

Homework 9

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Consider the colon data in the R package "survival". It gives adjuvant chemotherapy data for colon cancer. Levamisole is a low-toxicity compound previously used to treat worm infestations in animals; 5-FU is a moderately toxic (as these things go) chemotherapy agent. There are two records per person, one for recurrence (etype=1) and one for death (etype=2). Other important variables include:

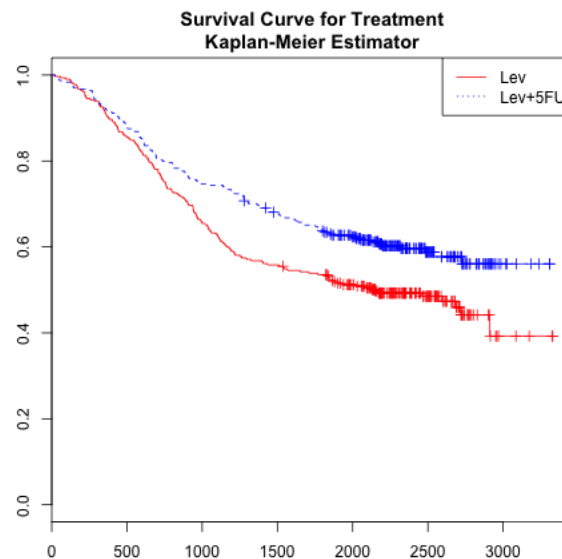
- rx: Treatment: Obs(ervation), Lev(amisole), Lev(amisole)+5-FU
- sex: 1=male
- age: in years
- time: days until event or censoring
- status: censoring status

For the following, consider survival to be Days until Death, i.e., etype=2.

Problem 1

Using the Kaplan-Meier method, estimate the survival curve for each treatment group: Lev(amisole) and Lev(amisole)+5-FU.

Using Kaplan-Meier method, fit the survival estimator, the estimated survival curve is as follows:



Problem 2

Estimate the median survival time for each of the two treatment groups, using the estimated survival curves.

Using Kaplan-Meier survival curve, the result is as follows:

Kaplan-Meier Estimated Curve

Call: `survfit(formula = Surv(time, status) ~ rx, data = survival_colon)`

| | n | events | median | 0.95LCL | 0.95UCL |
|------------|-----|--------|--------|---------|---------|
| rx=Lev | 310 | 161 | 2152 | 1540 | NA |
| rx=Lev+5FU | 304 | 123 | NA | 2725 | NA |

So the estimated median is:

Table 1: Estimated Median for two treatment groups

| Treatment | Lev | Lev+5FU |
|-----------|------|---------|
| Median | 2152 | NA |

The median is calculated as the smallest survival time for which the survivor function is less than or equal to 0.5.

- For treatment Lev, the estimated median is 2152.
- For treatment Lev+5FU, since it never gets to the point where $s(t) \leq 0.5$, then the median for treatment Lev+5FU is NA.

Problem 3

Using the log-rank test, determine whether there is a difference in survival between the two groups.

Using Log-rank test, the null hypothesis and alternative hypothesis are:

H_0 : there is no difference between the two treatment of survival curves

H_1 : there is difference between the two treatment of survival curves

the result is as follows:

Log-rank Test Result

Call:

`survdif(formula = Surv(time, status) ~ rx, data = survival_colon)`

| | N | Observed | Expected | (O-E)^2/E | (O-E)^2/V |
|------------|-----|----------|----------|-----------|-----------|
| rx=Lev | 310 | 161 | 137 | 4.24 | 8.21 |
| rx=Lev+5FU | 304 | 123 | 147 | 3.95 | 8.21 |

Chisq= 8.2 on 1 degrees of freedom, p= 0.00417

Since the p-value of log-rank test is 0.00417, then we should reject the null hypothesis, i.e., concluding that there is a difference in survival between the two groups.

Problem 4

Using a Cox proportional hazards model, estimate the hazard ratio for Levamisole relative to 5-FU, adjusting for Age and Sex.

Using Cox proportional hazards model and adjusting for Age and Sex, the result is as follows:

Cox proportional hazards model adjusting for age and sex Result

Call:

coxph(formula = Surv(time, status) ~ rx_d + age + sex, data = survival_colon)

n= 614, number of events= 284

| | coef | exp(coef) | se(coef) | z | Pr(> z) |
|------|-----------|-----------|----------|--------|-----------|
| rx_d | 0.344635 | 1.411474 | 0.120079 | 2.870 | 0.0041 ** |
| age | 0.000920 | 1.000921 | 0.005119 | 0.180 | 0.8574 |
| sex | -0.043126 | 0.957791 | 0.118948 | -0.363 | 0.7169 |

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

| | exp(coef) | exp(-coef) | lower .95 | upper .95 |
|------|-----------|------------|-----------|-----------|
| rx_d | 1.4115 | 0.7085 | 1.1155 | 1.786 |
| age | 1.0009 | 0.9991 | 0.9909 | 1.011 |
| sex | 0.9578 | 1.0441 | 0.7586 | 1.209 |

Concordance= 0.549 (se = 0.018)

Rsquare= 0.014 (max possible= 0.996)

Likelihood ratio test= 8.38 on 3 df, p=0.0388

Wald test = 8.29 on 3 df, p=0.04033

Score (logrank) test = 8.37 on 3 df, p=0.03892

Since we want to get the hazard ratio for Levamisole relative to 5-FU, then we simply set the Lev+5FU as the baseline. Since from the result we can see, the hazard ratio for the second group relative to the first group, that is, rxLev relative to rxLev+5FU with adjusting for age and sex is 1.4115.

Problem 5

Give a 95% confidence interval for the hazard ratio in 4.

From the result above, we can see that the 95% confidence interval for hazard ratio in Problem 4 is:

[1.1155, 1.786]

R Code:

```

rm(list = ls())
library(survival)
data("colon")

#Meier Estimator for treatment Lev, Lev+5FU
survival_colon <- subset(colon, etype==2 & rx %in% c("Lev", "Lev+5FU"))
fit_trt <- survfit(formula = Surv(time, status) ~ rx, data = survival_colon, type = "kaplan-meier")
sink('/Users/raymond/Drive/STAT W4201/HW9/meiersum.txt')
summary(fit_trt)
sink()

#Plot the survival curve
png(filename = "/Users/raymond/Drive/STAT W4201/HW9/meiercurve.png")
plot(fit_trt, lty = c(1,2), col = c("red", "blue"))
title(main="Survival Curve for Treatment")
title(main="Kaplan-Meier Estimator", line=0.5)
legend("topright", c("Lev", "Lev+5FU"), col=c("red", "blue"), lty=c(1,3))
dev.off()

#Estimate the median
sink('/Users/raymond/Drive/STAT W4201/HW9/meier.txt')
fit_trt
sink()

#Log-rank test for difference
log_rank <- survdiff(Surv(time, status) ~ rx, data=survival_colon)

sink('/Users/raymond/Drive/STAT W4201/HW9/logrank.txt')
log_rank
sink()

#Cox proportional hazards model
survival_colon$rx_d <- as.numeric(survival_colon$rx=="Lev")
cox <- coxph(Surv(time, status) ~ rx_d + age + sex, data=survival_colon)
sink('/Users/raymond/Drive/STAT W4201/HW9/cox.txt')
summary(cox)
sink()

```