

## 8.5

a)

```

Call:
coxph(formula = Surv(time, delta) ~ Z1 + Z2 + Z3, data = hodg,
      ties = "breslow")

n= 43, number of events= 26

      coef exp(coef) se(coef)   z Pr(>|z|)
Z1  1.8297    6.2323  0.6753 2.709  0.00674 **
Z2  0.6639    1.9423  0.5643 1.177  0.23939
Z3  0.1537    1.1662  0.5888 0.261  0.79406
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

      exp(coef) exp(-coef) lower .95 upper .95
Z1      6.232    0.1605   1.6589  23.414
Z2      1.942    0.5149   0.6427  5.870
Z3      1.166    0.8575   0.3677  3.698

Concordance= 0.605 (se = 0.058 )
Rsquare= 0.168 (max possible= 0.983 )
Likelihood ratio test= 7.89 on 3 df,  p=0.04825
Wald test       = 9.26 on 3 df,  p=0.02604
Score (logrank) test = 11.08 on 3 df,  p=0.01131

```

• Global Test :

Test	$\chi^2$	df	p-value
LR	7.89	3	0.048
Score	11.08	3	0.011
Wald	9.26	3	0.026

• ANOVA Table :

Var	df	Est.	SE	$\chi^2$	p-value
HOD Allo	1	1.83	0.68	7.34	0.007
NHL Auto	1	0.66	0.56	1.38	0.24
HOD Auto	1	0.15	0.59	0.07	0.79

b)

```

hodg$Z1b <- ifelse(hodg$gtype == 2, 1, 0)
hodg$Z2b <- ifelse(hodg$gtype == 2, 1, 0)
hodg$Z3b <- hodg$Z1b * hodg$Z2b
fit.hodg1 <- coxph(Surv(time, delta) ~ Z1b + Z2b + Z3b, ties = 'breslow', data = hodg)
summary(fit.hodg1)

fit.hodginter <- coxph(Surv(time, delta) ~ Z1b+Z2b, ties = 'breslow', data = hodg)
summary(fit.hodginter)
X2.lrt <- 2 * (fit.hodg1$loglik[2] - fit.hodginter$loglik[2])
1-pchisq(X2.lrt, 1)

b.null <- 0
X2.wald <- t(fit.hodg1$coefficients[3] - b.null) %%
  solve(fit.hodg1$var[3, 3]) %%
  (fit.hodg1$coefficients[3] - b.null)
1-pchisq(X2.wald, 1)

Call:
coxph(formula = Surv(time, delta) ~ Z1b + Z2b, data = hodg, ties = "breslow")

n= 43, number of events= 26

      coef exp(coef) se(coef)   z Pr(>|z|)
Z1b  0.66387  1.94229  0.56427 1.177  0.23939
Z2b  1.82974  6.23229  0.67532 2.709  0.00674 **
Z3b -2.33990  0.09634  0.85168 -2.747  0.00601 **

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

      exp(coef) exp(-coef) lower .95 upper .95
Z1b      0.94229  0.5149   0.64270  5.8697
Z2b      6.23229  0.1605   1.65887  23.4144
Z3b      0.09634  10.3802  0.01815   0.5114

Concordance= 0.605 (se = 0.058 )
Rsquare= 0.168 (max possible= 0.983 )
Likelihood ratio test= 7.89 on 3 df,  p=0.04825
Wald test       = 9.26 on 3 df,  p=0.02604
Score (logrank) test = 11.08 on 3 df,  p=0.01131

      exp(coef) exp(-coef) lower .95 upper .95
Z1b      0.7687    1.3010   0.3209   1.841
Z2b      1.3200    0.7575   0.5629   3.096

Concordance= 0.553 (se = 0.058 )
Rsquare= 0.012 (max possible= 0.983 )
Likelihood ratio test= 0.54 on 2 df,  p=0.7634
Wald test       = 0.53 on 2 df,  p=0.7653
Score (logrank) test = 0.54 on 2 df,  p=0.765

[1] 0.006690241  ← LR p-value
[1,]
[1,] 0.006006927  ← Wald p-value

```

Both Likelihood ratio and Wald p-value are  $< 0.05$ .

Therefore, we have enough evidence to conclude that there is a significant interaction between disease type & transplant type

c) Relative Risk for an NHL Auto to NHL Allo of 1.94 with 95% CL (0.64, 5.87)

(d)

```
#Allo patient
C <- c(1, 0, 0)
b0 <- c(0, 0, 0)
b <- fit.hodg$coefficients
V <- fit.hodg$var
chi_allo <- t(C %% b - C %% b0) %% solve(t(C) %% V %% C) %% (C %% b - C %% b0)
pchisq(chi_allo, df=1, lower.tail = F)

#Auto patient
C <- c(0, 1, -1)
b0 <- c(0, 0, 0)
b <- fit.hodg$coefficients
V <- fit.hodg$var
chi_allo <- t(C %% b - C %% b0) %% solve(t(C) %% V %% C) %% (C %% b - C %% b0)
pchisq(chi_allo, df=1, lower.tail = F)
```
[,1]
[1,] 0.006739661
[,1]
[1,] 0.312685
```

Allo : The p-value is 0.0067

Auto : The p-value is 0.31

e)

```
C <- rbind(c(0, 1, 0), c(1, 0, -1))
b0 <- c(0, 0, 0)
b <- fit.hodg$coefficients
V <- fit.hodg$var
chi_allo <- t(C %% b - C %% b0) %% solve(C %% V %% t(C)) %%
(C %% b - C %% b0)
pchisq(chi_allo, df=2, lower.tail = F)
```
[,1]
[1,] 0.01429393
```

The test stat is 8.50, df is 2, p-value is 0.014  $< 0.05$

which means statistically significant. We have enough evidence to reject  $H_0$ .

8.10

```

Call:
coxph(formula = Surv(ta, da) ~ z10, data = bmt, ties = "breslow")

  coef exp(coef) se(coef)   z     p
z10 -0.299    0.742    0.466 -0.64 0.52

Likelihood ratio test=0.43 on 1 df, p=0.51
n= 137, number of events= 26

```

- a) • Cox model test the hypothesis of no difference in the rate of development of AGVHD between MTX & no MTX.

$$Z_{10} = \begin{cases} 1 & \text{with MTX} \\ 0 & \text{without MTX} \end{cases}$$

$$\text{Cox model : } h(t) = h_0(t) \exp \{ \beta_1 Z_{10} \}$$

- Find a point estimate and a 95% C.I. for RR of AGVHD on the MTX protocol as compare to those not given MTX

$\exp(\hat{\beta}_1)$  can be seen as a measure of relative risk

$$\exp(\hat{\beta}_1) = \frac{h(t|Z_{10}=1)}{h(t|Z_{10}=0)} = 0.742$$

$$SE(\hat{\beta}_1) = 0.466 \Rightarrow SE \text{ of } \exp(\hat{\beta}_1)$$

```

```{r}
bmt$Z1 <- ifelse(bmt$group == 1, 1, 0)
bmt$Z2 <- ifelse(bmt$group == 2, 1, 0)
bmt$Z1_MTX <- bmt$Z1 * bmt$z10
bmt$Z2_MTX <- bmt$Z2 * bmt$z10
coxph(Surv(ta, da) ~ z10 + Z1 + Z2 + Z1_MTX + Z2_MTX, data = bmt, ties = 'breslow')
```

```

```

Call:
coxph(formula = Surv(ta, da) ~ z10 + Z1 + Z2 + Z1_MTX + Z2_MTX,
      data = bmt, ties = "breslow")

  coef exp(coef) se(coef)   z     p
z10    0.368    1.444    0.866  0.42 0.67
Z1     0.821    2.273    0.646  1.27 0.20
Z2     0.723    2.061    0.592  1.22 0.22
Z1_MTX -0.767    0.464   1.118 -0.69 0.49
Z2_MTX -1.350    0.259   1.360 -0.99 0.32

Likelihood ratio test=3.01 on 5 df, p=0.699
n= 137, number of events= 26

```

b)  $Z_1 = \begin{cases} 1 & \text{ALL} \\ 0 & \text{o.w.} \end{cases}$        $Z_2 = \begin{cases} 1 & \text{AML High} \\ 0 & \text{o.w.} \end{cases}$

$$\text{Cox model : } h(t) = h_0(t) \cdot \exp \{ \beta_1 Z_1 + \beta_2 Z_2 + \beta_3 Z_{10} + \beta_4 Z_1 Z_2 + \beta_5 Z_2 Z_3 \}$$

$$H_0: \beta_3 = 0 \quad p = 0.67 > 0.05 \quad \text{not statistically significant}$$

We don't have enough evidence to reject  $H_0$ , there's no effect of MTX on development of AGVHD, adjusting for 3 disease categories.

c)  $H_0: \beta_4 = 0 \ \& \ \beta_5 = 0$

pvalue = 0.49 & 0.32 both  $> 0.05$ , means not statistical significant

Therefore, there's no interaction effect on AGVHD between the disease categories and use MTX.

- d) Find the best model to test the primary hypo of on MTX effect on the occurrence of AGVHD  
Use "MASS" Package to find best model

```
```{r}
bmt$Q1 <- ifelse(bmt$group == 2, 1, 0)
bmt$Q2 <- ifelse(bmt$group == 3, 1, 0)
bmt$Q3 <- bmt$z7
bmt$Q4 <- ifelse(bmt$z8 == 1, 1, 0)
bmt$Q5 <- bmt$z10
bmt$Q6 <- ifelse(bmt$z4 == 1, 1, 0)
bmt$Q7 <- ifelse(bmt$z3 == 1, 1, 0)
bmt$Q8 <- bmt$Q6 * bmt$Q7
bmt$Q9 <- ifelse(bmt$z6 == 1, 1, 0)
bmt$Q10 <- ifelse(bmt$z5 == 1, 1, 0)
bmt$Q11 <- bmt$Q9 * bmt$Q10
bmt$Q12 <- bmt$z2 - 28
bmt$Q13 <- bmt$z1 - 28
bmt$Q14 <- bmt$Q12 * bmt$Q13

fit.AIC <- coxph(Surv(ta, da) ~ Q5, data = bmt, ties = "breslow")
stepAIC(fit.AIC, direction = "both", scope = list(upper = ~ Q1 + Q2 + Q3 + Q4 + Q5 + Q6 + Q7 + Q8 + Q9 + Q10 + Q11 + Q12 + Q13 + Q14, lower = ~ Q5))
```
Call:
coxph(formula = Surv(ta, da) ~ Q5 + Q13 + Q2 + Q9, data = bmt,
ties = "breslow")



coef	exp(coef)	se(coef)	z	p
Q5	-0.5993	0.5492	0.4715	-1.27 0.2037
Q13	0.0597	1.0615	0.0216	2.76 0.0057
Q2	-0.8031	0.4479	0.4767	-1.68 0.0920
Q9	0.6686	1.9515	0.4013	1.67 0.0957



Likelihood ratio test=12.6 on 4 df, p=0.0133
n= 137, number of events= 26
```

There're 4 variables :  $Q_5, Q_{13}, Q_2, Q_9$  and their coefficients shown above .

8.14

a) Cox PH model :  $h(t|x) = h_0(t) \cdot \exp(x^\top \beta)$

$$\text{Baseline} : \hat{S}_0(t) = \exp[-\hat{H}_0(t)]$$

$$\hat{S}(t|x_0) = \hat{S}_0(t) \exp(x_0^\top \hat{\beta})$$

Result shown below :

```

bmt$X1 <- ifelse(bmt$group == 2, 1, 0)
bmt$X2 <- ifelse(bmt$group == 3, 1, 0)
bmt$X1_MTX <- bmt$X1 * bmt$z10
bmt$X2_MTX <- bmt$X2 * bmt$z10

fit.bmt <- coxph(Surv(ta, da) ~ X1 + X2 + z10, data = bmt, ties = 'breslow')
b.haz <- basehaz(fit.bmt_14, centered = F)

t <- b.haz[, 2]

S.est <- cbind(exp(-b.haz[, 1]), t)

S.est <- fit.bmt_14$coefficients

S1_n <- S.est[, 1]^(exp(t(b.est) %% c(0, 0, 0))) # group 1 no MTX
S2_n <- S.est[, 1]^(exp(t(b.est) %% c(1, 0, 0))) # group 2 no MTX
S3_n <- S.est[, 1]^(exp(t(b.est) %% c(0, 1, 0))) # group 3 no MTX

S1 <- S.est[, 1]^(exp(t(b.est) %% c(0, 0, 1))) # group 1
S2 <- S.est[, 1]^(exp(t(b.est) %% c(1, 0, 1))) # group 2
S3 <- S.est[, 1]^(exp(t(b.est) %% c(0, 1, 1))) # group 3

res <- cbind(S1_n, S2_n, S3_n, S1, S2, S3)
colnames(res) <- c("ALL-no MTX", "AML low-no MTX", "AML high-no MTX",
                   "ALL- MTX", "AML low- MTX", "AML high- MTX")

ALL-no MTX AML low-no MTX AML high-no MTX ALL- MTX AML low- MTX AML high- MTX
[1,] 1.0000000 1.0000000 1.0000000 1.0000000 1.0000000 1.0000000
[2,] 1.0000000 1.0000000 1.0000000 1.0000000 1.0000000 1.0000000
[3,] 0.9796302 0.9826000 0.9889675 0.9856627 0.9877585 0.9922457
[4,] 0.9694026 0.9738436 0.9833883 0.9784305 0.9815737 0.9883145
[5,] 0.9591325 0.9650371 0.9777586 0.9711454 0.9753367 0.9843409
[6,] 0.9488786 0.9562306 0.9721099 0.9638484 0.9690827 0.9803471

```

b) 95% C.I. for survival function of AML High Risk patient at 80 days with

no MTX :

Call: survfit(formula = fit.bmt, newdata = data.frame(Q1 = 0, Q2 = 1, z10 = 0), se.fit = TRUE, conf.int = 0.95)

| time | n.risk | n.event | survival | std.err | lower | 95% CI | upper | 95% CI |
|------|--------|---------|----------|---------|-------|--------|-------|--------|
| 10   | 135    | 2       | 0.989    | 0.00877 | 0.972 | 1.000  |       |        |
| 16   | 132    | 1       | 0.983    | 0.01131 | 0.961 | 1.000  |       |        |
| 18   | 130    | 1       | 0.978    | 0.01369 | 0.951 | 1.000  |       |        |
| 20   | 129    | 1       | 0.972    | 0.01597 | 0.941 | 1.000  |       |        |
| 21   | 128    | 3       | 0.955    | 0.02240 | 0.912 | 1.000  |       |        |
| 22   | 125    | 1       | 0.950    | 0.02450 | 0.903 | 0.999  |       |        |
| 25   | 124    | 2       | 0.938    | 0.02863 | 0.884 | 0.996  |       |        |
| 28   | 122    | 2       | 0.927    | 0.03267 | 0.865 | 0.993  |       |        |
| 29   | 120    | 2       | 0.915    | 0.03667 | 0.846 | 0.990  |       |        |
| 30   | 118    | 1       | 0.909    | 0.03866 | 0.837 | 0.988  |       |        |
| 32   | 117    | 1       | 0.903    | 0.04063 | 0.827 | 0.987  |       |        |
| 36   | 115    | 1       | 0.898    | 0.04260 | 0.818 | 0.985  |       |        |
| 38   | 114    | 2       | 0.886    | 0.04649 | 0.799 | 0.982  |       |        |
| 39   | 112    | 1       | 0.880    | 0.04841 | 0.790 | 0.980  |       |        |
| 52   | 110    | 1       | 0.874    | 0.05033 | 0.781 | 0.978  |       |        |
| 67   | 107    | 1       | 0.868    | 0.05227 | 0.771 | 0.977  |       |        |
| 70   | 106    | 1       | 0.862    | 0.05421 | 0.762 | 0.975  |       |        |
| 72   | 105    | 1       | 0.856    | 0.05613 | 0.752 | 0.973  |       |        |
| 88   | 102    | 1       | 0.849    | 0.05807 | 0.743 | 0.971  |       |        |

$$S(80) = 0.856 , \text{ 95% CI : } (0.752, 0.973)$$

95% C.I. for survival function of AML High Risk patient at 80 days with

MTX :

Call: survfit(formula = fit.bmt, newdata = data.frame(Q1 = 0, Q2 = 1, z10 = 1), se.fit = TRUE, conf.int = 0.95)

| time | n.risk | n.event | survival | std.err | lower | 95% CI | upper | 95% CI |
|------|--------|---------|----------|---------|-------|--------|-------|--------|
| 10   | 135    | 2       | 0.992    | 0.00680 | 0.979 | 1      |       |        |
| 16   | 132    | 1       | 0.988    | 0.00907 | 0.971 | 1      |       |        |
| 18   | 130    | 1       | 0.984    | 0.01127 | 0.962 | 1      |       |        |
| 20   | 129    | 1       | 0.980    | 0.01343 | 0.954 | 1      |       |        |
| 21   | 128    | 3       | 0.968    | 0.01973 | 0.930 | 1      |       |        |
| 22   | 125    | 1       | 0.964    | 0.02182 | 0.922 | 1      |       |        |
| 25   | 124    | 2       | 0.956    | 0.02596 | 0.907 | 1      |       |        |
| 28   | 122    | 2       | 0.948    | 0.03008 | 0.891 | 1      |       |        |
| 29   | 120    | 2       | 0.940    | 0.03418 | 0.875 | 1      |       |        |
| 30   | 118    | 1       | 0.935    | 0.03624 | 0.867 | 1      |       |        |
| 32   | 117    | 1       | 0.931    | 0.03829 | 0.859 | 1      |       |        |
| 36   | 115    | 1       | 0.927    | 0.04035 | 0.851 | 1      |       |        |
| 38   | 114    | 2       | 0.918    | 0.04446 | 0.835 | 1      |       |        |
| 39   | 112    | 1       | 0.914    | 0.04652 | 0.827 | 1      |       |        |
| 52   | 110    | 1       | 0.910    | 0.04860 | 0.819 | 1      |       |        |
| 67   | 107    | 1       | 0.905    | 0.05073 | 0.811 | 1      |       |        |
| 70   | 106    | 1       | 0.901    | 0.05285 | 0.803 | 1      |       |        |
| 72   | 105    | 1       | 0.896    | 0.05496 | 0.795 | 1      |       |        |
| 88   | 102    | 1       | 0.892    | 0.05712 | 0.787 | 1      |       |        |

$$S(80) = 0.896 , \text{ 95% C.I. : } (0.785, 1)$$

## 9.1 Effect of ploidy on survival for patients with cancer of tongue.

$Z_2(t)$  : fixed time covariate of interest.  $Z_2(t) = Z_1 \cdot g(t)$

$$H_0: \beta_2 = 0$$

Test for the proportional hazard function.

$$Z_1 = \begin{cases} 1 & \text{Aneuploid} \\ 0 & \text{Diploid} \end{cases} \quad Z_2 = Z_1 \cdot \log(\text{time})$$

```

help("tongue")
data(tongue)
cut.points <- unique(tongue$time[tongue$delta == 1])
tongue1 <- survSplit(data = tongue, cut = cut.points, end = "time", start = "t0", event = "delta")

tongue1$X1 <- ifelse(tongue1$type == 2, 1, 0)
tongue1$X2 <- tongue1$X1 * log(tongue1$time)
fit.tongue <- coxph(Surv(t0, time, delta) ~ X1 + X2, data = tongue1, ties = 'breslow')
summary(fit.tongue)
```

```

Call:

```

coxph(formula = Surv(t0, time, delta) ~ X1 + X2, data = tongue1,
      ties = "breslow")

```

n= 1808, number of events= 53

	coef	exp(coef)	se(coef)	z	Pr(> z )
X1	0.9718	2.6427	0.7580	1.282	0.200
X2	-0.1557	0.8558	0.2148	-0.725	0.469

>0.05

	exp(coef)	exp(-coef)	lower .95	upper .95
X1	2.6427	0.3784	0.5982	11.674
X2	0.8558	1.1685	0.5618	1.304

Concordance= 0.564 (se = 0.036 )  
Rsquare= 0.002 (max possible= 0.197 )  
Likelihood ratio test= 3.14 on 2 df, p=0.2078  
Wald test = 3.2 on 2 df, p=0.2014  
Score (logrank) test = 3.33 on 2 df, p=0.1895

P-values > 0.05, which means statistically insignificant.

So we don't have evidence to reject  $H_0$ . We conclude that the hazard rates for two groups are proportional.

9.3

a)

```

fit.ct <- coxph(Surv(time, delta) ~ group, data = data, ties = "breslow")
summary(fit.ct)
```

Call:
coxph(formula = Surv(time, delta) ~ group, data = data, ties = "breslow")

n= 90, number of events= 82

      coef exp(coef) se(coef)      z Pr(>|z|)
group -0.1075    0.8981   0.2234 -0.481     0.63

      exp(coef) exp(-coef) lower .95 upper .95
group  0.8981     1.113    0.5797    1.391

Concordance= 0.562 (se = 0.031 )
Rsquare= 0.003 (max possible= 0.999 )
Likelihood ratio test= 0.23 on 1 df, p=0.6308
Wald test            = 0.23 on 1 df, p=0.6304
Score (logrank) test = 0.23 on 1 df, p=0.6303

```

Relative Risk = 0.8981 , 95% C.I. of RR = (0.5797, 1.391)

b)

```

cut.points_non <- unique(data$time[data$delta == 1])
data1 <- survSplit(data = data, cut = cut.points_non, end = "time", start = "t0", event = "delta")
data1$X1 <- data1$group * log(data1$time)
fit.non <- coxph(Surv(t0, time, delta) ~ group + X1, data = data1, ties = 'breslow')
summary(fit.non)
```

Call:
coxph(formula = Surv(t0, time, delta) ~ group + X1, data = data1,
ties = "breslow")

n= 3960, number of events= 82

      coef exp(coef) se(coef)      z Pr(>|z|)
group -3.8727    0.0208   1.4782 -2.62 0.00879 **
X1     0.6475    1.9108   0.2481  2.61 0.00906 **
```
Signif. codes: 0 '****' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

      exp(coef) exp(-coef) lower .95 upper .95
group  0.0208    48.0722  0.001148     0.377
X1     1.9108    0.5233  1.174937     3.107

Concordance= 0.575 (se = 0.031 )
Rsquare= 0.002 (max possible= 0.144 )
Likelihood ratio test= 8.56 on 2 df, p=0.01384
Wald test            = 6.88 on 2 df, p=0.032
Score (logrank) test = 7.6 on 2 df, p=0.02237

```

What p-value for  $X_1$  is 0.00906 , < 0.05 .

c)

```

loglik <- os.numeric(length(cut.points_non))
for(i in 1:length(cut.points_non)){
  data1$tdc1 <- ifelse(data1$time > cut.points_non[i], data1$group, 0)
  fit.tdc <- coxph(Surv(t0, time, delta) ~ group + tdc1, data = data1, ties = 'breslow')
  loglik[i] <- fit.tdc$loglik[2]
}
# cbind(cut.points_non, loglik)
opt_tau <- cut.points_non[which.max(loglik)]
opt_tau
```

Loglik converged before variable 1,2 ; beta may be infinite. X matrix deemed to be si
converged before variable 2 ; beta may be infinite. [1] 254

```

The cutpoint is at 254 days

```

data(larynx)
help(larynx)
#Create dummy variables for stage variable (s2, s3, s4)
larynx$s2 <- ifelse(larynx$stage == 2, 1, 0)
larynx$s3 <- ifelse(larynx$stage == 3, 1, 0)
larynx$s4 <- ifelse(larynx$stage == 4, 1, 0)
larynx$yr <- ifelse(larynx$diagyr < 75, 1, 0)

cut.points <- unique(larynx$time[larynx$delta == 1])
larynx1 <- survSplit(data = larynx, cut = cut.points, end = "time", start = "t0", event = "delta")
# stratify based on year
fit <- coxph(Surv(t0, time, delta) ~ s2+s3+s4+age+strata(yr), data = larynx1, ties = 'breslow')
fit

```

ANOVA Table Shown as below:

```

Call:
coxph(formula = Surv(t0, time, delta) ~ s2 + s3 + s4 + age +
    strata(yr), data = larynx1, ties = "breslow")

      coef exp(coef) se(coef)   z     p
s2  0.1122   1.1187  0.4641 0.24 0.80904
s3  0.6195   1.8580  0.3560 1.74 0.08181
s4  1.6970   5.4575  0.4403 3.85 0.00012
age 0.0170   1.0171  0.0149 1.14 0.25488

Likelihood ratio test=17.6 on 4 df, p=0.00149
n= 1919, number of events= 50

```

b)

```

larynx_yr0 <- larynx1[larynx1$yr == 0, ]
larynx_yr1 <- larynx1[larynx1$yr == 1, ]
fit0 <- coxph(Surv(t0, time, delta) ~ s2+s3+s4+age, data = larynx_yr0, ties = 'breslow')

fit1 <- coxph(Surv(t0, time, delta) ~ s2+s3+s4+age, data = larynx_yr1, ties = 'breslow')

#LR
X2 <- -2*(fit$loglik[2] - (fit0$loglik[2] + fit1$loglik[2])); X2
1 - pchisq(X2, 4)

```

LR test statistics  $\chi^2 = 3.062836$       P-value = 0.5473

c)

```

W1 <- (fit0$coefficients[1] - fit1$coefficients[1])^2 / (fit1$var[1,1] + fit0$var[1,1]); W1
1 - pchisq(W1, 1) #p-value

W2 <- (fit0$coefficients[2] - fit1$coefficients[2])^2 / (fit1$var[2,2] + fit0$var[2,2]); W2
1 - pchisq(W2, 1) #p-value

W3 <- (fit0$coefficients[3] - fit1$coefficients[3])^2 / (fit1$var[3,3] + fit0$var[3,3]); W3
1 - pchisq(W3, 1) #p-value

W4 <- (fit0$coefficients[4] - fit1$coefficients[4])^2 / (fit1$var[4,4] + fit0$var[4,4]); W4
1 - pchisq(W4, 1) #p-value

C <- rbind(c(1, 0, 0, 0), c(0, 1, 0, 0), c(0, 0, 1, 0), c(0, 0, 0, 1))
b0 <- fit0$coefficients
b1 <- fit1$coefficients
V <- fit0$var + fit1$var
wald <- t(b1 - b0) %*% solve(C %*% V %*% t(C)) %*% (b1 - b0)

wald
1 - pchisq(wald, 4)

```

} Individual Walt Test

} Overall Walt test

Walt test stat  $\chi^2 = 2.82$  , P-value = 0.59

9.8.

a)

```
cut.points <- unique(burn$T3[burn$D3 == 1])
burn1 <- survSplit(data = burn, cut = cut.points, end = "T3", start = "t0", event = "D3")
#Create time-dependent covariates
burn1$co <- ifelse(burn1$T3 >= burn1$T1 & burn1$D1 == 1, 1, 0) ← Covariate
fit <- coxph(Surv(t0, T3, D3) ~ co, data = burn1, ties = 'breslow')
summary(fit)
````
```

```
Call:
coxph(formula = Surv(t0, T3, D3) ~ co, data = burn1, ties = "breslow")

n= 2265, number of events= 48

      coef exp(coef) se(coef)   z Pr(>|z|)
co -0.8699    0.4190   0.4386 -1.983   0.0473 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

      exp(coef) exp(-coef) lower .95 upper .95
co     0.419      2.387    0.1773    0.9899

Concordance= 0.559  (se = 0.029 )
Rsquare= 0.002  (max possible= 0.176 )
Likelihood ratio test= 4.27  on 1 df,  p=0.03882
Wald test            = 3.93  on 1 df,  p=0.04735
Score (logrank) test = 4.01  on 1 df,  p=0.04516
```

b)

```
````{r}
burn1$co1 <- ifelse(burn1$T3 >= burn1$T2 & burn1$D2 == 1, 1, 0)
fit1 <- coxph(Surv(t0, T3, D3) ~ co1, data = burn1, ties = 'breslow') ← Another covariate
summary(fit1)
````
```

```
Call:
coxph(formula = Surv(t0, T3, D3) ~ co1, data = burn1, ties = "breslow")

n= 2265, number of events= 48

      coef exp(coef) se(coef)   z Pr(>|z|)
co1 -0.2162    0.8056   0.3537 -0.611    0.541

      exp(coef) exp(-coef) lower .95 upper .95
co1     0.8056      1.241    0.4028    1.611

Concordance= 0.519  (se = 0.031 )
Rsquare= 0  (max possible= 0.176 )
Likelihood ratio test= 0.38  on 1 df,  p=0.5364
Wald test            = 0.37  on 1 df,  p=0.541
Score (logrank) test = 0.37  on 1 df,  p=0.5405
```

c)

```
burn1$Z1_logt <- burn1$Z1 * log(burn1$T3)
burn1$Z2_logt <- burn1$Z2 * log(burn1$T3)
burn1$Z3_logt <- burn1$Z3 * log(burn1$T3)
burn1$Z4_logt <- burn1$Z4 * log(burn1$T3)
burn1$Z5_logt <- burn1$Z5 * log(burn1$T3)
burn1$Z6_logt <- burn1$Z6 * log(burn1$T3)
burn1$Z7_logt <- burn1$Z7 * log(burn1$T3)
burn1$Z8_logt <- burn1$Z8 * log(burn1$T3)
burn1$Z9_logt <- burn1$Z9 * log(burn1$T3)
burn1$Z10_logt <- burn1$Z10 * log(burn1$T3)
burn1$co_logt <- burn1$co * log(burn1$T3)
burn1$co1_logt <- burn1$co1 * log(burn1$T3)
burn1$Z11_1 <- ifelse(burn1$Z11 == 2, 1, 0)
burn1$Z11_2 <- ifelse(burn1$Z11 == 3, 1, 0)
burn1$Z11_3 <- ifelse(burn1$Z11 == 4, 1, 0)
burn1$Z11_1_logt <- burn1$Z11_1 * log(burn1$T3)
burn1$Z11_2_logt <- burn1$Z11_2 * log(burn1$T3)
burn1$Z11_3_logt <- burn1$Z11_3 * log(burn1$T3)
fit.burn_1 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+co+co1+Z9_logt, data = burn1, ties = 'breslow')
summary(fit.burn_1)
fit.burn_2 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+co+co1+Z11_1_logt, data = burn1, ties = 'breslow')
summary(fit.burn_2)
fit.burn_3 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+co+co1+Z11_3_logt, data = burn1, ties = 'breslow')
summary(fit.burn_3)
```

I attached R markdown file for this question  
The result was super long. The result showed that  $Z_9$ ,  $Z_{11(2)}$  &  $Z_{11(4)}$  are non-proportional hazard.

Then, we fit  $2^3=8$  Cox's models. Then, we use LR test to test whether the covariate effect of each stratified variable is the same.

```

d) ``{r}
burn2 <- burn[burn$D2==1,]
cut.points <- unique(burn2$T3[burn2$D3 == 1])
burn3 <- survSplit(data = burn2, cut = cut.points, end = "T3", start = "t0", event = "D3")
burn3$Z1_logt <- burn3$Z1 * log(burn3$T3)
burn3$Z2_logt <- burn3$Z2 * log(burn3$T3)
burn3$Z3_logt <- burn3$Z3 * log(burn3$T3)
burn3$Z4_logt <- burn3$Z4 * log(burn3$T3)
burn3$Z5_logt <- burn3$Z5 * log(burn3$T3)
burn3$Z6_logt <- burn3$Z6 * log(burn3$T3)
burn3$Z7_logt <- burn3$Z7 * log(burn3$T3)
burn3$Z8_logt <- burn3$Z8 * log(burn3$T3)
burn3$Z9_logt <- burn3$Z9 * log(burn3$T3)
burn3$Z10_logt <- burn3$Z10 * log(burn3$T3)
burn3$Z11_1 <- ifelse(burn3$Z11 == 2, 1, 0)
burn3$Z11_2 <- ifelse(burn3$Z11 == 3, 1, 0)
burn3$Z11_3 <- ifelse(burn3$Z11 == 4, 1, 0)
burn3$Z11_1_logt <- burn3$Z11_1 * log(burn3$T3)
burn3$Z11_2_logt <- burn3$Z11_2 * log(burn3$T3)
burn3$Z11_3_logt <- burn3$Z11_3 * log(burn3$T3)
burn3$X1 <- ifelse(burn3$T3 >= burn3$T1 & burn3$D1 == 1, 1, 0)
burn3$X2 <- ifelse(burn3$T3 >= burn3$T2 & burn3$D2 == 1, 1, 0)
burn3$X1_logt <- burn3$X1 * log(burn3$T3)
burn3$X2_logt <- burn3$X2 * log(burn3$T3)
fit.burn_4 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+X1+X2+Z11_3_logt, data = burn3, ties = 'breslow')
summary(fit.burn_4)
```

```

P-value for each variable multiplied by  $\log(3)$   $> 0.05$ .

There's no non-proportional variable need adjustly.

```

burn1$Z1_logt <- burn1$Z1 * log(burn1$T3)
burn1$Z2_logt <- burn1$Z2 * log(burn1$T3)
burn1$Z3_logt <- burn1$Z3 * log(burn1$T3)
burn1$Z4_logt <- burn1$Z4 * log(burn1$T3)
burn1$Z5_logt <- burn1$Z5 * log(burn1$T3)
burn1$Z6_logt <- burn1$Z6 * log(burn1$T3)
burn1$Z7_logt <- burn1$Z7 * log(burn1$T3)
burn1$Z8_logt <- burn1$Z8 * log(burn1$T3)
burn1$Z9_logt <- burn1$Z9 * log(burn1$T3)
burn1$Z10_logt <- burn1$Z10 * log(burn1$T3)
burn1$X1_logt <- burn1$X1 * log(burn1$T3)
burn1$X2_logt <- burn1$X2 * log(burn1$T3)
burn1$Z11_1 <- ifelse(burn1$Z11 == 2, 1, 0)
burn1$Z11_2 <- ifelse(burn1$Z11 == 3, 1, 0)
burn1$Z11_3 <- ifelse(burn1$Z11 == 4, 1, 0)
burn1$Z11_1_logt <- burn1$Z11_1 * log(burn1$T3)
burn1$Z11_2_logt <- burn1$Z11_2 * log(burn1$T3)
burn1$Z11_3_logt <- burn1$Z11_3 * log(burn1$T3)
fit.burn_1 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+X1+X2+Z9_logt, data = burn1, ties = 'breslow')
summary(fit.burn_1)

## Call:
## coxph(formula = Surv(t0, T3, D3) ~ Z1 + Z2 + Z3 + Z4 + Z5 + Z6 +
##        Z7 + Z8 + Z9 + Z10 + factor(Z11) + X1 + X2 + Z9_logt, data = burn1,
##        ties = "breslow")
##
##      n= 2265, number of events= 48
##
##              coef exp(coef)    se(coef)      z Pr(>|z|)
## Z1      -0.512046  0.599268  0.332452 -1.540   0.1235
## Z2      -0.533575  0.586505  0.409061 -1.304   0.1921
## Z3       2.232432  9.322512  1.041671  2.143   0.0321 *
## Z4       0.002227  1.002230  0.009750  0.228   0.8193
## Z5      -0.027148  0.973217  0.373909 -0.073   0.9421
## Z6       0.593789  1.810837  0.430185  1.380   0.1675
## Z7      -0.087971  0.915787  0.510760 -0.172   0.8633
## Z8      -0.161386  0.850964  0.390017 -0.414   0.6790
## Z9       1.187825  3.279940  0.814180  1.459   0.1446
## Z10      0.262749  1.300501  0.379058  0.693   0.4882
## factor(Z11)2 1.483047  4.406350  1.125233  1.318   0.1875
## factor(Z11)3 2.014883  7.499853  1.144508  1.760   0.0783 .
## factor(Z11)4 0.815790  2.260961  1.047933  0.778   0.4363
## X1      -0.656238  0.518800  0.488373 -1.344   0.1790
## X2      -0.111971  0.894070  0.381398 -0.294   0.7691
## Z9_logt  -0.769492  0.463248  0.385125 -1.998   0.0457 *

```

```

## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef)  exp(-coef) lower .95 upper .95
## Z1          0.5993     1.6687   0.3123   1.1498
## Z2          0.5865     1.7050   0.2631   1.3076
## Z3          9.3225     0.1073   1.2102  71.8133
## Z4          1.0022     0.9978   0.9833   1.0216
## Z5          0.9732     1.0275   0.4677   2.0253
## Z6          1.8108     0.5522   0.7793   4.2078
## Z7          0.9158     1.0920   0.3365   2.4920
## Z8          0.8510     1.1751   0.3962   1.8277
## Z9          3.2799     0.3049   0.6650  16.1770
## Z10         1.3005     0.7689   0.6187   2.7338
## factor(Z11)2 4.4063     0.2269   0.4856  39.9834
## factor(Z11)3 7.4999     0.1333   0.7959  70.6741
## factor(Z11)4 2.2610     0.4423   0.2899  17.6317
## X1          0.5188     1.9275   0.1992   1.3511
## X2          0.8941     1.1185   0.4234   1.8881
## Z9_logt      0.4632     2.1587   0.2178   0.9854
##
## Concordance= 0.742  (se = 0.046 )
## Rsquare= 0.014  (max possible= 0.176 )
## Likelihood ratio test= 33  on 16 df,  p=0.007398
## Wald test          = 26.54  on 16 df,  p=0.04695
## Score (logrank) test = 30.57  on 16 df,  p=0.01527

fit.burn_2 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+X1+X2+Z11_1_logt, data = burn1, ties = 'breslow')
summary(fit.burn_2)

## Call:
## coxph(formula = Surv(t0, T3, D3) ~ Z1 + Z2 + Z3 + Z4 + Z5 + Z6 +
##       Z7 + Z8 + Z9 + Z10 + factor(Z11) + X1 + X2 + Z11_1_logt,
##       data = burn1, ties = "breslow")
##
##    n= 2265, number of events= 48
##
##          coef  exp(coef)   se(coef)      z Pr(>|z|)
## Z1      -0.611424  0.542578  0.334821 -1.826   0.0678 .
## Z2      -0.517405  0.596065  0.408518 -1.267   0.2053
## Z3      2.107986  8.231642  1.035470  2.036   0.0418 *
## Z4      0.002824  1.002828  0.009747  0.290   0.7720
## Z5      -0.091639  0.912435  0.370390 -0.247   0.8046
## Z6      0.602352  1.826409  0.431211  1.397   0.1624
## Z7      0.012729  1.012810  0.510874  0.025   0.9801
## Z8      -0.202155  0.816968  0.395273 -0.511   0.6090
## Z9      -0.276036  0.758785  0.368864 -0.748   0.4543
## Z10     0.259425  1.296185  0.379265  0.684   0.4940
## factor(Z11)2 3.391876 29.721663  1.445321  2.347   0.0189 *
```

```

## factor(Z11)3 2.115241 8.291582 1.146546 1.845 0.0651 .
## factor(Z11)4 0.866786 2.379252 1.051673 0.824 0.4098
## X1 -0.618331 0.538843 0.486884 -1.270 0.2041
## X2 -0.046297 0.954759 0.379345 -0.122 0.9029
## Z11_1_logt -1.109465 0.329735 0.565092 -1.963 0.0496 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## Z1          0.5426   1.84305   0.2815   1.0458
## Z2          0.5961   1.67767   0.2676   1.3275
## Z3          8.2316   0.12148   1.0817   62.6440
## Z4          1.0028   0.99718   0.9839   1.0222
## Z5          0.9124   1.09597   0.4415   1.8857
## Z6          1.8264   0.54752   0.7844   4.2525
## Z7          1.0128   0.98735   0.3721   2.7567
## Z8          0.8170   1.22404   0.3765   1.7728
## Z9          0.7588   1.31790   0.3682   1.5635
## Z10         1.2962   0.77149   0.6164   2.7258
## factor(Z11)2 29.7217   0.03365   1.7491   505.0482
## factor(Z11)3 8.2916   0.12060   0.8764   78.4476
## factor(Z11)4 2.3793   0.42030   0.3029   18.6907
## X1          0.5388   1.85583   0.2075   1.3993
## X2          0.9548   1.04738   0.4539   2.0081
## Z11_1_logt 0.3297   3.03274   0.1089   0.9981
##
## Concordance= 0.75 (se = 0.046 )
## Rsquare= 0.015 (max possible= 0.176 )
## Likelihood ratio test= 33.45 on 16 df,  p=0.006437
## Wald test      = 28.39 on 16 df,  p=0.02838
## Score (logrank) test = 32.7 on 16 df,  p=0.008099

fit.burn_3 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+X1+X2+Z11_3_logt, data = burn1, ties = 'breslow')
summary(fit.burn_3)

## Call:
## coxph(formula = Surv(t0, T3, D3) ~ Z1 + Z2 + Z3 + Z4 + Z5 + Z6 +
##       Z7 + Z8 + Z9 + Z10 + factor(Z11) + X1 + X2 + Z11_3_logt,
##       data = burn1, ties = "breslow")
##
## n= 2265, number of events= 48
##
##          coef exp(coef)  se(coef)      z Pr(>|z|)
## Z1 -0.619562 0.538180 0.332304 -1.864 0.0623 .
## Z2 -0.538179 0.583810 0.408731 -1.317 0.1879
## Z3  2.150549 8.589573 1.035625  2.077 0.0378 *
## Z4  0.002803 1.002807 0.009736  0.288 0.7734
## Z5 -0.057916 0.943729 0.369671 -0.157 0.8755
## Z6  0.600562 1.823143 0.431758  1.391 0.1642

```

```

## Z7      -0.018792  0.981383  0.510207 -0.037   0.9706
## Z8      -0.209377  0.811089  0.392949 -0.533   0.5941
## Z9      -0.286154  0.751147  0.365956 -0.782   0.4343
## Z10     0.254382  1.289665  0.379729  0.670   0.5029
## factor(Z11)2 1.274127  3.575580  1.122947  1.135   0.2565
## factor(Z11)3 1.694910  5.446155  1.139273  1.488   0.1368
## factor(Z11)4 -1.526701  0.217251  1.418293 -1.076   0.2817
## X1      -0.668221  0.512620  0.482212 -1.386   0.1658
## X2      -0.026358  0.973986  0.377121 -0.070   0.9443
## Z11_3_logt 1.189838  3.286548  0.516537  2.303   0.0213 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## Z1      0.5382    1.8581   0.28059   1.032
## Z2      0.5838    1.7129   0.26203   1.301
## Z3      8.5896    0.1164   1.12835  65.388
## Z4      1.0028    0.9972   0.98385   1.022
## Z5      0.9437    1.0596   0.45728   1.948
## Z6      1.8231    0.5485   0.78218   4.249
## Z7      0.9814    1.0190   0.36104   2.668
## Z8      0.8111    1.2329   0.37548   1.752
## Z9      0.7511    1.3313   0.36663   1.539
## Z10     1.2897    0.7754   0.61270   2.715
## factor(Z11)2 3.5756    0.2797   0.39581  32.300
## factor(Z11)3 5.4462    0.1836   0.58390  50.797
## factor(Z11)4 0.2173    4.6030   0.01348   3.501
## X1      0.5126    1.9508   0.19922   1.319
## X2      0.9740    1.0267   0.46510   2.040
## Z11_3_logt 3.2865    0.3043   1.19416   9.045
##
## Concordance= 0.754  (se = 0.046 )
## Rsquare= 0.016  (max possible= 0.176 )
## Likelihood ratio test= 35.5 on 16 df,  p=0.003394
## Wald test           = 28.68 on 16 df,  p=0.0262
## Score (logrank) test = 34.64 on 16 df,  p=0.004448

burn2 <- burn[burn$D2==1,]
cut.points <- unique(burn2$T3[burn2$D3 == 1])
burn3 <- survSplit(data = burn2, cut = cut.points, end = "T3", start = "t0",
event = "D3")
burn3$Z1_logt <- burn3$Z1 * log(burn3$T3)
burn3$Z2_logt <- burn3$Z2 * log(burn3$T3)
burn3$Z3_logt <- burn3$Z3 * log(burn3$T3)
burn3$Z4_logt <- burn3$Z4 * log(burn3$T3)
burn3$Z5_logt <- burn3$Z5 * log(burn3$T3)
burn3$Z6_logt <- burn3$Z6 * log(burn3$T3)
burn3$Z7_logt <- burn3$Z7 * log(burn3$T3)
burn3$Z8_logt <- burn3$Z8 * log(burn3$T3)
burn3$Z9_logt <- burn3$Z9 * log(burn3$T3)

```

```

burn3$Z10_logt <- burn3$Z10 * log(burn3$T3)
burn3$Z11_1 <- ifelse(burn3$Z11 == 2, 1, 0)
burn3$Z11_2 <- ifelse(burn3$Z11 == 3, 1, 0)
burn3$Z11_3 <- ifelse(burn3$Z11 == 4, 1, 0)
burn3$Z11_1_logt <- burn3$Z11_1 * log(burn3$T3)
burn3$Z11_2_logt <- burn3$Z11_2 * log(burn3$T3)
burn3$Z11_3_logt <- burn3$Z11_3 * log(burn3$T3)
burn3$X1 <- ifelse(burn3$T3 >= burn3$T1 & burn3$D1 == 1, 1, 0)
burn3$X2 <- ifelse(burn3$T3 >= burn3$T2 & burn3$D2 == 1, 1, 0)
burn3$X1_logt <- burn3$X1 * log(burn3$T3)
burn3$X2_logt <- burn3$X2 * log(burn3$T3)
fit.burn_4 <- coxph(Surv(t0, T3, D3) ~ Z1+Z2+Z3+Z4+Z5+Z6+Z7+Z8+Z9+Z10+factor(Z11)+X1+X2+Z11_3_logt, data = burn3, ties = 'breslow')

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights,
:
## Loglik converged before variable 11,12,15 ; beta may be infinite.

summary(fit.burn_4)

## Call:
## coxph(formula = Surv(t0, T3, D3) ~ Z1 + Z2 + Z3 + Z4 + Z5 + Z6 +
##       Z7 + Z8 + Z9 + Z10 + factor(Z11) + X1 + X2 + Z11_3_logt,
##       data = burn3, ties = "breslow")
##
##    n= 590, number of events= 14
##
##              coef  exp(coef)   se(coef)      z Pr(>|z|)
## Z1      -3.530e-01 7.026e-01 6.206e-01 -0.569  0.5695
## Z2       1.462e-01 1.157e+00 6.477e-01  0.226  0.8215
## Z3      -2.898e-01 7.484e-01 1.168e+00 -0.248  0.8040
## Z4      -2.583e-02 9.745e-01 2.098e-02 -1.231  0.2184
## Z5       1.405e+00 4.074e+00 9.209e-01  1.525  0.1272
## Z6       2.725e+00 1.526e+01 1.135e+00  2.401  0.0163 *
## Z7       4.842e-01 1.623e+00 1.497e+00  0.323  0.7465
## Z8      -3.889e-01 6.778e-01 1.034e+00 -0.376  0.7069
## Z9      -9.674e-01 3.801e-01 8.259e-01 -1.171  0.2414
## Z10      5.629e-01 1.756e+00 6.965e-01  0.808  0.4189
## factor(Z11)2 -2.009e+01 1.888e-09 1.216e+04 -0.002  0.9987
## factor(Z11)3 -1.772e+01 2.006e-08 2.687e+04 -0.001  0.9995
## factor(Z11)4  6.687e+00 8.021e+02 1.866e+01  0.358  0.7201
## X1      -1.113e+00 3.284e-01 9.277e-01 -1.200  0.2301
## X2       2.082e+01 1.100e+09 1.010e+04  0.002  0.9984
## Z11_3_logt -2.362e+00 9.421e-02 6.461e+00 -0.366  0.7146
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## Z1       7.026e-01 1.423e+00 2.082e-01 2.371e+00
## Z2      1.157e+00 8.640e-01 3.252e-01 4.119e+00

```

```

## Z3      7.484e-01  1.336e+00  7.590e-02  7.380e+00
## Z4      9.745e-01  1.026e+00  9.352e-01  1.015e+00
## Z5      4.074e+00  2.455e-01  6.701e-01  2.477e+01
## Z6      1.526e+01  6.554e-02  1.650e+00  1.411e+02
## Z7      1.623e+00  6.162e-01  8.623e-02  3.054e+01
## Z8      6.778e-01  1.475e+00  8.929e-02  5.145e+00
## Z9      3.801e-01  2.631e+00  7.531e-02  1.918e+00
## Z10     1.756e+00  5.695e-01  4.484e-01  6.876e+00
## factor(Z11)2 1.888e-09  5.297e+08  0.000e+00      Inf
## factor(Z11)3 2.006e-08  4.986e+07  0.000e+00      Inf
## factor(Z11)4 8.021e+02  1.247e-03  1.046e-13  6.151e+18
## X1      3.284e-01  3.045e+00  5.330e-02  2.024e+00
## X2      1.100e+09  9.089e-10  0.000e+00      Inf
## Z11_3_logt 9.421e-02  1.061e+01  2.984e-07  2.974e+04
##
## Concordance= 0.89  (se = 0.086 )
## Rsquare= 0.05  (max possible= 0.158 )
## Likelihood ratio test= 30.38  on 16 df,  p=0.01615
## Wald test          = 11.99  on 16 df,  p=0.7449
## Score (logrank) test = 25.18  on 16 df,  p=0.06672

```