Assignment 10

(1) (a) $h(t) = \frac{1}{\sigma} \exp\left\{-\frac{1}{\sigma} x^T\beta\right\} t^{1/\sigma - 1}$, so

$h_0(t) = \frac{1}{\sigma} e^{-\beta_0/\sigma} t^{\frac{1}{\sigma} - 1}$

(b) The proportional hazards model is $h(t) = h_0(t) e^{x^T\beta}$, so $\vec{\beta}_1$ is estimating $-\frac{1}{\sigma}\vec{\beta}_1$

(2) We did this in an earlier assignment also.

$$H(t) = \int_0^t h(y)\,dy = \int_0^t \frac{f(y)}{S(y)}\,dy = \int_0^t \frac{f(y)}{1-F(y)}\,dy$$

Let $u = 1 - F(y)$, $du = -f(y)\,dy$

y	$u = 1 - F(y)$
t	$1 - F(t)$
0	1

$$= -\int_1^{1-F(t)} \frac{1}{u}\,du = \int_{1-F(t)}^1 \frac{1}{u}\,du$$

$$= \log u \Big|_{1-F(t)}^1 = \log(1) - \log(1 - F(t))$$

$$= 0 - \log S(t) \text{ so}$$

$$H(t) = -\log S(t) \iff \log S(t) = -H(t)$$

$$\iff S(t) = e^{-H(t)}$$

(3) From the last question,

$$S_0(t) = e^{-\int_0^t h_0(y)\,dy}, \text{ and}$$

$$S(t) = e^{-\int_0^t h(y)\,dy} = e^{-\int_0^t h_0(y) e^{x^T\beta}\,dy}$$

$$= e^{-e^{x^T\beta}\int_0^t h_0(y)\,dy} = \left(e^{-\int_0^t h_0(y)\,dy}\right)^{e^{x^T\beta}}$$

$$= S_0(t)^{\exp\{x^T\beta\}}$$

(4) (a) $h(t) = h_0(t)\, e^{\beta_1 x_1 + \beta_2 x_2 + \beta_3 c_1 + \beta_4 c_2 + \beta_5 c_3}$

(b)

	c_1	c_2	c_3	$h(t)$	
Squamous	1	0	0	$h_0(t)\, e^{\beta_1 x_1 + \beta_2 x_2}$	e^{β_3}
Small cell	0	1	0	$h_0(t)\, e^{\beta_1 x_1 + \beta_2 x_2}$	e^{β_4}
Adeno	0	0	1	$h_0(t)\, e^{\beta_1 x_1 + \beta_2 x_2}$	e^{β_5}
Large cell	0	0	0	$h_0(t)\, e^{\beta_1 x_1 + \beta_2 x_2}$	

(4c) $h_0(t)e^{45\beta_1 + 6\beta_2 + \beta_5}$

(d) e^{β_4}

(e) $e^{\beta_3 - \beta_5}$

(f) $H_0: \beta_3 = \beta_4 = \beta_5 = 0$

(g) (i) $h(t) = h_0(t)e^{\beta_1 x_1 + \beta_2 x_2}$

(ii)
$$\underset{L}{\begin{pmatrix} 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}} \underset{B}{\begin{pmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \end{pmatrix}} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}$$

(h) $H_0: \beta_1 = 0$

(i) $H_0: \beta_4 = 0$

(j) $H_0: \beta_3 = \beta_5$

```
R version 4.2.3 (2023-03-15) -- "Shortstop Beagle"
Copyright (C) 2023 The R Foundation for Statistical Computing
Platform: x86_64-apple-darwin17.0 (64-bit)

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'help.start()' for an HTML browser interface to help.
Type 'q()' to quit R.

[R.app GUI 1.79 (8198) x86_64-apple-darwin17.0]

[Workspace restored from /Users/brunner/.RData]
[History restored from /Users/brunner/.Rapp.history]

> # ---------------------- veteran ---------------------------- #
>
> rm(list=ls()); options(scipen=999)
> library(survival)
> help(veteran)
starting httpd help server ... done
> summary(veteran)
      trt             celltype       time           status           karno
 Min.   :1.000   squamous :35   Min.   :  1.0   Min.   :0.0000   Min.   :10.00
 1st Qu.:1.000   smallcell:48   1st Qu.: 25.0   1st Qu.:1.0000   1st Qu.:40.00
 Median :1.000   adeno    :27   Median : 80.0   Median :1.0000   Median :60.00
 Mean   :1.496   large    :27   Mean   :121.6   Mean   :0.9343   Mean   :58.57
 3rd Qu.:2.000                  3rd Qu.:144.0   3rd Qu.:1.0000   3rd Qu.:75.00
 Max.   :2.000                  Max.   :999.0   Max.   :1.0000   Max.   :99.00
    diagtime           age             prior
 Min.   : 1.000   Min.   :34.00   Min.   : 0.00
 1st Qu.: 3.000   1st Qu.:51.00   1st Qu.: 0.00
 Median : 5.000   Median :62.00   Median : 0.00
 Mean   : 8.774   Mean   :58.31   Mean   : 2.92
 3rd Qu.:11.000   3rd Qu.:66.00   3rd Qu.:10.00
 Max.   :87.000   Max.   :81.00   Max.   :10.00
> head(veteran)
  trt celltype time status karno diagtime age prior
1   1 squamous   72      1    60        7  69     0
2   1 squamous  411      1    70        5  64    10
3   1 squamous  228      1    60        3  38     0
4   1 squamous  126      1    60        9  63    10
5   1 squamous  118      1    70       11  65    10
6   1 squamous   10      1    20        5  49     0
```

```
>
>
> contrasts(veteran$celltype)
          smallcell adeno large
squamous          0     0     0
smallcell         1     0     0
adeno             0     1     0
large             0     0     1
> # Edit data frame
> vet = within(veteran,
+ {
+ trt = trt - 1 # Makes it indicator for test treatment; standard is reference.
+ prior = prior/10 # Now 1=yes.
+ })
>
> # Experimental treatment, cell type and Karnofsky score
> model1 = coxph(Surv(time,status) ~ trt + celltype + karno, data=vet); summary(model1)
Call:
coxph(formula = Surv(time, status) ~ trt + celltype + karno,
    data = vet)

  n= 137, number of events= 128

                      coef exp(coef)  se(coef)      z      Pr(>|z|)
trt                0.261744  1.299194  0.200923  1.303       0.19267
celltypesmallcell  0.824980  2.281836  0.268911  3.068       0.00216 **
celltypeadeno      1.153994  3.170833  0.295038  3.911 0.00009178351 ***
celltypelarge      0.394625  1.483828  0.282243  1.398       0.16206
karno             -0.031271  0.969213  0.005165 -6.054 0.00000000141 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                   exp(coef) exp(-coef) lower .95 upper .95
trt                   1.2992     0.7697    0.8763    1.9262
celltypesmallcell     2.2818     0.4382    1.3471    3.8653
celltypeadeno         3.1708     0.3154    1.7784    5.6534
celltypelarge         1.4838     0.6739    0.8534    2.5801
karno                 0.9692     1.0318    0.9595    0.9791

Concordance= 0.737  (se = 0.022 )
Likelihood ratio test= 61.07  on 5 df,   p=0.000000000007
Wald test            = 63.41  on 5 df,   p=0.000000000002
Score (logrank) test = 66.55  on 5 df,   p=0.0000000000005

>
> # If treatment is left alone,
> summary(coxph(Surv(time,status) ~ trt + celltype + karno, data=veteran))
Call:
coxph(formula = Surv(time, status) ~ trt + celltype + karno,
    data = veteran)

  n= 137, number of events= 128
```

```
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>
> nocelltype = update(model1, . ~ .-celltype)
> anova(nocelltype,model1)
Analysis of Deviance Table
 Cox model: response is  Surv(time, status)
 Model 1: ~ trt + karno
 Model 2: ~ trt + celltype + karno
   loglik  Chisq Df Pr(>|Chi|)
1 -483.97
2 -474.91 18.102  3   0.000419 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
>
> # Pairwise comparisons (use Wald tests)
> source("http://www.utstat.toronto.edu/~brunner/Rfunctions/Wtest.txt")
> Vn1 = vcov(model1); b1 = coefficients(model1)
> smallVSadeno = cbind(0, 1,-1, 0, 0)
> smallVSlarge = cbind(0, 1, 0,-1, 0)
> adenoVSlarge = cbind(0, 0, 1,-1, 0)
> Wtest(L=smallVSadeno, Tn=b1, Vn=Vn1)
        W        df   p-value
1.4953326 1.0000000 0.2213909
> Wtest(L=smallVSlarge, Tn=b1, Vn=Vn1)
        W        df   p-value
2.6803131 1.0000000 0.1015957
> Wtest(L=adenoVSlarge, Tn=b1, Vn=Vn1) # Quiz question on this one. Interpret.
         W         df    p-value
6.46489623 1.00000000 0.01100261
>
>
>
>
```

```
>
> # -------------------- cancer again -------------------------- #
>
> rm(list=ls());  options(scipen=999)
> # install.packages("survival",dependencies=TRUE) # Only need to do this once
> library(survival) # Do this every time
> # help(cancer)
> # summary(cancer)
>
> attach(cancer)
> status=status-1; sex = sex-1 # So 0=M, 1=F
> stime = Surv(time,status)
> table(ph.ecog)
ph.ecog
  0   1   2   3
 63 113  50   1
> summary(ph.ecog)
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.    NA's
 0.0000  0.0000  1.0000  0.9515  1.0000  3.0000       1
> # Eliminate the ph.ecog=3
> ecog = ph.ecog
> ecog[ecog==3] = NA
> table(ecog) # 0, 1, 2
ecog
  0   1   2
 63 113  50
> ecog = factor(ecog) # This makes zero (good) the ref category -- okay.
>
> model1 = coxph(stime ~ sex + ecog); summary(model1)
Call:
coxph(formula = stime ~ sex + ecog)

  n= 226, number of events= 163
   (2 observations deleted due to missingness)

         coef exp(coef) se(coef)      z  Pr(>|z|)
sex   -0.5447    0.5800   0.1681 -3.240    0.0012 **
ecog1  0.4180    1.5189   0.1995  2.096    0.0361 *
ecog2  0.9464    2.5765   0.2248  4.211 0.0000254 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

      exp(coef) exp(-coef) lower .95 upper .95
sex       0.580     1.7242    0.4172    0.8064
ecog1     1.519     0.6584    1.0274    2.2454
ecog2     2.577     0.3881    1.6585    4.0027

Concordance= 0.64  (se = 0.025 )
Likelihood ratio test= 27.58  on 3 df,   p=0.000004
Wald test            = 27.85  on 3 df,   p=0.000004
Score (logrank) test = 28.82  on 3 df,   p=0.000002

> # Test whether hazard ratio of 1 to 0 = hr of 2 to 1
```

```
> # H0: beta2 = beta3-beta2 <=> 2 beta2 = beta3
> LL = cbind(0,2,-1)
> source("http://www.utstat.toronto.edu/~brunner/Rfunctions/Wtest.txt")
> betahat = coefficients(model1); kov = vcov(model1)
> Wtest(L=LL, Tn=betahat, Vn=kov)
        W        df   p-value
0.1229529 1.0000000 0.7258537
>
> # ------------------------------------------------------------ #
>
```