free light chain

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Contents


```
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")
op <- par(no.readonly = TRUE)
pander::panderOptions('digits', 3)
#pander::panderOptions('table.split.table', 400)
pander::panderOptions('keep.trailing.zeros',TRUE)
```

1 RRPLOTS and flchain

```
odata <- flchain
odata$chapter <- NULL
table(odata$death)
```

```
##
##    0    1
## 5705 2169
```

```
rownames(odata) <- c(1:nrow(odata))
data <- as.data.frame(model.matrix(Surv(futime,death)~.*.,odata))

data$`(Intercept)` <- NULL
table(odata[rownames(data),"death"])
```

```
##
##    0    1
## 4562 1962
```

```
dataFL <- cbind(time=odata[rownames(data),"futime"],status=odata[rownames(data),"death"],data)
dataFL$time <- dataFL$time/365
colnames(dataFL) <-str_replace_all(colnames(dataFL)," ","")
colnames(dataFL) <-str_replace_all(colnames(dataFL),"\\.","_")
colnames(dataFL) <-str_replace_all(colnames(dataFL),":","_")
colnames(dataFL) <-str_replace_all(colnames(dataFL),"-","_")
colnames(dataFL) <-str_replace_all(colnames(dataFL),">","_")

trainsamples <- sample(nrow(dataFL),2000)
dataFLTrain <- dataFL[trainsamples,]
dataFLTest <- dataFL[-trainsamples,]

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

0	1
1406	594

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

0	1
3156	1368

1.1 Modeling

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

-

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

Table 3: Table continues below

	Estimate	lower	HR	upper	u.Accuracy
age	0.019209	1.018	1.019	1.021	0.709
age_lambda	0.017226	1.016	1.017	1.019	0.720
lambda	-1.352607	0.228	0.259	0.293	0.662
flc_grp	0.084179	1.079	1.088	1.096	0.604
age_creatinine	0.024430	1.022	1.025	1.027	0.728
sample_yr_creatinine	-0.000865	0.999	0.999	0.999	0.650
flc_grp_creatinine	0.006657	1.005	1.007	1.009	0.635
creatinine	0.207278	1.154	1.230	1.312	0.654
age_flc_grp	0.000491	1.000	1.000	1.001	0.656

Table 4: Table continues below

	r.Accuracy	full.Accuracy	u.AUC	r.AUC
age	0.635	0.721	0.730	0.621
age_lambda	0.604	0.731	0.686	0.626
lambda	0.639	0.731	0.617	0.643
flc_grp	0.714	0.731	0.626	0.732
age_creatinine	0.658	0.729	0.703	0.669
sample_yr_creatinine	0.670	0.729	0.582	0.680
flc_grp_creatinine	0.709	0.721	0.621	0.730
creatinine	0.729	0.731	0.584	0.727
age_flc_grp	0.718	0.729	0.669	0.735

Table 5: Table continues below

	full.AUC	IDI	NRI	z.IDI	z.NRI
age	0.739	0.25702	0.911	26.49	21.57
age_lambda	0.732	0.12007	0.702	15.13	15.96
lambda	0.732	0.10513	0.693	13.86	15.76
flc_grp	0.732	0.04424	0.501	11.17	10.82
age_creatinine	0.744	0.08810	0.595	11.14	13.02
sample_yr_creatinine	0.744	0.08324	0.603	11.05	13.24
flc_grp_creatinine	0.739	0.01325	0.317	6.79	6.54
creatinine	0.732	0.01099	0.437	6.30	9.15
age_flc_grp	0.744	0.00863	0.249	3.18	5.16

	Delta.AUC	Frequency
age	0.118044	1
age_lambda	0.105883	1
lambda	0.088543	1
flc_grp	0.000424	1
age_creatinine	0.074935	1
sample_yr_creatinine	0.064100	1
flc_grp_creatinine	0.009021	1
creatinine	0.004825	1

	Delta.AUC	Frequency
age_flc_grp	0.008926	1

1.2 Cox Model Performance

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

1.2.1 The evaluation of the raw Cox model with RRPlot()

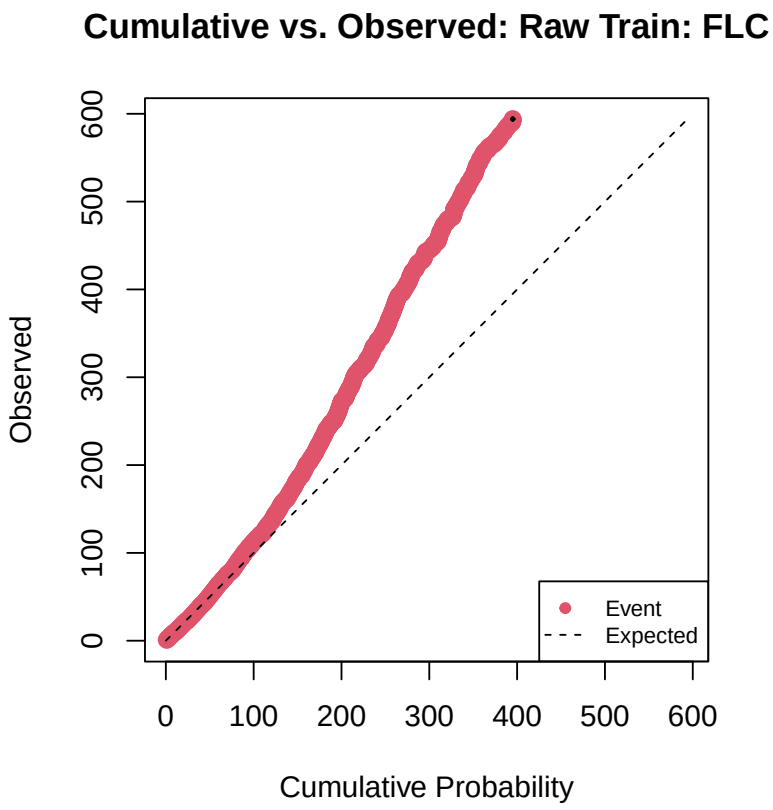
Here we will use the predicted event probability assuming a baseline hazard for events withing 5 years

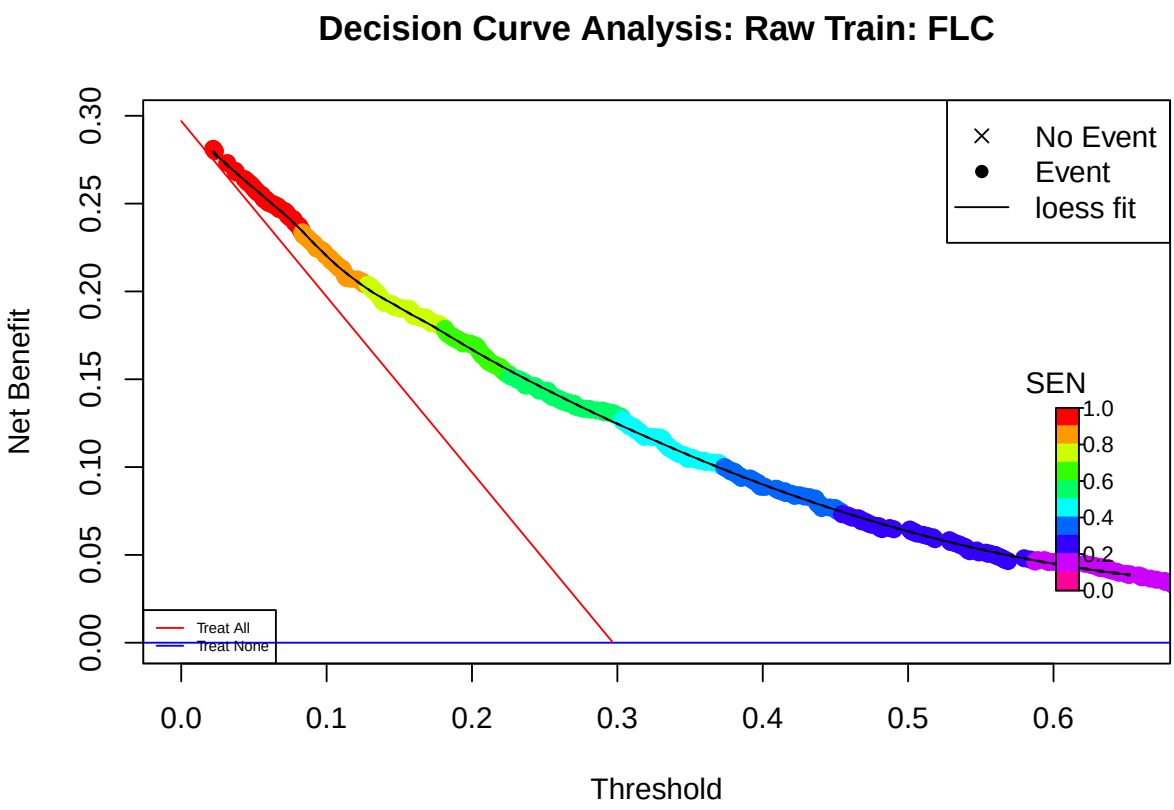
```
timeinterval <- mean(subset(dataFLTrain,status==1)$time)

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

pander::pander(t(c(h0=h0,timeinterval=timeinterval)),caption="Initial Parameters")
```

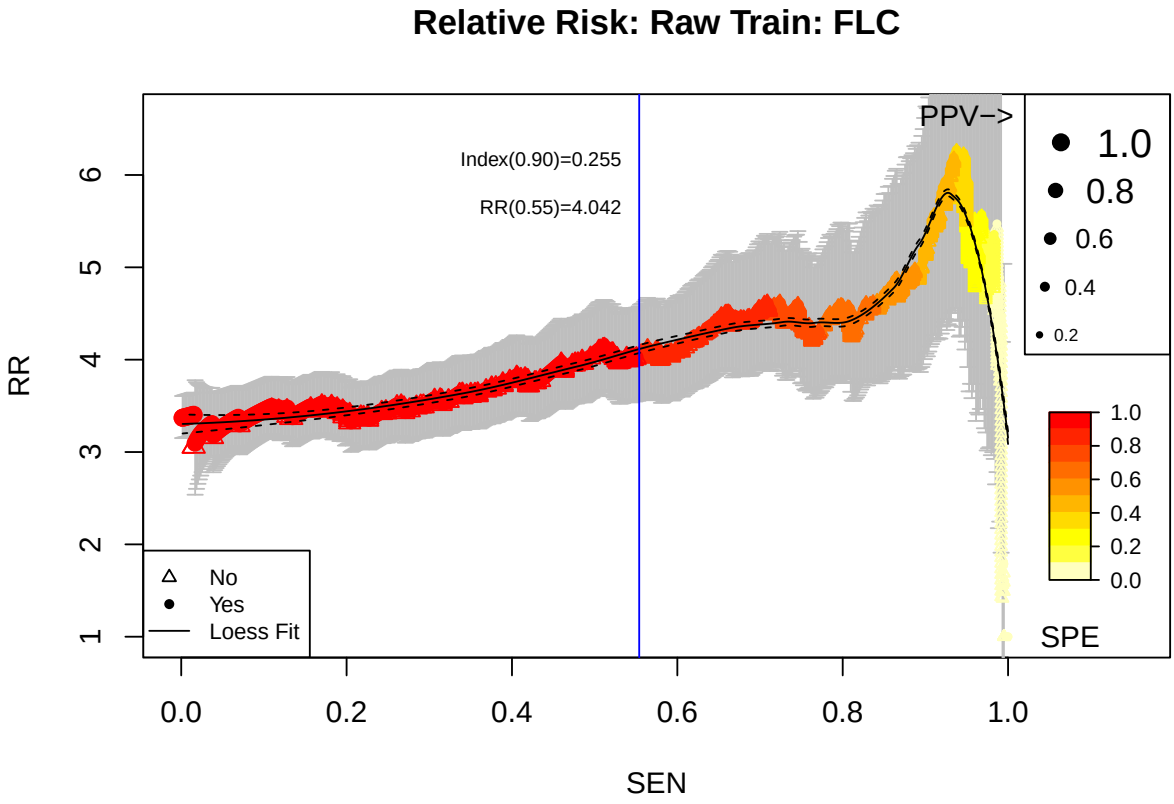
Table 7: Initial Parameters

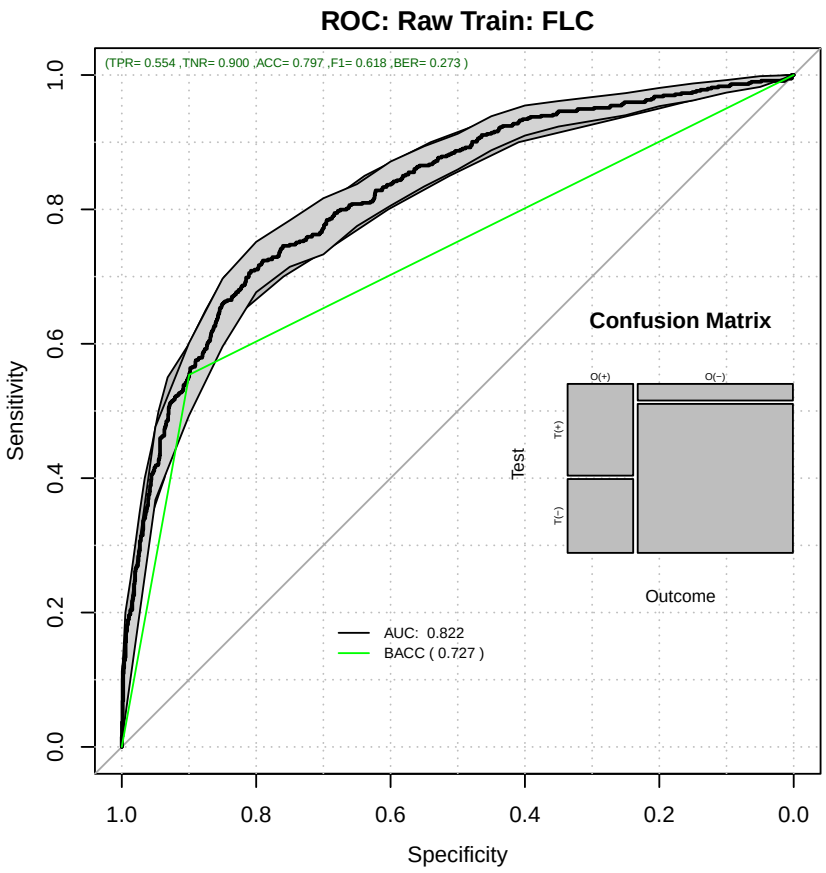
h0	timeinterval
0.153	5.82

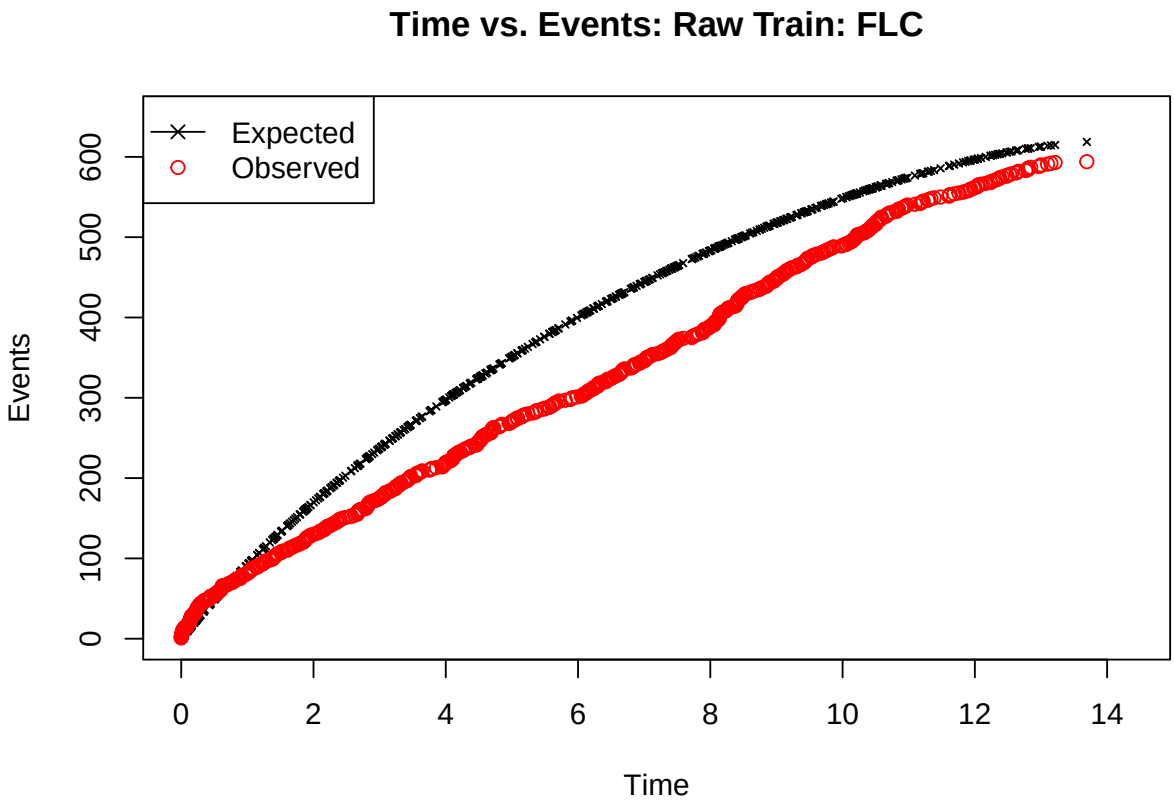
```
index <- predict(ml,dataFLTrain)
rdata <- cbind(dataFLTrain$status,ppoisGzero(index,h0))

rrAnalysisTrain <- RRPlot(rdata,atProb=c(0.90,0.80),
                      timetoEvent=dataFLTrain$time,
                      title="Raw Train: FLC",
                      ysurvlim=c(0.00,1.0),
                      riskTimeInterval=timeinterval)
```

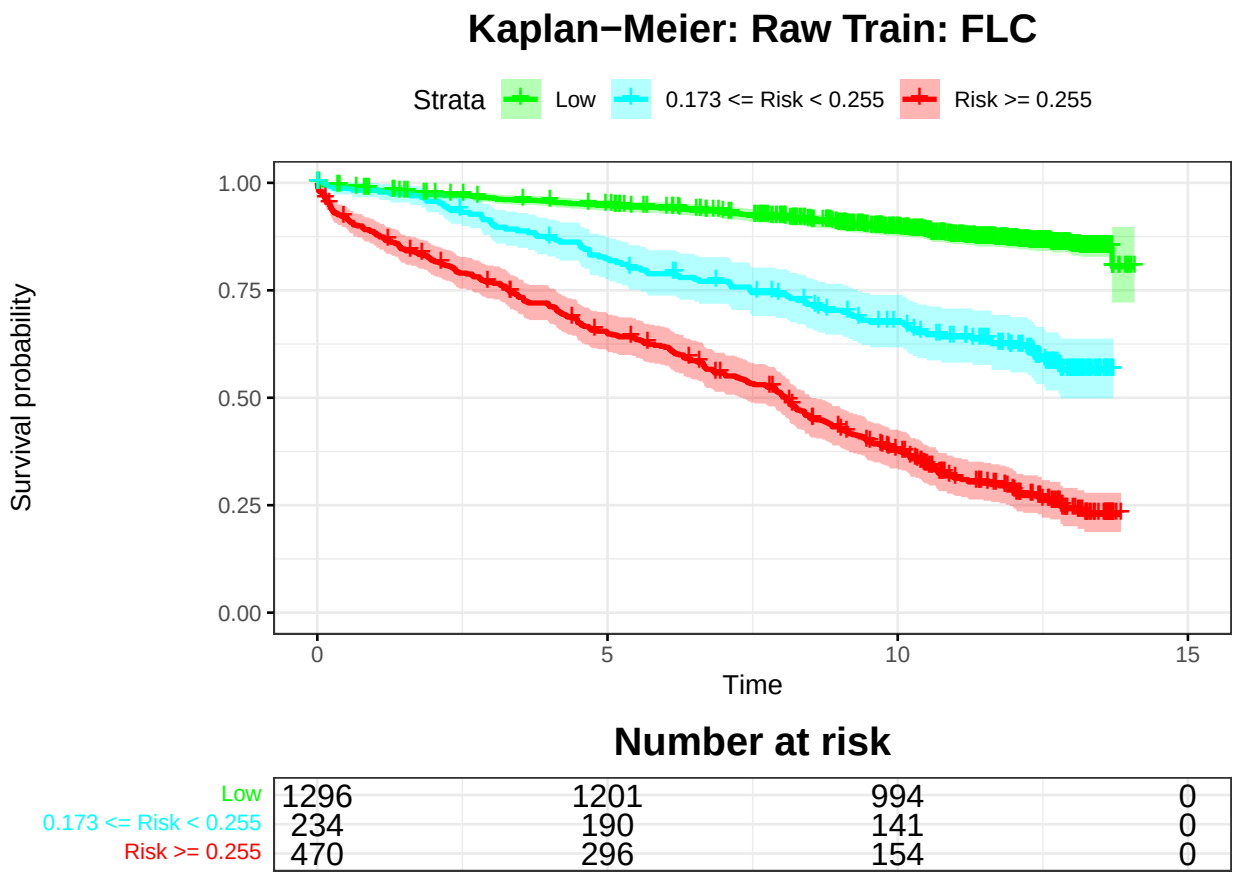

Cumulative vs. Observed: Raw Train: FLC
Observed
0
100
200
300
400
500
600
Cumulative Probability
Event
Expected


Decision Curve Analysis: Raw Train: FLC
Net Benefit
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.0
0.1
0.2
0.3
0.4
0.5
0.6
Threshold
No Event
Event
loess fit
SEN
1.0
0.8
0.6
0.4
0.2
0.0
Treat All
Treat None


Relative Risk: Raw Train: FLC
Index(0.90)=0.255
RR(0.55)=4.042
PPV–>
1.0
0.8
0.6
0.4
0.2
SPE
No
Yes
Loess Fit
RR
SEN
0.0
0.2
0.4
0.6
0.8
1.0
1
2
3
4
5
6


ROC: Raw Train: FLC
(TPR= 0.554 ,TNR= 0.900 ,ACC= 0.797 ,F1= 0.618 ,BER= 0.273)
Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
AUC: 0.822
BACC (0.727)
Confusion Matrix
O(+)
O(−)
T(+)
T(−)
Test
Outcome


Time vs. Events: Raw Train: FLC
Expected
Observed
Events
0
100
200
300
400
500
600
0
2
4
6
8
10
12
14
Time



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

1.2.2 Uncalibrated Performance Report

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

Table 8: O/E Ratio

est	lower	upper
0.96	0.884	1.04

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

Table 9: O/E Ratio

mean	50%	2.5%	97.5%
0.838	0.838	0.83	0.847

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

Table 10: O/Acum Ratio

mean	50%	2.5%	97.5%
1.44	1.44	1.43	1.44

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

Table 11: C. Index

mean.C Index	median	lower	upper
0.78	0.779	0.759	0.799

```
#pander::pander(rrAnalysisTrain$c.index,caption="C. Index")
pander::pander(t(rrAnalysisTrain$ROCAnalysis$aucs),caption="ROC AUC")
```

Table 12: ROC AUC

est	lower	upper
0.822	0.801	0.843

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

Table 13: Sensitivity

est	lower	upper
0.554	0.513	0.594

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

Table 14: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 15: Probability Thresholds

90%	80%
0.255	0.173

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

Table 16: Risk Ratio

est	lower	upper
4.04	3.57	4.58

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

Table 17: Logrank test Chisq = 709.746789 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1296	172	427.9	153.00	553
class=1	234	93	67.4	9.72	11
class=2	470	329	98.7	536.99	653

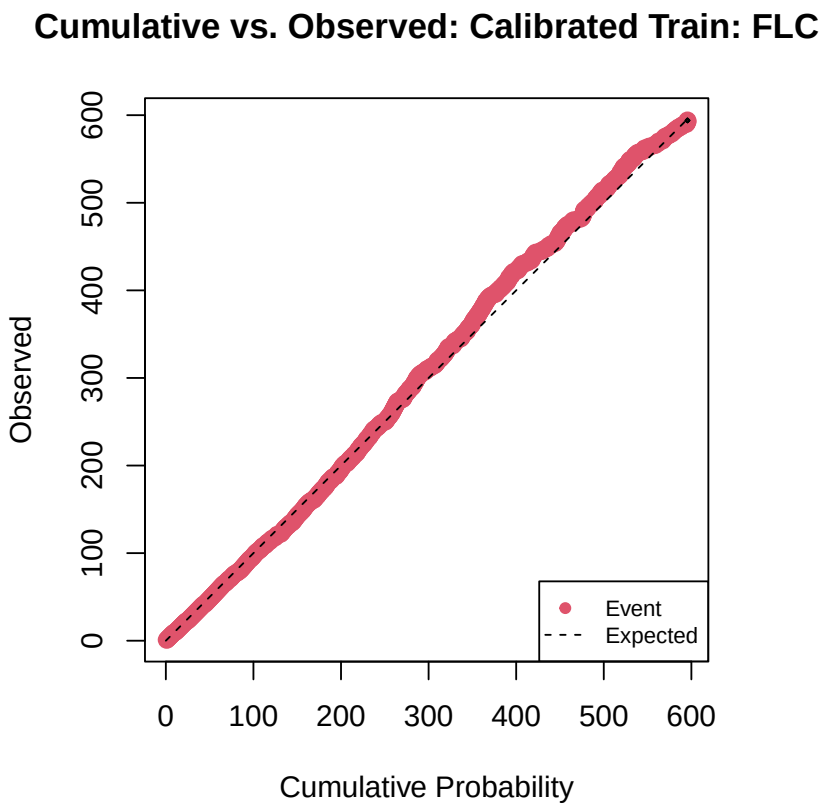
1.2.3 Cox Calibration

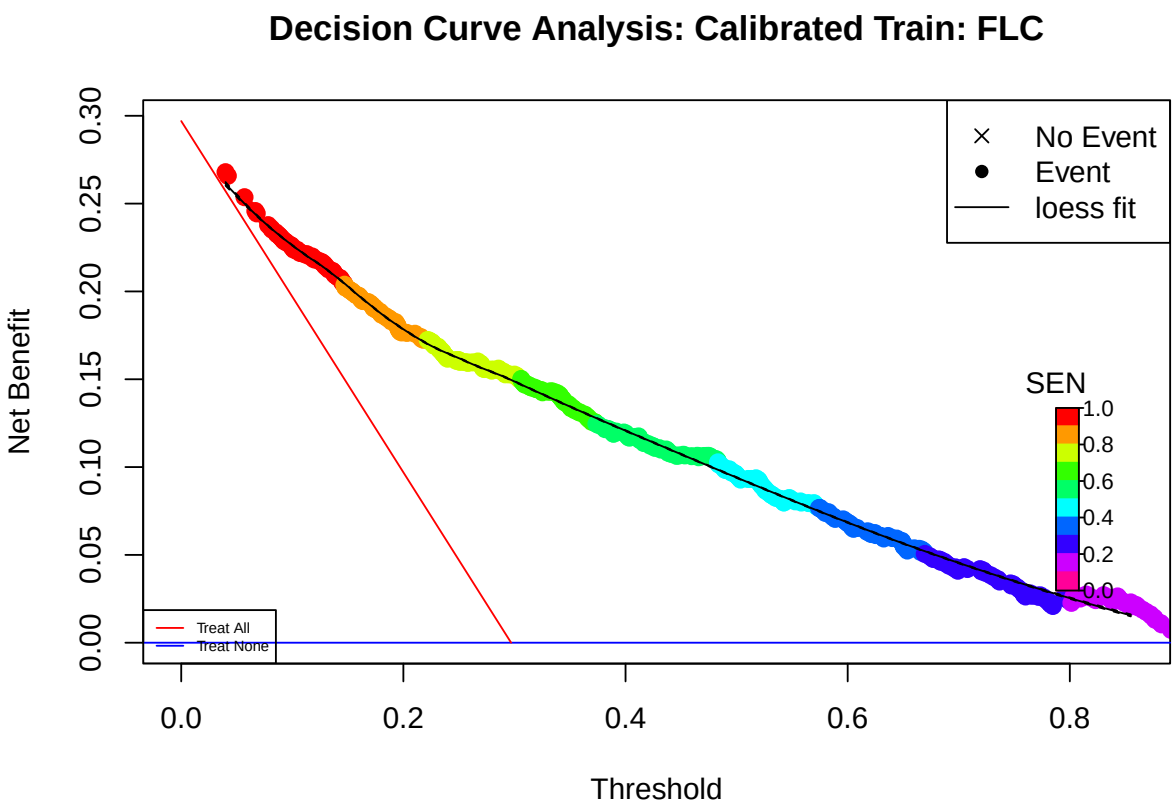
```
op <- par(no.readonly = TRUE)


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

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

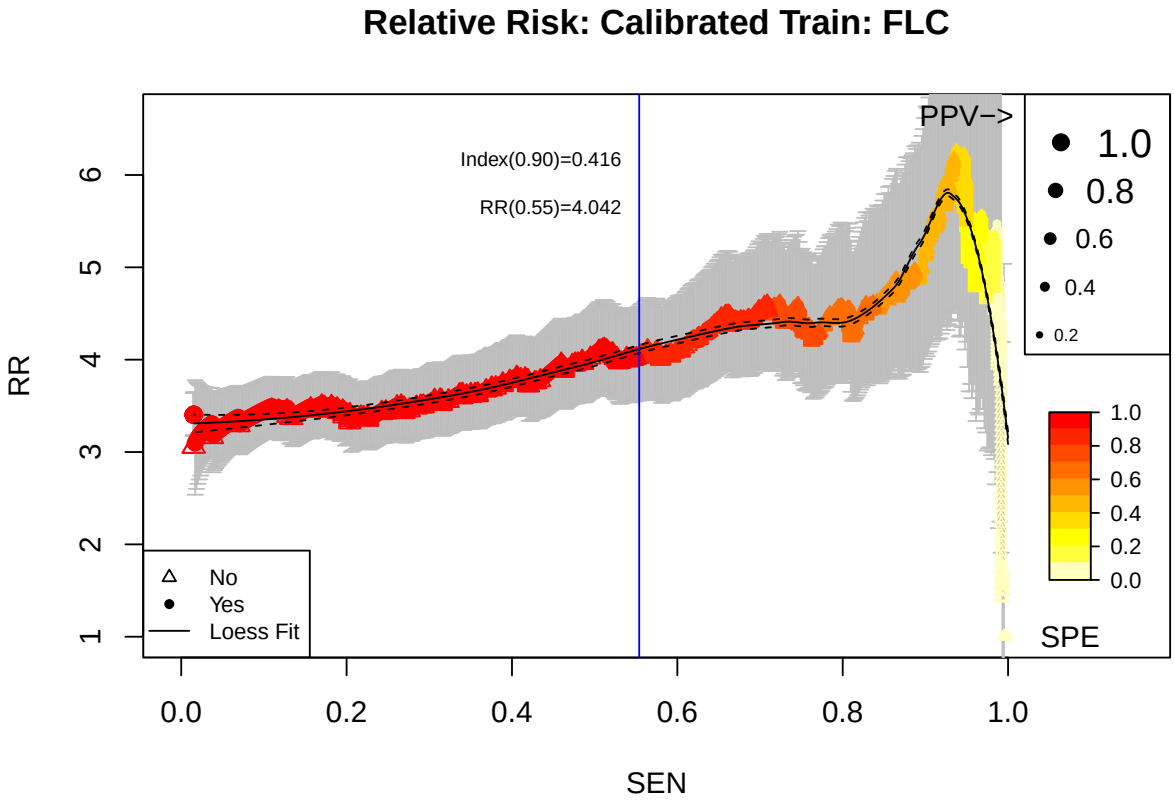
h0	Gain	DeltaTime
0.279	0.794	13.2

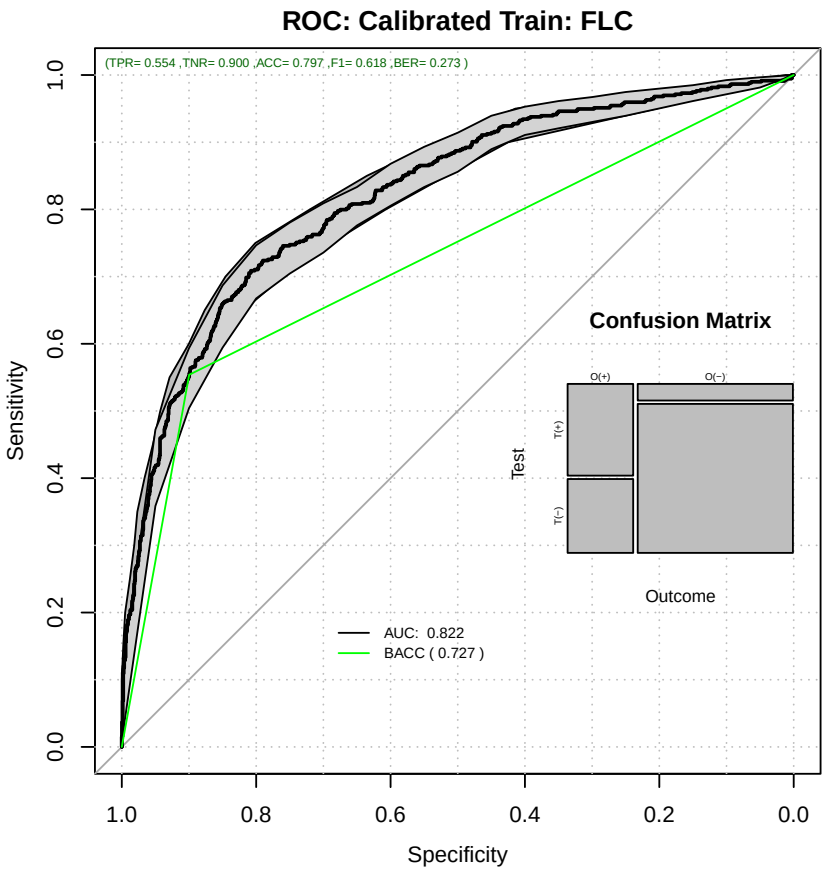
1.2.4 The RRplot() of the calibrated model

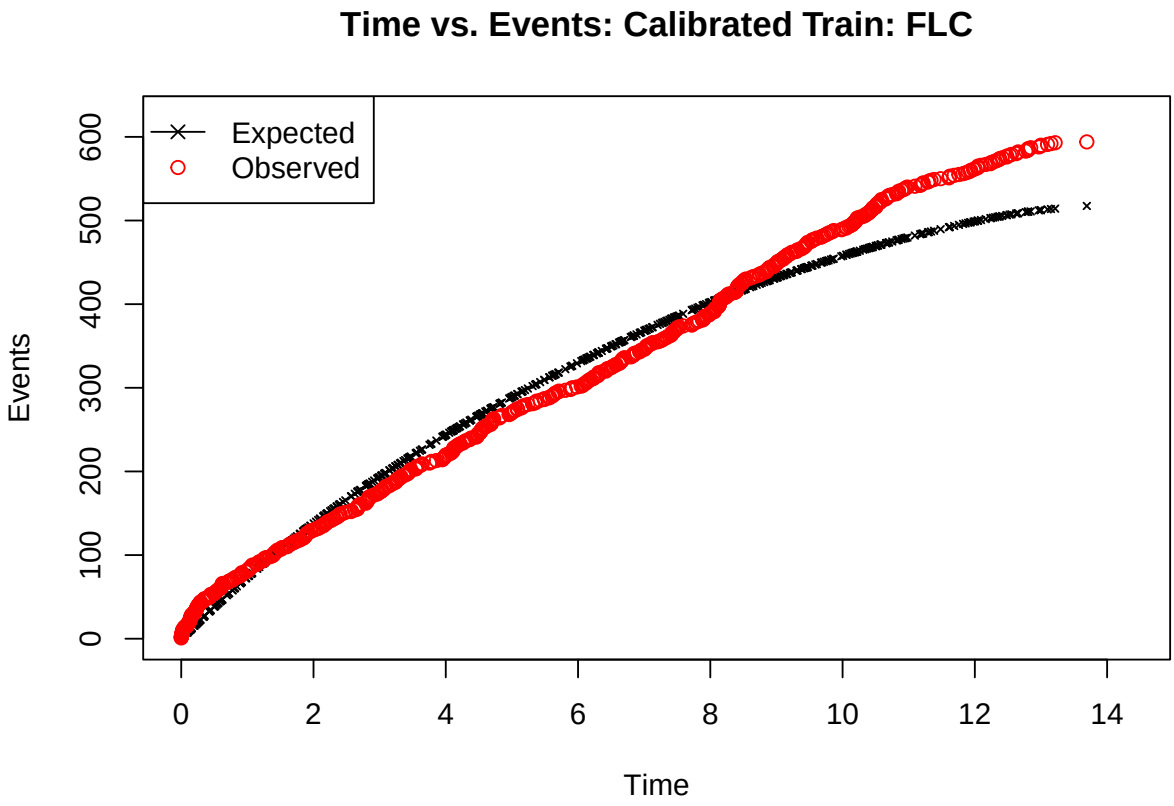
```
h0 <- calprob$h0
timeinterval <- calprob$timeInterval;

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


rrAnalysisTrain <- RRPlot(rdata,atProb=c(0.90,0.80),
                      timetoEvent=dataFLTrain$time,
                      title="Calibrated Train: FLC",
                      ysurvlim=c(0.00,1.0),
                      riskTimeInterval=timeinterval)
```

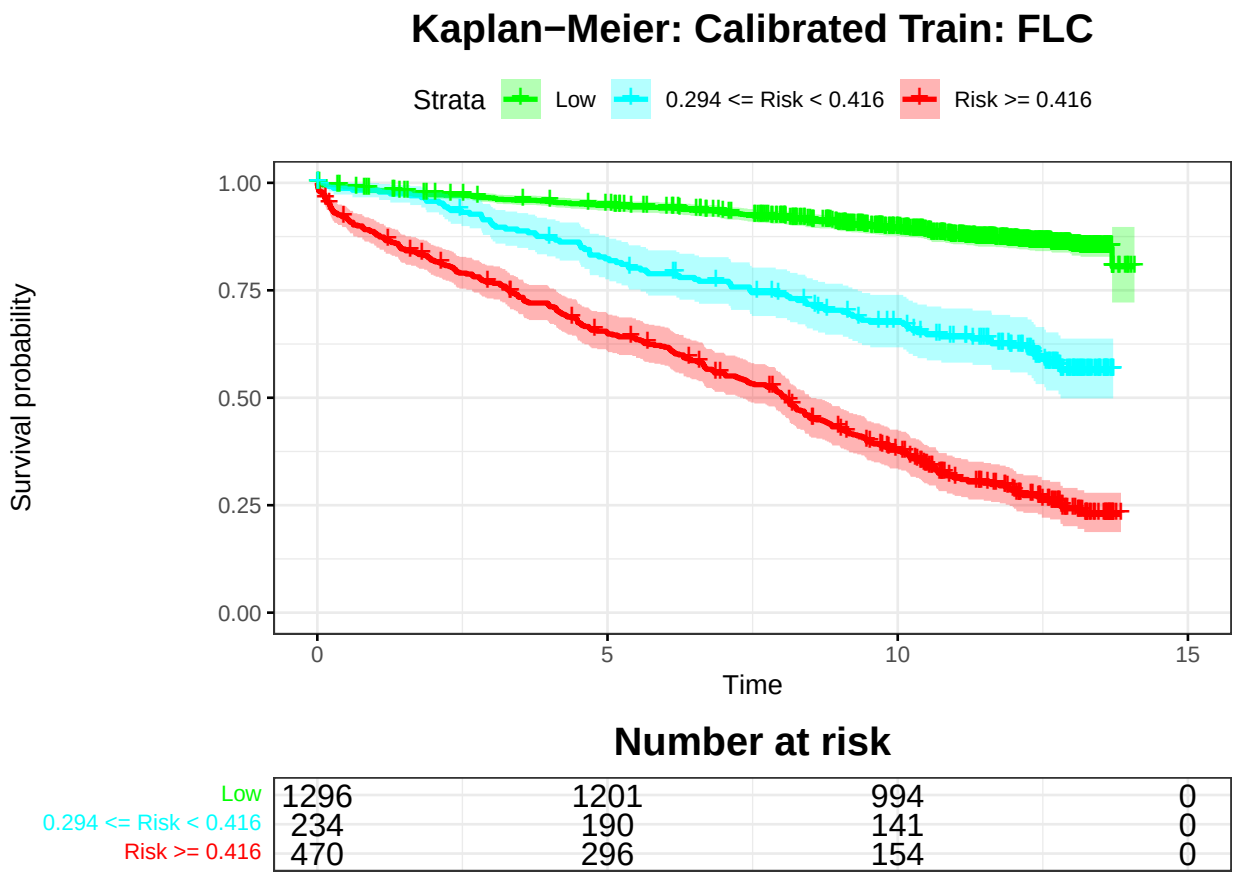

Cumulative vs. Observed: Calibrated Train: FLC
Observed
0
100
200
300
400
500
600
Cumulative Probability
Event
Expected


Decision Curve Analysis: Calibrated Train: FLC
Net Benefit
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.0
0.2
0.4
0.6
0.8
Threshold
No Event
Event
loess fit
SEN
1.0
0.8
0.6
0.4
0.2
0.0
Treat All
Treat None


Relative Risk: Calibrated Train: FLC
Index(0.90)=0.416
RR(0.55)=4.042
PPV–>
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
6
0.0
0.2
0.4
0.6
0.8
1.0


ROC: Calibrated Train: FLC
(TPR= 0.554 ,TNR= 0.900 ,ACC= 0.797 ,F1= 0.618 ,BER= 0.273)
Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
Confusion Matrix
O(+)
O(−)
T(+)
T(−)
Test
Outcome
AUC: 0.822
BACC (0.727)


Time vs. Events: Calibrated Train: FLC
Expected
Observed
Events
0
100
200
300
400
500
600
0
2
4
6
8
10
12
14
Time



1.2.5 Calibrated Train Performance

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

Table 19: O/E Ratio

est	lower	upper
1.15	1.06	1.24

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

Table 20: O/E Ratio

mean	50%	2.5%	97.5%
1.01	1.01	1	1.02

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

Table 21: O/Acum Ratio

mean	50%	2.5%	97.5%
1.02	1.02	1.02	1.02

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

Table 22: C. Index

mean.C Index	median	lower	upper
0.78	0.78	0.76	0.799

```
#pander::pander(rrAnalysisTrain$c.index,caption="C. Index")
pander::pander(t(rrAnalysisTrain$ROCAnalysis$aucs),caption="ROC AUC")
```

Table 23: ROC AUC

est	lower	upper
0.822	0.801	0.843

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

Table 24: Sensitivity

est	lower	upper
0.554	0.513	0.594

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

Table 25: Specificity

est	lower	upper
0.9	0.883	0.915

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

Table 26: Probability Thresholds

90%	80%
0.416	0.294

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

Table 27: Risk Ratio

est	lower	upper
4.04	3.57	4.58

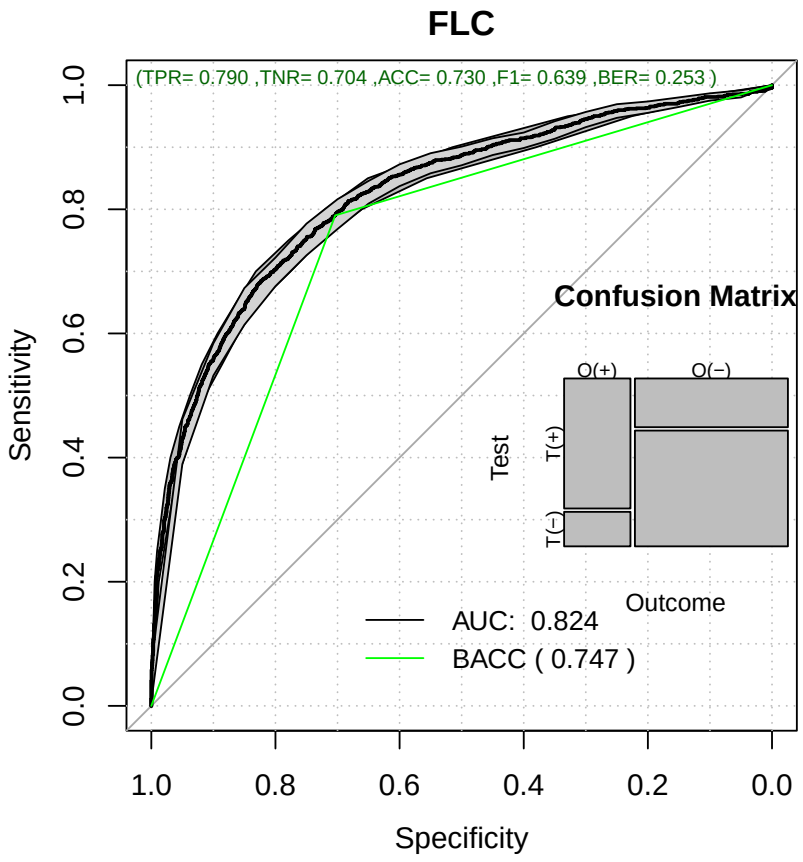
```
pander::pander(rrAnalysisTrain$surdif,caption="Logrank test")
```

Table 28: Logrank test Chisq = 709.746789 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	1296	172	427.9	153.00	553
class=1	234	93	67.4	9.72	11
class=2	470	329	98.7	536.99	653

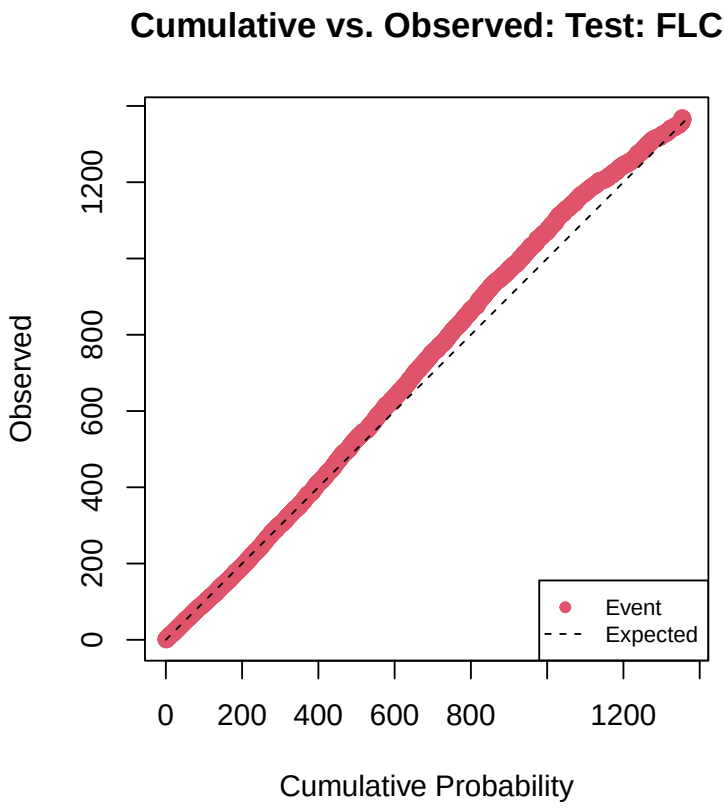
1.3 Performance on the test data set

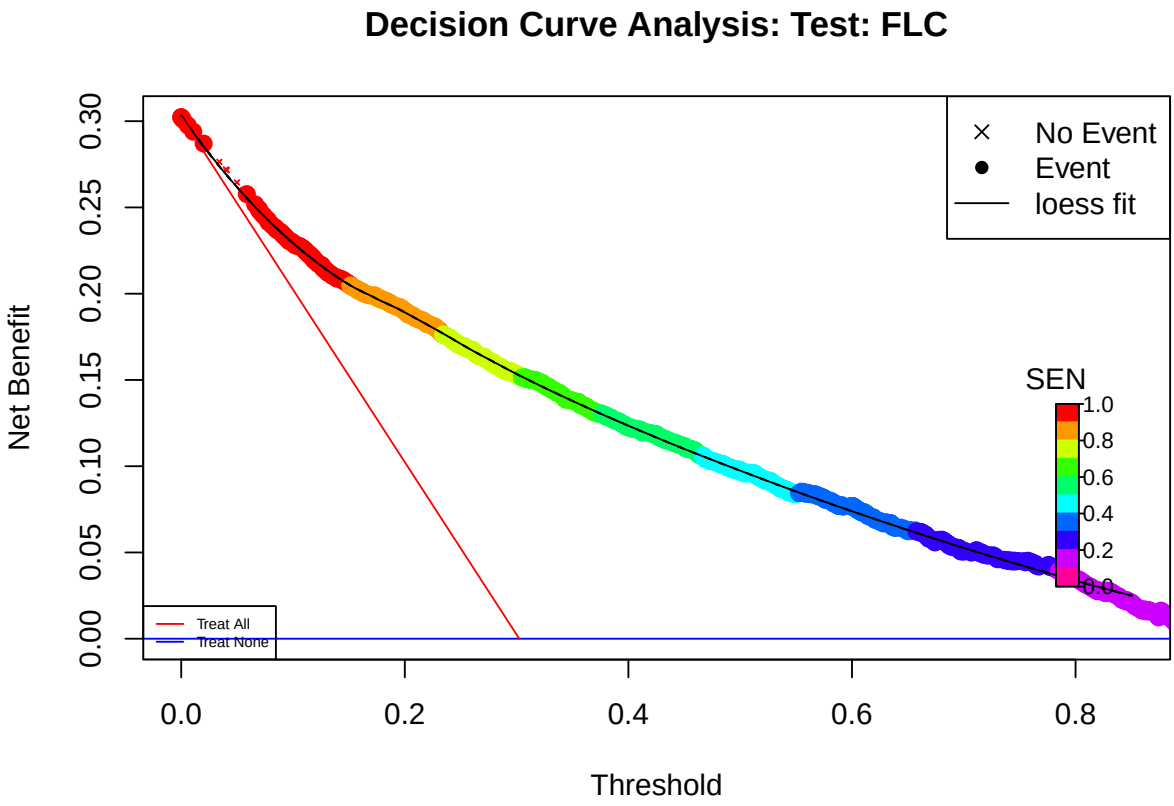
```
index <- predict(ml,dataFLTest)
pp <- predictionStats_binary(cbind(dataFLTest$status,index),plotname="FLC")
```

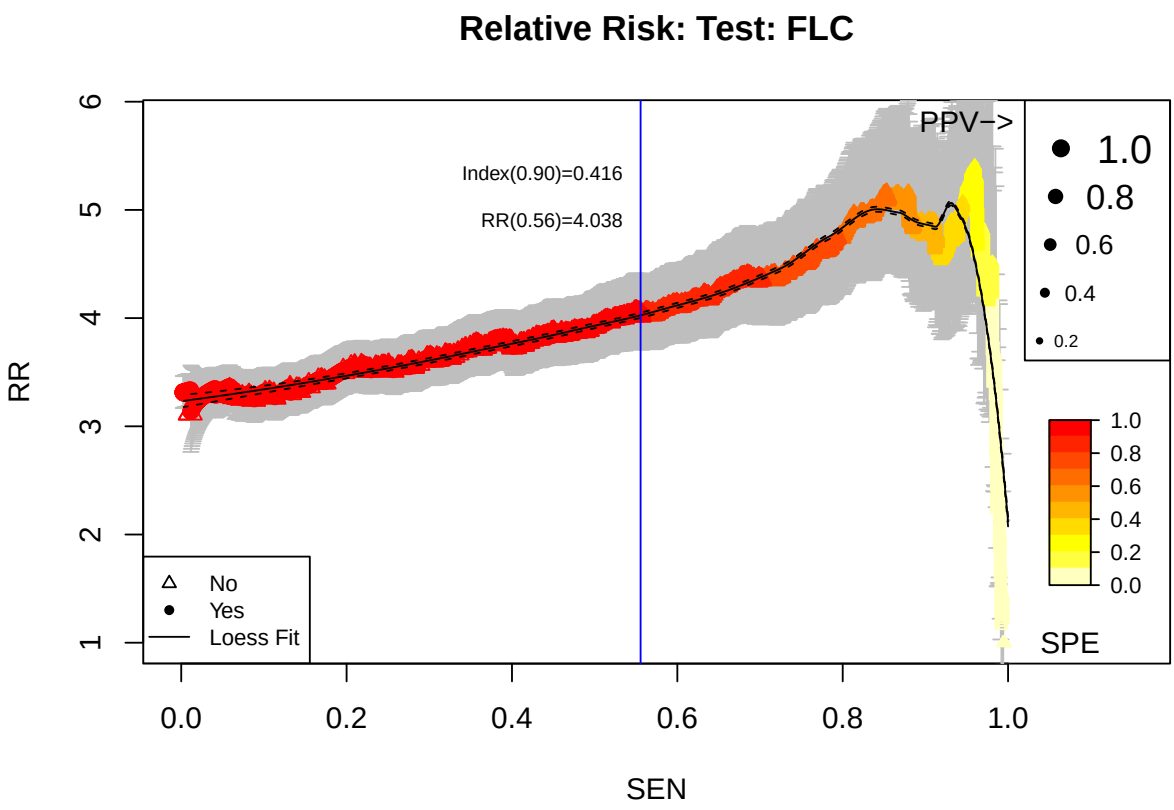


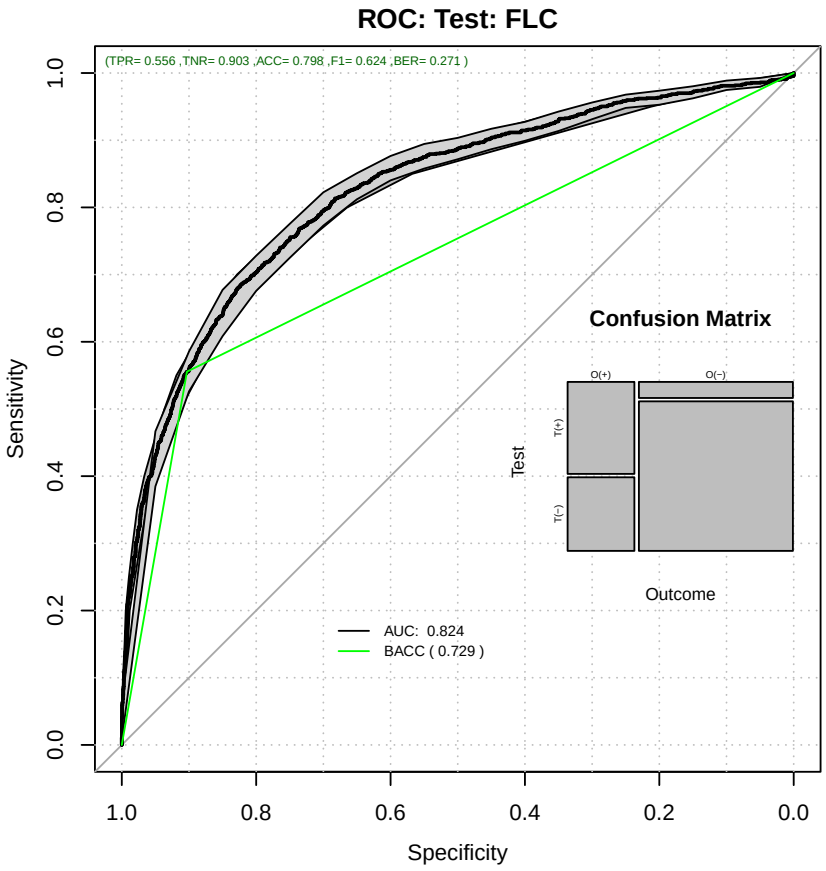

```
par(op)
```

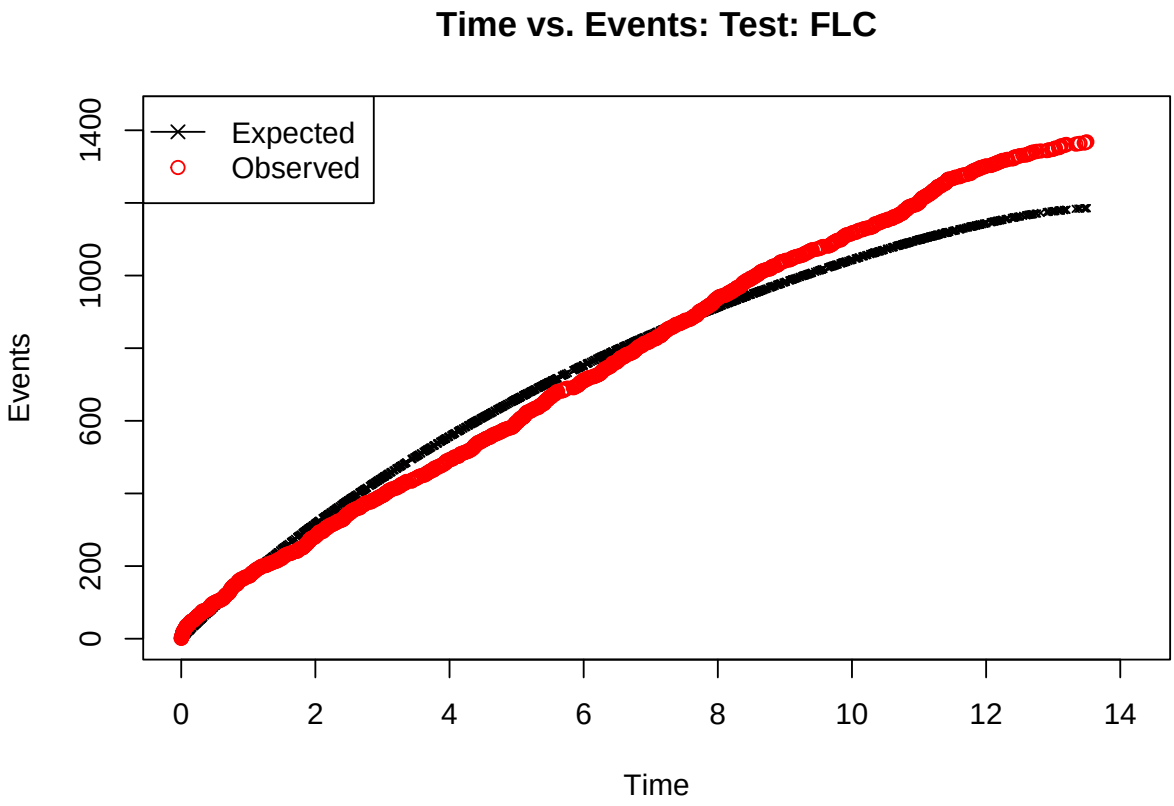
```
prob <- ppoisGzero(index,h0)
rdata <- cbind(dataFLTest$status,prob)
rrAnalysis <- RRPlot(rdata,atThr=rrAnalysisTrain$thr_atP,
                     timetoEvent=dataFLTest$time,
                     title="Test: FLC",
                     ysurvlim=c(0.00,1.0),
                     riskTimeInterval=timeinterval)
```

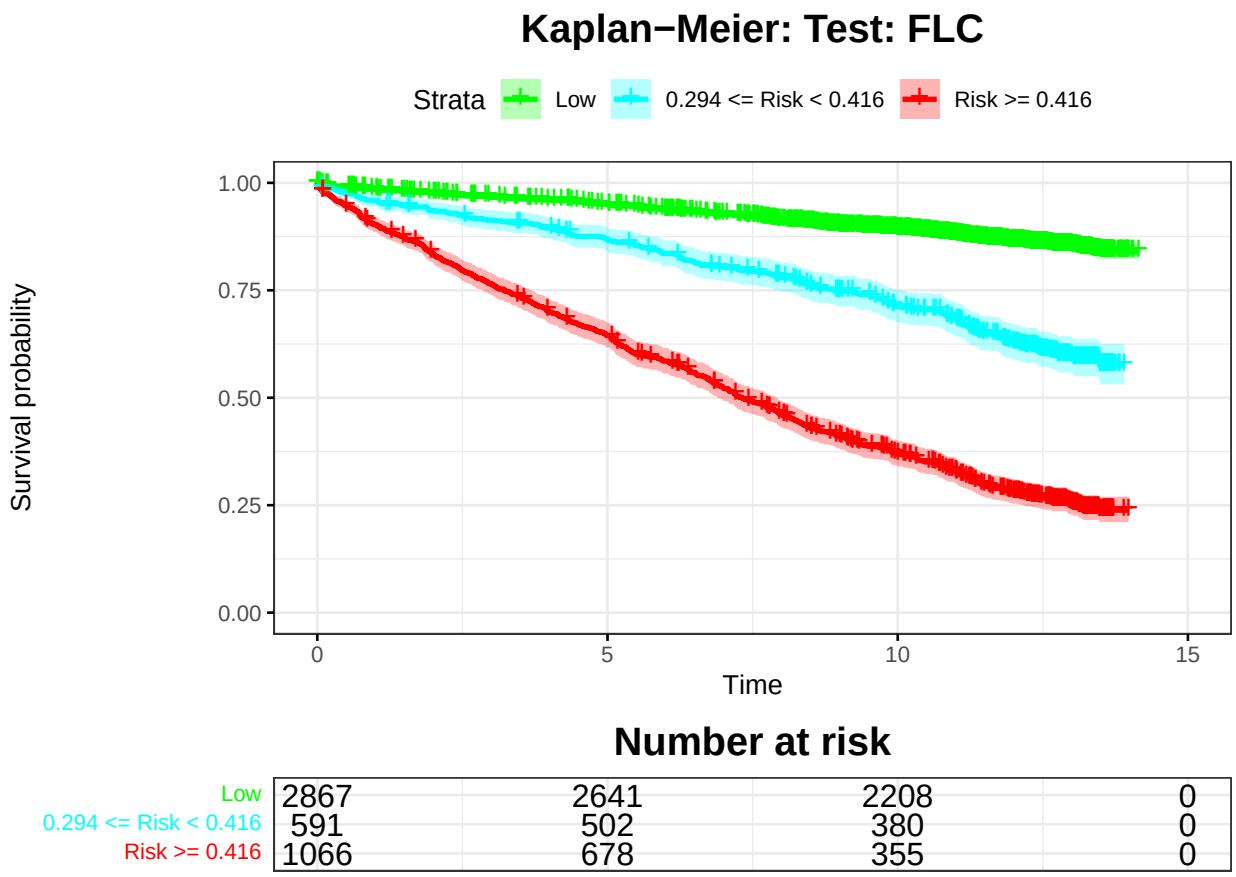



Decision Curve Analysis: Test: FLC
No Event
Event
loess fit
SEN
1.0
0.8
0.6
0.4
0.2
0.0
Treat All
Treat None
Net Benefit
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.0
0.2
0.4
0.6
0.8
Threshold


Relative Risk: Test: FLC
RR
SEN
PPV–>
Index(0.90)=0.416
RR(0.56)=4.038
No
Yes
Loess Fit
SPE
1.0
0.8
0.6
0.4
0.2
0.0


ROC: Test: FLC
(TPR= 0.556 ,TNR= 0.903 ,ACC= 0.798 ,F1= 0.624 ,BER= 0.271)
Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
AUC: 0.824
BACC (0.729)
Confusion Matrix
O(+)
O(−)
T(+)
T(−)
Test
Outcome


Time vs. Events: Test: FLC
Expected
Observed
Events
0
200
600
1000
1400
0
2
4
6
8
10
12
14
Time




```
par(op)
```

1.3.1 External Data Report

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

Table 29: O/E Ratio

est	lower	upper
1.15	1.09	1.22

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

Table 30: O/E Ratio

mean	50%	2.5%	97.5%
0.991	0.991	0.986	0.995

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

Table 31: O/Acum Ratio

mean	50%	2.5%	97.5%
1.04	1.04	1.04	1.04

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

Table 32: C. Index

mean.C Index	median	lower	upper
0.778	0.778	0.765	0.791

```
#pander::pander(rrAnalysis$c.index,caption="C. Index")
pander::pander(t(rrAnalysis$ROCAnalysis$aucs),caption="ROC AUC")
```

Table 33: ROC AUC

est	lower	upper
0.824	0.81	0.838

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

Table 34: Sensitivity

est	lower	upper
0.556	0.529	0.582

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

Table 35: Specificity

est	lower	upper
0.903	0.892	0.913

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

Table 36: Probability Thresholds

90%	80%
0.416	0.294

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

Table 37: Risk Ratio

est	lower	upper
4.04	3.72	4.38

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

Table 38: Logrank test Chisq = 1603.704759 on 2 degrees of freedom, p = 0.000000

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
class=0	2867	386	960	342.8	1157.9
class=1	591	222	179	10.2	11.7
class=2	1066	760	229	1230.3	1496.4