Homework 5

Denis Ostroushko

Exercise 1

(a)

R output for a regression model is given below. All three tests suggest that there is evidence to conclude that some variables included in the model are helpful at explaining the outcome.

```
Call:
coxph(formula = Surv(time = time, event = delta) ~ age + stage,
    data = larynx)

  n= 90, number of events= 50

          coef exp(coef) se(coef)     z Pr(>|z|)
age    0.01903   1.01921  0.01426 1.335   0.1820
stage2 0.14004   1.15032  0.46249 0.303   0.7620
stage3 0.64238   1.90100  0.35611 1.804   0.0712 .
stage4 1.70598   5.50678  0.42191 4.043 5.27e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

       exp(coef) exp(-coef) lower .95 upper .95
age        1.019     0.9811    0.9911     1.048
stage2     1.150     0.8693    0.4647     2.848
stage3     1.901     0.5260    0.9459     3.820
stage4     5.507     0.1816    2.4086    12.590

Concordance= 0.682  (se = 0.039 )
Likelihood ratio test= 18.31  on 4 df,   p=0.001
Wald test            = 21.15  on 4 df,   p=3e-04
Score (logrank) test = 24.78  on 4 df,   p=6e-05
```

(b)

Stratification by diagnosis year produces similar results. Coefficients, and therefore hazard rations, tell a similar story between the two models. Standard errors appear similar as well.

```
Call:
coxph(formula = Surv(time = time, event = delta) ~ age + stage +
    strata(diagyr_strata), data = larynx)

  n= 90, number of events= 50

          coef exp(coef) se(coef)     z Pr(>|z|)
age    0.01715   1.01730  0.01492 1.149   0.2504
stage2 0.11378   1.12050  0.46420 0.245   0.8064
stage3 0.62377   1.86595  0.35606 1.752   0.0798 .
stage4 1.71820   5.57447  0.43941 3.910 9.22e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

       exp(coef) exp(-coef) lower .95 upper .95
age        1.017     0.9830    0.9880     1.047
stage2     1.121     0.8925    0.4511     2.783
stage3     1.866     0.5359    0.9286     3.750
stage4     5.574     0.1794    2.3560    13.190

Concordance= 0.674  (se = 0.042 )
Likelihood ratio test= 17.96  on 4 df,   p=0.001
Wald test            = 20.69  on 4 df,   p=4e-04
Score (logrank) test = 24.12  on 4 df,   p=8e-05
```

(c)

Code below conducts a likelihood test for the two models.

```
anova(cox_1_a, cox_1_b, test="Chisq")
```

```
Analysis of Deviance Table
 Cox model: response is  Surv(time = time, event = delta)
 Model 1: ~ age + stage
 Model 2: ~ age + stage + strata(diagyr_strata)
   loglik  Chisq Df Pr(>|Chi|)
```

```
1 -187.71
2 -161.38 52.659  0  < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

While we saw that the results of the two models' estimates are similar, it appears that the inclusion of the stratification variable improves model fit.

(d)

I am including code below that I used to conduct the Wald test. Following the book instructions, I am comparing each corresponding estimate between the two strata.

Walk test suggests that model parameters are similar for the two strata.

```
coef1 <- summary(cox_1_a)$coefficients
coef2 <- summary(cox_1_b)$coefficients

waldtest_table <-
  data.frame(
    test_stat = (coef1[,1] - coef2[,1])^2 / (coef1[,3]^2 + coef2[,3]^2)
  )

waldtest_table$p_val = pchisq(waldtest_table$test_stat, lower.tail = F, df = 1)

waldtest_table
```

```
          test_stat      p_val
age     0.0082974613 0.9274208
stage2  0.0016065128 0.9680283
stage3  0.0013660023 0.9705173
stage4  0.0004022519 0.9839985
```

Exercise 2

(a)

Exponentiated coefficient and end points of the confidence interval produce desired output for the non-stratified cox regression model

```
[1] 2.471126


       2.5 %    97.5 %
trt 1.326257 4.604285
```

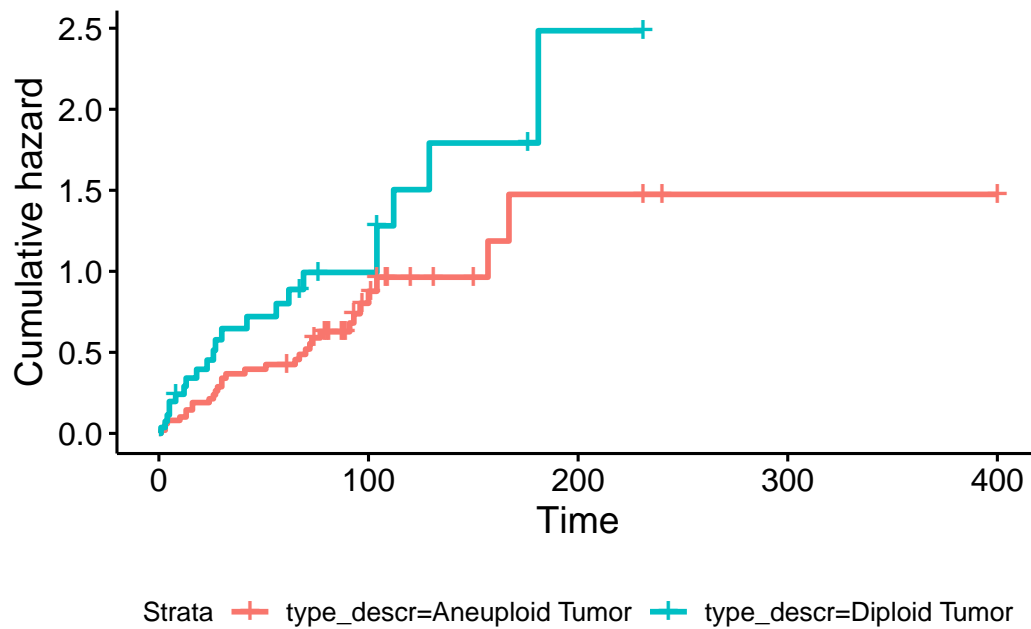**(b)**

Stratified model produce similar output and results.

```
[1] 2.410976


       2.5 %    97.5 %
trt 1.151142 5.049597
```
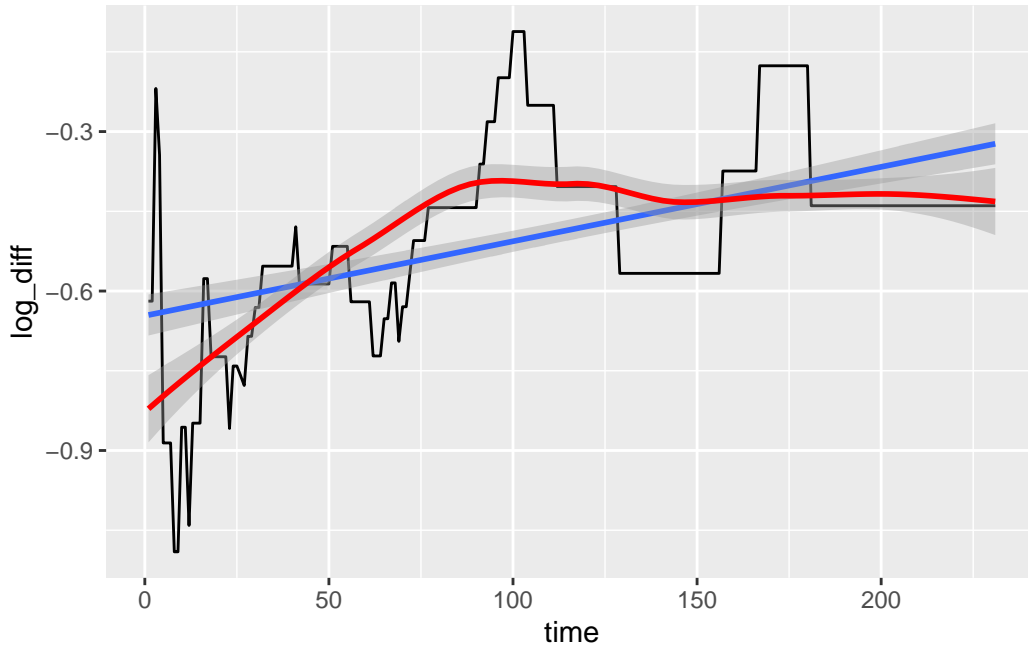
Exercise 3

(a)

Plot below provides cumulative hazards for the two groups. Visually, they do not appear proportional over time.

(b)

Using some manipulation of the data used for part (a), I carry observed values of cumulative hazard forward and have some data at each time point 1,2,3 …

Plot below provides differences of log cumualtive hazards between the two groups.

Smooth LOESS red regression line shows that the hazards rate proportion seems to increase until approximate time 75, after which the rates are proportional. There is a lot of variance in the poprtion of hazards between the two groups.

(c)
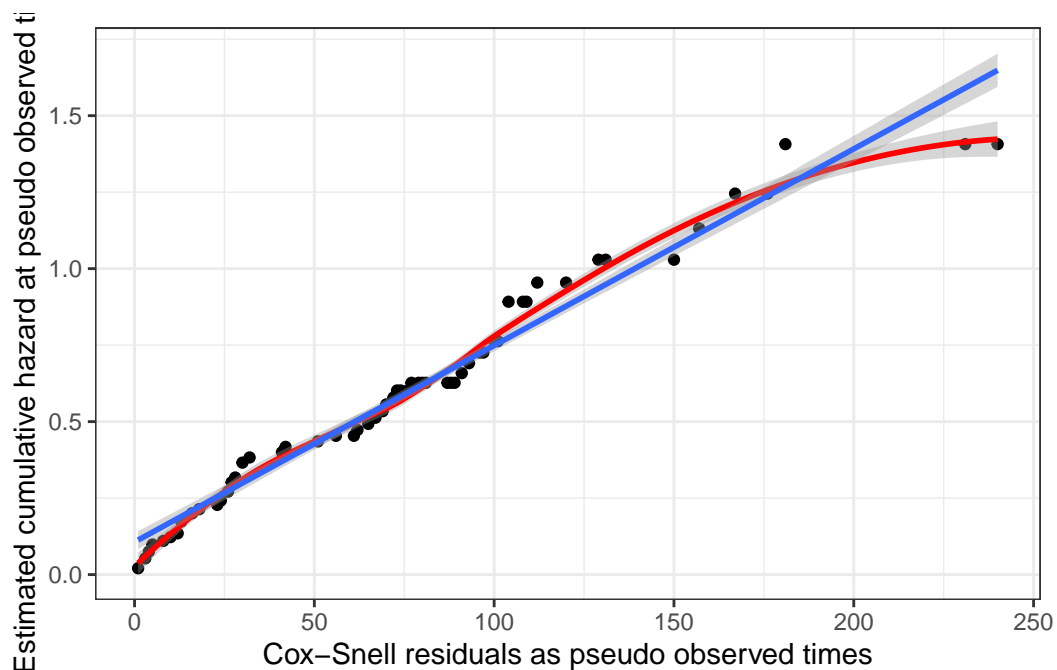
I chose to use cox snell residuals to evaluate model fit.

I removed an outlier that have observed time of around 400.

Residuals vs time has approximately linear trend, with more and more variance occurring at later times. Later observations have a poor fit to the linear trend, which is common for these sets of residuals

Exercise 4

(a)

I am using code below to obtain MLE estimates:

```
# https://stackoverflow.com/questions/9113872/interpreting-weibull-parameters-from-survreg

model <- survreg(Surv(time = time, event= delta) ~ 1, data = tongue, dist = "weibull")
summary(model)
```

```
Call:
survreg(formula = Surv(time = time, event = delta) ~ 1, data = tongue,
    dist = "weibull")
            Value Std. Error     z       p
(Intercept) 4.738      0.174 27.29 <2e-16
Log(scale)  0.227      0.117  1.95  0.051

Scale= 1.25

Weibull distribution
Loglik(model)= -300.7   Loglik(intercept only)= -300.7
Number of Newton-Raphson Iterations: 5
n= 80
```

```r
shape <- 1/model$scale
scale <- exp( coef(model) )
```

- Shape parameter: 0.8

- Scale parameter: 114.19

(b)

Using output above, we obtain test statistic and a p-value to conduct the test. Null hypothesis: shape parameter is equal to 1.

- test stat: 27.29

- p-value: 0

Conclusion: we have enough evidence to conclude that the shape parameter is very different from 1

(c)

Plugging in shape and scale MLE parameter into a function, and using 50% percentile of weibull distribution, we obtain an MLE for median survival time:

```r
med.surv <- qweibull(0.5, shape = shape, scale = scale)
med.surv
```

```
[1] 72.09234
```

(d)

```r
model2 <- survreg(Surv(time = time, event= delta) ~ type_descr, data = tongue, dist = "wei
summary(model2)
```

```
Call:
survreg(formula = Surv(time = time, event = delta) ~ type_descr,
    data = tongue, dist = "weibull")
                         Value Std. Error    z       p
(Intercept)              4.972      0.227 21.93 <2e-16
type_descrDiploid Tumor -0.669      0.351 -1.91  0.057
Log(scale)               0.216      0.116  1.87  0.062

Scale= 1.24

Weibull distribution
Loglik(model)= -298.9   Loglik(intercept only)= -300.7
    Chisq= 3.58 on 1 degrees of freedom, p= 0.059
Number of Newton-Raphson Iterations: 5
n= 80
```

- Null hypothesis: no effect of ploidy, i.e. the coefficient is equal to 1
- Test statistic: - 1.91
- p-value: 0.057

Conclusion: the p-value is above the accepted $\alpha = 0.05$, but it is extremely close. Therefore, we have a moderately strong belief that the effect of ploidy is statistically significant and is idfferent between the two groups.