Exercise 3-13 IUD data competing risk

The tabled data consist of on 32 women who used the intera-uterine prevention device (IUD). However, the text refers to 100 women, and supposedly the remaining 68 must be censored at the end of follow-up at 300 days. We will first do the exercise without the remaining 68 and then for comparison show the plots including these censored events.
Data are the times from insertion of the device until the 1st of 3 endpoints

- The IUD was expelled (10 women)
- The IUD was removed (19 women)
- Follow-up ended before expulsion or removal (3+68 w.)

This is a competing risk situation because there are two different essential outcomes (expulsion or removal).

Data file

Data were read in to a file "iud"

```
> library(survival)

> iud[1:15,]
   time stat
1     2    1
2    14    2
3   166    2
4    86    0
5     8    1
6    21    2
7   178    2
8   203    0
9    10    1
10   27    2
11  183    2
12  207    0
13   25    1
14   40    2
15  272    2
```

Cumulative hazards for IUD data

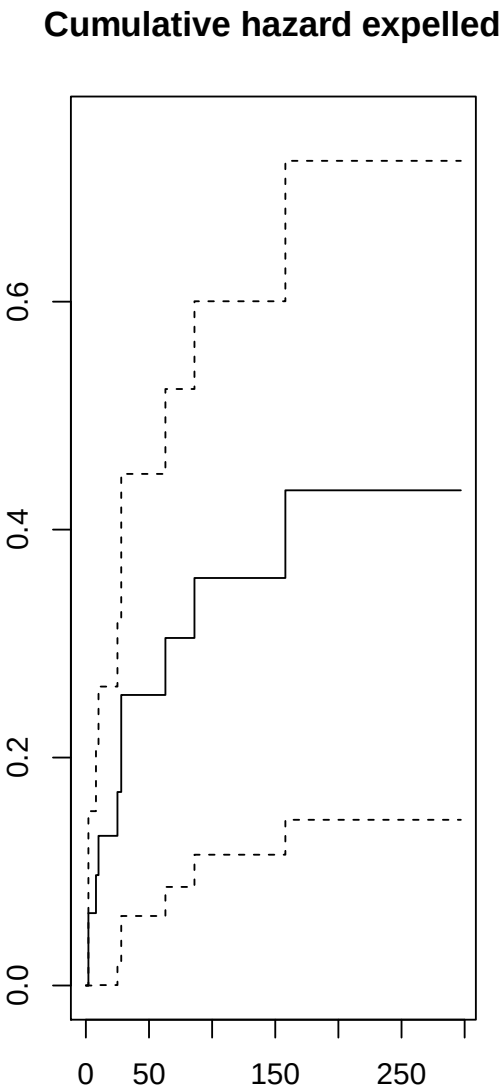
can be obtained in R through the `survfit` function in the standard way, using the other event as censoring.

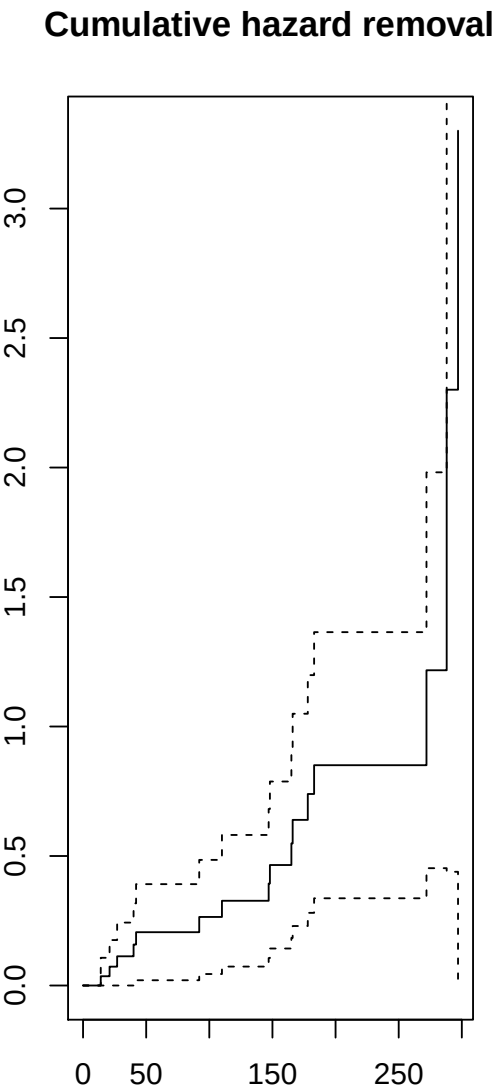
```
iudcumhazexp=survfit(Surv(time,stat==1)~1,dat=iud,type="fh")
iudcumhazrem=survfit(Surv(time,stat==2)~1,dat=iud,type="fh")

par(mfrow=c(1,2))
plot(iudcumhazexp,fun="cumhaz",ylim=c(0,0.75),main="Cumulative hazard ex
plot(iudcumhazrem,fun="cumhaz",main="Cumulative hazard removal")
```

We note that

- The cumulative hazard for expelling the IUD is close to concave. This indicates a decreasing hazard
- The cumulative hazard for removal is close to convex. This indicates an increasing hazard.

Plots of cumulative hazards for IUD data





Cumulative incidence functions

The transition probabilities for competing risks are given as

$$P_{0h}(s,t) = P(X(t) = h | X(s) = 0)$$

can be estimated

$$\widehat{\mathrm{P}}_{00}(s,t) = \prod_{s<u\leq t} \left[1 - \frac{dN_0(u)}{Y_0(u)}\right],$$

for $h = 0$ and

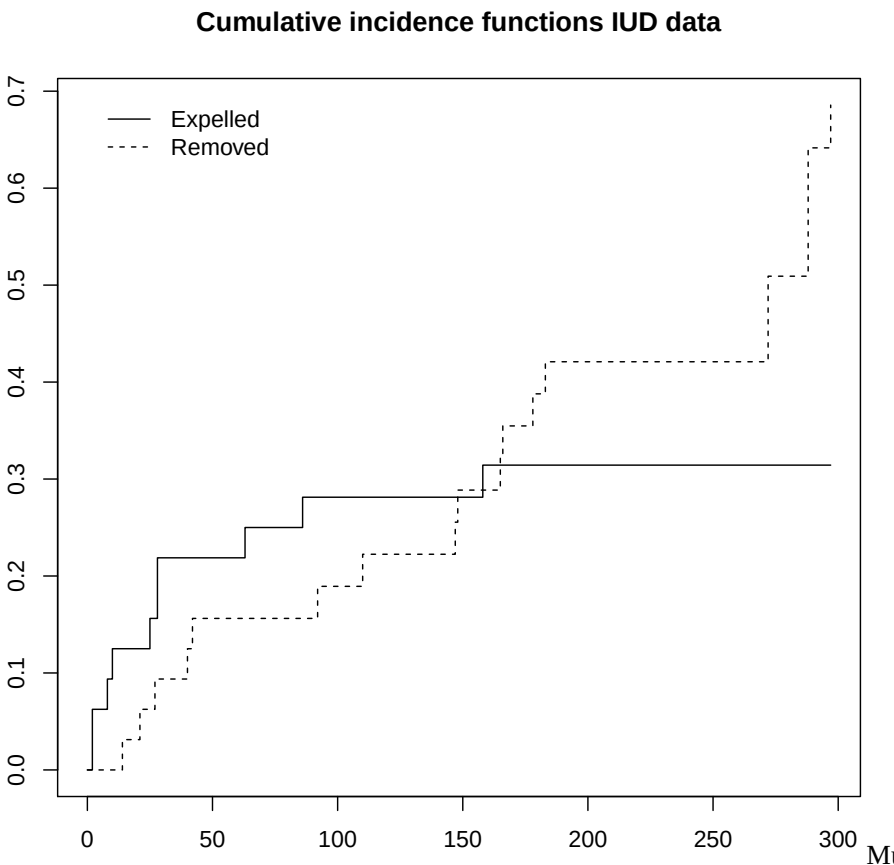
$$\hat{P}_{0h}(s,t) = \int_s^t \hat{P}_{00}(s,u-)\frac{dN_{0h}(u)}{Y_0(u)}$$

for $h = 1, \ldots, K$. The $\hat{P}_{0h}(s,t)$ for $h > 0$ are called cumulative incidence functions.

Cumulative incidence functions for IUD data

can be obtained in R also using the `survfit` function, but with "mstate" option.

```
iudcuminc=survfit(Surv(time,stat,type="mstate")~1,dat=iud)
par(mfrow=c(1,1))
plot(iudcuminc,lty=1:2,main="Cumulative incidence functions IUD data")
legend(0,0.7,lty=1:2,c("Expelled","Removed"),bty="n")
```

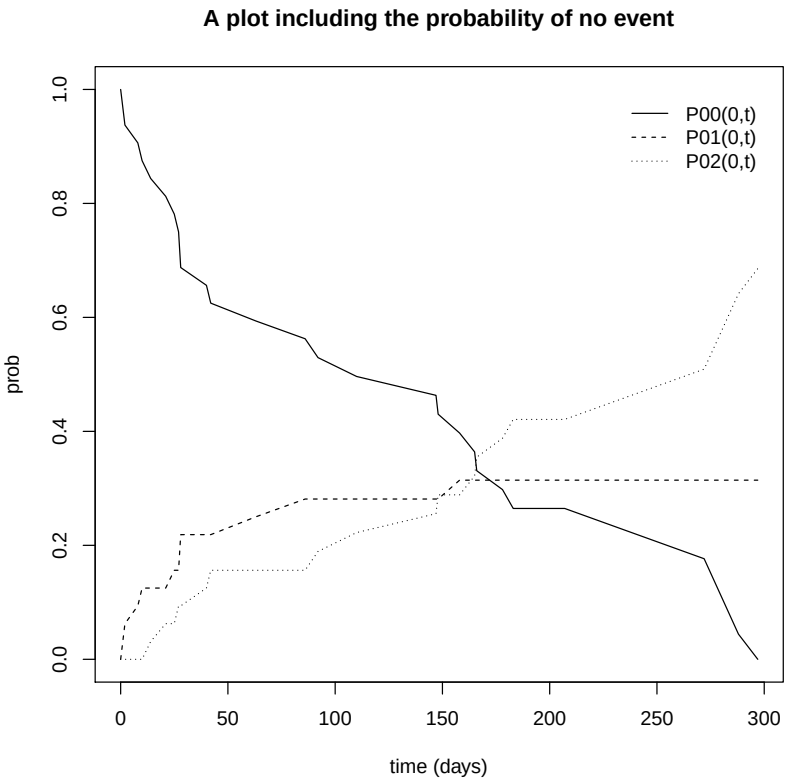


Comments

- $0 \leq \hat{\mathrm{P}}_{01}(0,t) \leq 1$ and $0 \leq \hat{\mathrm{P}}_{02}(0,t) \leq 1$
- $\hat{\mathrm{P}}_{01}(0,t) + \hat{\mathrm{P}}_{02}(0,t) \leq 1$
- $\hat{\mathrm{P}}_{01}(0,300) + \hat{\mathrm{P}}_{02}(0,300) = 1$

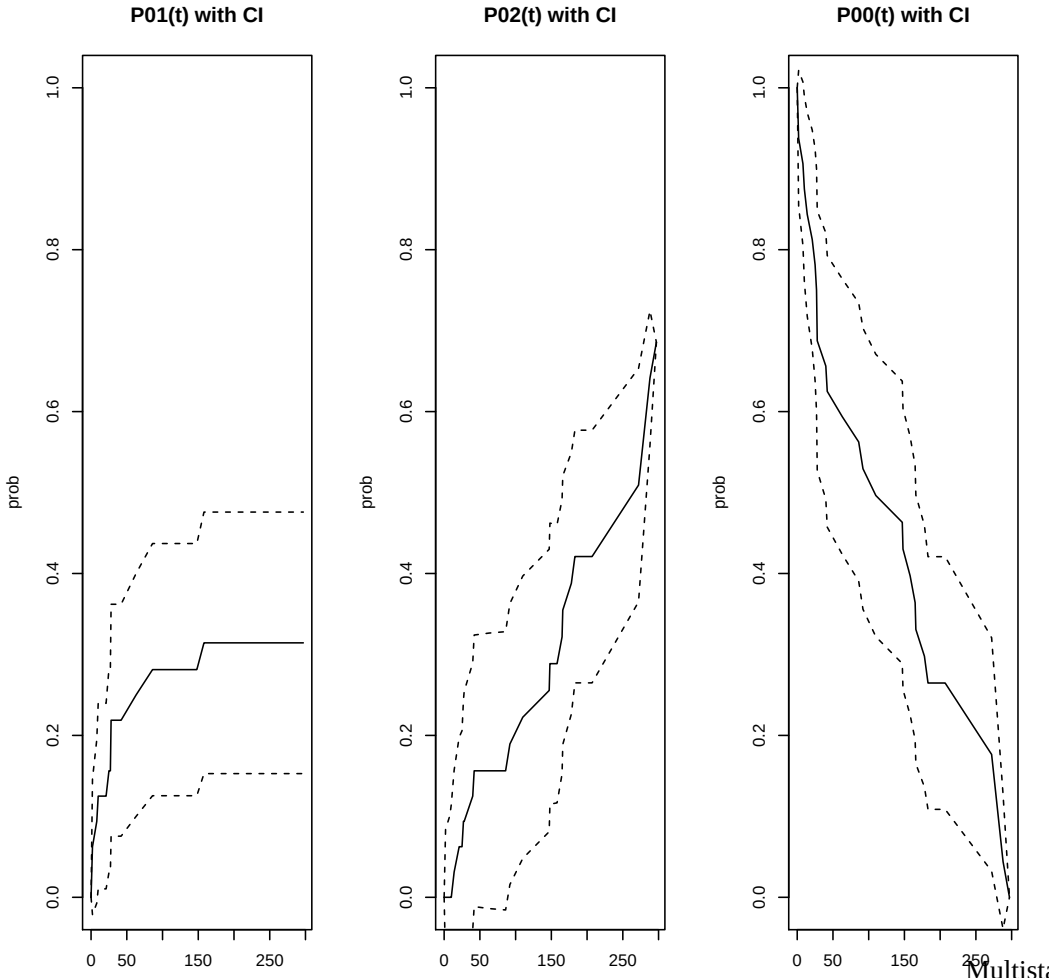
A plot including $\hat{\mathbf{P}}_{01}(0,t)$

```
prev=rbind(c(0,0,1),iudcuminc$prev)
tid=c(0,iudcuminc$time)
se=rbind(c(0,0,0),iudcuminc$std.err)
plot(tid,prev[,3],type="l",xlab="time (days)",ylab="prob")
lines(tid,prev[,1],lty=2)
lines(tid,prev[,2],lty=3)
legend(230,1,lty=1:3,c("P00(0,t)","P01(0,t)","P02(0,t)"),bty="n")
title("A plot including the probability of no event")
```



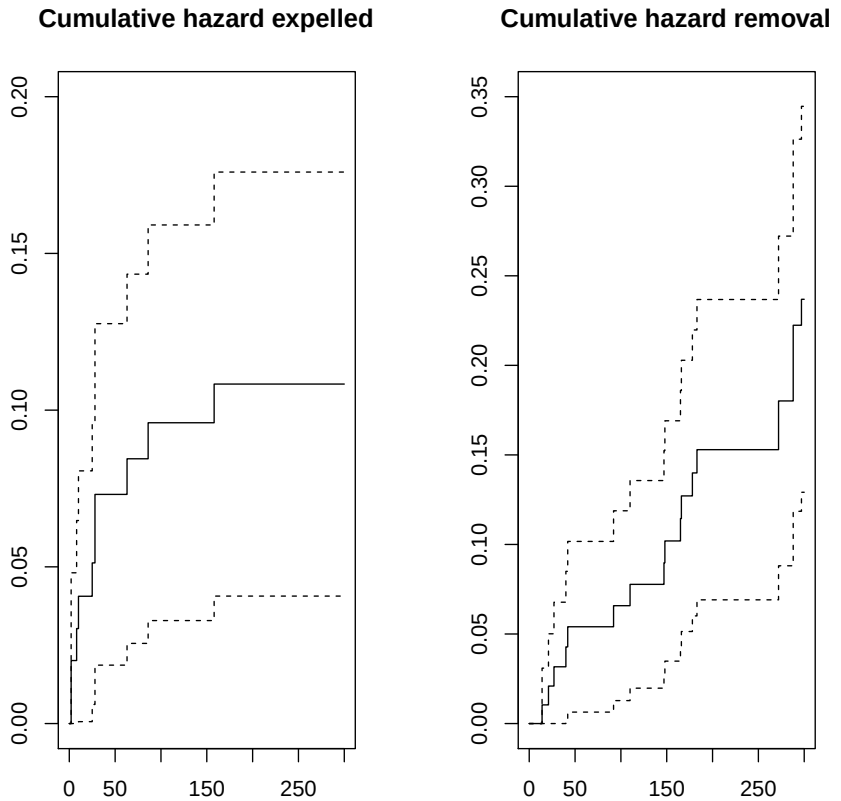
Plots of cumulative incidence including with CI's

```
plot(tid,prev[,1],type="l",xlab="time (days)",ylab="prob",ylim=c(0,1))
lines(tid,prev[,1]+1.96*se[,1],lty=2)
lines(tid,prev[,1]-1.96*se[,1],lty=2)
title("P01(t) with CI")
```



Including 68 censored women

```
additwomen=data.frame(cbind(rep(300,68),rep(0,68)))
names(additwomen)=names(iud)
iud=rbind(iud,additwomen)
iudcumhazexp=survfit(Surv(time,stat==1)~1,dat=iud,type="fh")
iudcumhazrem=survfit(Surv(time,stat==2)~1,dat=iud,type="fh")
plot(iudcumhazexp,fun="cumhaz",main="Cumulative hazard expelled")
plot(iudcumhazrem,fun="cumhaz",main="Cumulative hazard removal")
```

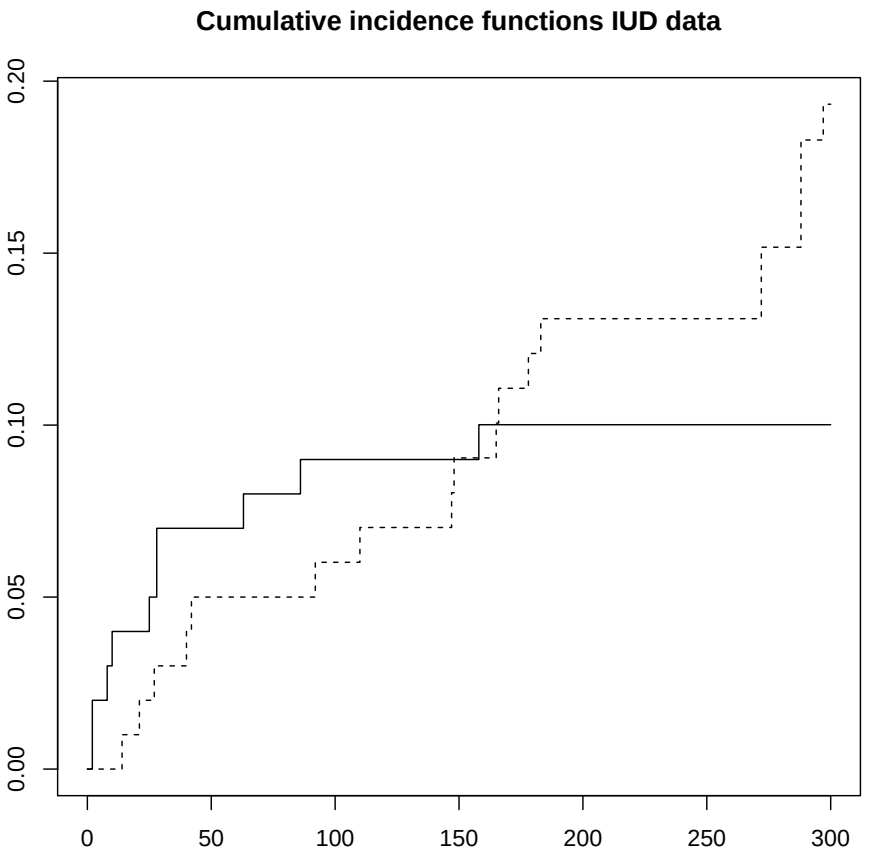


Summary of cumulative hazards

Compared to the analyses where the 68 censored women were not included we note

- The absolute value (y-axis) of the cumulative hazards is much smaller.
- This is natural since the overall rate of expulsion and removal must be smaller.
- The cumulative hazard for expelling the IUD is still close to concave. So still a decreasing hazard.
- The cumulative hazard for removal now closer to straight line. This indicates that a constant hazard may be OK.

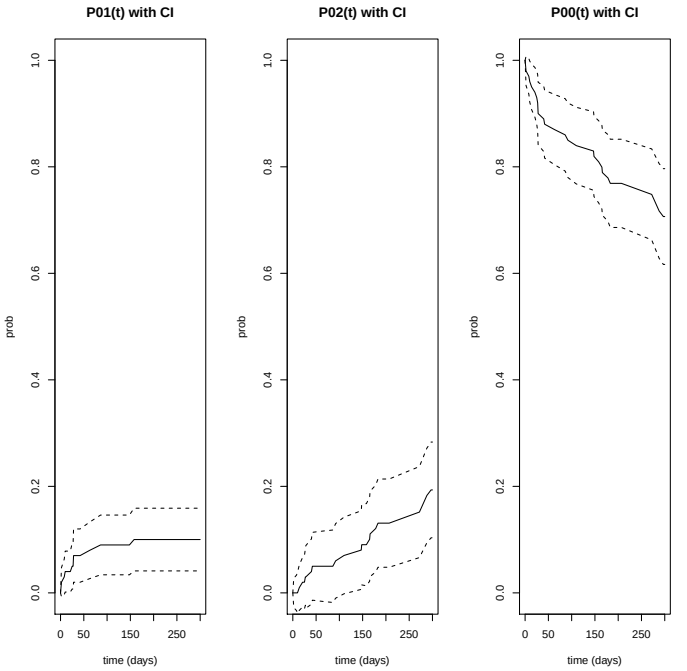
Cumulative incidence functions for extended IUD data



Note:

- The cumulative incidences now only go to 10% and 20%
- The rather steep increase towards 300 days for removal is no longer present

Plots of cumulative incidence including with CI's



When including the 68 censored women we see

- again the smaller cumulative incidences
- larger probability of no event (going down to 70%)
- and clearly the symmetric CI is inappropriate for removal since the lower limit has negative values