Chapter 8

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Contents


```
# install.packages("asaur")    # this must be done once

# Section 8.1 Stanford heart transplant data
library(survival)
coxph(Surv(futime, fustat) ~ transplant + age + surgery, data=jasa) # naive analysis
```

```
## Call:
## coxph(formula = Surv(futime, fustat) ~ transplant + age + surgery,
##     data = jasa)
##
##               coef exp(coef) se(coef)     z       p
## transplant -1.7171    0.1796   0.2785 -6.16 7.1e-10
## age         0.0589    1.0607   0.0150  3.91 9.1e-05
## surgery    -0.4190    0.6577   0.3712 -1.13    0.26
##
## Likelihood ratio test=45.9  on 3 df, p=6.11e-10
## n= 103, number of events= 75
```

```
# landmark method, with landmark set to 30 days
ind30 <- jasa$futime >= 30
sum(ind30)
```

```
## [1] 79
```

```
transplant30 <- {{jasa$transplant == 1} & {jasa$wait.time < 30}}
sum(transplant30)
```

```
## [1] 39
```

```
coxph(Surv(futime, fustat) ~ transplant30 + age + surgery, data=jasa, subset=ind30)
```

```
## Call:
## coxph(formula = Surv(futime, fustat) ~ transplant30 + age + surgery,
##     data = jasa, subset = ind30)
##
##                       coef exp(coef) se(coef)     z     p
## transplant30TRUE -0.0421    0.9587   0.2838 -0.15 0.882
## age               0.0372    1.0379   0.0171  2.17 0.030
## surgery          -0.8197    0.4406   0.4130 -1.98 0.047
##
## Likelihood ratio test=9.5  on 3 df, p=0.0233
## n= 79, number of events= 52
```

subset example

```
id <- 1:nrow(jasa)
jasaT <- data.frame(id, jasa)
id.simple <- c(2, 5, 10, 12, 28, 95)
heart.simple <- jasaT[id.simple,c(1, 10, 9, 6, 11)]
heart.simple
```

```
##    id wait.time futime fustat transplant
## 2   2        NA      5      1          0
## 5   5        NA     17      1          0
## 10 10        11     57      1          1
## 12 12        NA      7      1          0
## 28 28        70     71      1          1
## 95 95         1     15      1          1
```

```
coxph(Surv(futime, fustat) ~ transplant, data=heart.simple) # naive analysis
```

```
## Call:
## coxph(formula = Surv(futime, fustat) ~ transplant, data = heart.simple)
##
##              coef exp(coef) se(coef)     z    p
## transplant -1.688     0.185    1.172 -1.44 0.15
##
## Likelihood ratio test=2.47  on 1 df, p=0.116
## n= 6, number of events= 6
```

put data into counting process format

```
sdata <- tmerge(heart.simple, heart.simple, id=id,
                death=event(futime, fustat),
                transpl=tdc(wait.time))
sdata
```

```
##   id wait.time futime fustat transplant tstart tstop death transpl
## 1  2        NA      5      1          0      0     5     1       0
## 2  5        NA     17      1          0      0    17     1       0
## 3 10        11     57      1          1      0    11     0       0
## 4 10        11     57      1          1     11    57     1       1
## 5 12        NA      7      1          0      0     7     1       0
## 6 28        70     71      1          1      0    70     0       0
## 7 28        70     71      1          1     70    71     1       1
## 8 95         1     15      1          1      0     1     0       0
## 9 95         1     15      1          1      1    15     1       1
```

```
heart.simple.counting <- sdata[,-(2:5)]
heart.simple.counting
```

```
##   id tstart tstop death transpl
## 1  2      0     5     1       0
## 2  5      0    17     1       0
## 3 10      0    11     0       0
## 4 10     11    57     1       1
## 5 12      0     7     1       0
## 6 28      0    70     0       0
## 7 28     70    71     1       1
## 8 95      0     1     0       0
## 9 95      1    15     1       1
```

```
coxph.heart.simple.counting <- coxph(Surv(tstart, tstop, death) ~ transpl,
   data=heart.simple.counting)
summary(coxph.heart.simple.counting)   # time-dependent analysis
```

```
## Call:
## coxph(formula = Surv(tstart, tstop, death) ~ transpl, data = heart.simple.counting)
##
##   n= 9, number of events= 6
##
##           coef exp(coef) se(coef)     z Pr(>|z|)
## transpl 0.2846    1.3292   0.9609 0.296    0.767
##
```

```
##         exp(coef) exp(-coef) lower .95 upper .95
## transpl     1.329     0.7523    0.2021      8.74
##
## Concordance= 0.5  (se = 0.133 )
## Rsquare= 0.01   (max possible= 0.768 )
## Likelihood ratio test= 0.09  on 1 df,   p=0.7691
## Wald test            = 0.09  on 1 df,   p=0.7671
## Score (logrank) test = 0.09  on 1 df,   p=0.7666
```

counting process format for entire Stanford heart transplant data

See Therneau and Crowson (2015) Using time dependent covariates and time-dependent coefficients in the Cox model. Vignette for R survival package http://cran.r-project.org/web/packages/survival

```
tdata <- jasa[, -c(1:4, 11:14)]  #leave off the dates and transplant-specific covariates,
tdata$futime <- pmax(.5, tdata$futime)  # the death on day 0
indx <- {{tdata$wait.time == tdata$futime} & !is.na(tdata$wait.time)}
#indx <- with(tdata, which(wait.time == futime))
tdata$wait.time[indx] <- tdata$wait.time[indx] - .5  #the tied transplant
id <- 1:nrow(tdata)
tdata$id <- id
head(sdata)
```

```
##   id wait.time futime fustat transplant tstart tstop death transpl
## 1  2        NA      5      1          0      0     5     1       0
## 2  5        NA     17      1          0      0    17     1       0
## 3 10        11     57      1          1      0    11     0       0
## 4 10        11     57      1          1     11    57     1       1
## 5 12        NA      7      1          0      0     7     1       0
## 6 28        70     71      1          1      0    70     0       0
```

```
sdata <- tmerge(tdata, tdata, id=id,
                death = event(futime, fustat),
                trans = tdc(wait.time))
jasa.counting <- sdata[,c(7:11, 2:3)]
head(jasa.counting)
```

```
##   id tstart tstop death trans surgery      age
## 1  1      0    49     1     0       0 30.84463
## 2  2      0     5     1     0       0 51.83573
## 3  3      0    15     1     1       0 54.29706
```

```
## 4  4      0    35     0     0       0 40.26283
## 5  4     35    38     1     1       0 40.26283
## 6  5      0    17     1     0       0 20.78576
```

```
summary(coxph(Surv(tstart, tstop, death) ~ trans + surgery + age, data=jasa.counting))
```

```
## Call:
## coxph(formula = Surv(tstart, tstop, death) ~ trans + surgery +
##     age, data = jasa.counting)
##
##   n= 170, number of events= 75
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## trans    0.01405   1.01415  0.30822  0.046   0.9636
## surgery -0.77326   0.46150  0.35966 -2.150   0.0316 *
## age      0.03055   1.03103  0.01389  2.199   0.0279 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##         exp(coef) exp(-coef) lower .95 upper .95
## trans      1.0142     0.9860    0.5543    1.8555
## surgery    0.4615     2.1668    0.2280    0.9339
## age        1.0310     0.9699    1.0033    1.0595
##
## Concordance= 0.599  (se = 0.037 )
## Rsquare= 0.061   (max possible= 0.97 )
## Likelihood ratio test= 10.72  on 3 df,   p=0.01335
## Wald test            = 9.68  on 3 df,   p=0.02153
## Score (logrank) test = 10  on 3 df,   p=0.01855
```

Section 8.2.1 predictable time-dependent variables

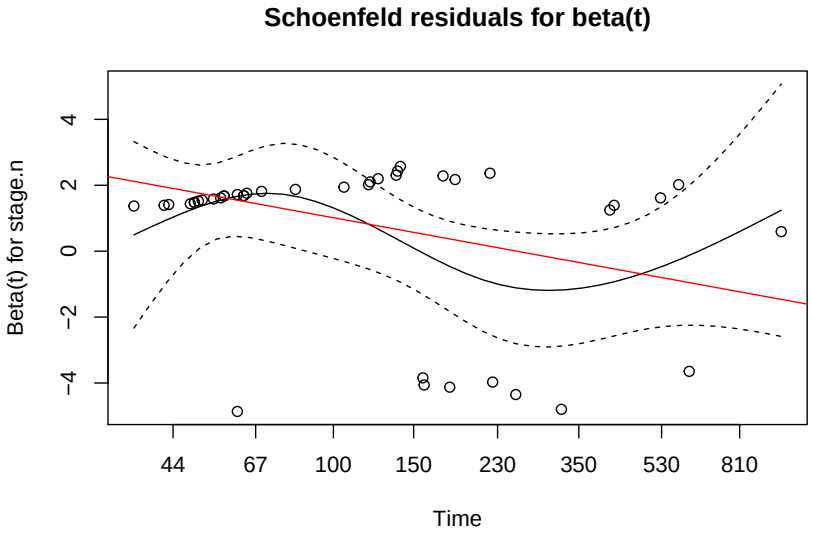
```
library(asaur)

attach(pancreatic2)

stage.n <- rep(0, nrow(pancreatic2))
stage.n[pancreatic2$stage == "M"] <- 1

result.panc <- coxph(Surv(pfs) ~ stage.n)   # this is the log-rank test
result.panc
```

```
## Call:
## coxph(formula = Surv(pfs) ~ stage.n)
##
##          coef exp(coef) se(coef)    z    p
## stage.n 0.593     1.810    0.401 1.48 0.14
##
## Likelihood ratio test=2.43  on 1 df, p=0.119
## n= 41, number of events= 41
```

```
result.panc2.tt <- coxph(Surv(pfs) ~ stage.n + tt(stage.n),
    tt=function(x,t, ...) x*log(t))
result.panc2.tt
```

```
## Call:
## coxph(formula = Surv(pfs) ~ stage.n + tt(stage.n), tt = function(x,
##     t, ...) x * log(t))
##
##                coef exp(coef) se(coef)     z     p
## stage.n       6.010   407.339    3.060  1.96 0.050
## tt(stage.n)  -1.086     0.338    0.589 -1.84 0.065
##
## Likelihood ratio test=6.33  on 2 df, p=0.0423
## n= 41, number of events= 41
```

```
result.sch.resid <- cox.zph(result.panc, transform=function(pfs) log(pfs))
plot(result.sch.resid)
abline(coef(result.panc2.tt), col="red")
title('Schoenfeld residuals for beta(t)')
```




```
result.panc2.tt2 <- coxph(Surv(pfs) ~ stage.n + tt(stage.n),
    tt=function(x,t, ...) x*t)
result.panc2.tt2
```

```
## Call:
## coxph(formula = Surv(pfs) ~ stage.n + tt(stage.n), tt = function(x,
##     t, ...) x * t)
##
##                  coef exp(coef) se(coef)     z     p
## stage.n      1.27810   3.58981  0.66103  1.93 0.053
## tt(stage.n) -0.00366   0.99635  0.00253 -1.44 0.149
##
## Likelihood ratio test=4.56  on 2 df, p=0.102
## n= 41, number of events= 41
```

```
detach(pancreatic2)
```

Section 8.2.2

```
?lung
```

```
## starting httpd help server ... done
```

```
summary(lung)
```

```
##       inst             time            status           age        
##  Min.   : 1.00   Min.   :   5.0   Min.   :1.000   Min.   :39.00  
##  1st Qu.: 3.00   1st Qu.: 166.8   1st Qu.:1.000   1st Qu.:56.00  
##  Median :11.00   Median : 255.5   Median :2.000   Median :63.00  
##  Mean   :11.09   Mean   : 305.2   Mean   :1.724   Mean   :62.45  
##  3rd Qu.:16.00   3rd Qu.: 396.5   3rd Qu.:2.000   3rd Qu.:69.00  
##  Max.   :33.00   Max.   :1022.0   Max.   :2.000   Max.   :82.00  
##  NA's   :1                                                       
##       sex           ph.ecog          ph.karno        pat.karno     
##  Min.   :1.000   Min.   :0.0000   Min.   : 50.00   Min.   : 30.00  
##  1st Qu.:1.000   1st Qu.:0.0000   1st Qu.: 75.00   1st Qu.: 70.00  
##  Median :1.000   Median :1.0000   Median : 80.00   Median : 80.00  
##  Mean   :1.395   Mean   :0.9515   Mean   : 81.94   Mean   : 79.96  
##  3rd Qu.:2.000   3rd Qu.:1.0000   3rd Qu.: 90.00   3rd Qu.: 90.00  
##  Max.   :2.000   Max.   :3.0000   Max.   :100.00   Max.   :100.00  
##                  NA's   :1        NA's   :1        NA's   :3       
##     meal.cal         wt.loss        
##  Min.   :  96.0   Min.   :-24.000  
##  1st Qu.: 635.0   1st Qu.:  0.000  
##  Median : 975.0   Median :  7.000  
##  Mean   : 928.8   Mean   :  9.832  
##  3rd Qu.:1150.0   3rd Qu.: 15.750  
##  Max.   :2600.0   Max.   : 68.000  
##  NA's   :47       NA's   :14       
```

```
coxph(Surv(time, status==2) ~ age, data=lung)
```

```
## Call:
## coxph(formula = Surv(time, status == 2) ~ age, data = lung)
##
##       coef exp(coef) se(coef)    z     p
## age 0.0187    1.0189   0.0092 2.03 0.042
##
## Likelihood ratio test=4.24  on 1 df, p=0.0395
## n= 228, number of events= 165
```

```
# the following enters age as time-dependent, but gives the same result:
coxph(Surv(time, status==2) ~ tt(age), data=lung,
  tt=function(x, t, ...) {
    age <- x + t/365.25
    age})
```

```
## Call:
## coxph(formula = Surv(time, status == 2) ~ tt(age), data = lung,
##     tt = function(x, t, ...) {
##         age <- x + t/365.25
##         age
##     })
##
##           coef exp(coef) se(coef)    z     p
## tt(age) 0.0187    1.0189   0.0092 2.03 0.042
##
## Likelihood ratio test=4.24  on 1 df, p=0.0395
## n= 228, number of events= 165
```