

Colon Cancer

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1 RRPlot and the Colon data set

1.0.1 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(corrplot)
#source("~/GitHub/FRESA.CAD/R/RRPlot.R")
#source("~/GitHub/FRESA.CAD/R/PoissonEventRiskCalibration.R")
op <- par(no.readonly = TRUE)
pander::panderOptions('digits', 3)
```

```
#pander::panderOptions('table.split.table', 400)
pander::panderOptions('keep.trailing.zeros', TRUE)
```

1.1 The data set

```
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~.*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
301	320

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

0	1
141	126

1.2 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
age_nodes	0.000458	1.000	1.000	1.001	0.607
age	-0.020172	0.973	0.980	0.987	0.502
age_node4	0.005125	1.003	1.005	1.007	0.614
age_extent	0.005018	1.003	1.005	1.007	0.536
extent	0.187439	1.107	1.206	1.314	0.580
node4	0.187704	1.100	1.206	1.323	0.614
rxLev_5FU_age	-0.002388	0.996	0.998	0.999	0.586
rxLev_5FU	-0.190602	0.748	0.826	0.913	0.586
adhere	0.432738	1.202	1.541	1.976	0.530
age_adhere	-0.005721	0.990	0.994	0.998	0.530
nodes	0.018295	1.004	1.018	1.034	0.618

Table 4: Table continues below

	r.Accuracy	full.Accuracy	u.AUC	r.AUC	full.AUC
age_nodes	0.564	0.623	0.612	0.570	0.626
age	0.620	0.640	0.504	0.624	0.641
age_node4	0.624	0.640	0.621	0.622	0.641
age_extent	0.628	0.640	0.535	0.632	0.641
extent	0.622	0.658	0.569	0.627	0.658
node4	0.639	0.658	0.621	0.639	0.658
rxLev_5FU_age	0.630	0.658	0.581	0.636	0.658
rxLev_5FU	0.624	0.640	0.581	0.628	0.641
adhere	0.602	0.615	0.541	0.607	0.620
age_adhere	0.609	0.615	0.541	0.613	0.620
nodes	0.648	0.658	0.623	0.645	0.660

	IDI	NRI	z.IDI	z.NRI	Delta.AUC	Frequency
age_nodes	0.03263	0.379	6.04	5.11	0.05648	1.0
age	0.03251	0.272	5.22	3.42	0.01636	1.0
age_node4	0.02950	0.422	4.99	6.23	0.01836	1.0
age_extent	0.02683	0.277	4.56	4.80	0.00865	1.0
extent	0.02368	0.272	4.28	4.71	0.03110	1.0
node4	0.01870	0.398	4.07	5.97	0.01985	1.0
rxLev_5FU_age	0.01677	0.324	3.97	4.35	0.02218	1.0
rxLev_5FU	0.01463	0.324	3.75	4.35	0.01279	1.0
adhere	0.00951	0.367	3.41	6.52	0.01329	0.7
age_adhere	0.00664	0.486	2.88	6.63	0.00724	0.7
nodes	0.00570	0.158	2.43	2.04	0.01560	1.0

1.3 Cox Model Performance

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

1.3.1 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

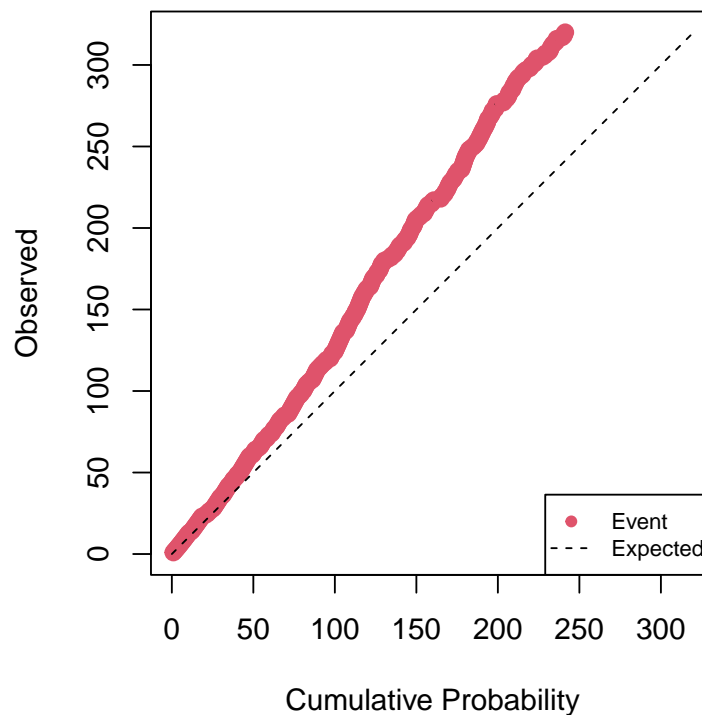
```
index <- predict(ml,dataColonTrain)
timeinterval <- 2*mean(subset(dataColonTrain,status==1)$time)

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

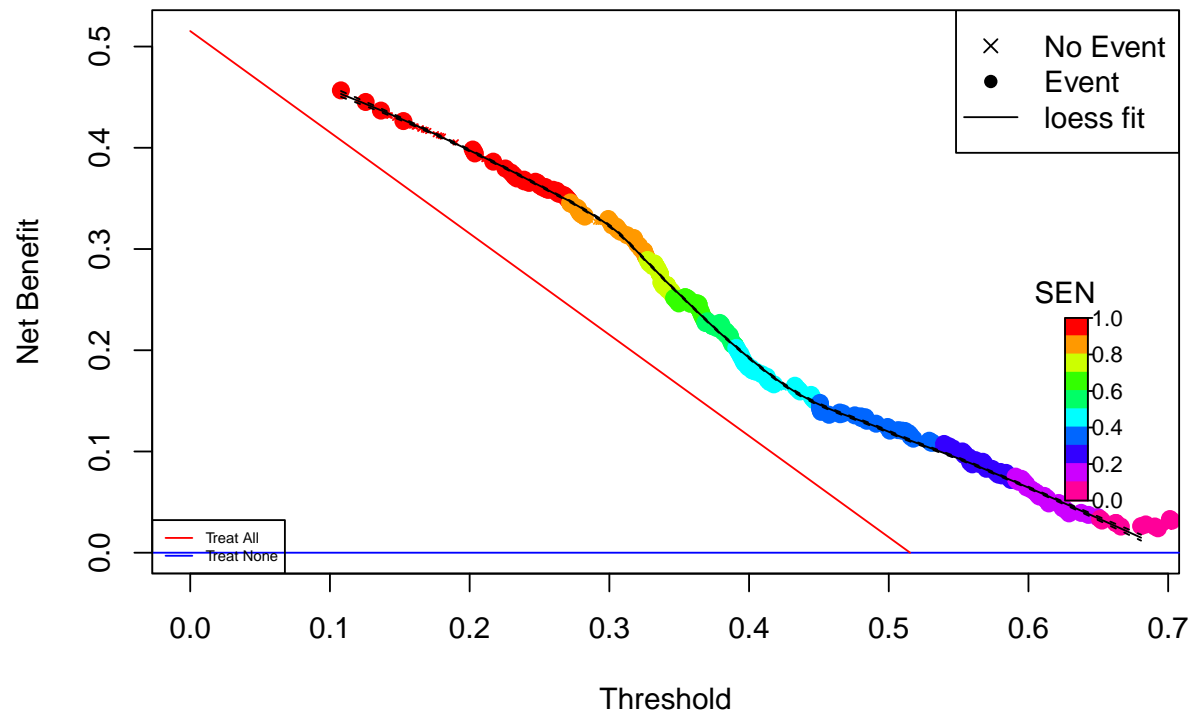
rdata <- cbind(dataColonTrain$status,ppoisGzero(index,h0))

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

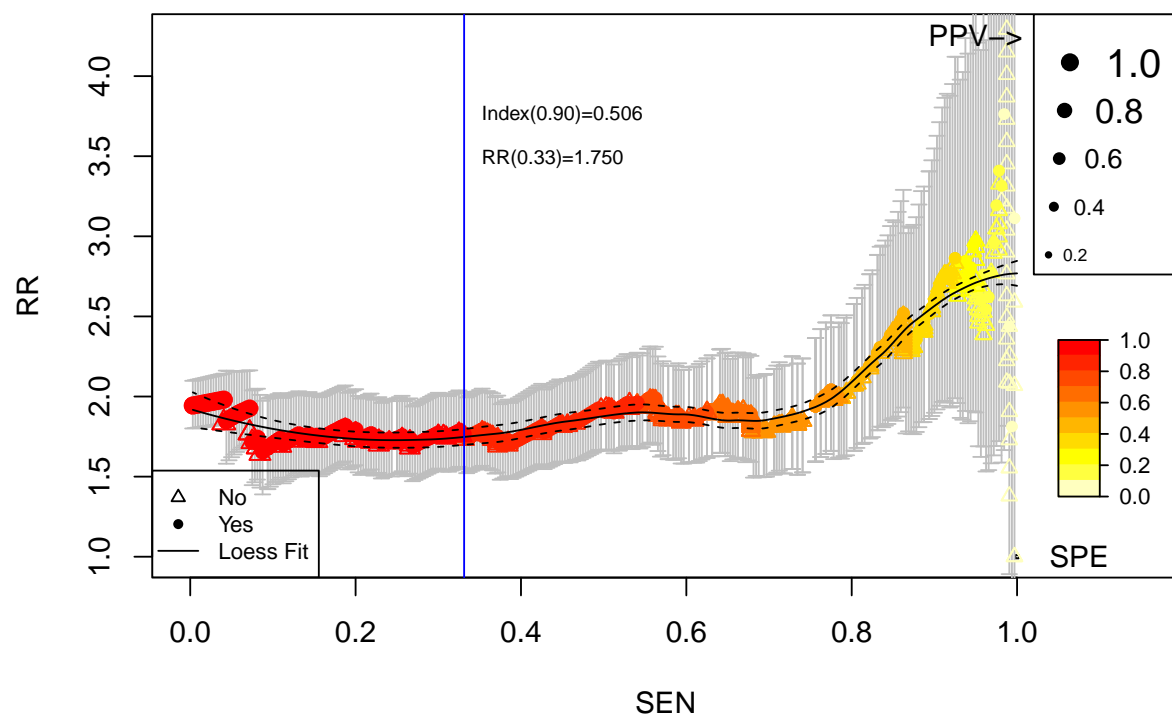
Cumulative vs. Observed: Raw Train: Colon Cancer

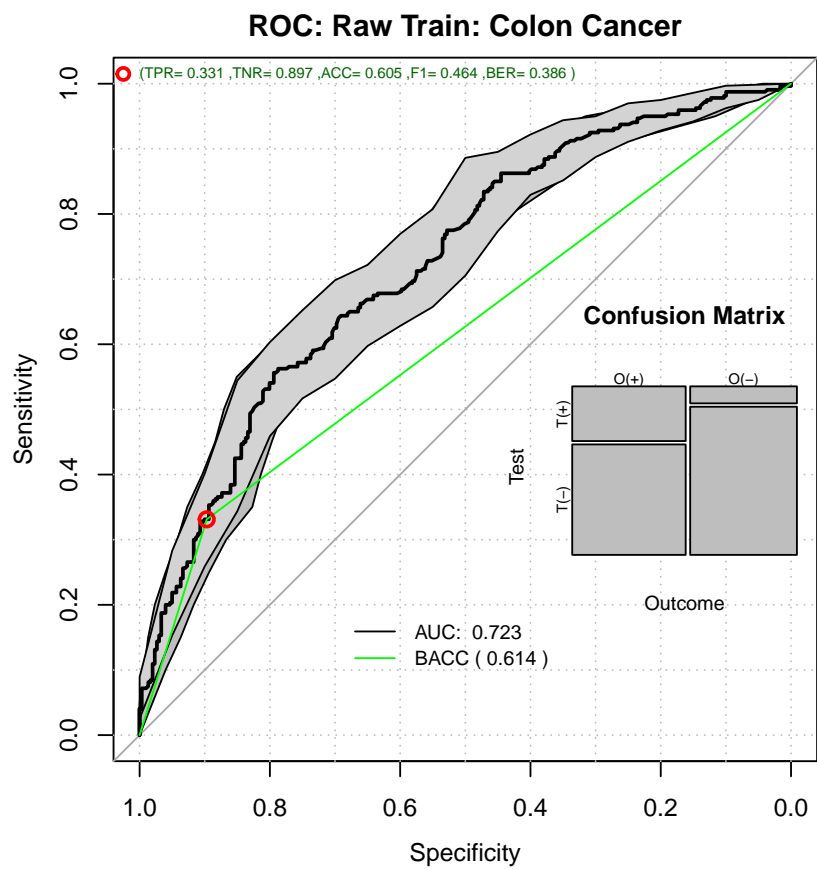


Decision Curve Analysis: Raw Train: Colon Cancer

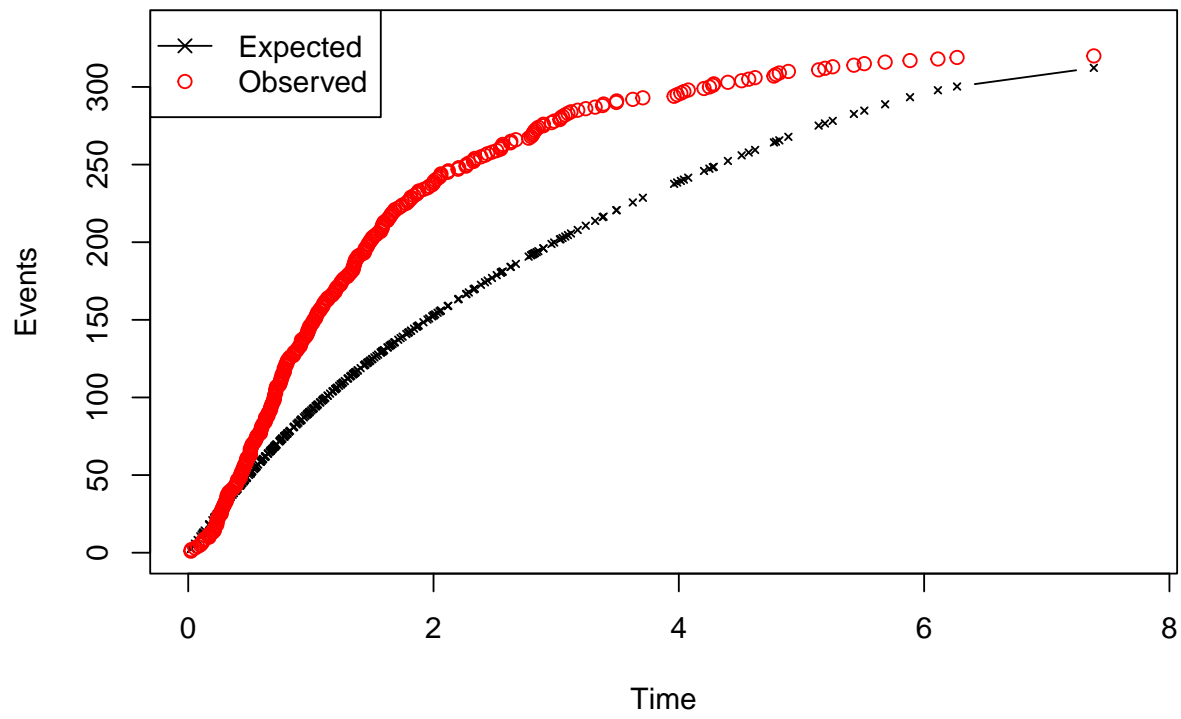


Relative Risk: Raw Train: Colon Cancer

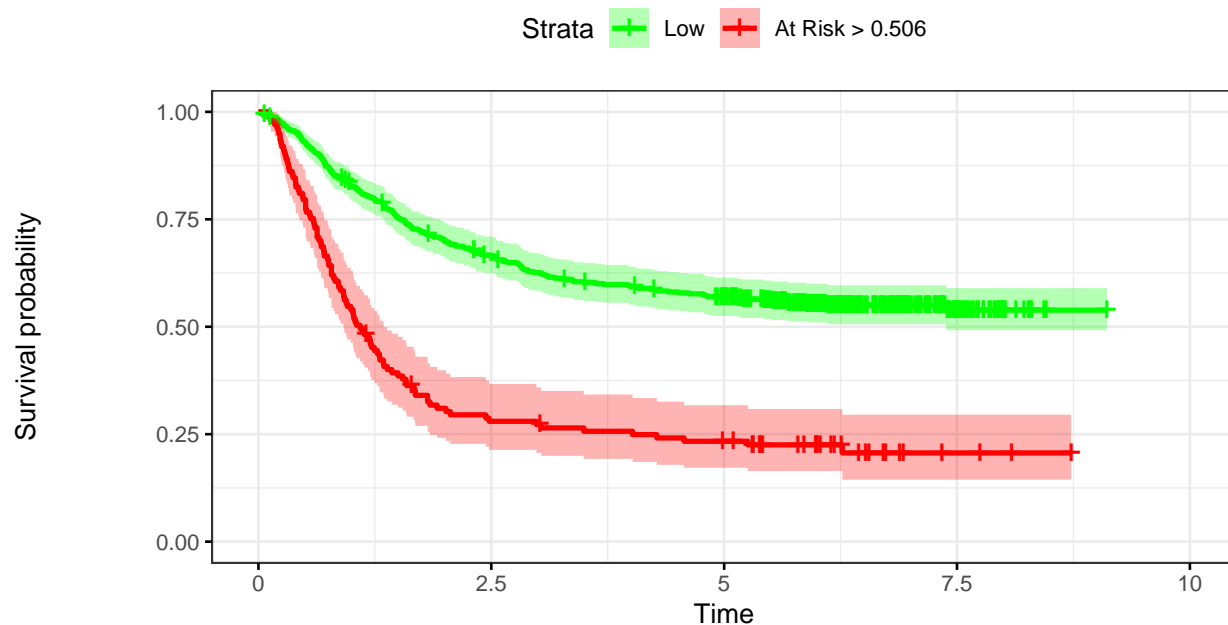




Time vs. Events: Raw Train: Colon Cancer



Kaplan–Meier: Raw Train: Colon Cancer



Number at risk

Low	484	314	257	39	0
At Risk > 0.506	137	37	29	3	0

1.3.2 Uncalibrated Performance Report

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

Table 6: Threshold values

	@:0.9	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.506	0.380	0.217	0.108	0.501
RR	1.750	1.990	3.410	1.000	1.750
SEN	0.331	0.556	0.978	1.000	0.338
SPE	0.897	0.794	0.123	0.000	0.894
BACC	0.614	0.675	0.551	0.500	0.616

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

Table 7: O/E Ratio

O/E	Low	Upper	p.value
1.02	0.915	1.14	0.651

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

Table 8: O/E Mean

mean	50%	2.5%	97.5%
1.45	1.44	1.42	1.47

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

Table 9: O/Acum Mean

mean	50%	2.5%	97.5%
1.32	1.32	1.32	1.33

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

mean.C Index	median	lower	upper
0.677	0.677	0.647	0.704

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

Table 11: ROC AUC

est	lower	upper
0.723	0.684	0.763

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

Table 12: Sensitivity

est	lower	upper
0.331	0.28	0.386

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

Table 13: Specificity

est	lower	upper
0.897	0.857	0.929

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

Table 14: Probability Thresholds

90%
0.506

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

Table 15: Risk Ratio

est	lower	upper
1.75	1.53	2

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

Table 16: Logrank test Chisq = 81.803097 on 1 degrees of freedom,
p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	484	214	271.6	12.2	81.8
class=1	137	106	48.4	68.5	81.8

1.3.3 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
0.702	1.51	3.15

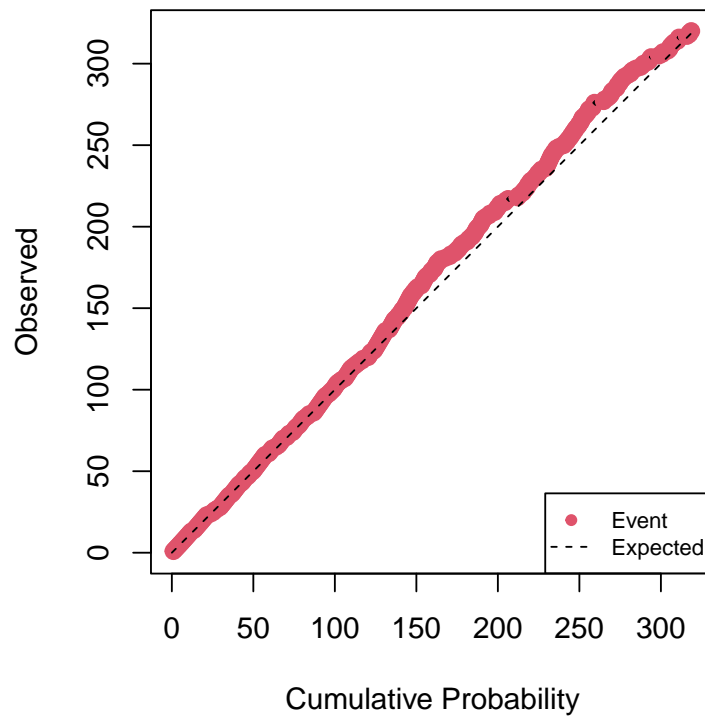
1.3.4 The RRplot() of the calibrated model

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

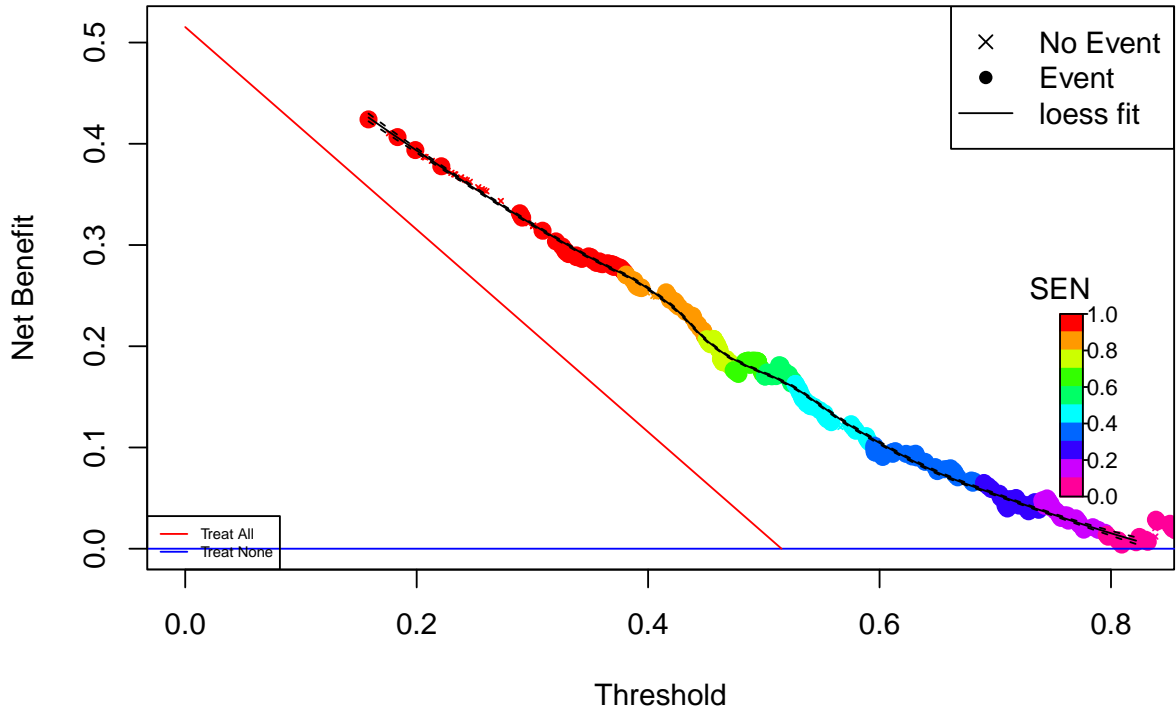
rdata <- cbind(dataColonTrain$status,calprob$prob)

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

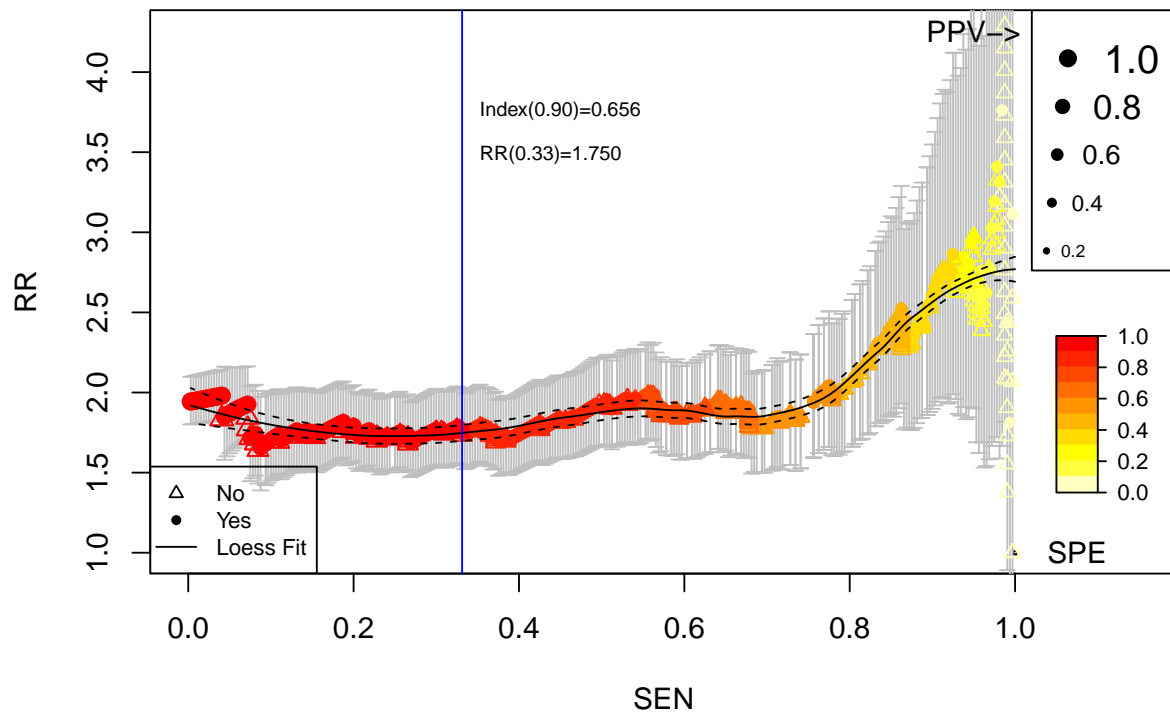
Cumulative vs. Observed: Calibrated Train: Colon

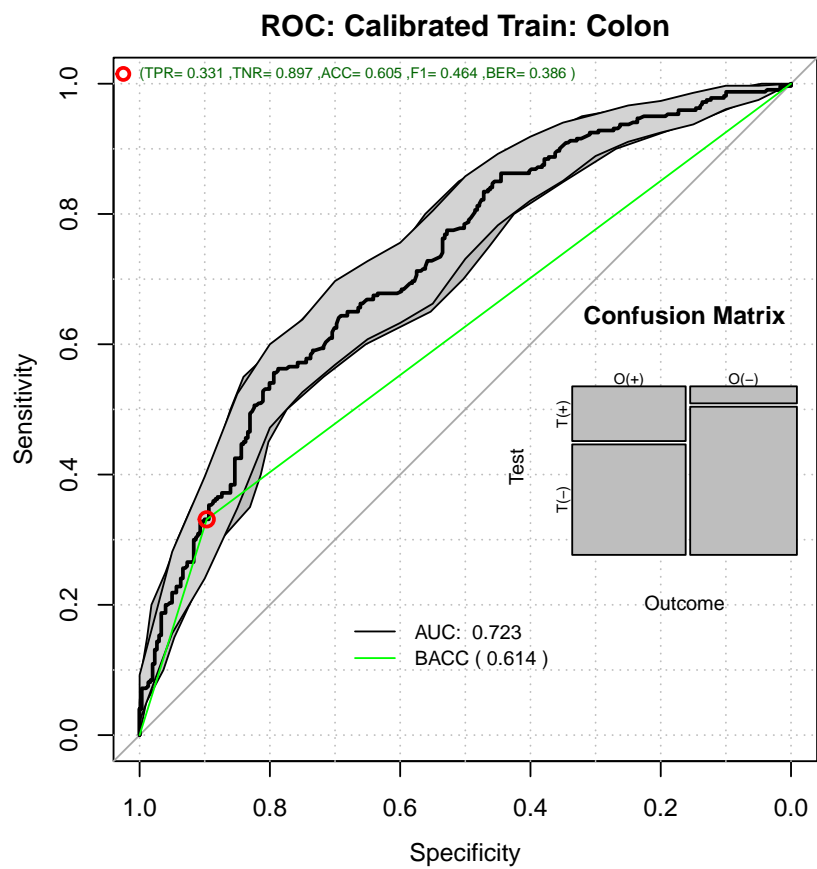


Decision Curve Analysis: Calibrated Train: Colon

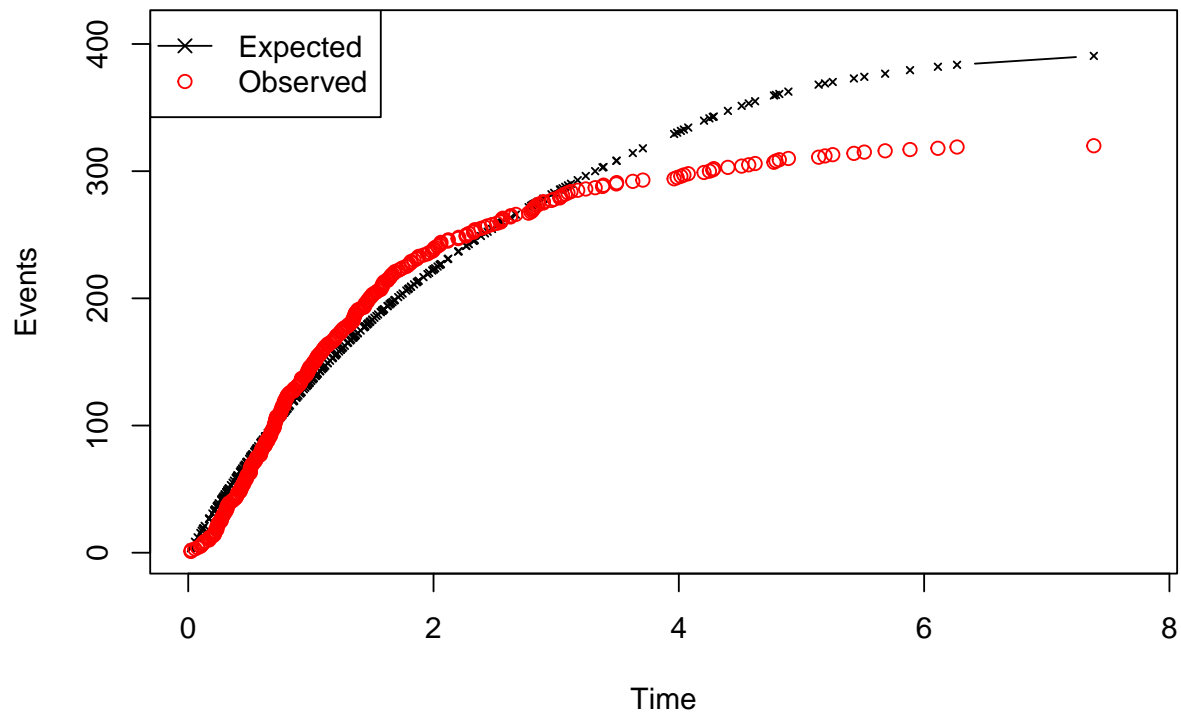


Relative Risk: Calibrated Train: Colon

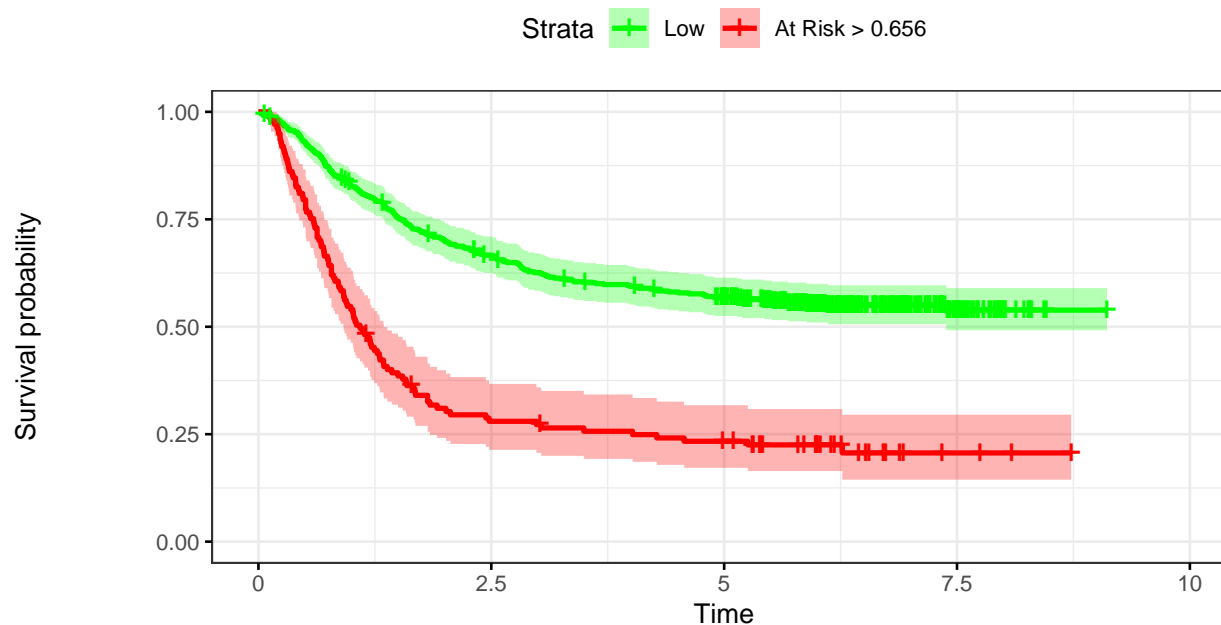




Time vs. Events: Calibrated Train: Colon



Kaplan–Meier: Calibrated Train: Colon



Number at risk

Low	484	314	257	39	0
At Risk > 0.656	137	37	29	3	0

1.3.5 Calibrated Train Performance

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

Table 18: Threshold values

	@:0.9	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.656	0.514	0.309	0.158	0.500
RR	1.750	1.990	3.410	1.000	1.863
SEN	0.331	0.556	0.978	1.000	0.603
SPE	0.897	0.794	0.123	0.000	0.714
BACC	0.614	0.675	0.551	0.500	0.659

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

Table 19: O/E Ratio

O/E	Low	Upper	p.value
0.819	0.732	0.914	0.000267

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

Table 20: O/E Mean

mean	50%	2.5%	97.5%
0.994	0.994	0.981	1.01

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

Table 21: O/Acum Mean

mean	50%	2.5%	97.5%
1.04	1.04	1.03	1.04

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

mean.C Index	median	lower	upper
0.677	0.677	0.649	0.705

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

Table 23: ROC AUC

est	lower	upper
0.723	0.684	0.763

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

Table 24: Sensitivity

est	lower	upper
0.331	0.28	0.386

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

Table 25: Specificity

est	lower	upper
0.897	0.857	0.929

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

Table 26: Probability Thresholds

90%
0.656

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

Table 27: Risk Ratio

est	lower	upper
1.75	1.53	2

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

Table 28: Logrank test Chisq = 81.803097 on 1 degrees of freedom,
p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	484	214	271.6	12.2	81.8
class=1	137	106	48.4	68.5	81.8

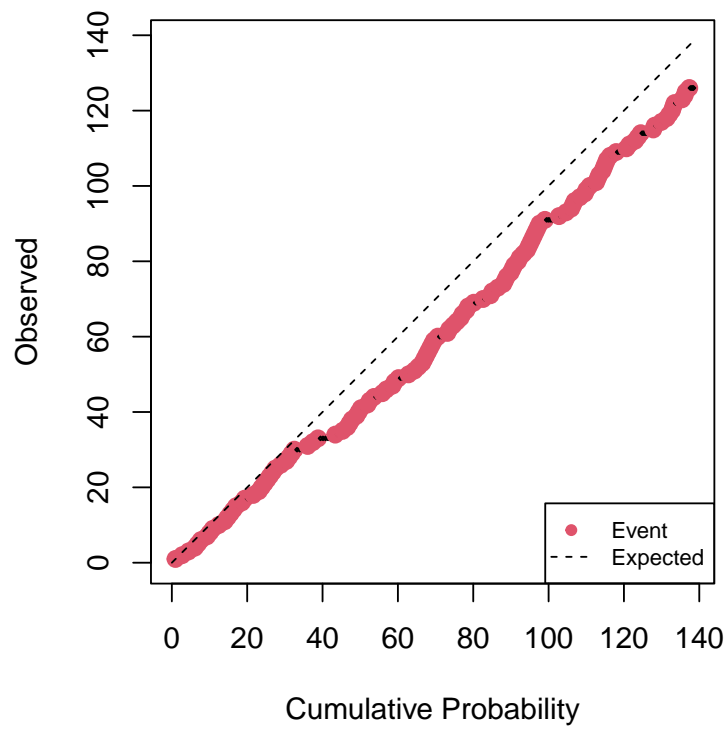
1.3.6 Evaluating on the test set

The calibrated h0 and timeinterval were estimated on the training set

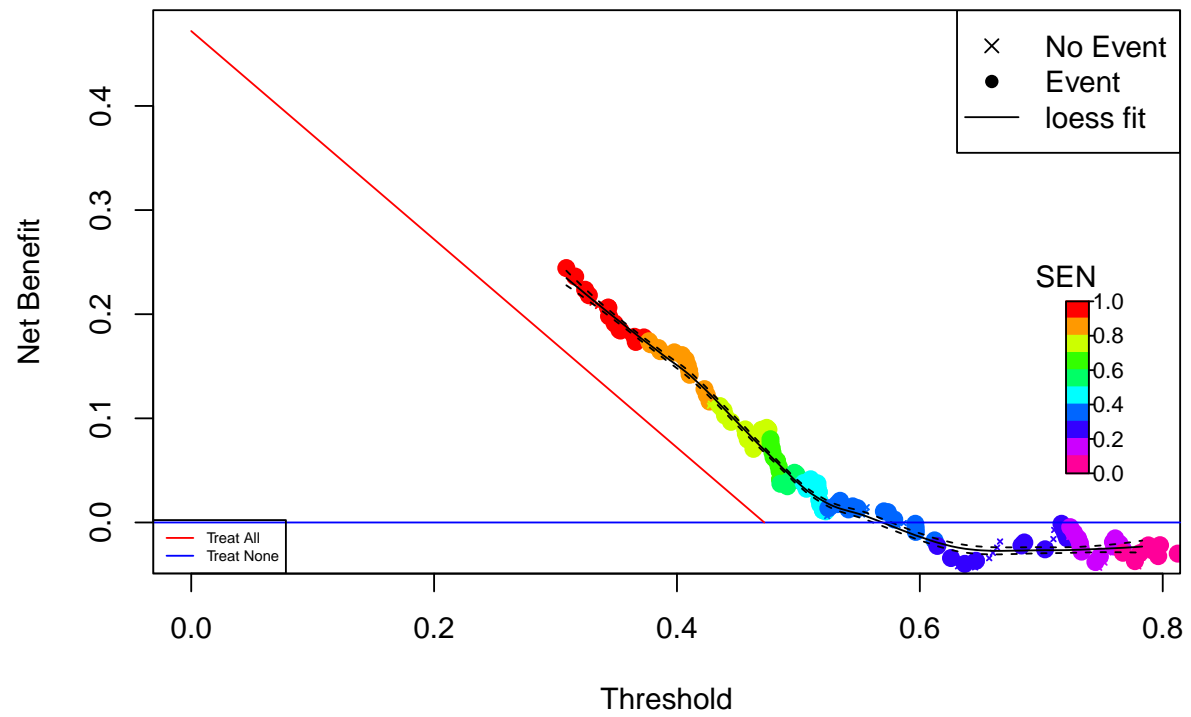
```
index <- predict(ml,dataColonTest)
rdata <- cbind(dataColonTest$status,ppoisGzero(index,h0))

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

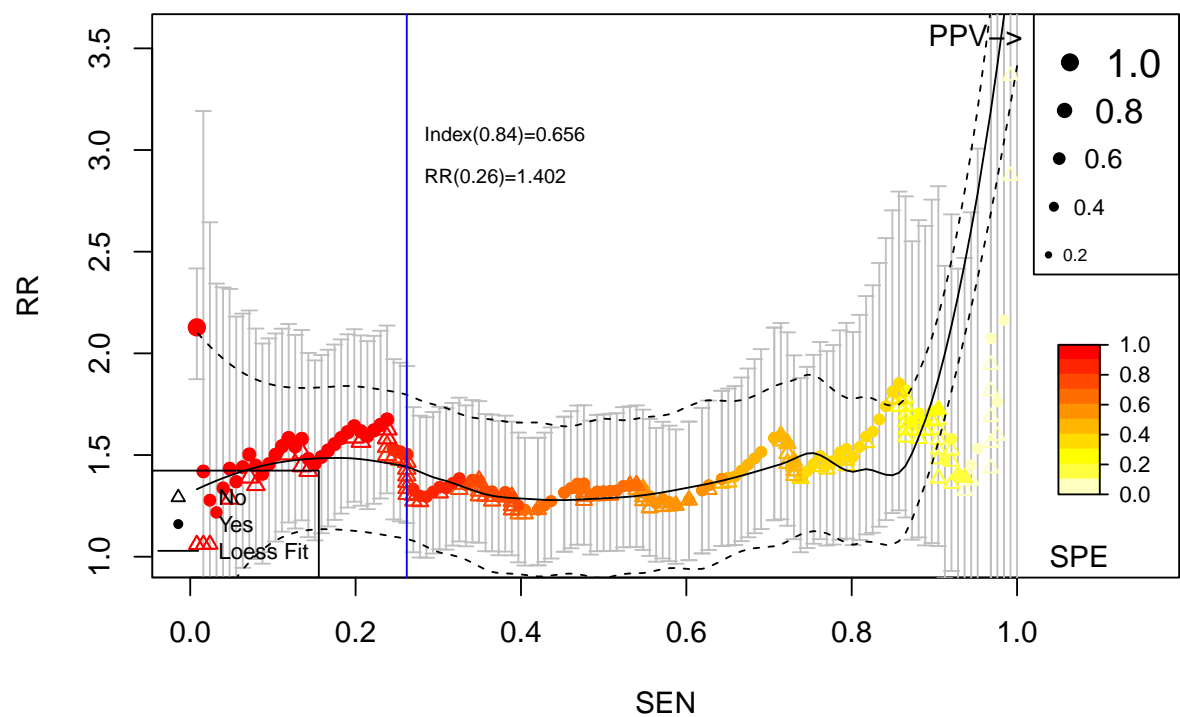
Cumulative vs. Observed: Test: Colon Cancer

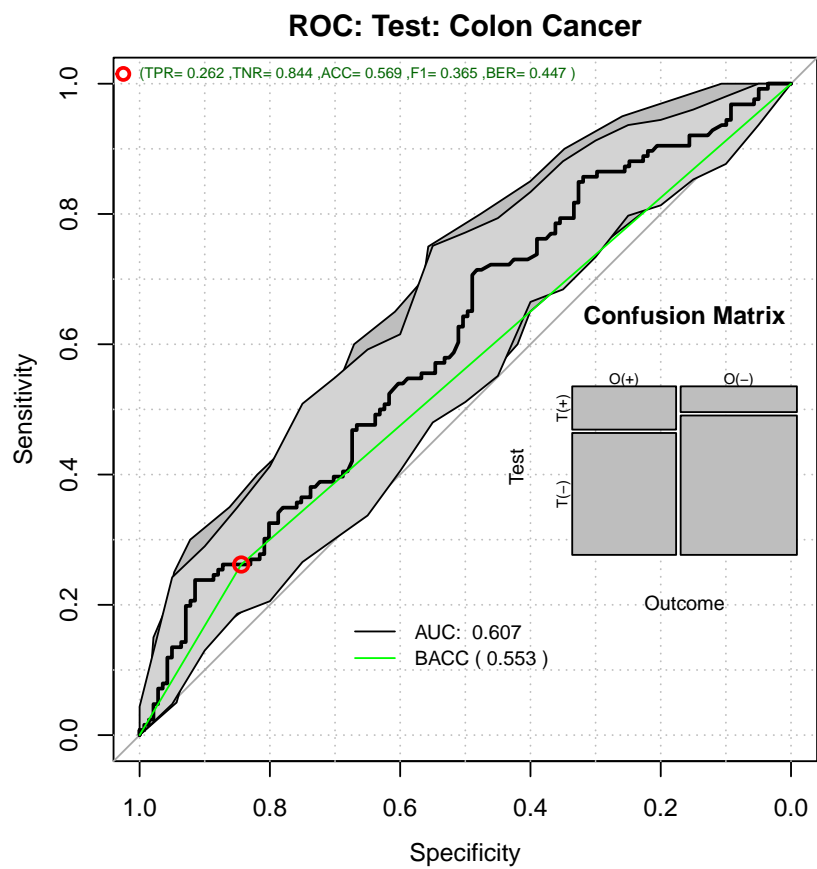


Decision Curve Analysis: Test: Colon Cancer

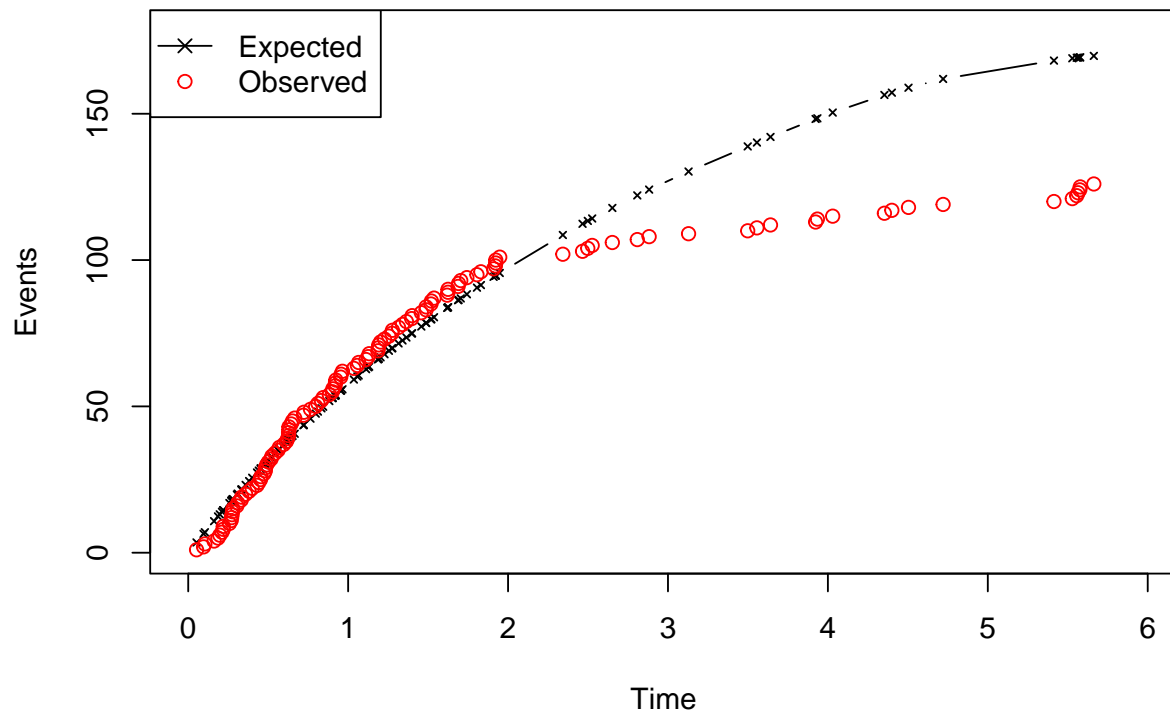


Relative Risk: Test: Colon Cancer

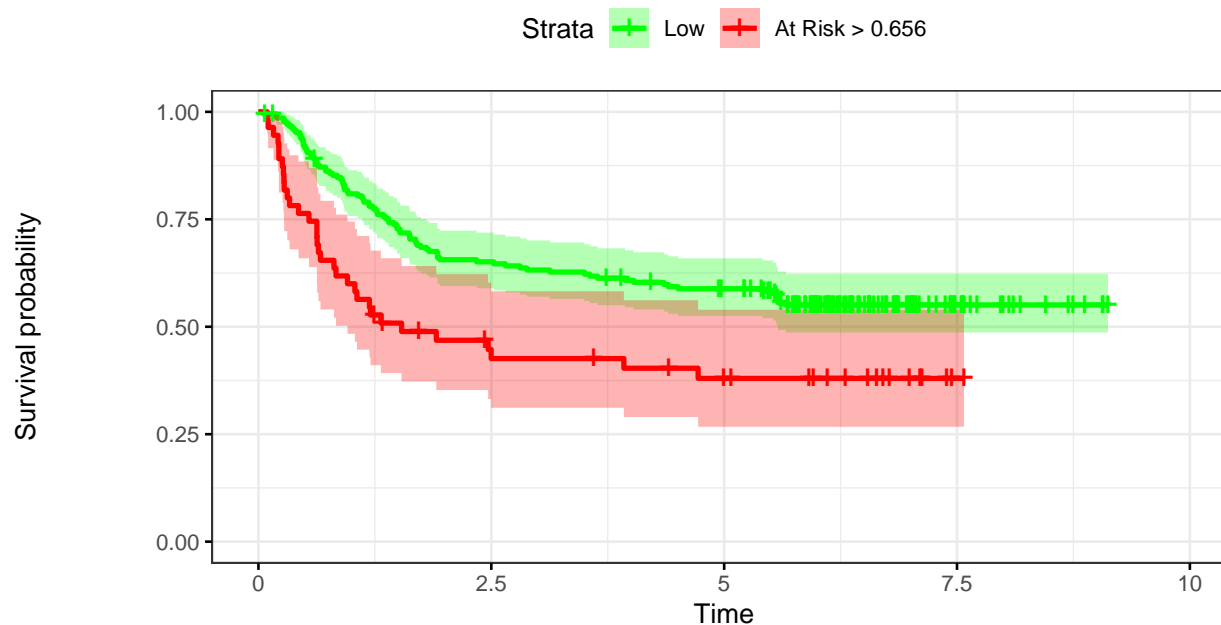




Time vs. Events: Test: Colon Cancer



Kaplan–Meier: Test: Colon Cancer



Number at risk

Low	212	136	118	19	0
At Risk > 0.656	55	20	15	1	0

1.3.7 Test Performance

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

Table 29: Threshold values

	@:0.66	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.657	0.474	0.404	0.3089	0.500
RR	1.368	1.595	1.853	24.0458	1.325
SEN	0.262	0.714	0.857	1.0000	0.516
SPE	0.844	0.482	0.319	0.0355	0.617
BACC	0.553	0.598	0.588	0.5177	0.566

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

Table 30: O/E Ratio

O/E	Low	Upper	p.value
0.742	0.618	0.884	0.000544

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

Table 31: O/E Mean

mean	50%	2.5%	97.5%
0.971	0.97	0.946	0.993

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

Table 32: O/Acum Mean

mean	50%	2.5%	97.5%
0.866	0.866	0.861	0.872

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

mean.C Index	median	lower	upper
0.607	0.606	0.551	0.655

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

Table 34: ROC AUC

est	lower	upper
0.607	0.54	0.675

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

Table 35: Sensitivity

est	lower	upper
0.262	0.188	0.348

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

Table 36: Specificity

est	lower	upper
0.844	0.773	0.9

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

Table 37: Probability Thresholds

90%
0.656

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

Table 38: Risk Ratio

est	lower	upper
1.4	1.08	1.82

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

Table 39: Logrank test Chisq = 10.116219 on 1 degrees of freedom,
p = 0.001470

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	212	93	106	1.60	10.1
class=1	55	33	20	8.47	10.1

1.4 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: 854 Avg. Se-
lected: 9.5 Min Tests: 1 Max Tests: 10 Mean Tests: 4.953162 . MAD: 0.4641621 .[+++).[++].[++++-
].[++++].[++].[++++].[++++-].[++++-].[++++-].[++++-]20 Tested: 885 Avg. Selected: 9.2 Min Tests: 1 Max
Tests: 20 Mean Tests: 9.559322 . MAD: 0.4660532 .[+-].[++-].[+-].[+-].[+-].[+-].[+-].[+-].[+-].[+-]30 Tested: 888 Avg. Selected: 9.066667 Min Tests: 1 Max Tests: 30 Mean Tests:
14.29054 . MAD: 0.4659471 .[++++-].[++++].[++++-].[++++].[++++].[++++-].[++++-].[+-].[++++].[++++]40
Tested: 888 Avg. Selected: 9.075 Min Tests: 3 Max Tests: 40 Mean Tests: 19.05405 . MAD: 0.4660608
.[+-].[++++-].[++++-].[+-].[++++].[++++-].[++++].[++++-].[++++-].[+-]50 Tested: 888 Avg. Selected:
8.94 Min Tests: 5 Max Tests: 50 Mean Tests: 23.81757 . MAD: 0.4661358
```

```
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,]
```

```

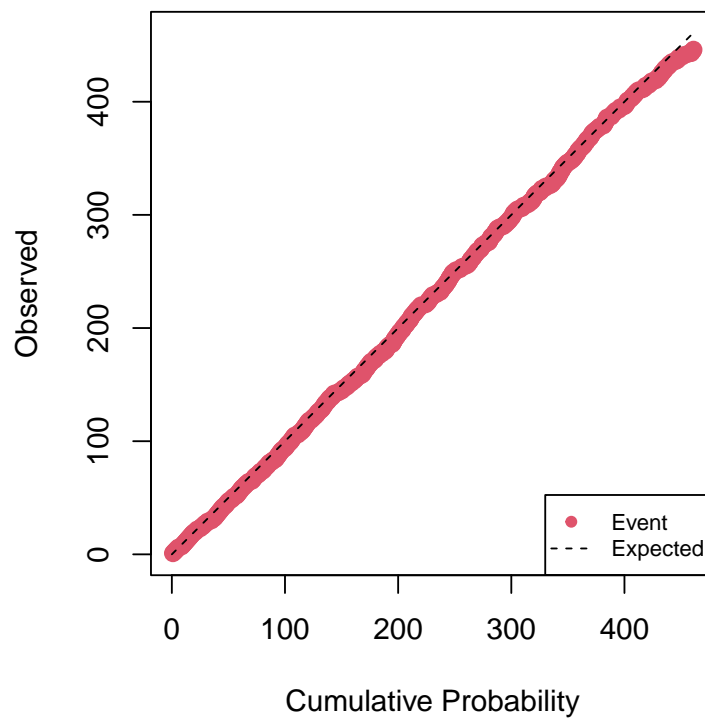
prob <- ppoisGzero(boxplot(unlist(stp[,4])~rownames(stp),plot=FALSE)$stats[3,],h0)

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

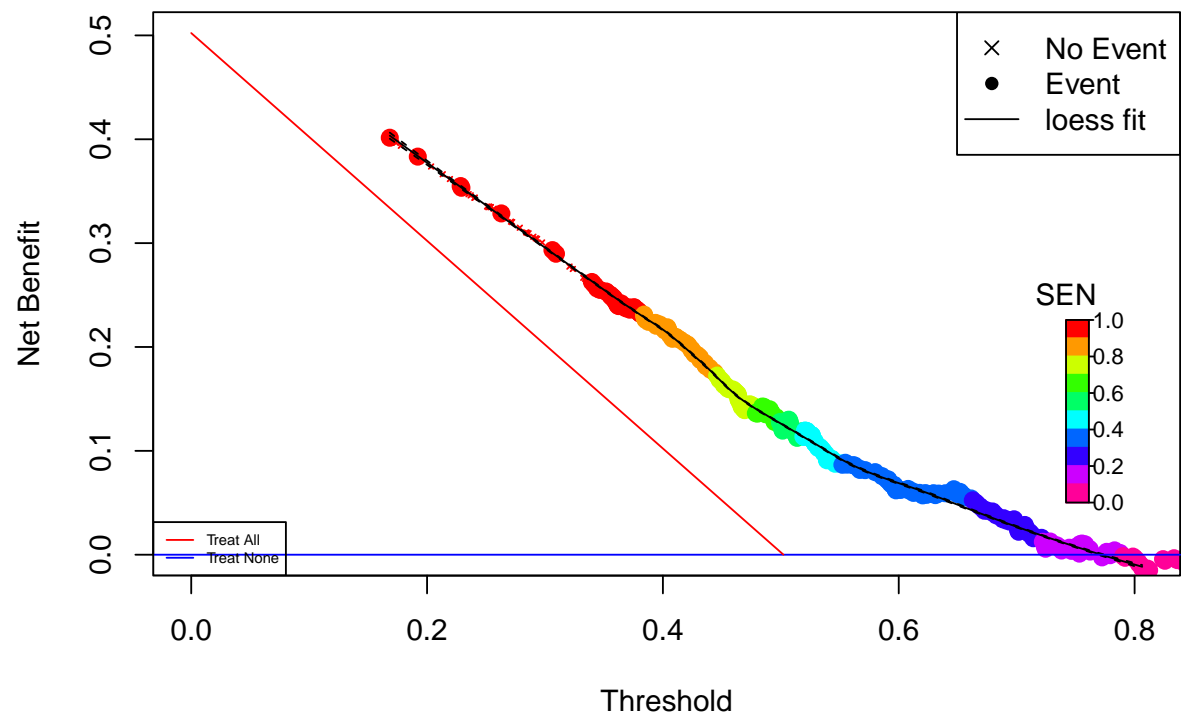
rrAnalysisCVTest <- RRPlot(rdatacv,atThr = rrAnalysisTrain$thr_atP,
                           timetoEvent=times,
                           title="CV Test: Colon Cancer",
                           ysurvlim=c(0.00,1.0),
                           riskTimeInterval=timeinterval)

```

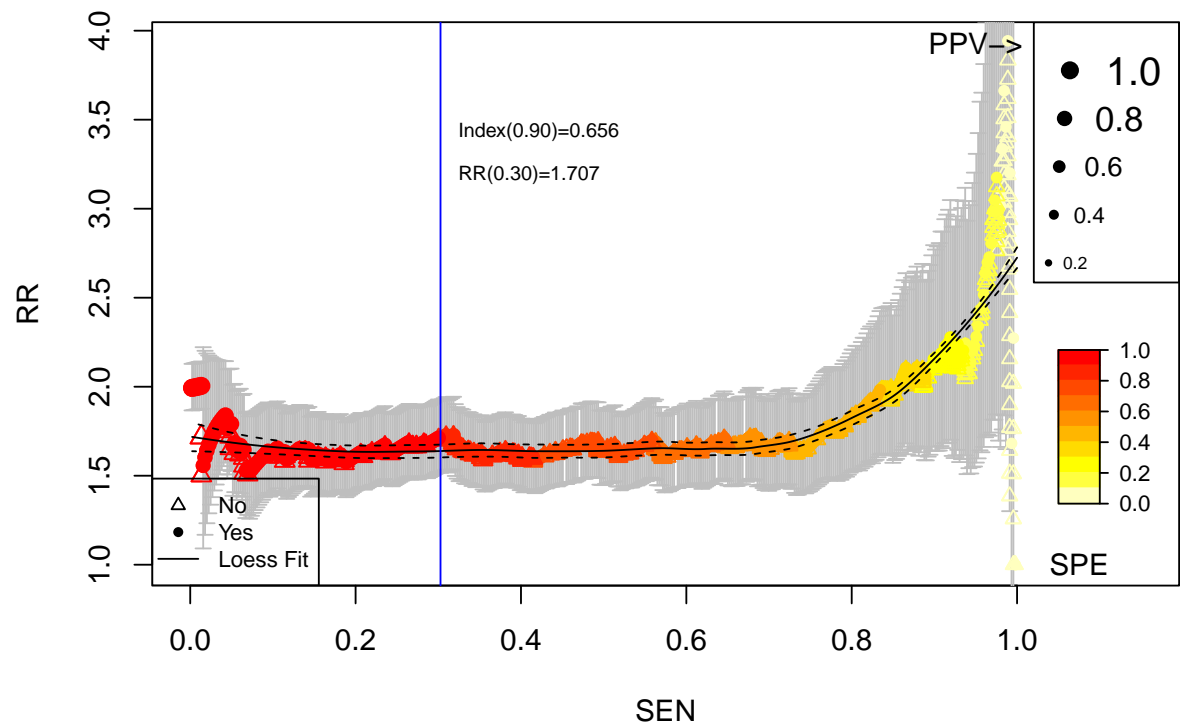
Cumulative vs. Observed: CV Test: Colon Cancer

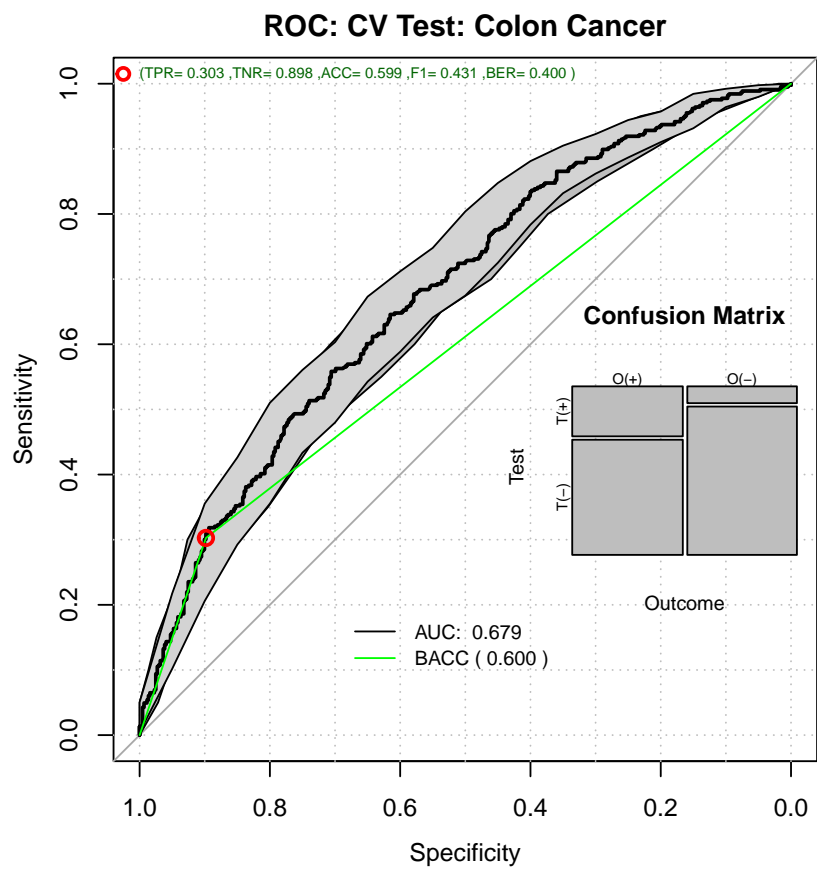


Decision Curve Analysis: CV Test: Colon Cancer

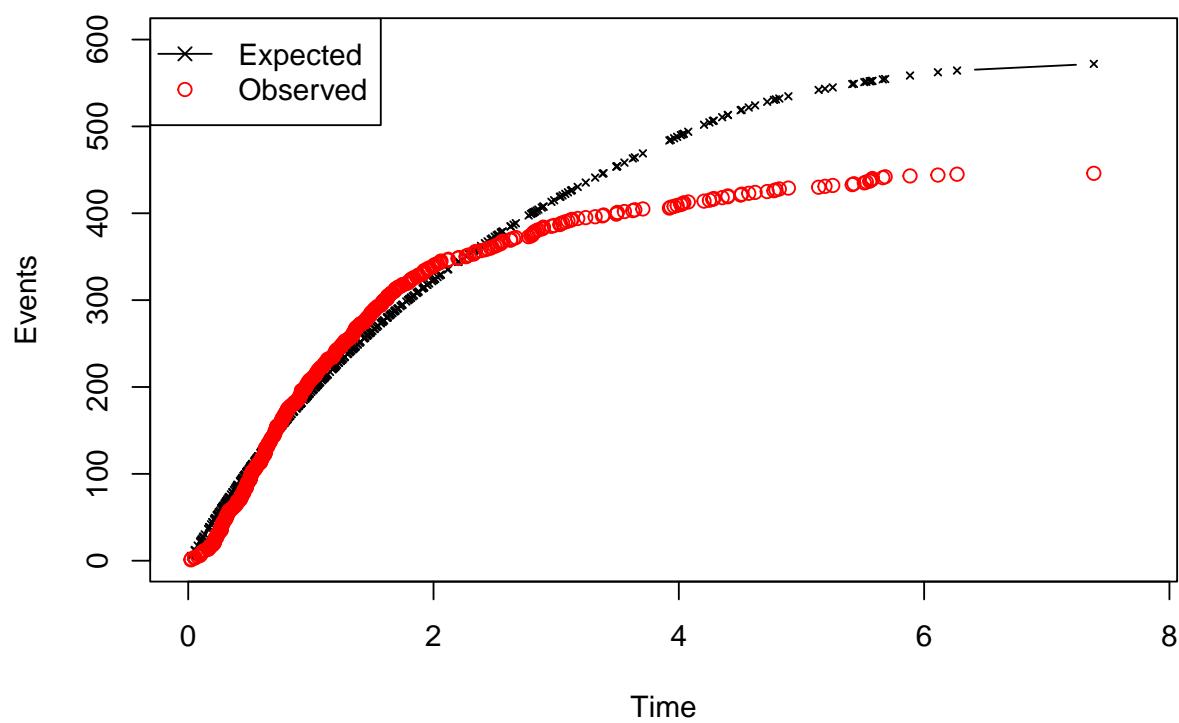


Relative Risk: CV Test: Colon Cancer

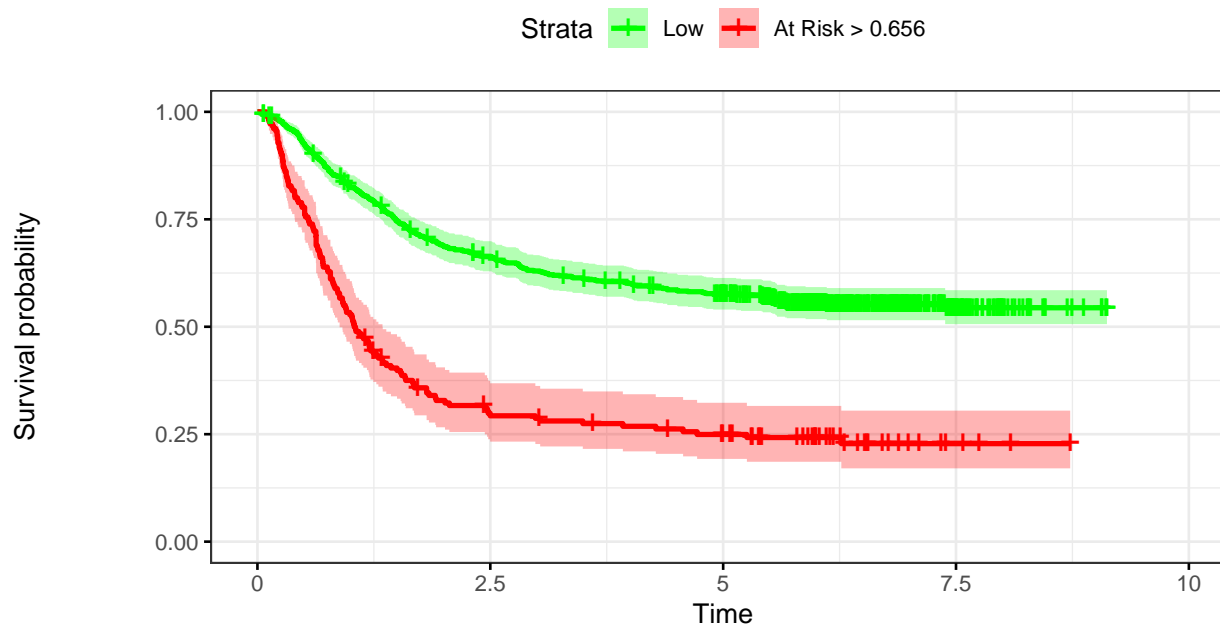




Time vs. Events: CV Test: Colon Cancer



Kaplan–Meier: CV Test: Colon Cancer



Number at risk

Low	708	458	382	58	0
At Risk > 0.656	180	49	37	4	0

1.4.1 CV Test Performance

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

Table 40: Threshold values

	@:0.66	@MAX_BACC	@MAX_RR	@SPE100	p(0.5)
Thr	0.655	0.507	0.352	0.168	0.500
RR	1.714	1.698	3.175	1.000	1.639
SEN	0.305	0.558	0.975	1.000	0.594
SPE	0.898	0.706	0.124	0.000	0.652
BACC	0.602	0.632	0.550	0.500	0.623

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

Table 41: O/E Ratio

O/E	Low	Upper	p.value
0.78	0.709	0.856	5.32e-08

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

Table 42: O/E Mean

mean	50%	2.5%	97.5%
0.973	0.973	0.962	0.984

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

Table 43: O/Acum Mean

mean	50%	2.5%	97.5%
0.977	0.977	0.976	0.979

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

mean.C Index	median	lower	upper
0.652	0.652	0.627	0.677

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

Table 45: ROC AUC

est	lower	upper
0.679	0.645	0.714

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

Table 46: Sensitivity

est	lower	upper
0.303	0.26	0.348

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

Table 47: Specificity

est	lower	upper
0.898	0.866	0.925

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

Table 48: Probability Thresholds

90%
0.656

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

Table 49: Risk Ratio

est	lower	upper
1.71	1.52	1.92

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

Table 50: Logrank test Chisq = 102.535013 on 1 degrees of freedom,
p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	708	311	384.4	14.0	103
class=1	180	135	61.6	87.4	103