

Analyzing Competing Risk Data Using the R timereg Package

Worked example (Follicular cell lymphoma study)

```
rm(list = ls())
```

```
library(timereg)
```

```
fol <- read.table("https://raw.githubusercontent.com/scheike/update-code-for-jss-comp.risk/master/folli")
```

```
head(fol)
```

```
##   age path1 hgb ldh clinstg blktxcat relsite ch rt   survtime stat
## 1  56  NH04 140  NA      2        1      B   Y  0.6981520    1
## 2  36  NH02 130  NA      2        1      D   Y 14.5023956    1
## 3  39  NH02 140  NA      2        3      Y   Y  4.9144422    1
## 4  37  NH03 140  NA      1        1      Y   Y 15.6851472    1
## 5  61  NH04 110  NA      2        2      Y   Y  0.2354552    1
## 6  69  NH02 120  NA      1        1      Y   Y  8.4188912    1
##           dftime dfcens resp stnum
## 1  0.238193018      1   CR      1
## 2 12.418891170      1   CR      2
## 3  0.002737851      1  NR      3
## 4 15.685147159      1   CR      4
## 5  0.002737851      1  NR      5
## 6  8.418891170      1   CR      6
```

```
table(fol$resp,useNA = "always")
```

```
##
##   CR   NR <NA>
## 517   24     0
```

```
table(fol$relsite,useNA = "always")
```

```
##
##           B    D    L <NA>
## 293    18  214   16     0
```

```
table(fol$stat,useNA = "always")
```

```
##
##    0    1 <NA>
## 285 256     0
```

```

evcens <- (fol$resp=="NR" | fol$rebsite!="")
# no treatment response OR relapse
crcens <- (fol$resp=="CR" & fol$rebsite==" " & fol$stat==1)
# death AND without relapse AND after Complete treatment response
cause <- ifelse(evcens==1,1,ifelse(crcens==1,2,0))
table(cause)

```

```

## cause
##    0    1    2
## 193 272   76

```

272 no treatment response or relapse 76 competing risk events (death without relapse) 193 censored

```

stage <- as.numeric(fol$clinstg==2)
fol$chemo<-as.numeric(fol$ch=="Y")
times1=sort(unique(fol$dftime[cause==1]))
fol$age <- scale(fol$age)

```

```

library("timereg")
library("cmprsk")

```

```

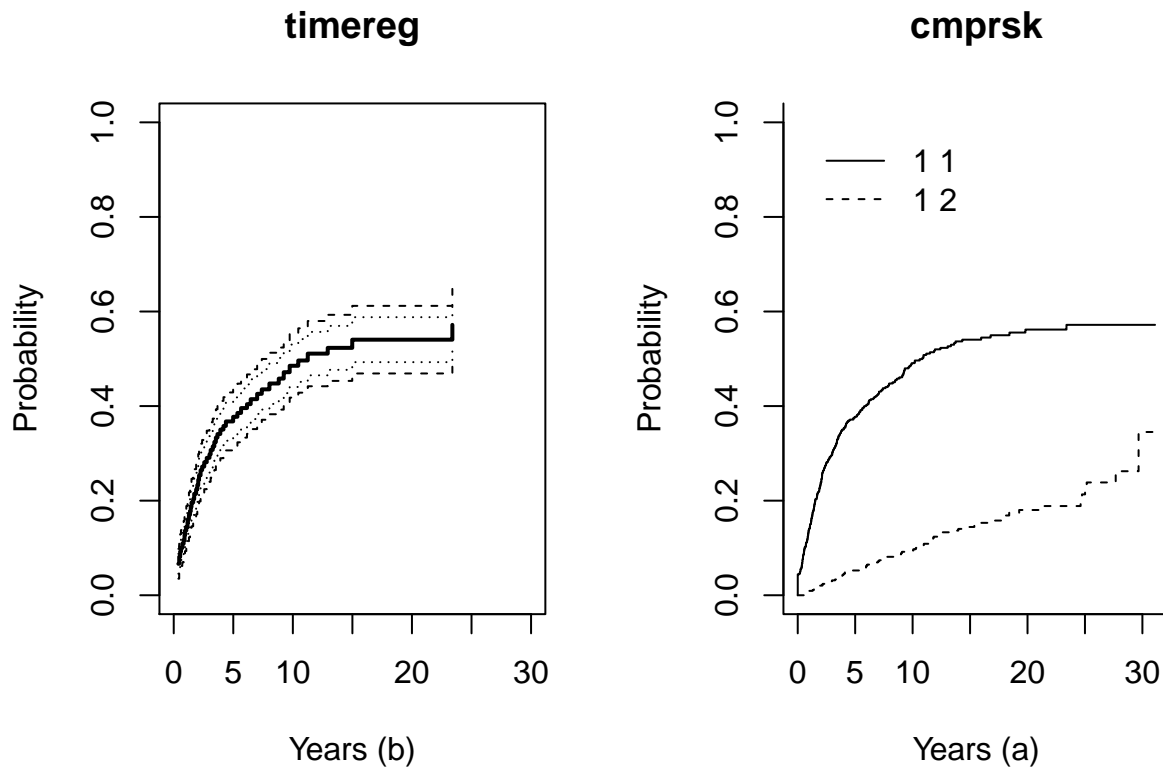
out1 <-comp.risk(Event(dftime,cause)~ 1,data=fol,cause=1,model="additive")
pout1 <- predict(out1,X=1)
fit<-cuminc(fol$dftime,cause,cencode=0)

```

```

par(mfrow=c(1,2))
plot(pout1,xlim=c(0,30),xlab="Years (b)",main="timereg",uniform=2,se=3)
plot(fit,main="cmprsk",xlab="Years (a)")

```



```
## problems with convergence when hgb included
outf<-comp.risk(Event(dftime,cause)~stage+age+chemo,
data=fol,cause=1,n.sim=5000,model="prop",cens.model="cox")
summary(outf)
```

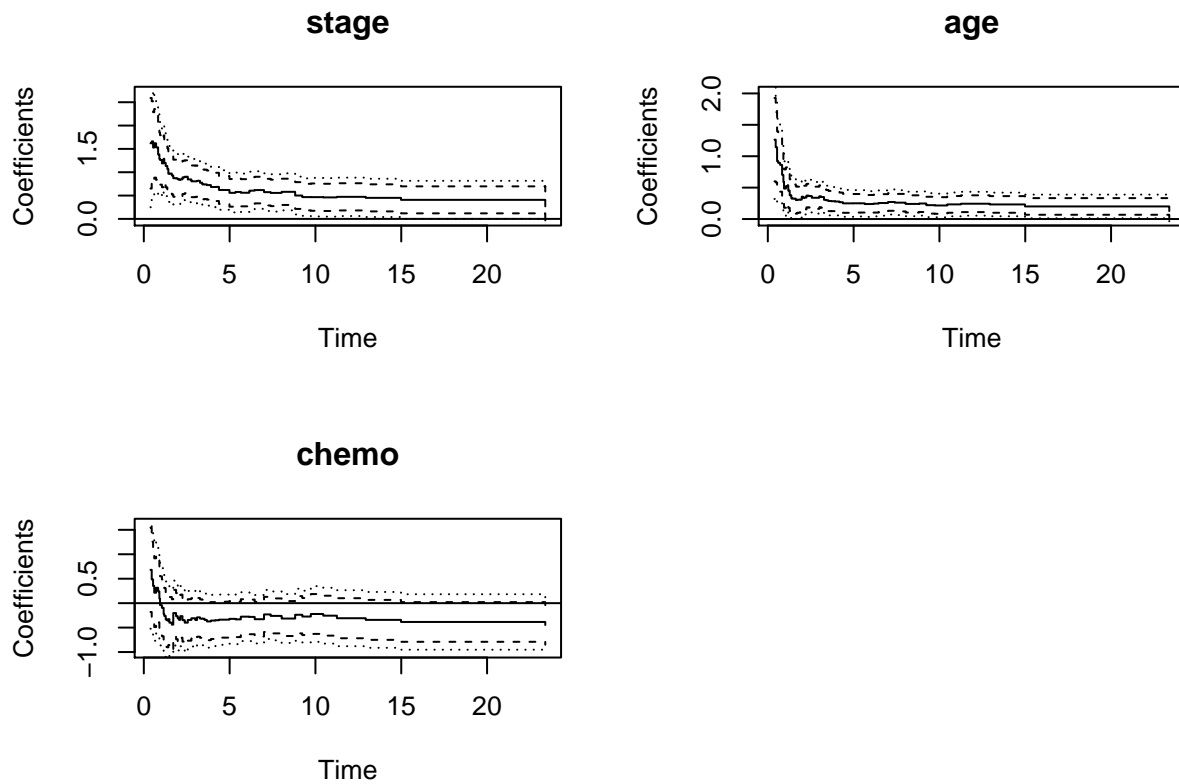
```
## Competing risks Model
##
## Test for nonparametric terms
##
## Test for non-significant effects
##      Supremum-test of significance p-value H_0: B(t)=0
## (Intercept)                12.10                0.000
## stage                      5.04                 0.000
## age                        4.07                 0.000
## chemo                      2.18                 0.179
##
## Test for time invariant effects
##      Kolmogorov-Smirnov test p-value H_0:constant effect
## (Intercept)                2.980                0.0000
## stage                      0.950                0.0180
## age                        0.853                0.0022
## chemo                      0.760                0.0190
##
##      Cramer von Mises test p-value H_0:constant effect
## (Intercept)               13.200                0.0000
## stage                     2.660                0.0006
## age                      0.457                0.0028
```

```
## chemo
```

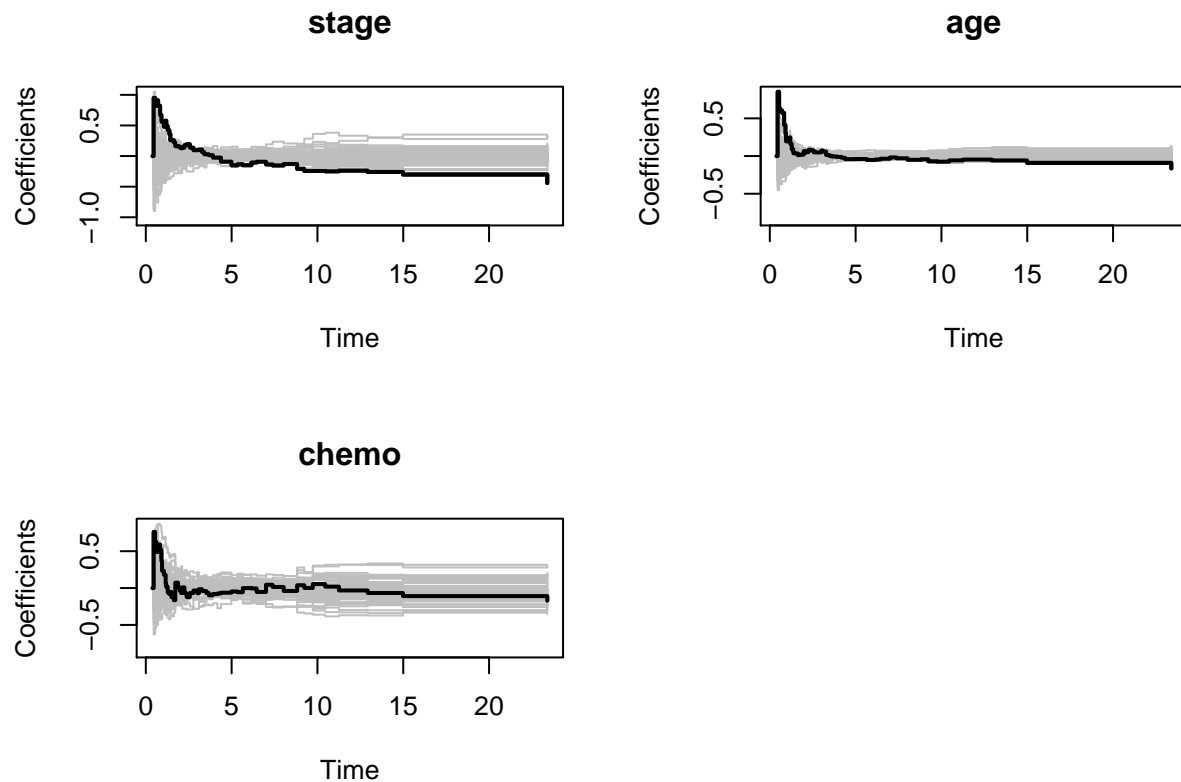
0.482

0.3490

```
par(mfrow=c(2,2))  
plot(outf,specific.comps=2:4,pointwise.ci=2,sim.ci=3)
```



```
par(mfrow=c(2,2))  
plot(outf,specific.comps=2:4,score=1)
```



```
outf1<-comp.risk(Event(dftime,cause)~stage+age+const(hgb)+chemo,
data=fol,cause=1,times=times1,model="prop")
summary(outf1)
```

```
## Competing risks Model
##
## No test for non-parametric terms
## Parametric terms :
##          Coef.      SE Robust SE      z P-val lower2.5% upper97.5%
## const(hgb) 0.000387 0.00406    0.00406 0.0953 0.924  -0.00757    0.00834
##
```

```
outfg<-comp.risk(Event(dftime,cause)~const(stage)+const(age)+
const(hgb)+const(chemo),data=fol,cause=1,times=times1,model="prop",cens.model="cox")
summary(outfg)
```

```
## Competing risks Model
##
## No test for non-parametric terms
## Parametric terms :
##          Coef.      SE Robust SE      z  P-val lower2.5%
## const(stage) 0.678000 0.13900    0.13900 4.8800 1.05e-06    0.40600
## const(age)   0.280000 0.07210    0.07210 3.8900 1.02e-04    0.13900
## const(hgb)   0.000149 0.00413    0.00413 0.0362 9.71e-01   -0.00795
```

```
## const(chemo) -0.302000 0.17600 0.17600 -1.7200 8.59e-02 -0.64700
##               upper97.5%
## const(stage) 0.95000
## const(age)   0.42100
## const(hgb)   0.00824
## const(chemo) 0.04300
##
```

```
## predictions for fg model and outf1
```

```
newdata=data.frame(stage=c(0,1),age=c(-1,0.3),hgb=rep(138,2),chemo=c(0,1))
```

```
poutf1<-predict(outf1,newdata)
poutfg<-predict(outfg,newdata)
```

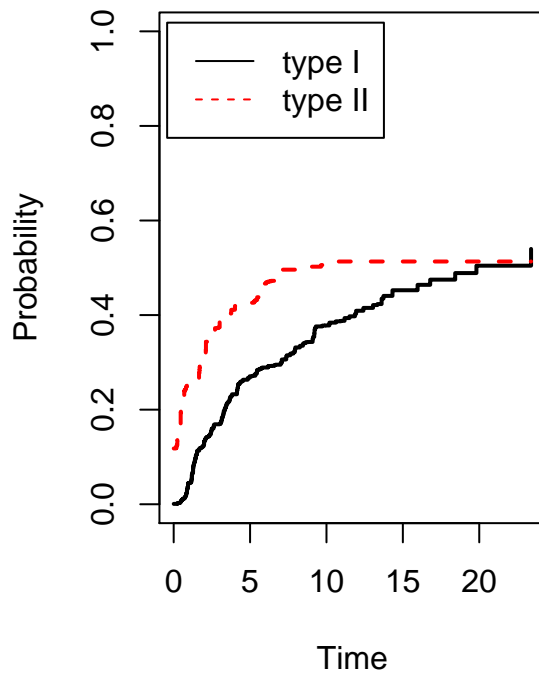
```
newdata
```

```
##   stage age hgb chemo
## 1     0 -1.0 138     0
## 2     1  0.3 138     1
```

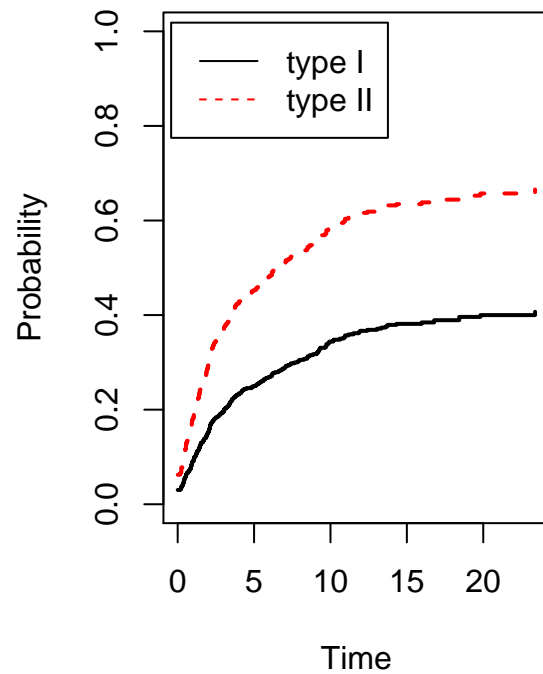
```
par(mfrow=c(1,2))
plot(poutf1,multiple=1,se=0,uniform=0,col=1:2,lty=1:2)
legend("topleft",inset = .02 ,lty = 1:2,col = 1:2,c("type I","type II"))
title(main="Flexible model predictions")

plot(poutfg,multiple=1,se=0,uniform=0,col=1:2,lty=1:2)
legend("topleft",inset = .02,lty = 1:2,col = 1:2,c("type I","type II"))
title(main="Fine-Gray model predictions")
```

Flexible model predictions



Fine-Gray model predictions

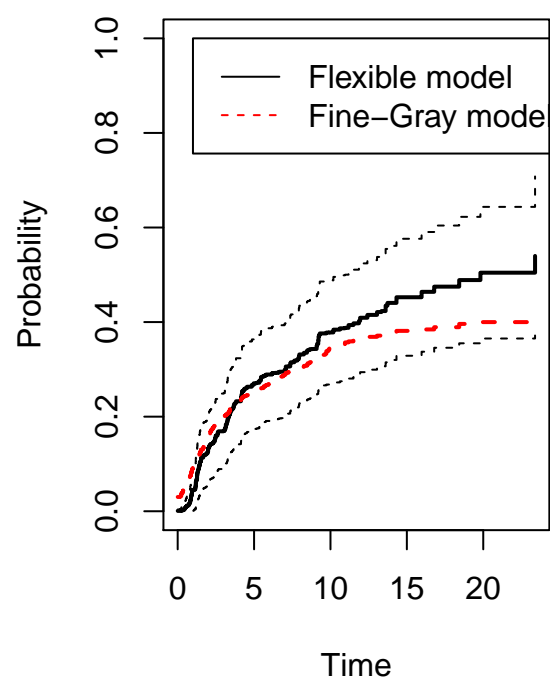


```
par(mfrow=c(1,2))
plot(poutf1,se=0,uniform=2,col=1,lty=1,specific.comps=1)
plot(poutfg,new=0,se=0,uniform=0,col=2,lty=2,specific.comps=1)

title(main="Type I patients")
legend(1,1.0,c("Flexible model","Fine-Gray model"),lty=1:2,col=1:2)

plot(poutf1,se=0,uniform=1,col=1,lty=1,specific.comps=2)
plot(poutfg,new=0,se=0,uniform=0,col=2,lty=2,specific.comps=2)
title(main="Type II patients")
legend(1,1.0,c("Flexible model","Fine-Gray model"),lty=1:2,col=1:2)
```

Type I patients



Type II patients

