UTHM
Universiti Tun Hussein Onn Malaysia

UNIVERSITI TUN HUSSEIN ONN MALAYSIA

FINAL EXAMINATION
SEMESTER I
SESSION 2015/2016

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COURSE NAME	:	SURVIVAL ANALYSIS
COURSE CODE	:	BWB 42903
PROGRAMME	:	3 BWQ
EXAMINATION DATE	:	DECEMBER 2015 / JANUARY 2016
DURATION	:	3 HOURS
INSTRUCTION	:	ANSWER ALL QUESTIONS

THIS QUESTION PAPER CONSISTS OF **SIX (6)** PAGES

Q1   (a)   State two properties of hazard function.

(4 marks)

(b)   Show clearly the relationship of $S(t)$ to $h(t)$.

(4 marks)

(c)   Describe any two major approaches to analyze the relationship of a set of predictor variables with the survival time.

(4 marks)

(d)   Explain briefly the ideas behind the accelerated failure time model and the Cox proportional hazards model for incorporating covariates into a survival model.

(4 marks)

Q2   (a)   Given the following survival time data in weeks for $n = 25$ participants

12.3+, 5.4, 8.2, 12.2+, 11.7, 10.0, 5.7, 9.8, 2.6, 11.0, 9.2, 12.1+,

6.6, 2.2, 1.8, 10.2, 10.7, 11.1, 5.3, 3.5, 9.2, 2.5, 8.7, 3.8, 3.0

where + denotes censored data.

(i)   Calculate the average survival time ($\overline{T}$) and the average hazard rate ($\overline{h}$).

(4 marks)

(ii)   Construct the estimated survival curve. From the curve, estimate the median survival time.

(10 marks)

(b)   Consider the comparison of the following two survivor curves.
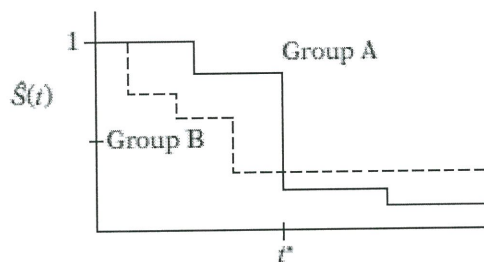
(i)   Which group has a better survival prognosis based on $t*$?

(2 marks)

(ii)   Which group has a longer median survival time?

(1 mark)

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Q3 Consider the survival data for 137 patients from the Veteran's Administration Lung Cancer Trial. The variables in this dataset are listed in **Table Q3**.

Table Q3 Survival Data on Lung Cancer Trial

Variable	Variable Name	Coding
1	Treatment	Standard = 1, Test = 2
2	Cell type 1	Large = 1, other = 0
3	Cell type 2	Adeno = 1, other = 0
4	Cell type 3	Small =1, other = 0
5	Cell type 4	Squamous =1, other =0
6	Survival time	Days
7	Performance status	0 = worst....100 = best
8	Disease duration	Months
9	Age	Years
10	Prior therapy	None = 0, some = 1
11	Status	0 = censored, 1=died

For these data, a Cox PH model was fitted yielding the following edited computer results:

Response: survival time

Variable Name	Coef.	Std. Err.	$p > |z|$	Haz. Ratio	[95% Conf. interval]	
1 Treatment	0.290	0.207	0.162	1.336	0.890	2.006
3 Adeno cell	0.789	0.303	0.009	2.200	1.216	3.982
4 Small cell	0.457	0.266	0.086	1.579	0.937	2.661
5 Squamous cell	-0.400	0.283	0.157	0.671	0.385	1.167
7 Perf. Status	-0.033	0.006	0.000	0.968	0.958	0.978
8 Disease dur.	0.000	0.009	0.992	1.000	0.982	1.018
9 Age	-0.009	0.009	0.358	0.991	0.974	1.010
10 Prior Therapy	0.007	0.023	0.755	1.007	0.962	1.054

Log likelihood = - 475.180

(a) State the Cox PH model used to obtain the above computer results.

(2 marks)

(b) From the output, what is the hazard ratio for the Cox PH model that compares persons having Adeno cell type

(i) with persons with large cell type?

(4 marks)

(ii) with persons with Squamous cell type?

(4 marks)

(c) Is there any effect of treatment on survival time? Justify your answer by using $\alpha = 0.05$.

(5 marks)

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(d) Write a model for the estimated survival curve for a person who was given the best test treatment and who had a squamous cell type, where the variables to be adjusted are performance status, disease duration, age and prior therapy.

(2 marks)

Q4 The data consists of 50 persons from 1967 – 1980 Evans Count Study. There are two basic independent variables of interest: AGE and chronic disease status (CHR), where CHR is coded as: None = 0 and Chronic disease = 1. A product term of the form AGE X CHR is also considered. The dependent variable is time until death, and the event is death. The primary question of interest concerns whether CHR, considered as the exposure variable, is related to survival time, controlling for AGE. The edited output of computer results for this question is given as follows:

Model 1:

Variable	Coef.	Std. Err.	Chi-sq.	p > |z|
CHR	0.8595	0.3116	7.61	.0058

Log likelihood = -142.87

Model 2:

Variable	Coef.	Std. Err.	Chi-sq.	p > |z|
CHR	0.8051	0.3252	6.13	.0133
AGE	0.0856	0.0193	19.63	.0000

Log likelihood = -132.45

Model 3:

Variable	Coef.	Std. Err.	Chi-sq.	p > |z|
CHR	1.0009	2.2556	0.20	.6572
AGE	0.0874	0.0276	10.01	.0016
CHR x AGE	-0.0030	0.0345	0.01	.9301

Log likelihood = -132.35

(a) State the Cox PH model that allows for main effects of CHR and AGE as well as the interaction effect of CHR with AGE.

(2 marks)

(b) Test for significant interaction and draw you conclusions by using $\alpha = 0.05$.

(5 marks)

(c) Assuming no interaction, should AGE be controlled? Explain your answer on the basis of cofounding and precision considerations.

(8 marks)

(d) When considering plots of various hazard functions over time, the hazard function for persons with CHR = 1 crosses the hazard function for persons with CHR = 0, what does this indicate about the use of any of the three models provided in the output.

(4 marks)

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(e)   Using model 2, find an equation for the estimated survival curve for persons with CHR = 1, adjusted for AGE. Also, write down an equation for the estimated survival curve for persons with CHR = 0, adjusted for AGE.

(4 marks)

(f)   What is your overall conclusion about the effect of CHR on survival time based on the output provided?

(2 marks)

Q5   A clinical trial data based on heroin drug addicts was run by using Weibull model. The predictor of interest is CLINIC (coded 1 or 2) for two methadone clinics for heroin addicts. Covariates include DOSE for methadone dose (mg/day), PRISON (coded 1 if patient has a prison record and 0 if not), and a prison-dose product term called PRIDOSE. The outcome is time (in days) until the person dropped out of the clinic or was censored. The computer output for both the accelerated failure time (AFT) and proportional hazard (PH) forms are presented as follows:

Weibull regression
accelerated failure-time form

Log likelihood = -260.74854

_t	Coef.	Std.Err.	z	p>|z|
clinic	.698	.158	4.42	0.000
prison	.145	.558	0.26	0.795
dose	.027	.006	4.60	0.000
prisdose	-.006	.009	-0.69	0.492
_cons	3.977	.376	10.58	0.000
/ln_p	.315	.068	4.67	0.000
P	1.370467			
1/p	.729678			

Weibull regression
Log relative-hazard form

Log likelihood = -260.74854

_t	Coef.	Std.Err.	z	p>|z|
clinic	-.957	.213	-4.49	0.000
prison	-.198	.765	-0.26	0.795
dose	-.037	.008	-4.63	0.000
prisdose	.009	.013	0.69	0.491
_cons	-5.450	.702	-7.76	0.000
/ln_p	.315	.068	4.67	0.000
P	1.370467			
1/p	.729678			

(a)   Estimate the acceleration factor with a 99% confidence interval comparing CLINIC = 2 versus CLINIC = 1. Interpret the result.

(4 marks)

(b)   Estimate the hazard ratio with a 99% confidence interval comparing CLINIC = 2 versus CLINIC = 1. Interpret the result.

(4 marks)

(c)   Estimate the coefficient for CLINIC in the PH Weibull model using the results in the output from the AFT form of the model. [Hint: the coefficients for a Weibull PH and AFT model are related $\beta = -\alpha_j p$ for the jth covariate].

(2 marks)

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(d)   Is the product term PRISDOSE included in the model to account for potential interaction or potential confounding of the effect of CLINIC on survival?

              (2 marks)

(e)   Based on the output, estimate the median survival time for a patient from CLINIC = 1 and CLINIC = 2 who has a prison record, receives a methadone dose of 50 mg/day and exist an interaction between PRISON and DOSE. Based on both median values, find the ratio. How does this ratio relate to the acceleration factor?

              (8 marks)

(f)   Frailty component is now included in the Weibull model in AFT form. A gamma distribution of mean 1 and variance θ is assumed for the frailty. The output shown one additional parameter estimate for θ is given below.

```
Weibull regression
Accelerated failure-time form
Gamma frailty


Log likelihood = -260.74854
```

_t	Coef.	Std.Err.	z	p>|z|
clinic	.698	.158	4.42	0.000
prison	.145	.558	0.26	0.795
dose	.027	.006	4.60	0.000
prisdose	-.006	.009	-0.69	0.492
_cons	3.977	.376	10.58	0.000
/ln_p	.315	.068	4.67	0.000
P	1.370467			
1/p	.729678			
theta	.00000002		.0000262	

```
Likelihood ratio test of theta = 0;
Chibar2(01) = 0.00
Prob>=chibar2 = 1.000
```

Did the addition of the frailty component changes any of the other parameter estimates? Justify your answer in terms of θ value.

              (4 marks)

- END OF QUESTION -