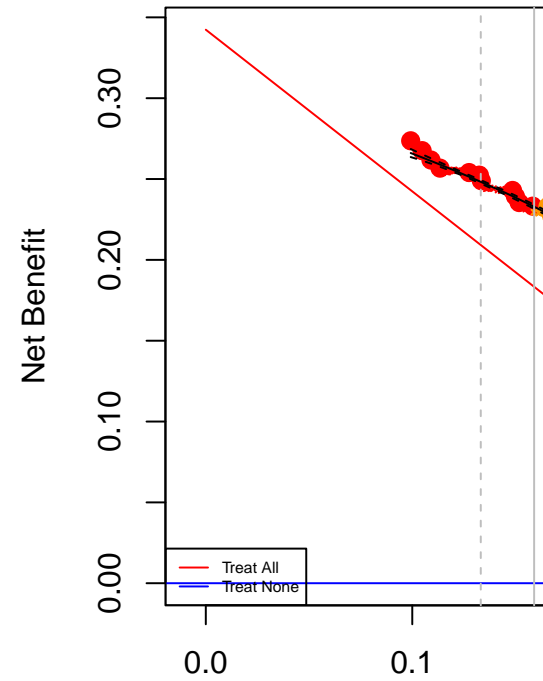
```
index <- predict(mcox,pdata)
rdata <- cbind(pdata$TTMevent,ppoisGzero(index,h0))

RRAnalysisAdCox <- RRPlot(rdata,atRate=c(0.90,0.95),
  timetoEvent=pdata$RFS,
  title="Adjusted: Breast Cancer",
  ysurvlim=c(0.00,1.0),
  riskTimeInterval=timeinterval)
```

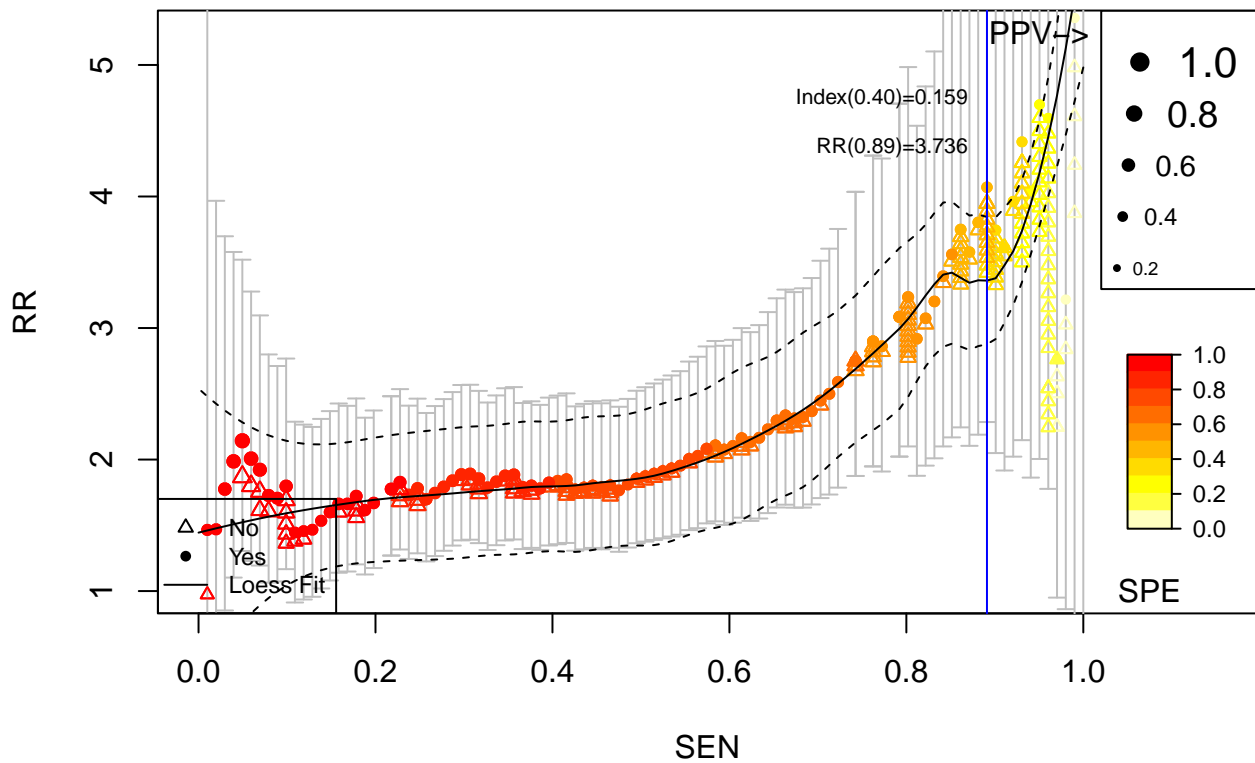
Cumulative vs. Observed: Adjusted: Breast Cancer

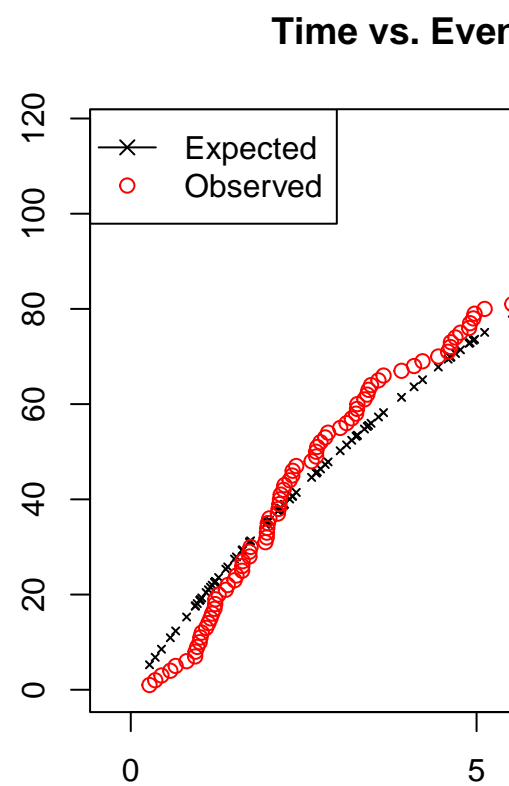
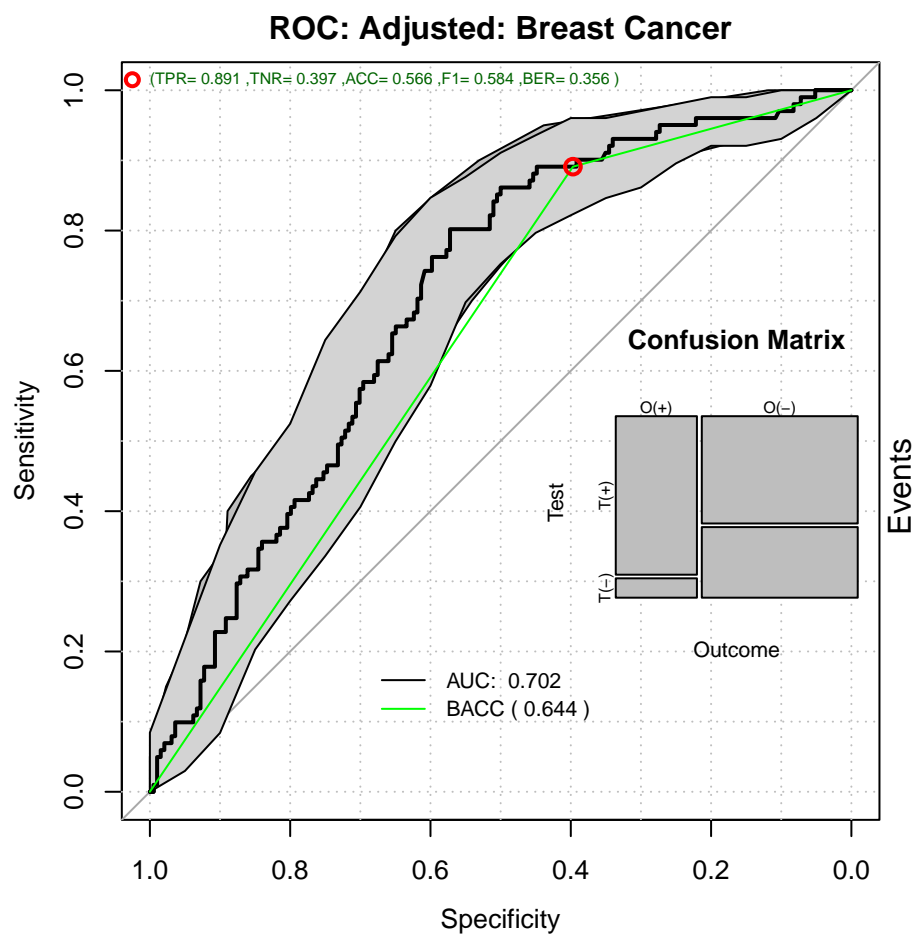


Decision Curve

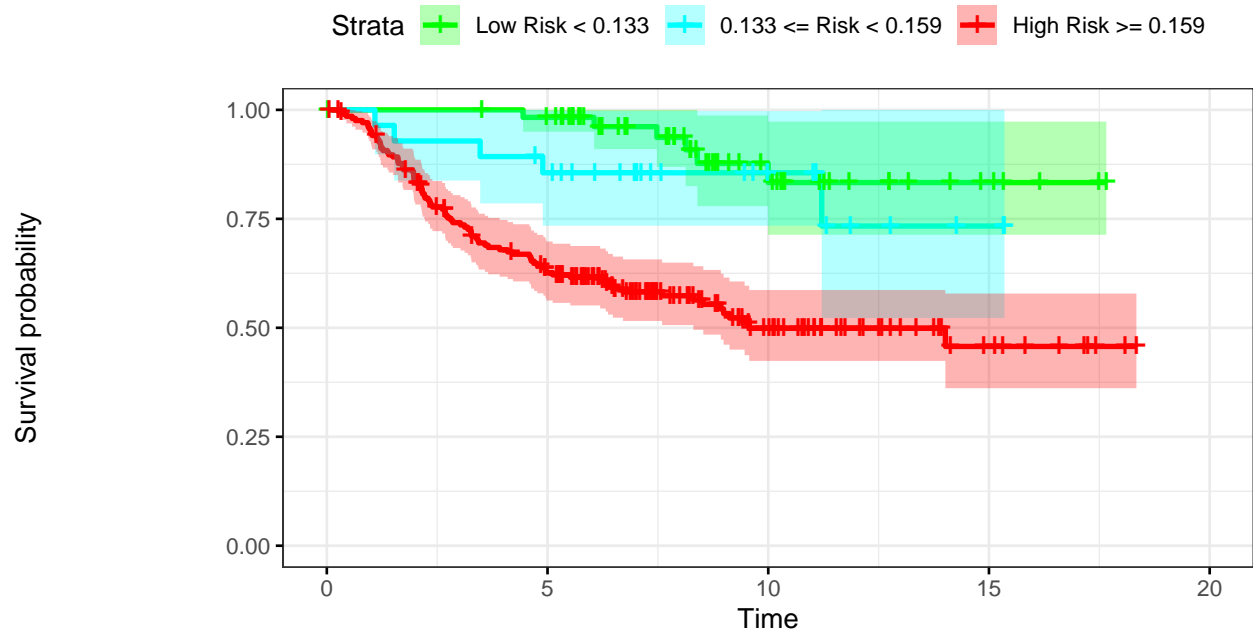


Relative Risk: Adjusted: Breast Cancer





Kaplan–Meier: Adjusted: Breast Cancer



Number at risk

Low Risk < 0.133	60	56	19	5	0
0.133 <= Risk < 0.159	28	23	9	2	0
High Risk >= 0.159	207	117	40	9	0

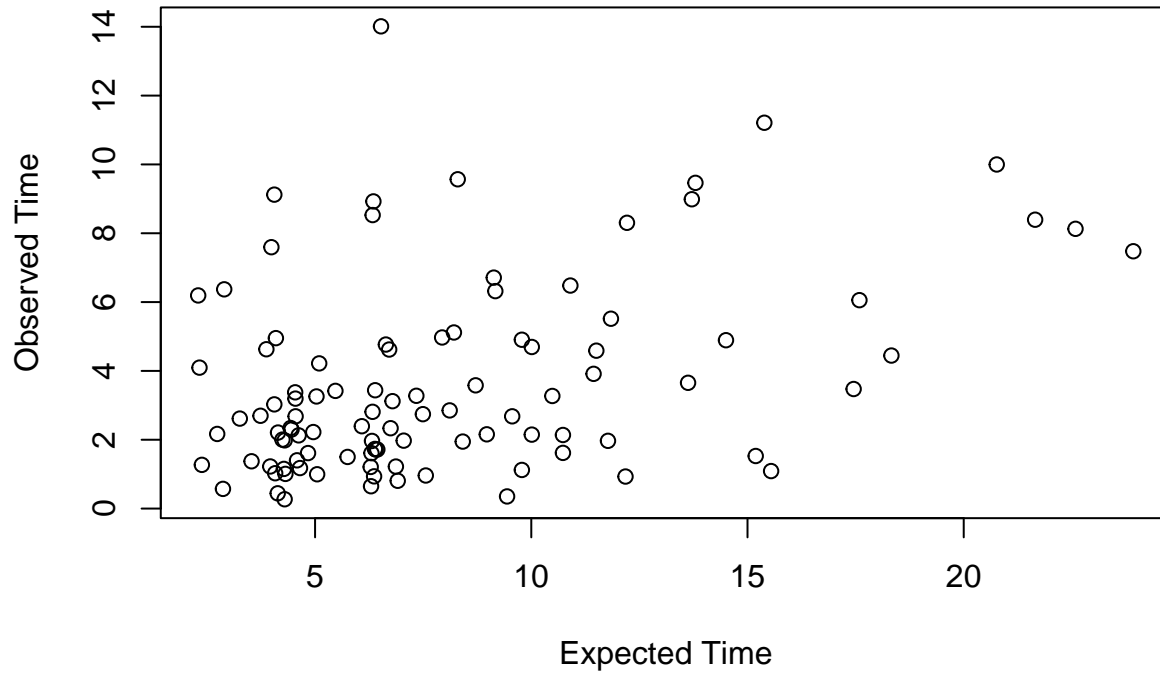
```
par(op)
```

Expected time to event

```
timetoEvent <- meanTimeToEvent(rdata[rdata[,1]==1,2],timeinterval)
```

```
plot(timetoEvent,pdata[rdata[,1]==1,"RFS"],xlab="Expected Time",ylab="Observed Time",main="Expected vs.
```


Expected vs. Observed



```
pander::pander(cor.test(timetoEvent, pdata[rdata[,1]==1, "RFS"], method="spearman"))
```

```
## Warning in cor.test.default(timetoEvent, pdata[rdata[, 1] == 1, "RFS"], :  
## Cannot compute exact p-value with ties
```

Table 37: Spearman's rank correlation rho: timetoEvent and
pdata[rdata[, 1] == 1, "RFS"]

Test statistic	P value	Alternative hypothesis	rho
117931	0.00143 * *	two.sided	0.313

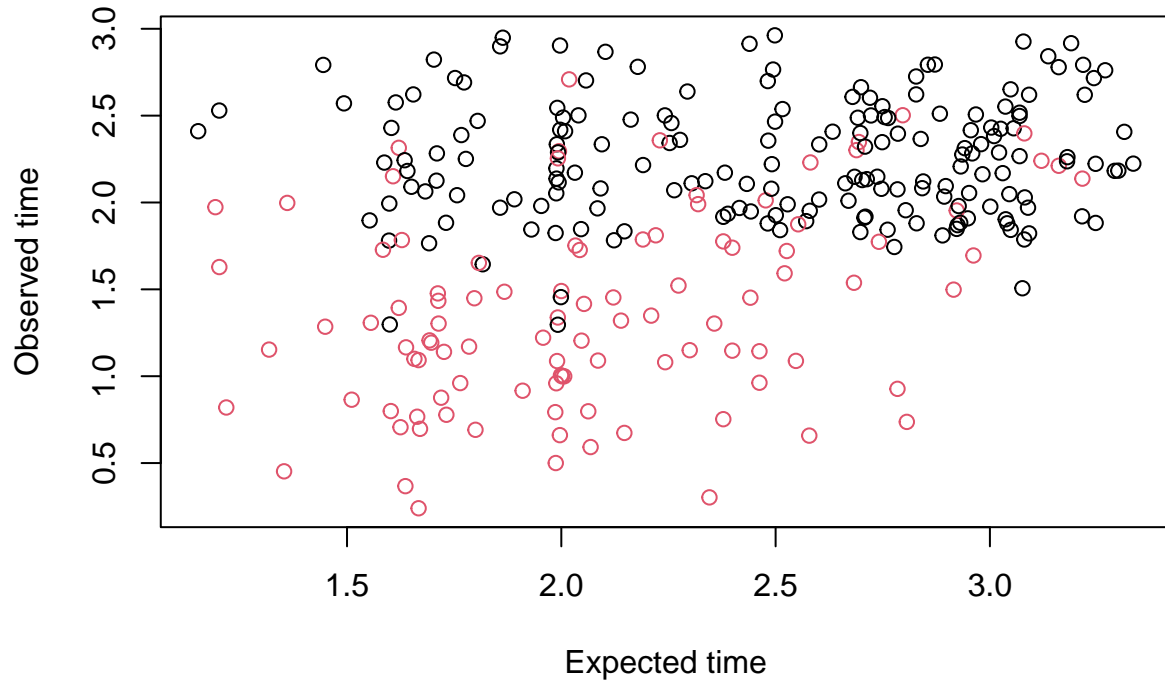
```
MADerror <- c(MADerror, mean(abs(timetoEvent - pdata[rdata[,1]==1, "RFS"])))  
pander::pander(MADerror)
```

4.75 and 5.02

```
timetoEvent <- log(1.0 + meanTimeToEvent(rdata[tinclude, 2], timeinterval))
```

```
plot(timetoEvent, obstiemToEvent,  
     col=1+rdata[tinclude, 1],  
     xlab="Expected time",  
     ylab="Observed time", main="Expected vs. Observed")
```

Expected vs. Observed



```
pander::pander(cor.test(timetoEvent,obstiemToEvent,method="kendall"))
```

Table 38: Kendall's rank correlation tau: `timetoEvent` and `obstiemToEvent`

Test statistic	P value	Alternative hypothesis	tau
5.82	5.83e-09 * * *	two.sided	0.231

```
MADerror2 <-c(MADerror2,mean(abs(timetoEvent-obstiemToEvent)))
pander::pander(MADerror2)
```

0.595 and 0.649

Adjusted Cox Performance

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

Table 39: Threshold values

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.159	0.133	0.205	0.133	9.92e-02	0.50740
RR	3.422	4.043	3.235	4.699	3.54e+01	1.72657
RR_LCI	1.928	1.863	2.100	2.004	7.42e-02	1.06501
RR_UCI	6.075	8.773	4.984	11.015	1.69e+04	2.79908
SEN	0.891	0.941	0.802	0.950	1.00e+00	0.07921
SPE	0.392	0.278	0.572	0.273	5.15e-02	0.96907
BACC	0.641	0.609	0.687	0.612	5.26e-01	0.52414

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
NetBenefit	0.230	0.249	0.202	0.252	2.74e-01	0.00617

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

Table 40: O/E Ratio

O/E	Low	Upper	p.value
0.904	0.737	1.1	0.344

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

Table 41: O/E Mean

mean	50%	2.5%	97.5%
0.98	0.98	0.954	1.01

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

Table 42: O/Acum Mean

mean	50%	2.5%	97.5%
1.24	1.24	1.22	1.25

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

mean.C Index	median	lower	upper
0.707	0.707	0.662	0.751

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

Table 44: ROC AUC

est	lower	upper
0.702	0.642	0.763

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

Table 45: Sensitivity

est	lower	upper
0.891	0.813	0.944

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

Table 46: Specificity

est	lower	upper
0.397	0.328	0.469

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

Table 47: Probability Thresholds

10%	5%
0.159	0.133

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

Table 48: Logrank test Chisq = 28.504862 on 2 degrees of freedom,
p = 0.000001

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	60	6	25.3	14.73	19.76
class=1	28	5	11.2	3.45	3.89
class=2	207	90	64.5	10.11	28.16

Calibrating the index

```
calprob <- CoxRiskCalibration(mcox,pdata,"TTMevent", "RFS")
pander::pander(c(h0=calprob$h0,
  Gain=calprob$hazardGain,
  DeltaTime=calprob$timeInterval),
  caption="Cox Calibration Parameters")
```

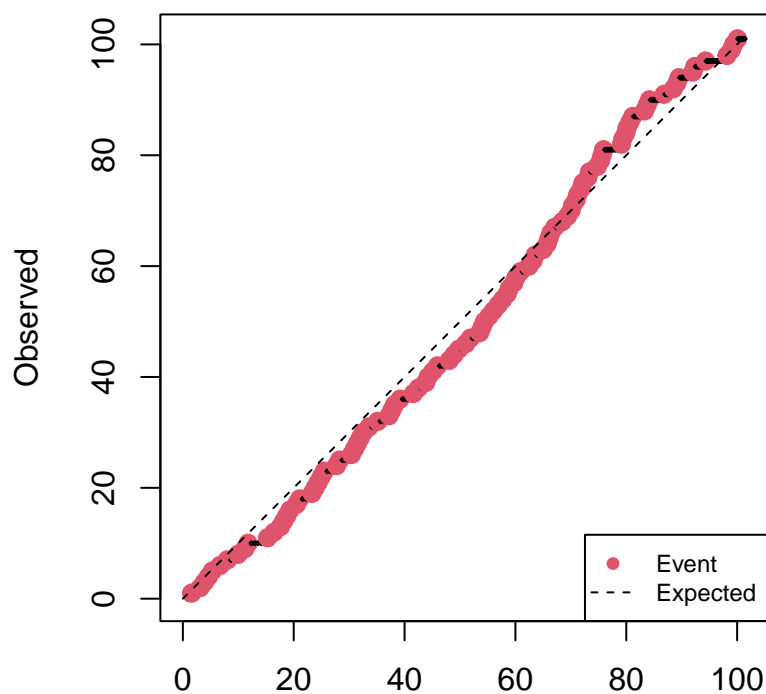
h0	Gain	DeltaTime
0.401	0.987	7.16

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

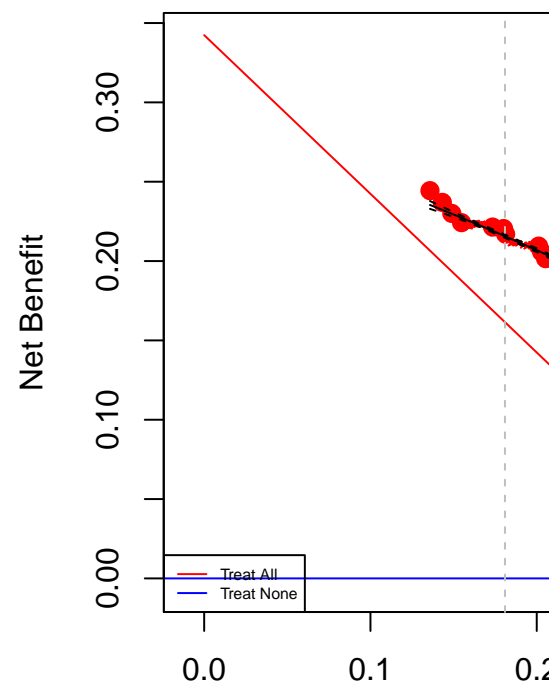
rdata <- cbind(pdata$TTMevent,calprob$prob)

RRAnalysisCalAdCox <- RRPlot(rdata,atRate=c(0.90,0.95),
  timetoEvent=pdata$RFS,
  title="Cal. NIK: Breast Cancer",
  ysurvlim=c(0.00,1.0),
  riskTimeInterval=timeinterval)
```

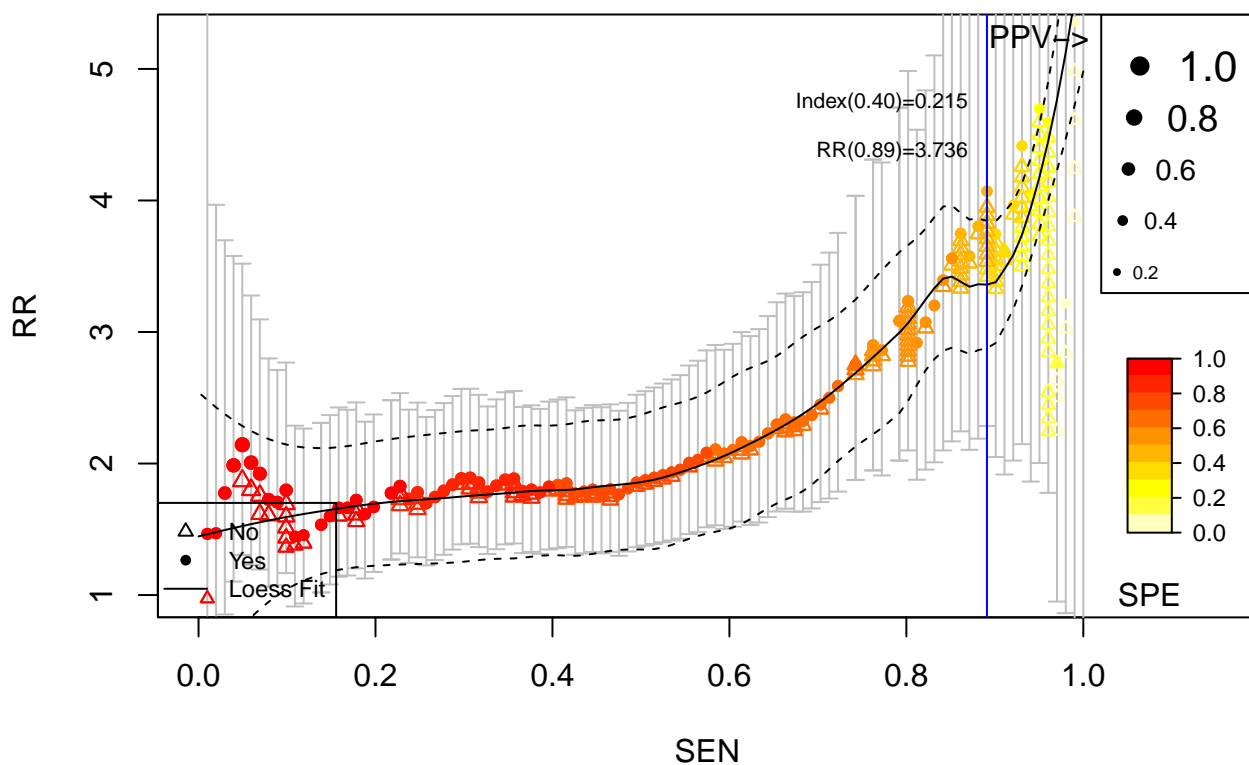
Cumulative vs. Observed: Cal. NIK: Breast Cancer

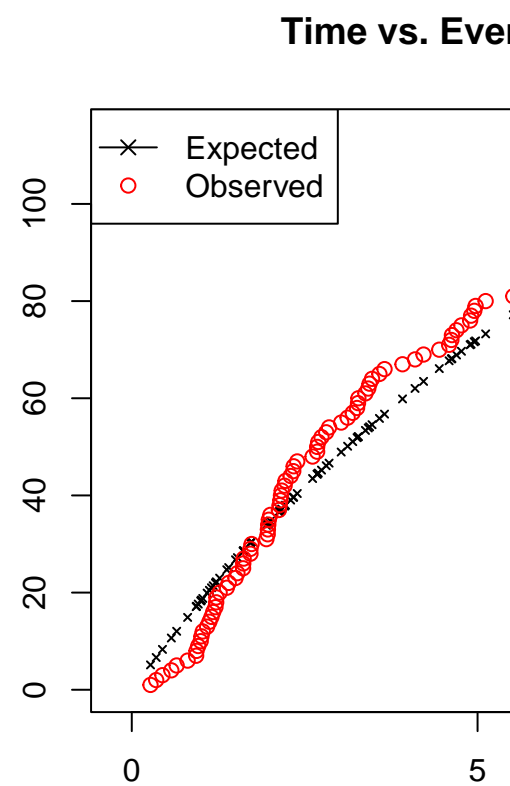
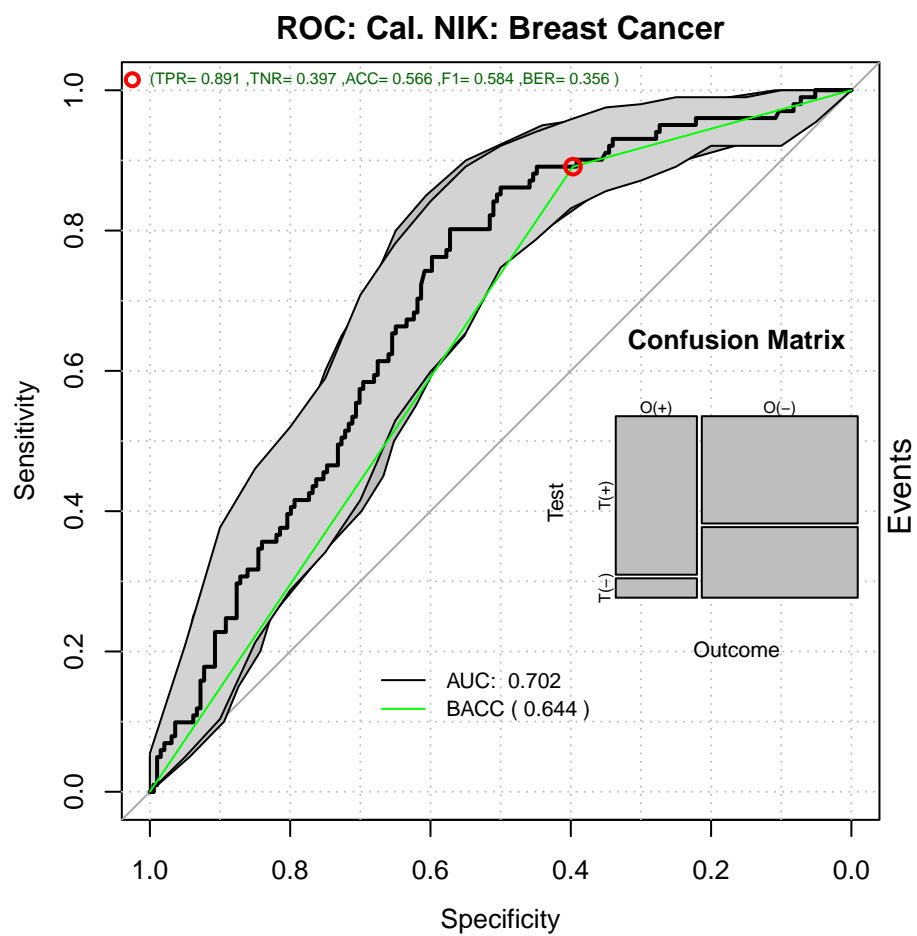


Decision Curve

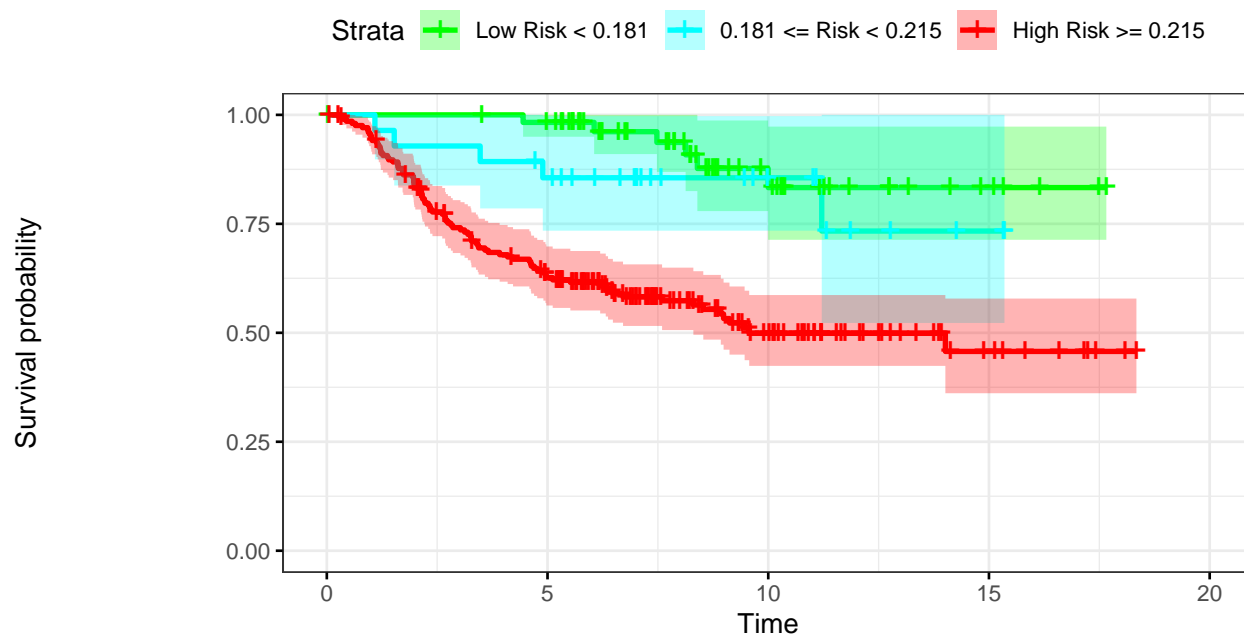


Relative Risk: Cal. NIK: Breast Cancer





Kaplan–Meier: Cal. NIK: Breast Cancer



Number at risk

Low Risk < 0.181	60	56	19	5	0
0.181 <= Risk < 0.215	28	23	9	2	0
High Risk >= 0.215	207	117	40	9	0

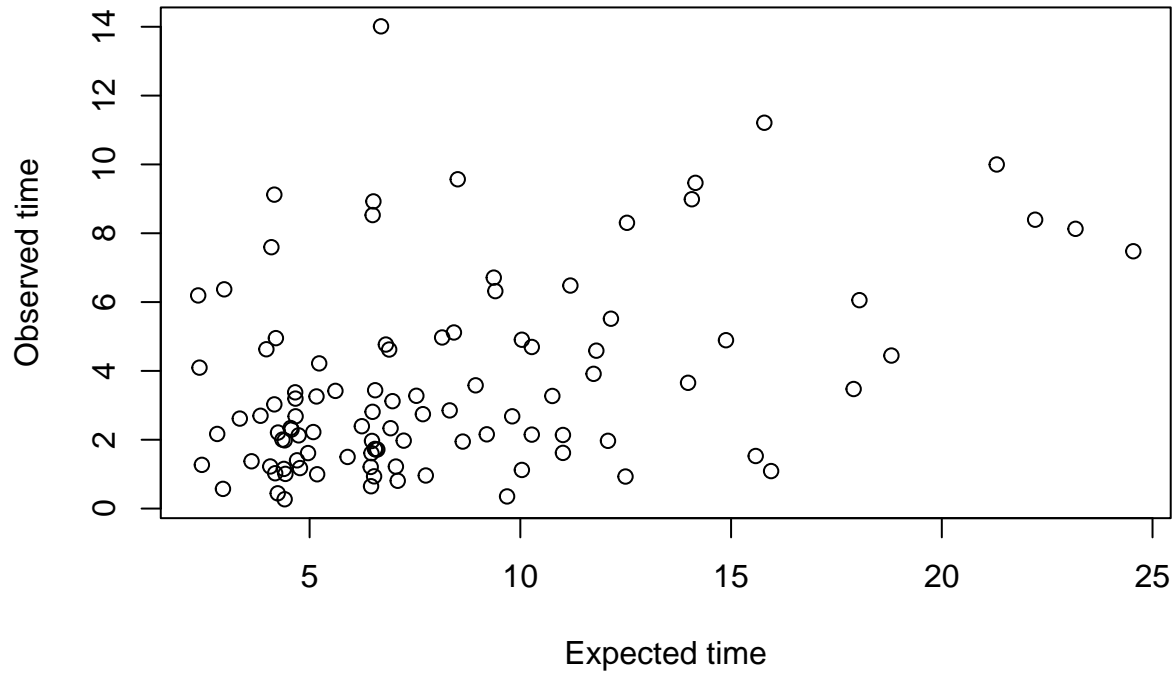
```
par(op)
```

Expected time to event

```
timetoEvent <- meanTimeToEvent(rdata[rdata[,1]==1,2],timeinterval)
```

```
plot(timetoEvent,pdata[rdata[,1]==1,"RFS"],xlab="Expected time",ylab="Observed time",main="Expected vs.
```

Expected vs. Observed



```
pander::pander(cor.test(timetoEvent, pdata[rdata[,1]==1, "RFS"], method="spearman"))
```

```
## Warning in cor.test.default(timetoEvent, pdata[rdata[, 1] == 1, "RFS"], :  
## Cannot compute exact p-value with ties
```

Table 50: Spearman's rank correlation rho: timetoEvent and
pdata[rdata[, 1] == 1, "RFS"]

Test statistic	P value	Alternative hypothesis	rho
117931	0.00143 * *	two.sided	0.313

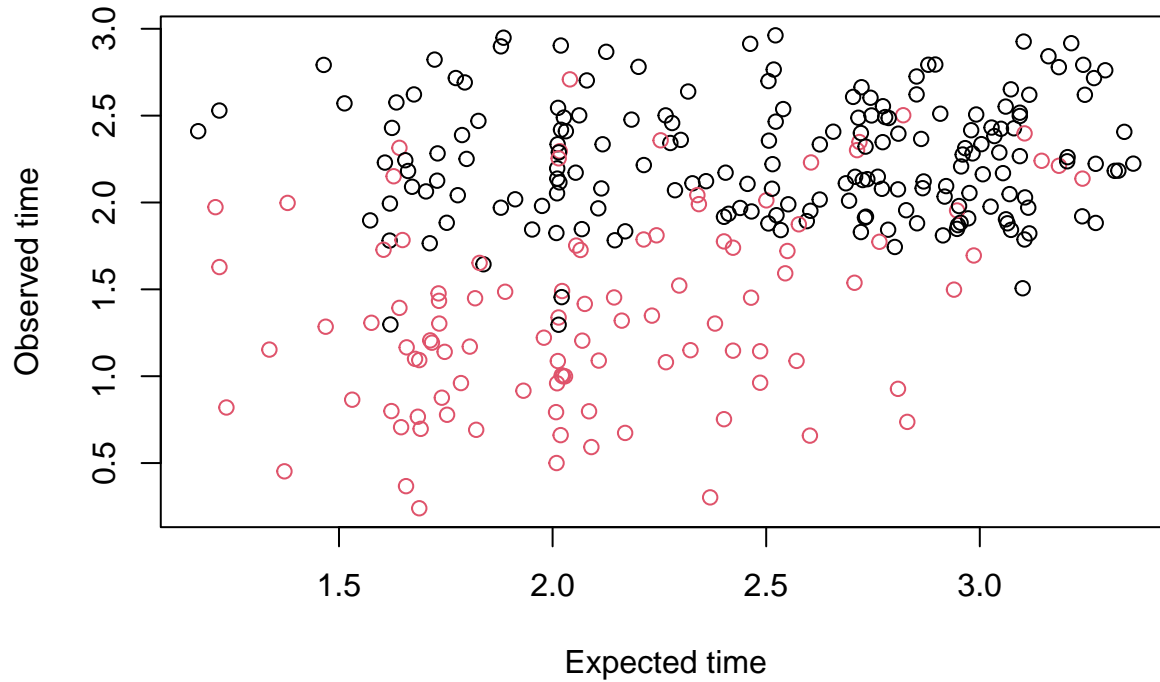
```
MADerror <- c(MADerror, mean(abs(timetoEvent - pdata[rdata[,1]==1, "RFS"])))  
pander::pander(MADerror)
```

4.75, 5.02 and 5.20

```
timetoEvent <- log(1.0 + meanTimeToEvent(rdata[tinclude, 2], timeinterval))
```

```
plot(timetoEvent, obstiemToEvent,  
     col=1+rdata[tinclude, 1],  
     xlab="Expected time",  
     ylab="Observed time", main="Expected vs. Observed")
```


Expected vs. Observed



```
pander::pander(cor.test(timetoEvent,obstiemToEvent,method="kendall"))
```

Table 51: Kendall's rank correlation tau: `timetoEvent` and `obstiemToEvent`

Test statistic	P value	Alternative hypothesis	tau
5.82	5.83e-09 * * *	two.sided	0.231

```
MADerror2 <-c(MADerror2,mean(abs(timetoEvent-obstiemToEvent)))
pander::pander(MADerror2)
```

0.595, 0.649 and 0.661

Calibrated and Adjusted Cox Performance

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

Table 52: Threshold values

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.215	0.181	0.274	0.180	1.36e-01	0.5003
RR	3.422	4.043	3.235	4.699	3.54e+01	1.8316
RR_LCI	1.928	1.863	2.100	2.004	7.42e-02	1.3487
RR_UCI	6.075	8.773	4.984	11.015	1.69e+04	2.4875
SEN	0.891	0.941	0.802	0.950	1.00e+00	0.3366
SPE	0.392	0.278	0.572	0.273	5.15e-02	0.8454
BACC	0.641	0.609	0.687	0.612	5.26e-01	0.5910

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
NetBenefit	0.196	0.217	0.168	0.220	2.44e-01	0.0135

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

Table 53: O/E Ratio

O/E	Low	Upper	p.value
0.923	0.752	1.12	0.445

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

Table 54: O/E Mean

mean	50%	2.5%	97.5%
1.01	1.01	0.978	1.03

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

Table 55: O/Acum Mean

mean	50%	2.5%	97.5%
0.973	0.973	0.963	0.982

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

mean.C Index	median	lower	upper
0.707	0.707	0.662	0.752

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

Table 57: ROC AUC

est	lower	upper
0.702	0.642	0.763

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

Table 58: Sensitivity

est	lower	upper
0.891	0.813	0.944

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

Table 59: Specificity

est	lower	upper
0.397	0.328	0.469

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

Table 60: Probability Thresholds

10%	5%
0.215	0.181

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

Table 61: Logrank test Chisq = 28.504862 on 2 degrees of freedom,
p = 0.000001

	N	Observed	Expected	(O-E) ² /E	(O-E) ² /V
class=0	60	6	25.3	14.73	19.76
class=1	28	5	11.2	3.45	3.89
class=2	207	90	64.5	10.11	28.16

Comparing Risks

Comparing concordance Index

```
## Correlation Index
cindex <- RRAnalysisCI$c.index$cstatCI
## Cox Index
cindex <- rbind(cindex,RRAnalysisCox$c.index$cstatCI)
## Adjusted Cox Index
cindex <- rbind(cindex,RRAnalysisAdCox$c.index$cstatCI)
## Adjusted and Calibrated Cox Index
cindex <- rbind(cindex,RRAnalysisCalAdCox$c.index$cstatCI)
rownames(cindex) <- c("CI","Cox","Adj. Cox","Cal. Adj. Cox")

pander::pander(cindex)
```

	mean.C Index	median	lower	upper
CI	0.698	0.698	0.648	0.745
Cox	0.698	0.698	0.653	0.745
Adj. Cox	0.707	0.707	0.662	0.751
Cal. Adj. Cox	0.707	0.707	0.662	0.752

Comparing Risk Ratios Index

```
## Correlation Index
RRratio <- c(RR=RRAnalysisCI$keyPoints$RR[1],
             LCI=RRAnalysisCI$keyPoints$RR_LCI[1],
             UCI=RRAnalysisCI$keyPoints$RR_UCI[1])
## Cox Index
RRratio <- rbind(RRratio,c(RR=RRAnalysisCox$keyPoints$RR[1],
                           LCI=RRAnalysisCox$keyPoints$RR_LCI[1],
                           UCI=RRAnalysisCox$keyPoints$RR_UCI[1]))
## Adjusted Cox Index
RRratio <- rbind(RRratio,c(RR=RRAnalysisAdCox$keyPoints$RR[1],
                           LCI=RRAnalysisAdCox$keyPoints$RR_LCI[1],
                           UCI=RRAnalysisAdCox$keyPoints$RR_UCI[1]))
## Adjusted and Calibrated Cox Index
RRratio <- rbind(RRratio,c(RR=RRAnalysisCalAdCox$keyPoints$RR[1],
                           LCI=RRAnalysisCalAdCox$keyPoints$RR_LCI[1],
                           UCI=RRAnalysisCalAdCox$keyPoints$RR_UCI[1]))
rownames(RRratio) <- c("CI", "Cox", "Adj. Cox", "Cal. Adj. Cox")
pander::pander(RRratio)
```

	RR	LCI	UCI
CI	3.81	2.08	6.96
Cox	3.81	2.08	6.96
Adj. Cox	3.42	1.93	6.07
Cal. Adj. Cox	3.42	1.93	6.07

Comparing logRank values

```
## Correlation Index
SurvDif <- c(chisq=RRAnalysisCI$surdif$chisq,pvalue=RRAnalysisCI$surdif$pvalue)
## Cox Index
SurvDif <- rbind(SurvDif,c(chisq=RRAnalysisCox$surdif$chisq,pvalue=RRAnalysisCox$surdif$pvalue))
## Adjusted Cox Index
SurvDif <- rbind(SurvDif,c(chisq=RRAnalysisAdCox$surdif$chisq,pvalue=RRAnalysisAdCox$surdif$pvalue))
## Adjusted and Calibrated Cox Index
SurvDif <- rbind(SurvDif,c(chisq=RRAnalysisCalAdCox$surdif$chisq,pvalue=RRAnalysisCalAdCox$surdif$pvalue))
rownames(SurvDif) <- c("CI", "Cox", "Adj. Cox", "Cal. Adj. Cox")
pander::pander(SurvDif)
```

	chisq	pvalue
CI	28.1	7.97e-07
Cox	28.1	7.97e-07
Adj. Cox	28.5	6.46e-07
Cal. Adj. Cox	28.5	6.46e-07

Comparing Sensitivity

```
## Correlation Index
sensi <- RRAnalysisCI$ROCAAnalysis$sensitivity
## Cox Index
```

```

sensi <- rbind(sensi,RRAnalysisCox$ROCAAnalysis$sensitivity)
## Adjusted Cox Index
sensi <- rbind(sensi,RRAnalysisAdCox$ROCAAnalysis$sensitivity)
## Adjusted and Calibrated Cox Index
sensi <- rbind(sensi,RRAnalysisCalAdCox$ROCAAnalysis$sensitivity)
rownames(sensi) <- c("CI","Cox","Adj. Cox","Cal. Adj. Cox")

pander::pander(sensi)

```

	est	lower	upper
CI	0.891	0.813	0.944
Cox	0.891	0.813	0.944
Adj. Cox	0.891	0.813	0.944
Cal. Adj. Cox	0.891	0.813	0.944

Comparing Specificity

```

## Correlation Index
speci <- RRAnalysisCI$ROCAAnalysis$specificity
## Cox Index
speci <- rbind(speci,RRAnalysisCox$ROCAAnalysis$specificity)
## Adjusted Cox Index
speci <- rbind(speci,RRAnalysisAdCox$ROCAAnalysis$specificity)
## Adjusted and Calibrated Cox Index
speci <- rbind(speci,RRAnalysisCalAdCox$ROCAAnalysis$specificity)
rownames(speci) <- c("CI","Cox","Adj. Cox","Cal. Adj. Cox")
pander::pander(speci)

```

	est	lower	upper
CI	0.397	0.328	0.469
Cox	0.397	0.328	0.469
Adj. Cox	0.397	0.328	0.469
Cal. Adj. Cox	0.397	0.328	0.469

Comparing O/E

```

OERatio <- NULL
## Cox Index
OERatio <- rbind(OERatio,RRAnalysisCox$OERatio$estimate)
## Adjusted Cox Index
OERatio <- rbind(OERatio,RRAnalysisAdCox$OERatio$estimate)
## Adjusted and Calibrated Cox Index
OERatio <- rbind(OERatio,RRAnalysisCalAdCox$OERatio$estimate)
rownames(OERatio) <- c("Cox","Adj. Cox","Cal. Adj. Cox")

pander::pander(OERatio)

```

	O/E	Low	Upper	p.value
Cox	0.871	0.709	1.06	0.178

	O/E	Low	Upper	p.value
Adj. Cox	0.904	0.737	1.10	0.344
Cal. Adj. Cox	0.923	0.752	1.12	0.445

Comparing O/Acum

```
OARatio <- NULL
## Cox Index
OARatio <- rbind(OARatio,RRAnalysisCox$OARatio$estimate)
## Adjusted Cox Index
OARatio <- rbind(OARatio,RRAnalysisAdCox$OARatio$estimate)
## Adjusted and Calibrated Cox Index
OARatio <- rbind(OARatio,RRAnalysisCalAdCox$OARatio$estimate)
rownames(OARatio) <- c("Cox","Adj. Cox","Cal. Adj. Cox")
pander::pander(OARatio)
```

	O/A	Low	Upper	p.value
Cox	1.263	1.029	1.53	0.0217
Adj. Cox	1.290	1.051	1.57	0.0128
Cal. Adj. Cox	0.997	0.812	1.21	1.0000

Comparing NetBenefit

```
NetBen <- NULL
## Cox Index
NetBen <- rbind(NetBen,RRAnalysisCox$keyPoints$NetBenefit)
## Adjusted Cox Index
NetBen <- rbind(NetBen,RRAnalysisAdCox$keyPoints$NetBenefit)
## Adjusted and Calibrated Cox Index
NetBen <- rbind(NetBen,RRAnalysisCalAdCox$keyPoints$NetBenefit)
colnames(NetBen) <- rownames(RRAnalysisCox$keyPoints)
rownames(NetBen) <- c("Cox","Adj. Cox","Cal. Adj. Cox")
pander::pander(NetBen)
```

	@:0.9	@:0.95	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Cox	0.223	0.232	0.222	0.239	0.252	-0.02795
Adj. Cox	0.230	0.249	0.202	0.252	0.274	0.00617
Cal. Adj. Cox	0.196	0.217	0.168	0.220	0.244	0.01345

Compare the ROC AUC

```
pander::pander(pROC::roc.test(RRAnalysisCI$ROCRAnalysis$ROC.analysis$roc.predictor,
                              RRAnalysisAdCox$ROCRAnalysis$ROC.analysis$roc.predictor))
```

Table 70: DeLong's test for two correlated ROC curves:
`RRAnalysisCI$ROCAalysis$ROC.analysis$roc.predictor` and
`RRAnalysisAdCox$ROCAalysis$ROC.analysis$roc.predictor`

Test statistic	P value	Alternative hypothesis	AUC of roc1	AUC of roc2
-0.988	0.323	two.sided	0.692	0.702