Time-Dependent Survival Analysis

Weisi Chen

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Contents

# Load the needed packages  
library(ggplot2)  
library(dplyr)  
library(lubridate)  
library(survival)  
library(ggsurvfit)  
library(gtsummary)  
library(here)  
library(survminer)  
library(broom)  
library(forestploter)  
library(tidyr)

# Load the data  
data(BMT, package="SemiCompRisks")  
  
head(BMT[, c("T1", "delta1", "TA", "deltaA")])

#> T1 delta1 TA deltaA  
#> 1 2081 0 67 1  
#> 2 1602 0 1602 0  
#> 3 1496 0 1496 0  
#> 4 1462 0 70 1  
#> 5 1433 0 1433 0  
#> 6 1377 0 1377 0

**Time-dependent covariate approach**

This is used when if the value of a covariate is changing over time.

### About the sample data

The data comes from the pbc and pdcseq dataset, available from the *survival* package.

The pdc dataset contains baseline data and follow-up status for a set of subjects with primary biliary cirrhosis, while the pdcseq dataset contains repeated laboratory values for those subjects.

Some important variables: status: status at endpoint, 0/1/2 for censored, transplant, dead albumin: serum albumin (g/dl) ascites: presence of ascites bili: serum bilirunbin (mg/dl) protime: standardised blood clotting time stage: histologic stage of disease (needs biopsy)

# Load the data  
pbc <- survival::pbc  
pbcseq <- survival::pbcseq

### Organize the dataset structure for time-dependent survival analysis

# baseline info  
pbc <- subset(pbc, select=c(id:sex,stage)) |>  
 mutate(sex\_f = case\_when(sex == "f" ~ "Female",  
 sex == "m" ~ "Male"),  
 sex\_f = factor(sex\_f, levels=c("Male", "Female")),  
 stage\_f = factor(stage))  
   
# set range  
pbc2 <- tmerge(pbc, pbc, id=id, death = event(time,status))  
# add time-varying covariates  
pbc3 <- tmerge(pbc2, pbcseq, id=id, ascites = tdc(day, ascites),   
 bili = tdc(day, bili), albumin = tdc(day, albumin),  
 protime = tdc(day, protime), alk.phos = tdc(day, alk.phos))

### Fit the time-dependent cox model

tbl\_regression(coxph(Surv(tstart, tstop, death == 2) ~ log(bili) + log(protime), data = pbc3),exponentiate = TRUE)

| **Characteristic** | **HR***1* | **95% CI***1* | **p-value** |
| --- | --- | --- | --- |
| log(bili) | 3.46 | 2.86, 4.18 | <0.001 |
| log(protime) | 53.7 | 22.9, 126 | <0.001 |
| *1*HR = Hazard Ratio, CI = Confidence Interval | | | |

**Interpretation**: For one-unit increase in log(bili), the hazard of death increases by a factor of 3.46, holding other covariates constant.

-> A 2.718 times increases in serum bilirunbin level, hoding all other covariates constant, increases the hazard of death by a factor of 3.46