Colon Cancer

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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
```

```
#library(corrplot)
source("~/GitHub/FRESA.CAD/R/RRPlot.R")
source("~/GitHub/FRESA.CAD/R/PoissonEventRiskCalibration.R")
```

```
data(cancer)
colon <- subset(colon,etype==1)
colon$etype <- NULL
rownames(colon) <- colon$id
colon$id <- NULL
colon <- colon[complete.cases(colon),]
time <- colon$time
status <- colon$status
data <- colon
data$time <- NULL
data$study <- NULL
table(data$status)
```

0 1 442 446

```
#dataColon <- as.data.frame(model.matrix(status~.*.,data))
dataColon <- as.data.frame(model.matrix(status~.*age,data))
dataColon$`(Intercept)` <- NULL
dataColon$time <- time/365
dataColon$status <- status
colnames(dataColon) <-str_replace_all(colnames(dataColon),":","_")
colnames(dataColon) <-str_replace_all(colnames(dataColon),"\\.","_")
colnames(dataColon) <-str_replace_all(colnames(dataColon),"\\+","_")
data <- NULL

trainsamples <- sample(nrow(dataColon),0.7*nrow(dataColon))
dataColonTrain <- dataColon[trainsamples,]
dataColonTest <- dataColon[-trainsamples,]


pander::pander(table(dataColonTrain$status))
```

0	1
313	308

```
pander::pander(table(dataColonTest$status))
```

0	1
129	138

Modeling

```
ml <- BSWiMS.model(Surv(time,status)~1,data=dataColonTrain,NumberofRepeats = 10)
```

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

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

Table 3: Table continues below

	Estimate	lower	HR	upper	u.Accuracy
rxLev__5FU__age	-0.004031	0.9942	0.996	0.9977	0.5845
rxLev__5FU	-0.1961	0.7487	0.8219	0.9023	0.5845
age__node4	0.003271	1.002	1.003	1.005	0.5974
age__nodes	0.0003607	1	1	1.001	0.6006
node4	0.204	1.082	1.226	1.389	0.5974
nodes	0.03575	1.008	1.036	1.065	0.6055
extent	0.1219	1.027	1.13	1.243	0.525
adhere	0.08741	1.012	1.091	1.177	0.5314
differ	4.082e-07	1	1	1	0.5362
age	-0.001283	0.9976	0.9987	0.9999	0.5056
rxLev	9.671e-08	1	1	1	0.5378

Table 4: Table continues below

	r.Accuracy	full.Accuracy	u.AUC	r.AUC	full.AUC
rxLev_5FU_age	0.6009	0.6169	0.5858	0.5992	0.6163
rxLev_5FU	0.6017	0.6028	0.5858	0.6001	0.6031
age_node4	0.5917	0.6017	0.5955	0.5927	0.6022
age_nodes	0.5712	0.6103	0.5994	0.572	0.6099
node4	0.612	0.6142	0.5955	0.6122	0.6134
nodes	0.6046	0.6169	0.6043	0.6036	0.6163
extent	0.6023	0.6084	0.528	0.6013	0.6079
adhere	0.6075	0.611	0.5284	0.6064	0.61
differ	0.496	0.5362	0.5336	0.5	0.5336
age	0.5996	0.6156	0.5053	0.5987	0.6149
rxLev	0.496	0.5378	0.5363	0.5	0.5363

	IDI	NRI	z.IDI	z.NRI	Delta.AUC	Frequency
rxLev_5FU_age	0.02345	0.3431	4.443	4.572	0.0171	1
rxLev_5FU	0.02107	0.3422	4.198	4.558	0.002999	1
age_node4	0.02022	0.349	4.008	5.055	0.009442	1
age_nodes	0.01824	0.2767	3.912	3.637	0.03789	1
node4	0.01186	0.2969	3.309	4.366	0.001207	1
nodes	0.006881	0.1462	2.589	1.913	0.01266	1
extent	0.009369	0.1136	2.556	2.114	0.006613	0.9
adhere	0.00603	0.1181	2.419	2.182	0.003684	0.8
differ	0.00803	0.1342	2.241	2.246	0.03356	0.7
age	0.00557	0.1491	2.204	1.867	0.01617	0.2
rxLev	0.004556	0.1453	1.957	1.961	0.03632	0.2

Cox Model Performance

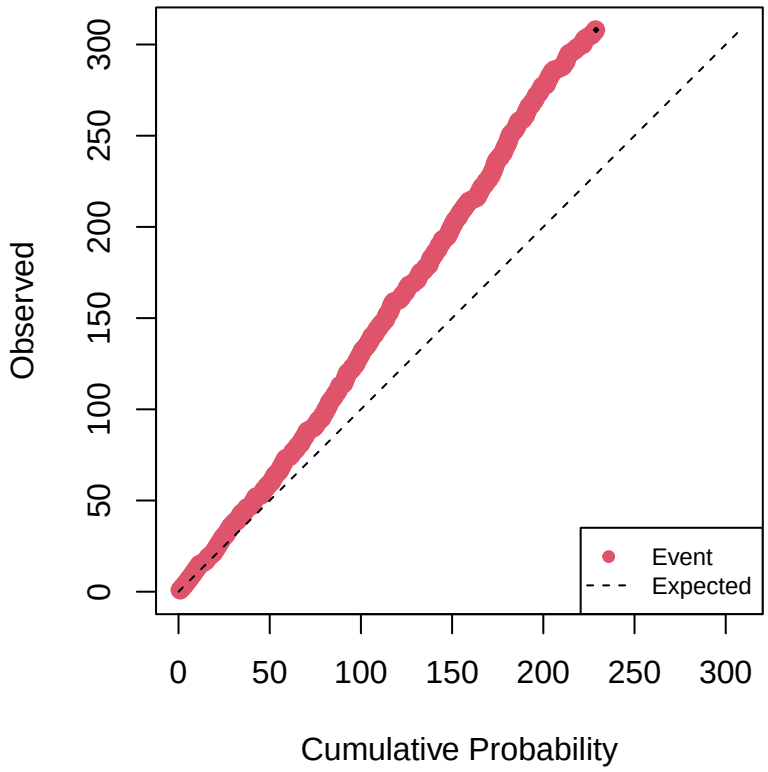
Here we evaluate the model using the RRPlot() function.

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

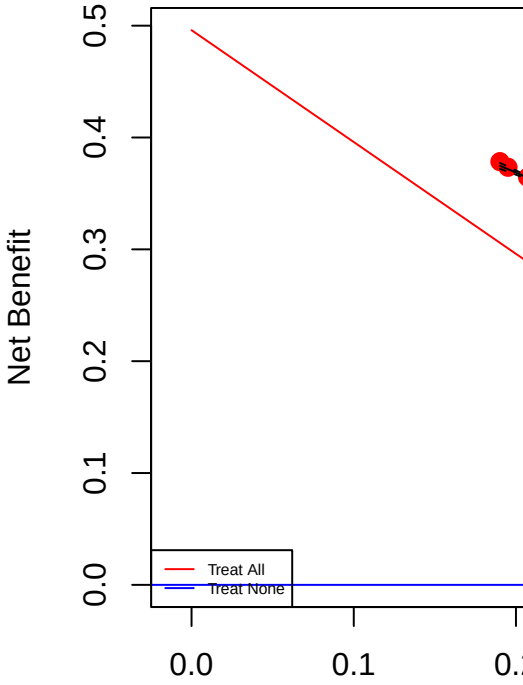
```
index <- predict(ml,dataColonTrain)
timeinterval <- 2*mean(subset(dataColonTrain,status==1)$time)

h0 <- sum(dataColonTrain$status & dataColonTrain$time <= timeinterval)
h0 <- h0/sum((dataColonTrain$time > timeinterval) | (dataColonTrain$status==1))

rdata <- cbind(dataColonTrain$status,ppoisGzero(index,h0))

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

Cumulative vs. Observed: Raw Train: Colon Cancer

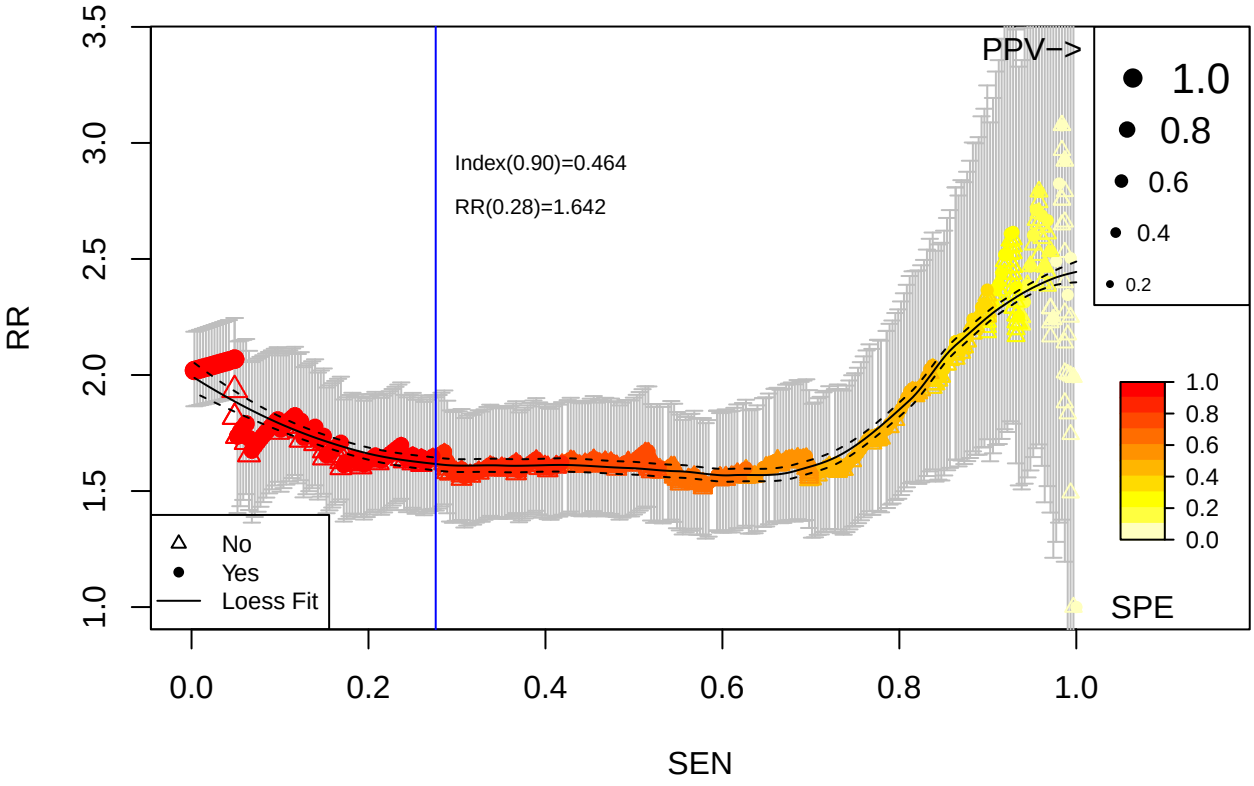


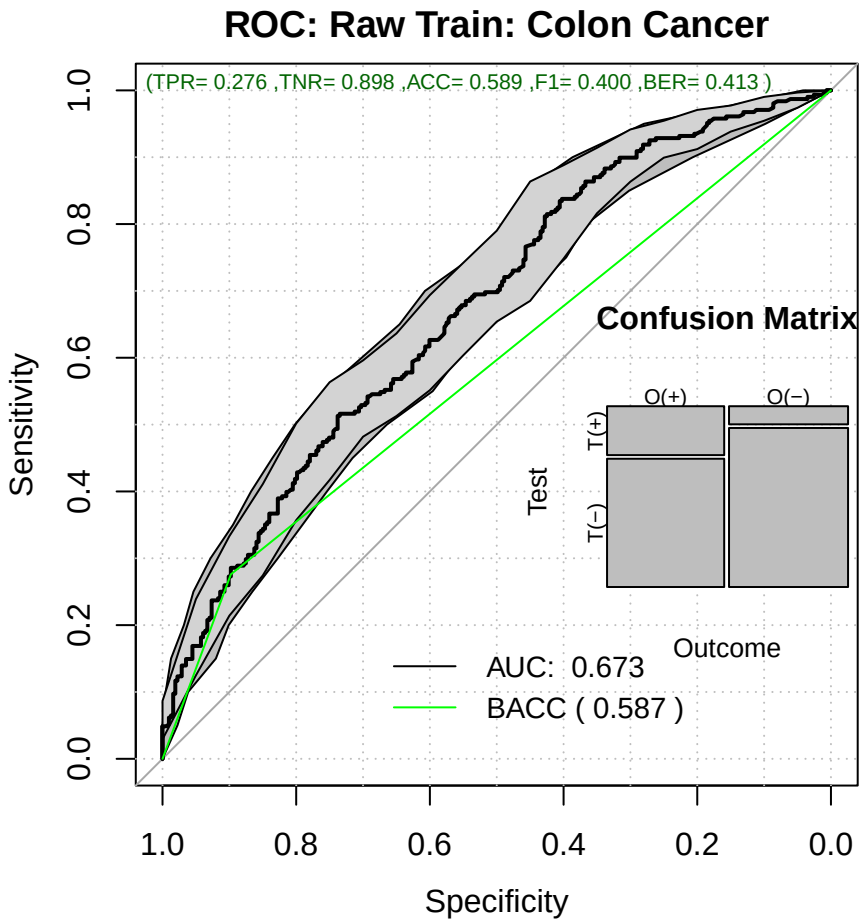
Cumulative Probability

Decision Curve

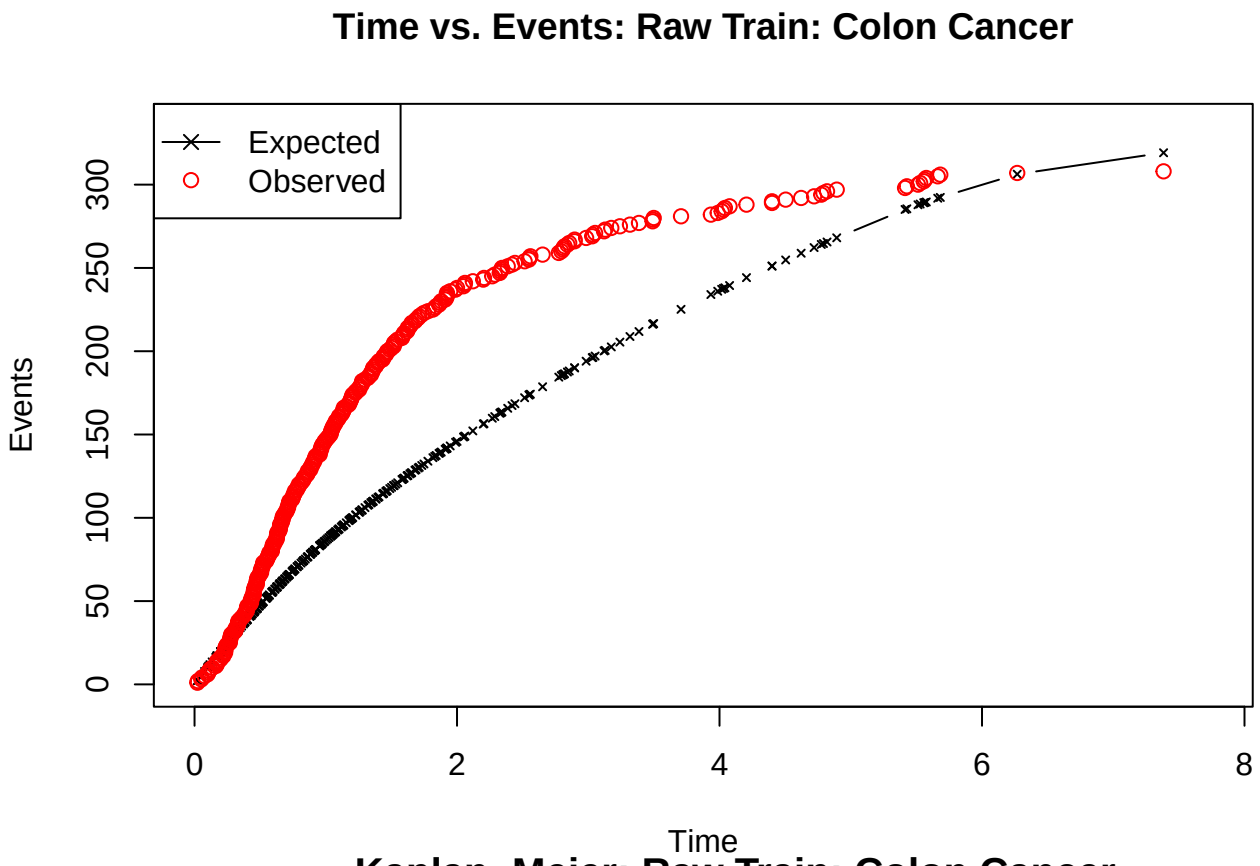


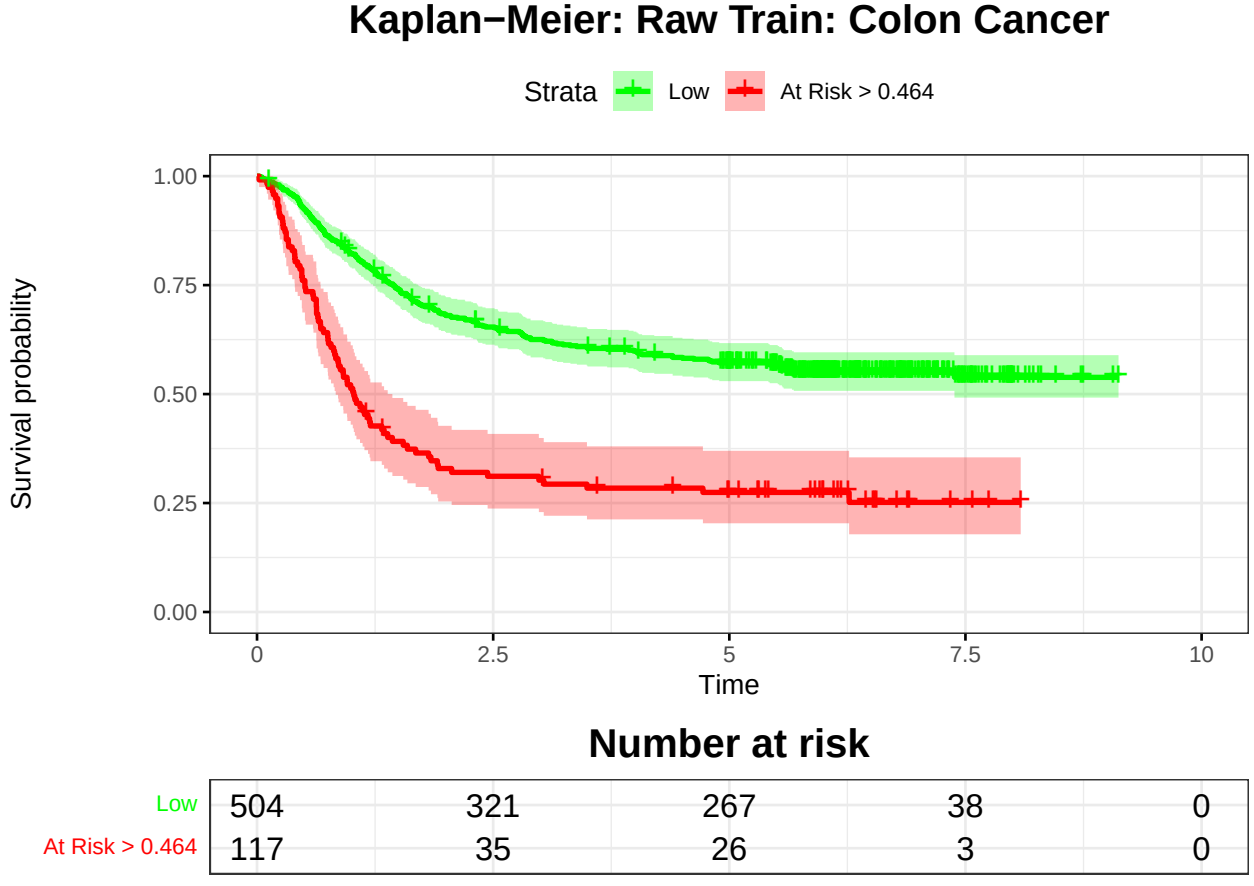
Relative Risk: Raw Train: Colon Cancer





ROC: Raw Train: Colon Cancer





Number at risk

Low	504	321	267	38	0
At Risk > 0.464	117	35	26	3	0

Uncalibrated Performance Report

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

Table 6: O/E Ratio

est	lower	upper
0.9651	0.8603	1.079

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

Table 7: O/E Ratio

mean	50%	2.5%	97.5%
1.479	1.479	1.453	1.508

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

Table 8: O/Acum Ratio

mean	50%	2.5%	97.5%
1.311	1.312	1.306	1.316

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

mean.C Index	median	lower	upper
0.6525	0.6523	0.6214	0.681

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

Table 10: ROC AUC

est	lower	upper
0.6734	0.6316	0.7152

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

Table 11: Sensitivity

est	lower	upper
0.276	0.2268	0.3295

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

Table 12: Specificity

est	lower	upper
0.8978	0.8587	0.929

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

Table 13: Probability Thresholds

90%
0.4643

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

Table 14: Risk Ratio

est	lower	upper
1.642	1.416	1.904

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

Table 15: Logrank test Chisq = 59.085144 on 1 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	504	223	268.1	7.585	59.09
class=1	117	85	39.9	50.96	59.09

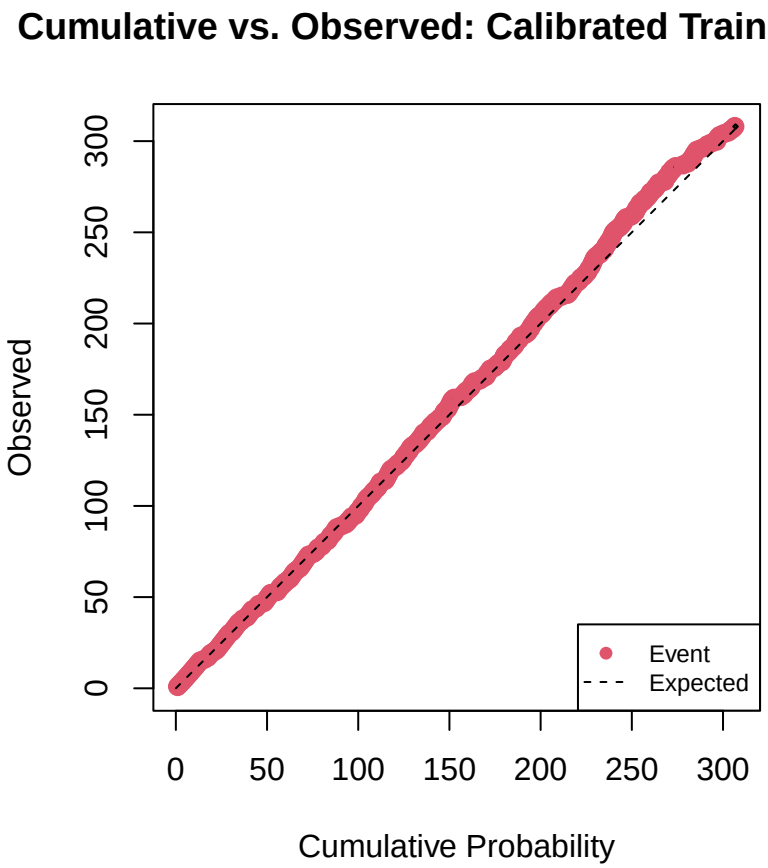
Cox Calibration

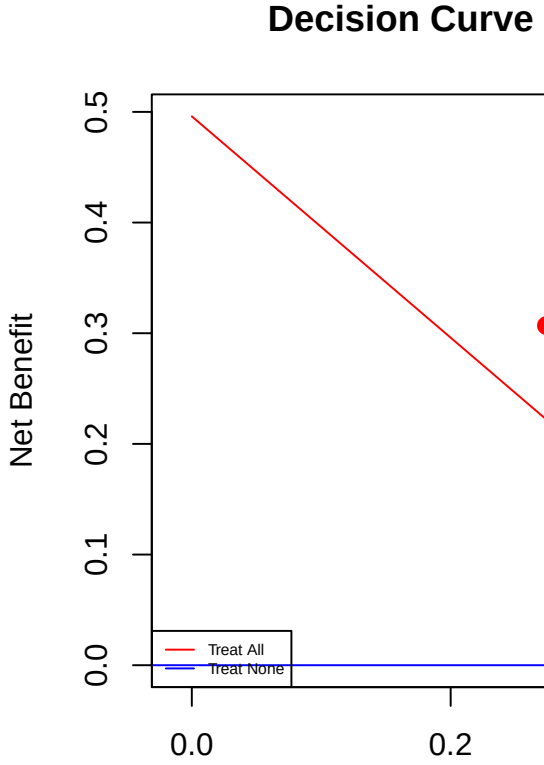
```
op <- par(no.readonly = TRUE)


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

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

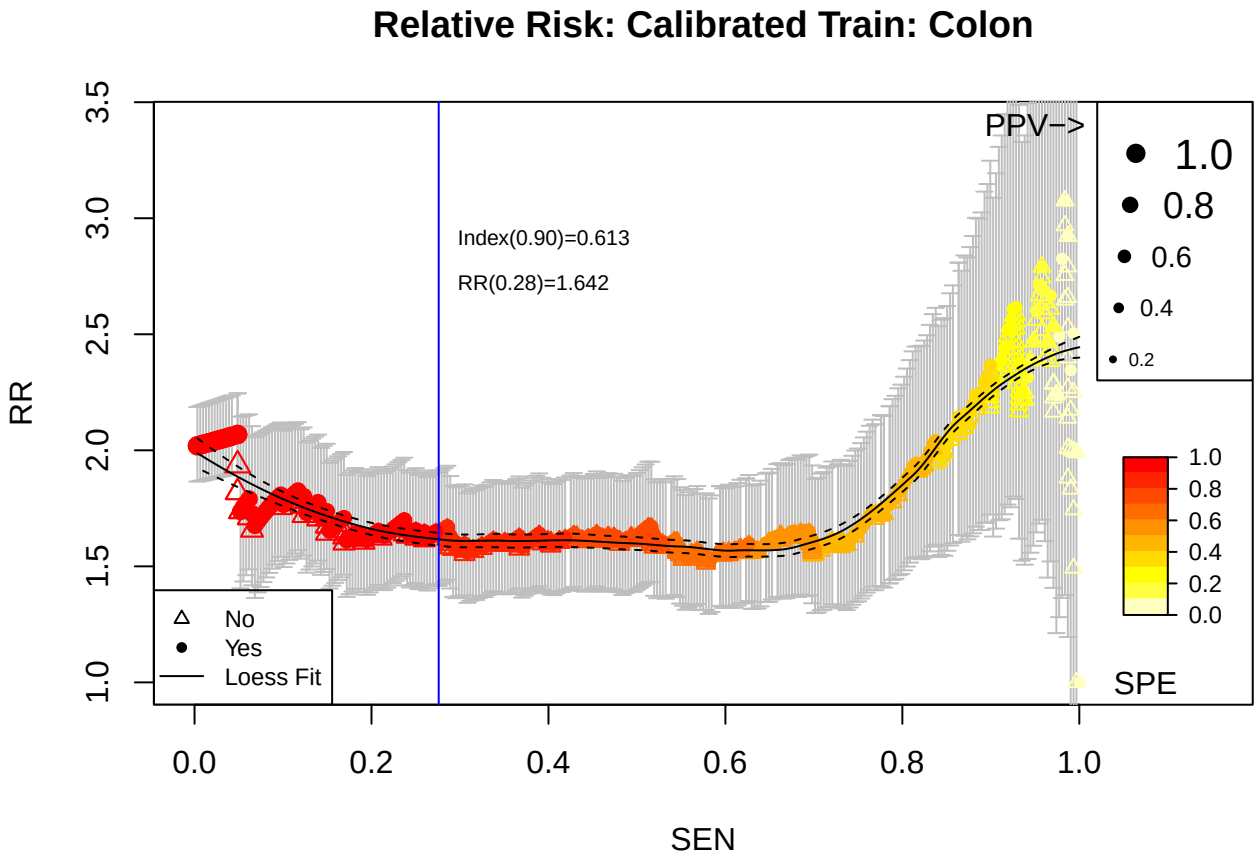
h0	Gain	DeltaTime
0.6696	1.519	2.942

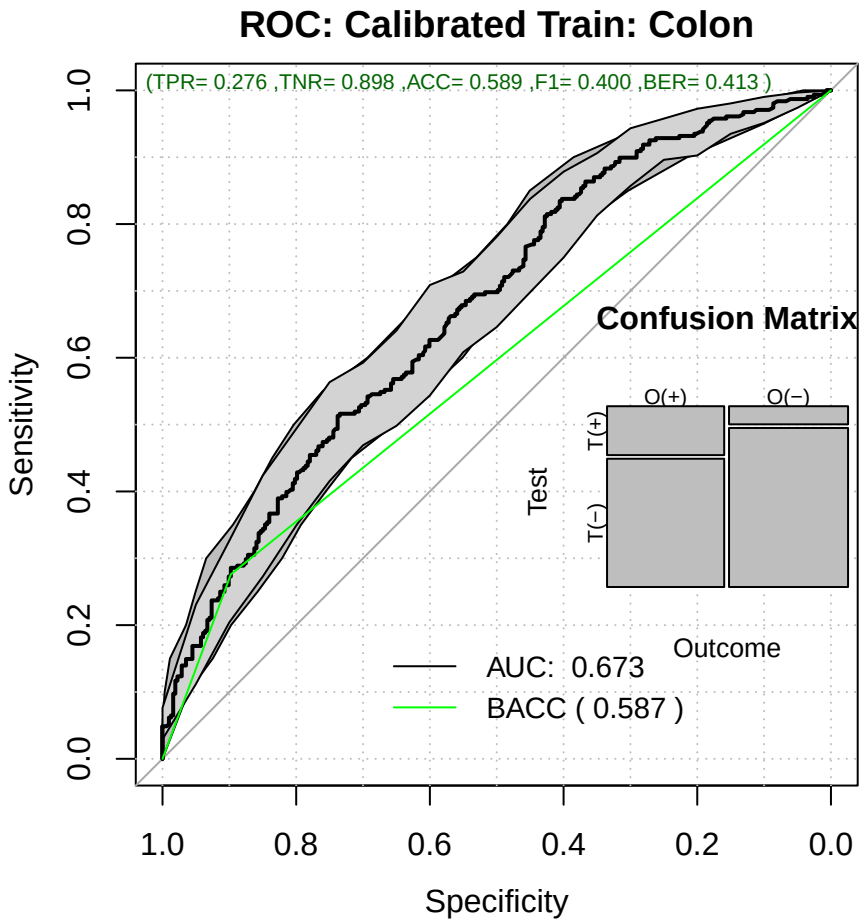
The RRplot() of the calibrated model

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

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


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

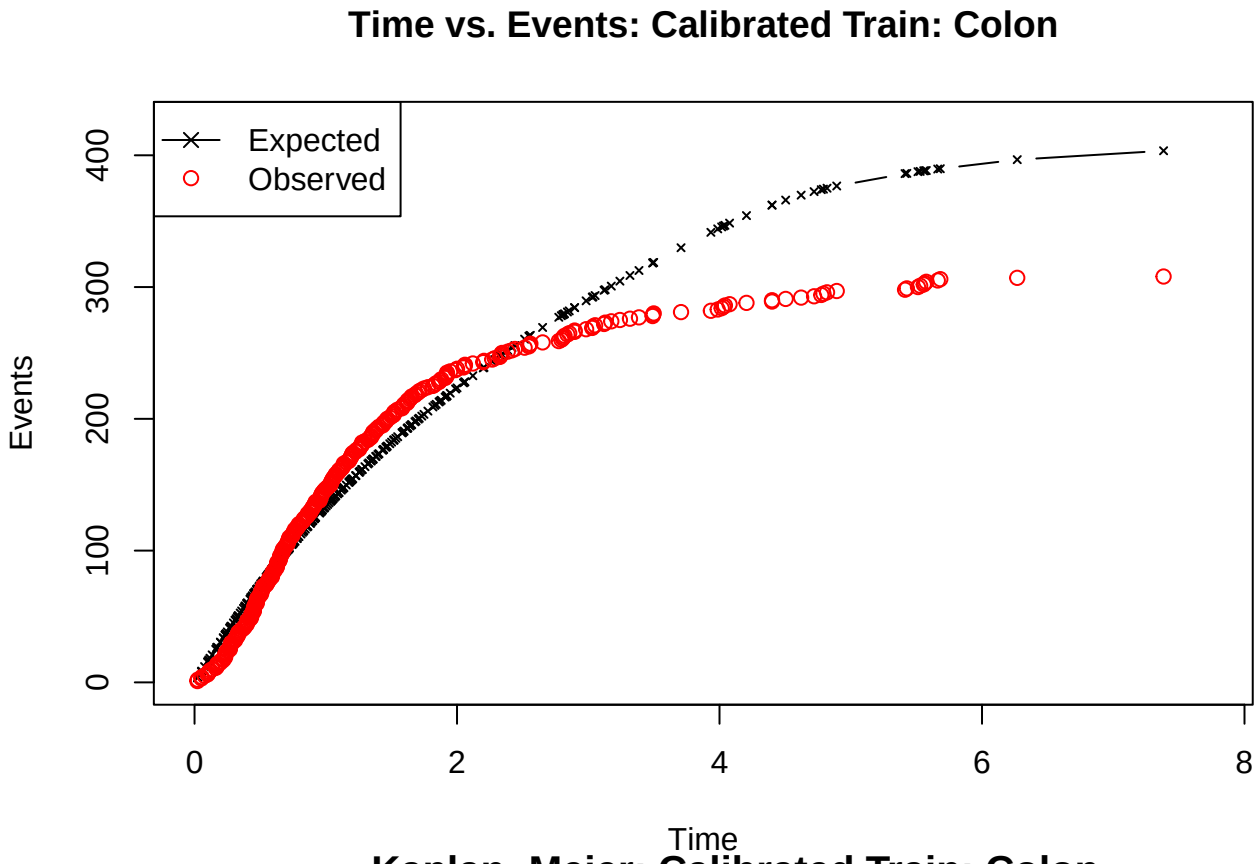


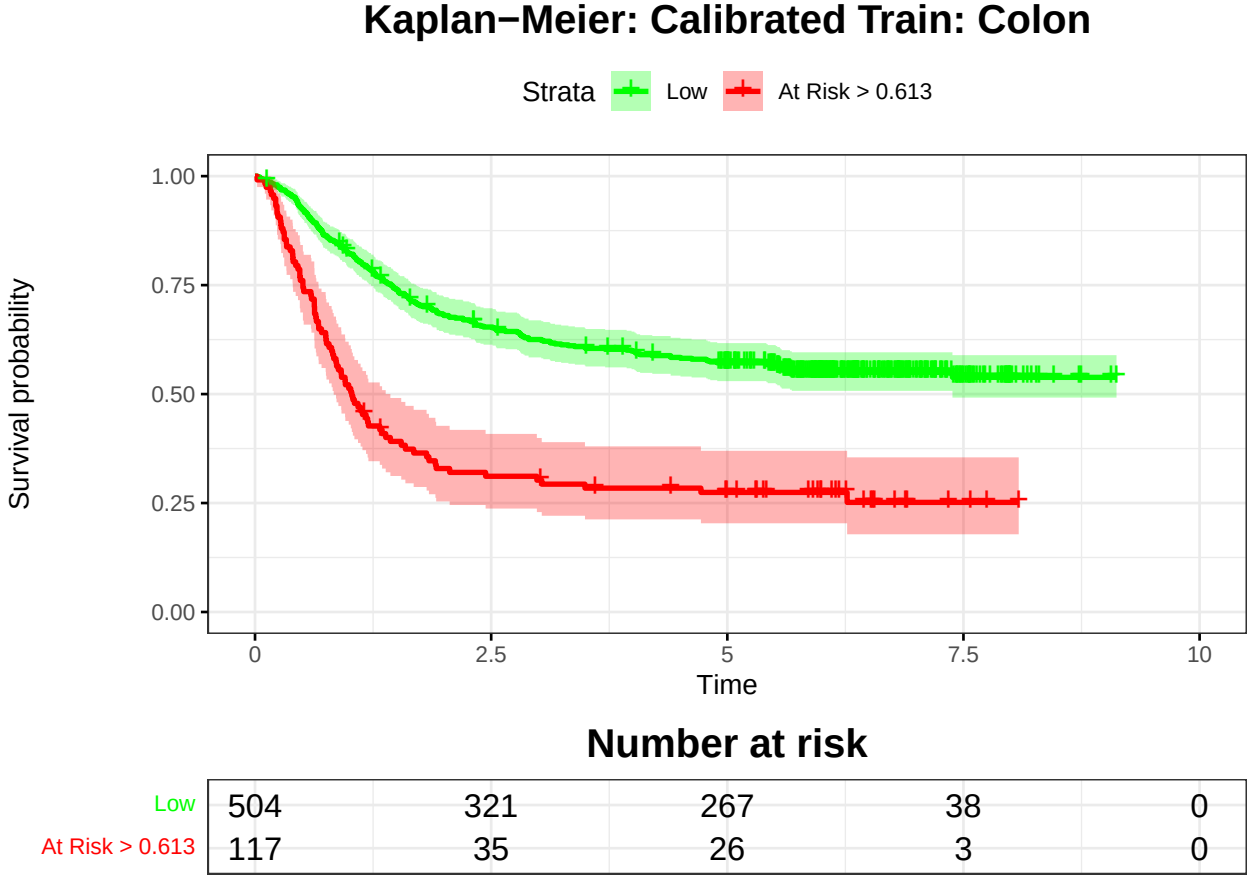



Relative Risk: Calibrated Train: Colon
RR
SEN
PPV−>
SPE
Index(0.90)=0.613
RR(0.28)=1.642
No
Yes
Loess Fit
1.0
0.8
0.6
0.4
0.2
0.0
3.5
3.0
2.5
2.0
1.5
1.0
0.0
0.2
0.4
0.6
0.8
1.0



ROC: Calibrated Train: Colon





Number at risk

Low	504	321	267	38	0
At Risk > 0.613	117	35	26	3	0

Calibrated Train Performance

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

Table 17: O/E Ratio

est	lower	upper
0.7634	0.6805	0.8536

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

Table 18: O/E Ratio

mean	50%	2.5%	97.5%
0.9684	0.9687	0.9507	0.9851

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

Table 19: O/Acum Ratio

mean	50%	2.5%	97.5%
1.013	1.013	1.011	1.015

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

mean.C Index	median	lower	upper
0.6525	0.6524	0.6246	0.6798

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

Table 21: ROC AUC

est	lower	upper
0.6734	0.6316	0.7152

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

Table 22: Sensitivity

est	lower	upper
0.276	0.2268	0.3295

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

Table 23: Specificity

est	lower	upper
0.8978	0.8587	0.929

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

Table 24: Probability Thresholds

90%
0.6125

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

Table 25: Risk Ratio

est	lower	upper
1.642	1.416	1.904

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

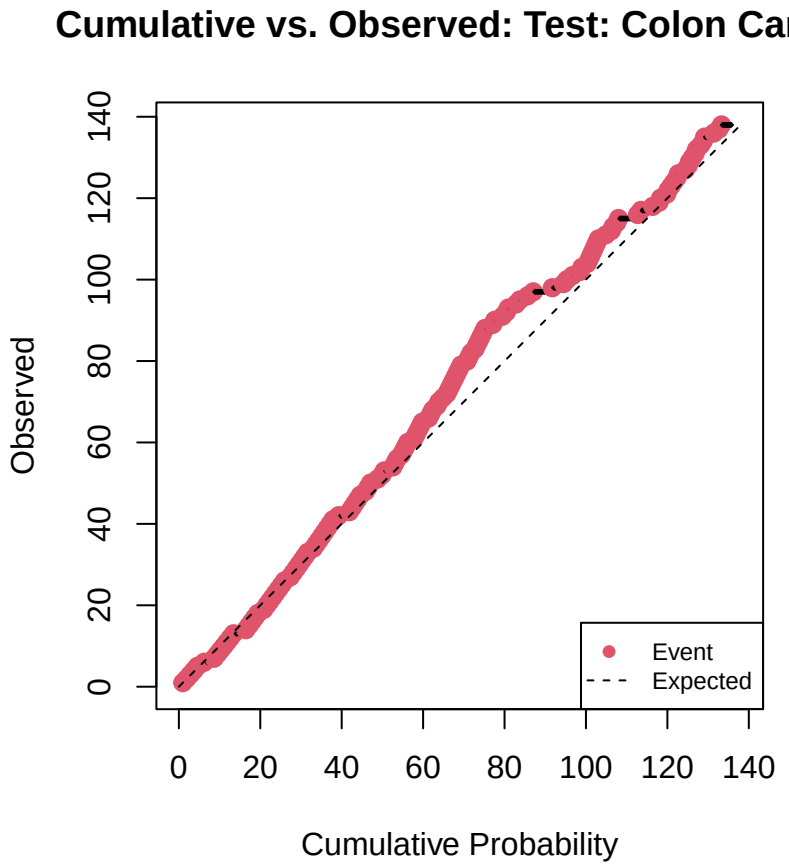
Table 26: Logrank test Chisq = 59.085144 on 1 degrees of freedom, p = 0.000000

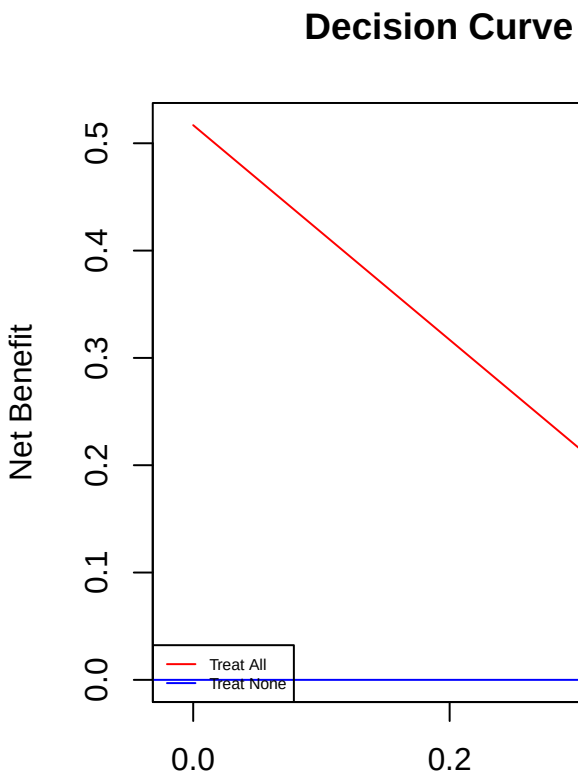
	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	504	223	268.1	7.585	59.09
class=1	117	85	39.9	50.96	59.09

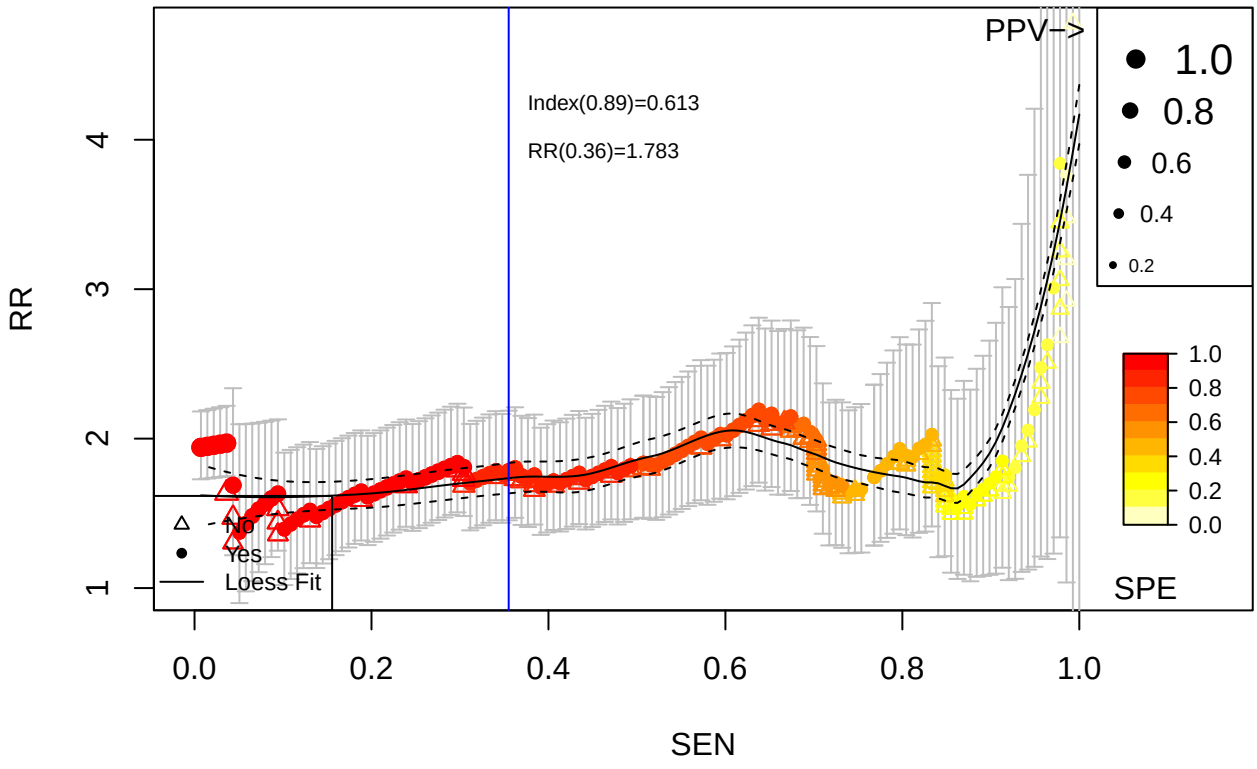
Evaluating on the test set

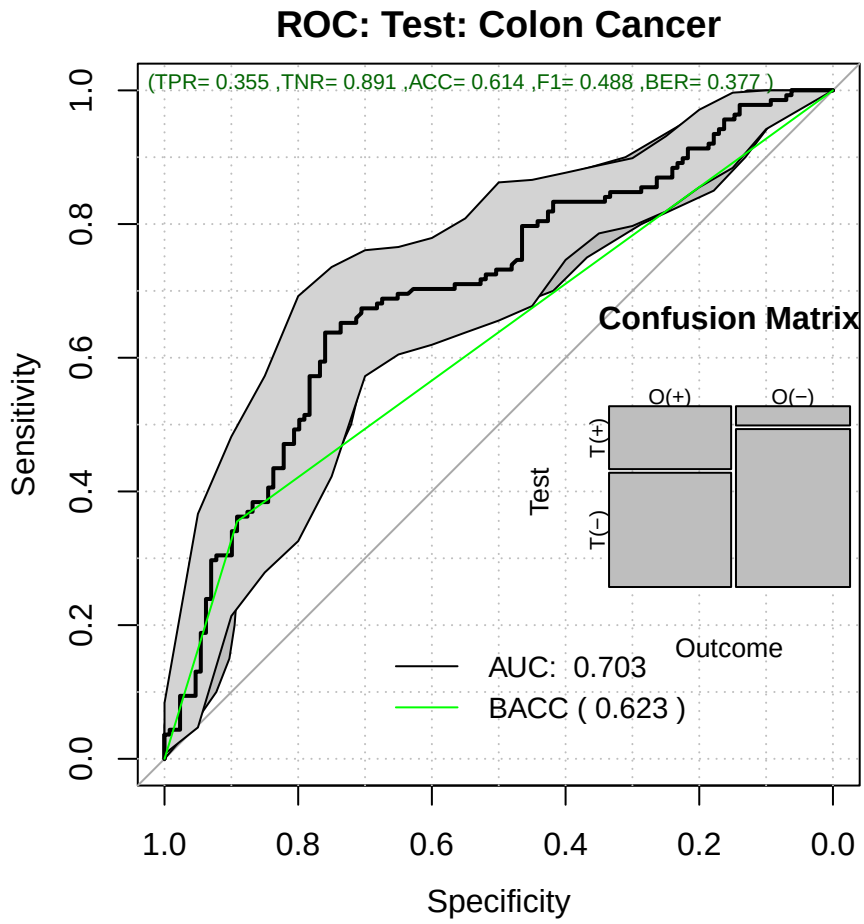
The calibrated h0 and timeinterval were estimated on the training set

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

rrAnalysisTest <- RRPlot(rdata,atThr = rrAnalysisTrain$thr_atP,
                    timetoEvent=dataColonTest$time,
                    title="Test: Colon Cancer",
                    ysurvlim=c(0.00,1.0),
                    riskTimeInterval=timeinterval)
```

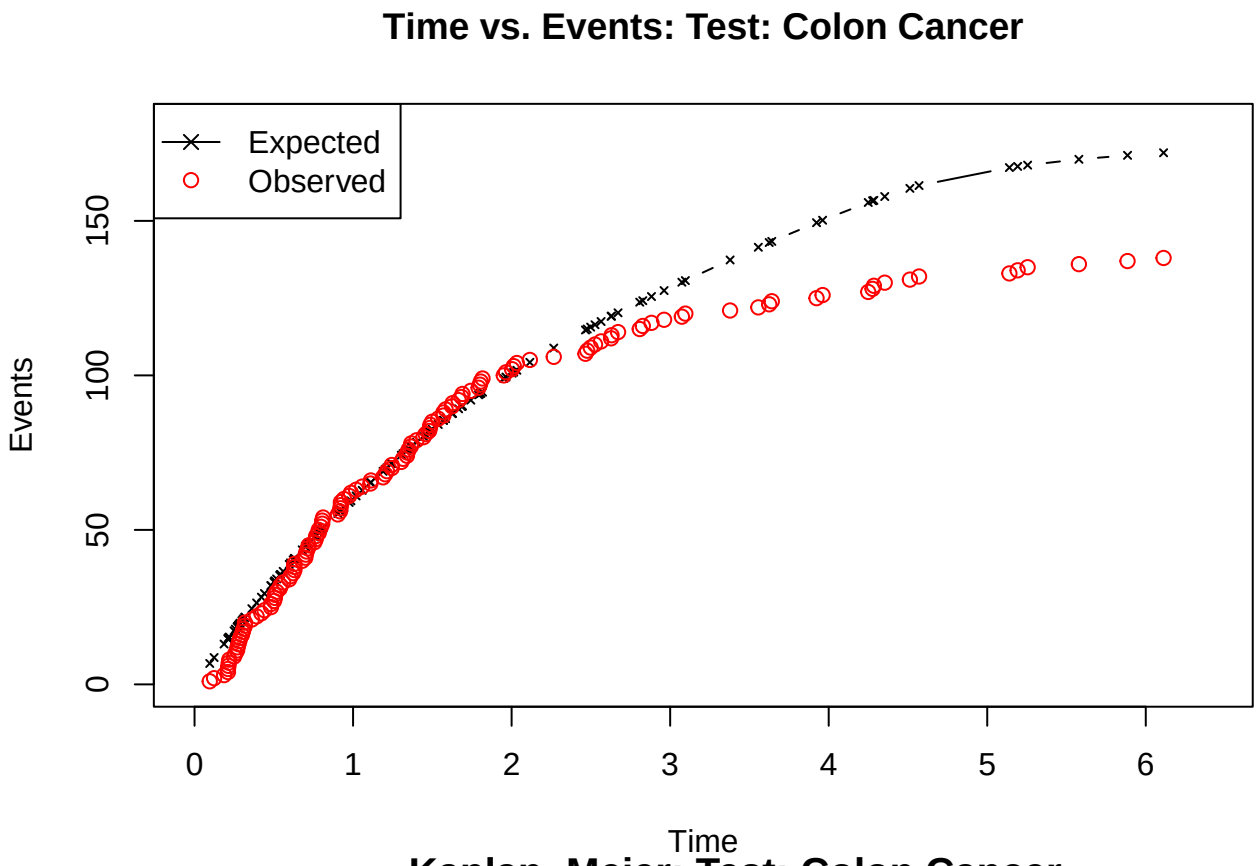

Cumulative vs. Observed: Test: Colon Cancer
Observed
0
20
40
60
80
100
120
140
Event
Expected
Cumulative Probability

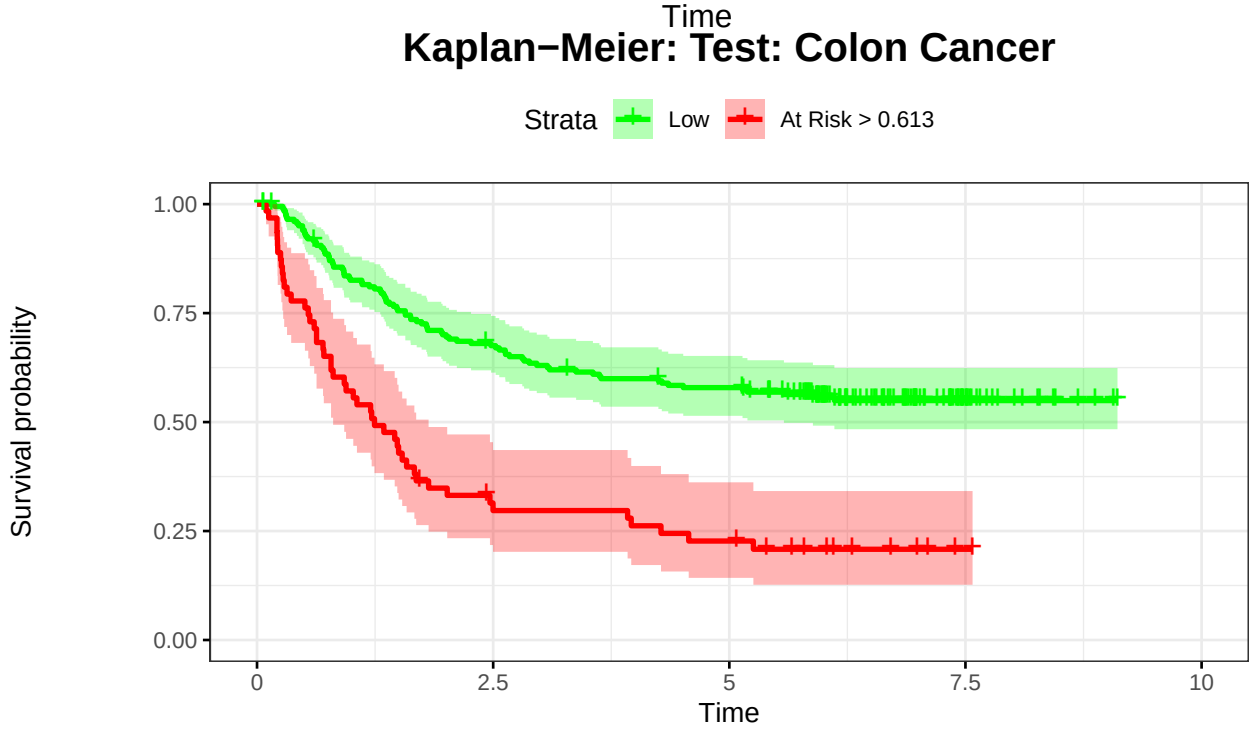

Decision Curve
Net Benefit
0.0
0.1
0.2
0.3
0.4
0.5
Treat All
Treat None
0.0
0.2


Relative Risk: Test: Colon Cancer
RR
1
2
3
4
PPV–>
1.0
0.8
0.6
0.4
0.2
Index(0.89)=0.613
RR(0.36)=1.783
No
Yes
Loess Fit
1.0
0.8
0.6
0.4
0.2
0.0
SPE
0.0
0.2
0.4
0.6
0.8
1.0
SEN



ROC: Test: Colon Cancer





Number at risk

Low	204	134	113	20	0
At Risk > 0.613	63	17	13	1	0

Test Performance

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

Table 27: O/E Ratio

est	lower	upper
0.8021	0.6739	0.9476

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

Table 28: O/E Ratio

mean	50%	2.5%	97.5%
0.9212	0.921	0.9002	0.941

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

Table 29: O/Acum Ratio

mean	50%	2.5%	97.5%
1.046	1.046	1.039	1.053

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

mean.C Index	median	lower	upper
0.6525	0.6526	0.6058	0.6979

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

Table 31: ROC AUC

est	lower	upper
0.7033	0.6405	0.766

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

Table 32: Sensitivity

est	lower	upper
0.3551	0.2755	0.441

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

Table 33: Specificity

est	lower	upper
0.8915	0.8246	0.9394

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

Table 34: Probability Thresholds

90%
0.6125

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

Table 35: Risk Ratio

est	lower	upper
1.783	1.453	2.187

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

Table 36: Logrank test Chisq = 36.794054 on 1 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	204	89	115.3	5.988	36.79
class=1	63	49	22.73	30.37	36.79

Cross-Validation

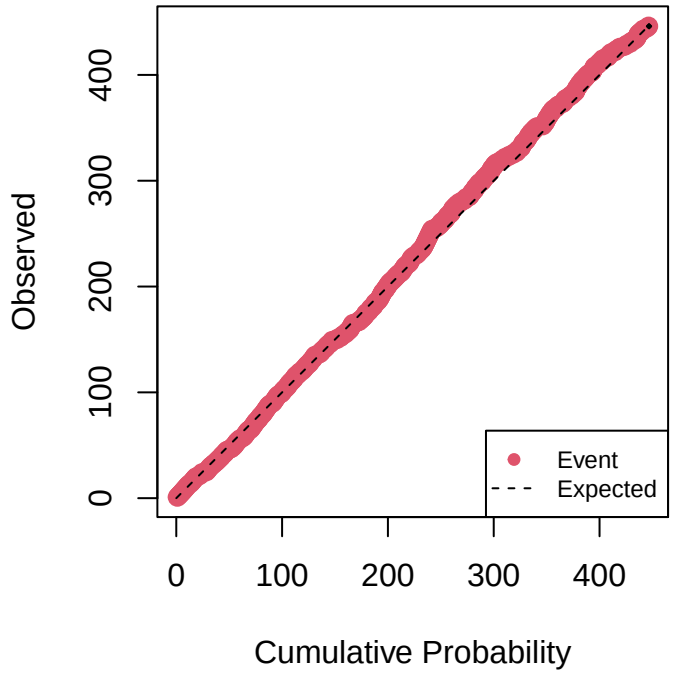
Here we will cross validate the training set and evaluate also on the testing set. The h0 and the timeinterval are the ones estimated on the calibration process

```
rcv <- randomCV(theData=dataColonTrain,
                theOutcome = Surv(time,status)~1,
                fittingFunction=BSWiMS.model,
                trainFraction = 0.75,
                repetitions=50,
                classSamplingType = "Pro",
                testingSet=dataColonTest
         )
```

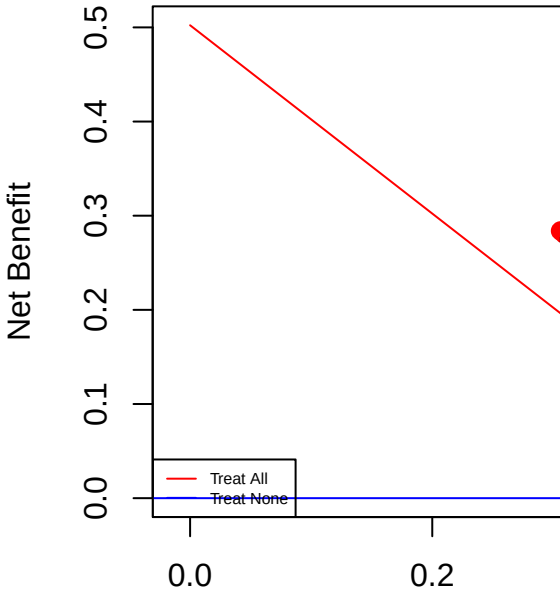
```
## .[+++++].[++++].[+++].[+++-].[+++++].[+++-].[++++].[+++++].[+++++].[+++]10  Tested: 848 Avg. Selecte
## .[++++-].[++++].[++++++].[++++-].[+++].[++++].[++].[+++].[+++].[++]20  Tested: 886 Avg. Selected: 8.
## .[+++-].[+++-].[+++++].[++++].[+++].[++++-].[++].[+++++++].[++++--].[++++-]30  Tested: 888 Avg. Sele
## .[+++-].[++++].[+++-].[+++].[+++].[++++].[+++].[++-].[+++++].[+++-]40  Tested: 888 Avg. Selected: 8
## .[++++].[+++-].[+++++].[+++-].[+++].[+++--].[++++].[+++].[++++-].[++++-]50  Tested: 888 Avg. Selecte
##
```

```
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

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

Cumulative vs. Observed: CV Test: Colon Cancer



Decision Curve An

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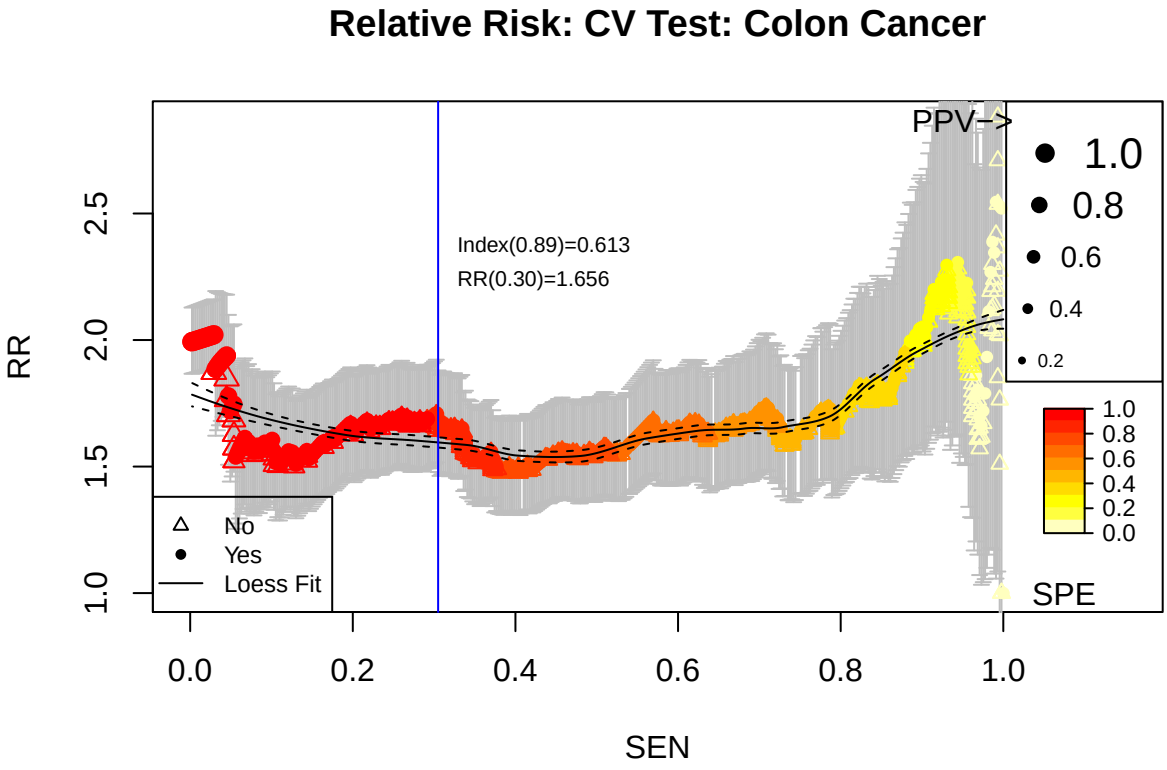
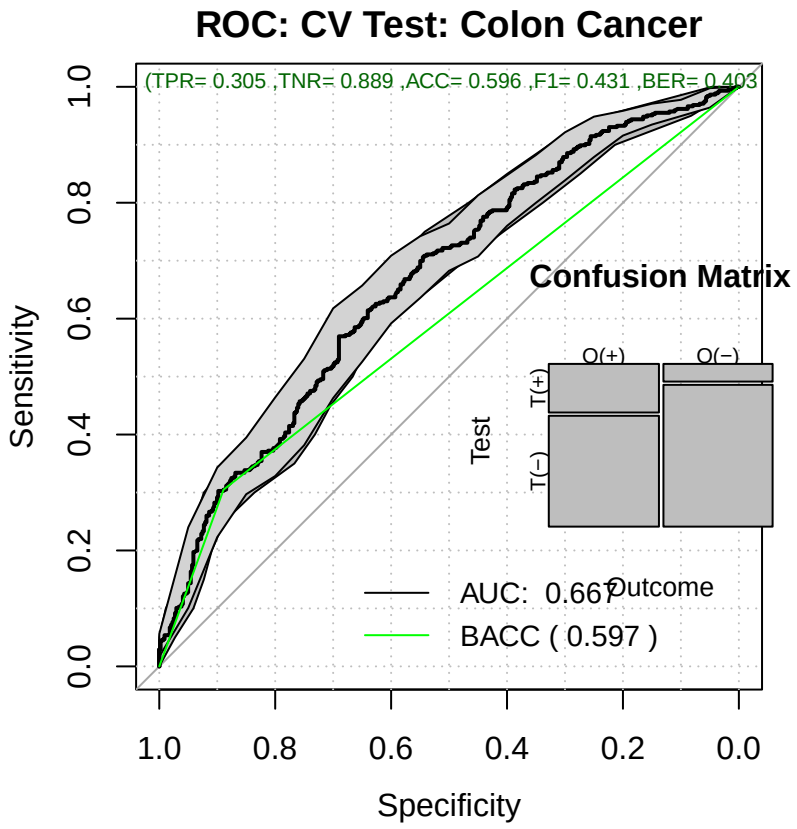
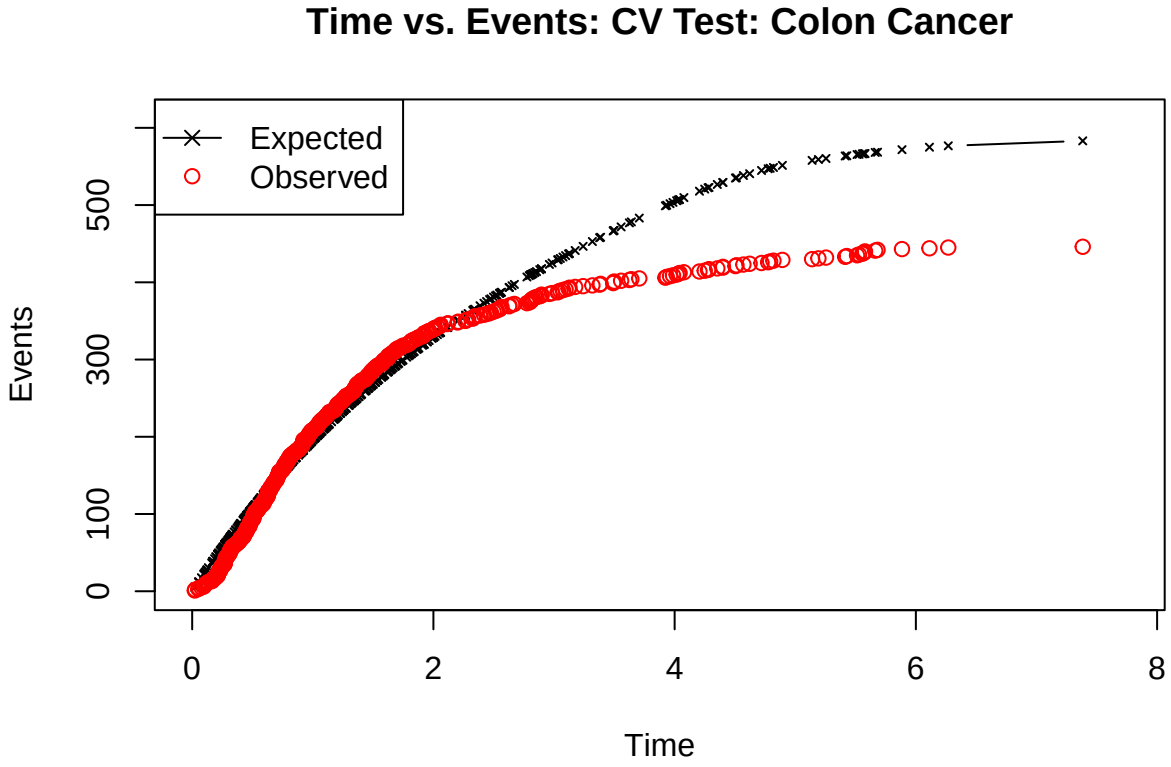
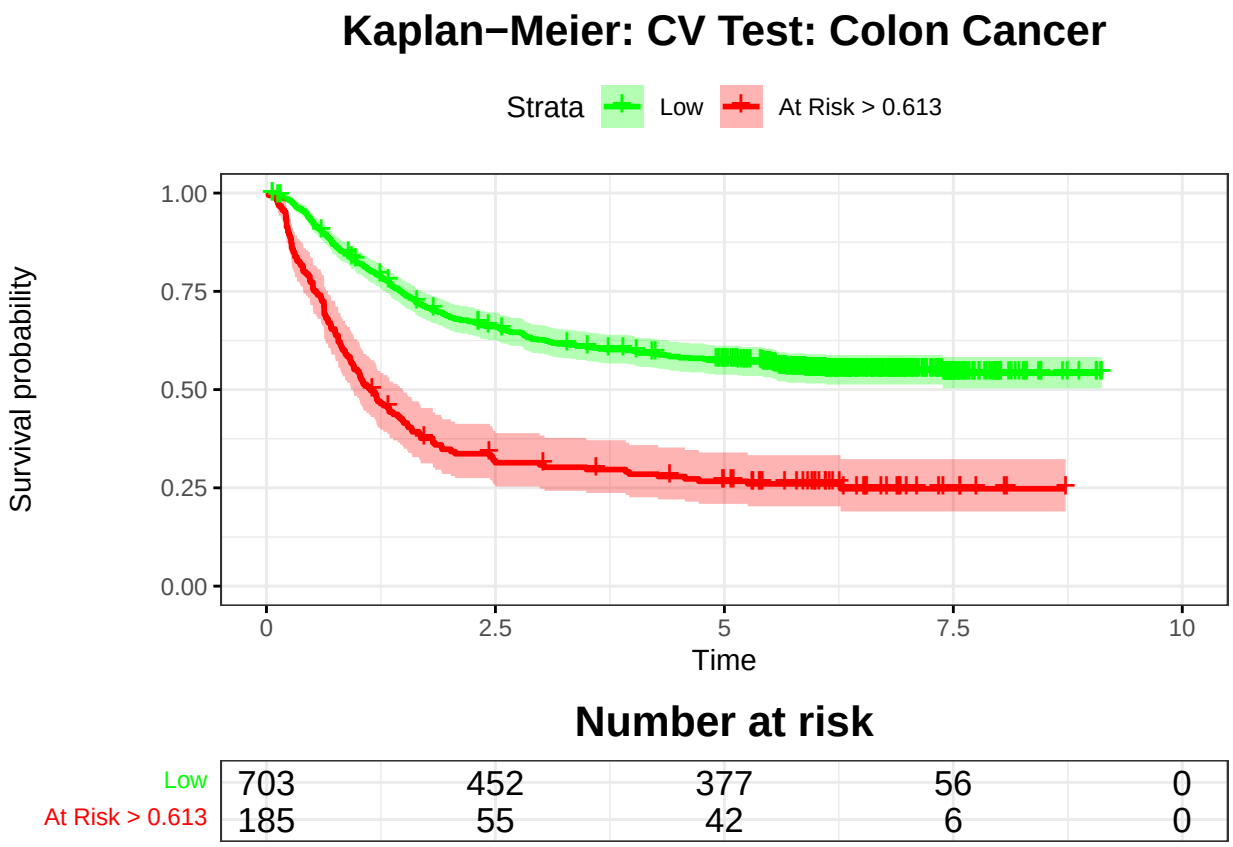



```
## ROC: CV Test: Colon Cancer
```




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





CV Test Performance

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

Table 37: O/E Ratio

est	lower	upper
0.7648	0.6955	0.8392

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

Table 38: O/E Ratio

mean	50%	2.5%	97.5%
0.9408	0.9413	0.9274	0.9535

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

Table 39: O/Acum Ratio

mean	50%	2.5%	97.5%
1.008	1.008	1.005	1.01

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

mean.C Index	median	lower	upper
0.6437	0.6435	0.6162	0.6689

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

Table 41: ROC AUC

est	lower	upper
0.6669	0.6316	0.7021

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

Table 42: Sensitivity

est	lower	upper
0.3049	0.2625	0.35

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

Table 43: Specificity

est	lower	upper
0.8891	0.8561	0.9169

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

Table 44: Probability Thresholds

90%
0.6125

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

Table 45: Risk Ratio

est	lower	upper
1.656	1.468	1.868

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

Table 46: Logrank test Chisq = 89.573729 on 1 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	703	310	380.5	13.05	89.57
class=1	185	136	65.55	75.73	89.57