Survival Analysis HW 5

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Question 8.1

In section 1.11, a study was conducted on the effects of ploidy on the prognosis of patients with cancer of the tongue. Tissue samples were examined to determine if the tumor had a aneuploid or diploid DNA profile. Times to death for these two groups of patients are recorded in Table 1.6. To analyze this data create a single indicator variable, Z, which reflects the type of tumor.

```
##   type time delta
## 1    1    1     1
## 2    1    3     1
## 3    1    3     1
## 4    1    4     1
## 5    1   10     1
## 6    1   13     1
```

```
data(kidney)

cox_model <- coxph(Surv(time = time, event = delta) ~ type, kidney)
summary(cox_model)

coxph(formula, data=, weights, subset,
      na.action, init, control,
      ties=c("efron","breslow","exact"),
      singular.ok=TRUE, robust=FALSE,
      model=FALSE, x=FALSE, y=TRUE, tt, method, ...)
```

(a) Test the hypothesis of no effect of ploidy on survival using the score test. Perform the test using the Breslow, Efron, and discrete method of handling ties and compare your results. (Parts (c) and (d) are included here.)

```
ques81a <- coxph(Surv(time = time, event = delta) ~ type, tongue, ties = "breslow")
summary(ques81a)
```

```
## Call:
## coxph(formula = Surv(time = time, event = delta) ~ type, data = tongue,
##     ties = "breslow")
##
##   n= 80, number of events= 53
##
##        coef exp(coef) se(coef)     z Pr(>|z|)
## type 0.4610    1.5856   0.2805 1.643      0.1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## type     1.586     0.6307     0.915     2.748
```

```
##
## Concordance= 0.564  (se = 0.036 )
## Rsquare= 0.032   (max possible= 0.993 )
## Likelihood ratio test= 2.61  on 1 df,   p=0.1061
## Wald test            = 2.7  on 1 df,   p=0.1004
## Score (logrank) test = 2.75  on 1 df,   p=0.09747
```

```
ques81a <- coxph(Surv(time = time, event = delta) ~ type, tongue, ties = "efron")
summary(ques81a)
```

```
## Call:
## coxph(formula = Surv(time = time, event = delta) ~ type, data = tongue,
##     ties = "efron")
##
##   n= 80, number of events= 53
##
##        coef exp(coef) se(coef)     z Pr(>|z|)
## type 0.4664    1.5942   0.2804 1.663   0.0963 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## type     1.594     0.6273    0.9201     2.762
##
## Concordance= 0.564  (se = 0.036 )
## Rsquare= 0.033   (max possible= 0.993 )
## Likelihood ratio test= 2.67  on 1 df,   p=0.102
## Wald test            = 2.77  on 1 df,   p=0.09632
## Score (logrank) test = 2.81  on 1 df,   p=0.09343
```

```
ques81a <- coxph(Surv(time = time, event = delta) ~ type, tongue, ties = "exact")
summary(ques81a)
```

```
## Call:
## coxph(formula = Surv(time = time, event = delta) ~ type, data = tongue,
##     ties = "exact")
##
##   n= 80, number of events= 53
##
##        coef exp(coef) se(coef)     z Pr(>|z|)
## type 0.4684    1.5974   0.2828 1.656   0.0977 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## type     1.597      0.626    0.9177     2.781
##
## Rsquare= 0.033   (max possible= 0.991 )
## Likelihood ratio test= 2.65  on 1 df,   p=0.1033
## Wald test            = 2.74  on 1 df,   p=0.09768
## Score (logrank) test = 2.79  on 1 df,   p=0.09487
```

(b) Estimate β and its standard error using all three methods of handling ties. Find a 95% confidence interval for the relative risk of death of an individual with an aneuploid tumor as

compared to an individual with a diploid tumor.
Using the results from part (a):

Breslow:

Efron:

Exact:

(c) Repeat (a) using the likelihood test. Compare your answer to that of part a.
Done in part (a).

(d) Repeat (a) using the Wald test. Compare your answer to those in parts a and c.
Done in part (a)

Question 8.2

In Exercise 7 of Chapter 7, three different treatments were administered to rats who had F98 glioma cells implanted into their brains. The data for the three groups of rats lists the death times (in days) in that exercise. Create two dummy variables, $Z_1 = 1$ if an animal is in the "radiation only" group, 0 otherwise; $Z_2 = 1$ if the animal is in the "radiation plus BPA" group, 0 otherwise.

```
##       group time event
## 1 Untreated   20     1
## 2 Untreated   21     1
## 3 Untreated   23     1
## 4 Untreated   24     1
## 5 Untreated   24     1
## 6 Untreated   26     1
```

(a) Estimate β_1 and β_2 and their respective standard errors. Also find an estimate of the covariance matrix of your estimates.

use vcov function vcov(cox_model)

(b) Test the global hypothesis of no effect of either radiation only or radiation plus BPA on survival. Perform the test using all three tests (Wald, likelihood ratio, and score test).

(c) Test the hypothesis that the effect of radiation only on survival is the same as the effect of radiation plus BPA (i.e., test $H_0 : \beta_1 = \beta_2$)

(d) Find an estimate and a 95% confidence interval for the relative risk of death for a radiation only animal compared to a radiation plus BPA animal.

(e) Test the hypothesis that any radiation given as a treatment (either radiation alone or with BPA) has a different effect on survival than no radiation. Use the likelihood ratio test.

(f) Repeat part (e) using a Wald test based on the results of part (a). Here you should test the hypothesis that $\beta_1 = \beta_2 = 0$

Question 8.3

In section 1.10, times to death or relapse (in days) are given for 23 non-Hodgkin's lymphoma (NHL) patients, 11 receiving an allogeneic (allo) transplant from an HLA-matched sibling donor and 12 patients receiving an autologous (auto) transplant. Also, data on 20 Hodgkin's lymphoma (HL) patients, 5 receiving an allogeneic (allo) transplant from an HLA-matched sibling donor and 15 patients receiving an autologous (auto) transplant is given in Table 1.5. Because there is potential for a different efficacy of the two types of transplants for the two types of lymphoma, a model with a main effect for type of transplant, a main effect for disease type, and an interaction term is of interest.

```
##   gtype dtype time delta score wtime
## 1     1     1   28     1    90    24
## 2     1     1   32     1    30     7
## 3     1     1   49     1    40     8
## 4     1     1   84     1    60    10
## 5     1     1  357     1    70    42
## 6     1     1  933     0    90     9
```

(a) Analyze this data by performing a global test of no effect of transplant type and disease state on survival. Construct an ANOVA table to summarize estimates of the risk coefficients and the results of the one-degree-of-freedom tests for each covariate in the model. Estimate the covariance matrix of your estimates.

(b) Test the hypothesis of disease type by type of transplant interaction using a likelihood ratio test.

(c) Find point estimates and 95% confidence intervals for the relative risk of death for an auto transplant NHL patient compared to a NHL allo transplant patient.

Question 8.6

In section 1.3, several event times are described for patients receiving a bone marrow transplant for leukemia. Consider the time to development of acute graft-versus-host disease (aGVHD). As a prophylactic treatment, patients at two of the hospitals were given a treatment combining methotrexate (MTX) with cyclosporine and possibly methylprednisilone. Patients at the other hospitals were not given methotrexate but rather a combination of cyclosporine and methylprednisilone. Of primary interest in studying aGVHD is a test of the effectiveness of the MTX regime to prevent aGVHD

```
##   group   t1   t2 d1 d2 d3   ta da  tc dc tp dp z1 z2 z3 z4 z5 z6   z7 z8
## 1     1 2081 2081  0  0  0   67  1 121  1 13  1 26 33  1  0  1  1   98  0
## 2     1 1602 1602  0  0  0 1602  0 139  1 18  1 21 37  1  1  0  0 1720  0
## 3     1 1496 1496  0  0  0 1496  0 307  1 12  1 26 35  1  1  1  0  127  0
## 4     1 1462 1462  0  0  0   70  1  95  1 13  1 17 21  0  1  0  0  168  0
## 5     1 1433 1433  0  0  0 1433  0 236  1 12  1 32 36  1  1  1  1   93  0
## 6     1 1377 1377  0  0  0 1377  0 123  1 12  1 22 31  1  1  1  1 2187  0
##   z9 z10
## 1  1   0
## 2  1   0
## 3  1   0
## 4  1   0
## 5  1   0
## 6  1   0
```

(a) Using an appropriate Cox model, test the hypothesis of no difference in the rate of development of aGVHD between MTX and no MTX patients. Find a point estimate and a 95% confidence interval for the relative risk of aGVHD for patients on the MTX protocol as compared to those not given MTX.

(b) Patients were also grouped into risk categories based on their status at the time of transplantation. These categories were as follows: acute lymphoblastic leukemia (ALL) with 38 patients and acute myeloctic leukemia (AML). The latter category was further subdivided into low-risk—first remission (54 patients) and high-risk—second remission or untreated first relapse or second or greater relapse or never in remission (45 patients). Test the hypothesis of interest (no effect of MTX on development of aGVHD) adjusting for the three disease categories.

(c) Test for the possibility of an interaction between the disease categories and the use of MTX on timing of aGVHD.

(d) Using the factors of age, sex, CMV status, FAB class, waiting time to transplant, and disease category as defined in Example 8.4, find the best model to test the primary hypothesis of no MTX effect on the occurence of aGVHD. Test the primary hypothesis and find an estimate of the relative risk of occurence of aGVHD for an MTX patient as compared to a non-MTX patient.

testing

```
data(kidney)

cox_model <- coxph(Surv(time = time, event = delta) ~ type, kidney)
```

```r
summary(cox_model)

coxph(formula, data=, weights, subset,
      na.action, init, control,
      ties=c("efron","breslow","exact"),
      singular.ok=TRUE, robust=FALSE,
      model=FALSE, x=FALSE, y=TRUE, tt, method, ...)
```