** Exercise 1

The recorded survival times, in years, of six patients following a heart bypass operation are given below.

\[
10.4^*, 6.6, 4.2, 6.2^*, 15.9, 6.3,
\]

where values followed by a * indicate right censored survival times. Also recorded for each patient is \( x \), the number of cigarettes smoked on average per week prior to the operation. These are

\[
0, 100, 60, 0, 0, 40,
\]

respectively.

(a) Assuming a Cox proportional hazards model with single covariate \( x \), find the partial likelihood \( L_P(\beta) \) of the coefficient \( \beta \) of \( x \) based on the above data.

Numerical maximisation of \( L_P(\beta) \) yields a maximum likelihood estimate \( \hat{\beta} = 0.017 \) and a maximised partial likelihood value \( L_P(\hat{\beta}) = e^{-3.439} \).

(b) What is the interpretation of the value \( \hat{\beta} \) in terms of the effect of smoking on the future lifetime of a patient who undergoes heart bypass operation?

(c) We wish to test the hypothesis \( H_0 \) that the number of cigarettes smoked does not have an effect on the distribution of the future lifetime of heart bypass patients. Still assuming a Cox proportional hazards model, perform

(i) the score test;
(ii) the likelihood ratio test.

* Exercise 2

The following table gives a small data set of survival times (in years), censoring status (1=failure, 0=censored) and a covariate \( x \).

<table>
<thead>
<tr>
<th>patient id</th>
<th>survival time</th>
<th>status</th>
<th>( x )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

Assume a Cox proportional hazards model.

(a) Write down the partial likelihood of \( \beta \) (the coefficient of \( x \)).
(b) Convince yourselves that the partial likelihood exhibits a single maximum as a function in $\beta$. In fact it does so at $\hat{\beta} \approx -1$.

(c) Find the asymptotic value of the standard error/deviation of $\hat{\beta}$.

** Exercise 3

(a) Define what is meant by a ‘proportional hazards’ model.

(b) Show that the model $T_i \sim \text{Weibull}(\lambda_i, \alpha)$ (see Section 1.2 in the lecture notes for information on the Weibull distribution), where $\lambda_i$ depends on the covariates associated with individual $i$, is a proportional hazards model.

*** Exercise 4

In an observational hip replacement study the time to revision of the prosthesis was analysed by a Cox proportional hazards model with two covariates. The table below gives the estimates for the regression coefficients (in the notation of the lecture notes these coefficients are $\beta_1$ and $\beta_2$) corresponding to the two covariates and their standard errors/deviations. The covariance between the two coefficients was estimated to be -0.00163.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Estimate</th>
<th>Stand. error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender(male)</td>
<td>0.69</td>
<td>0.18</td>
</tr>
<tr>
<td>Previous hip surgery</td>
<td>0.39</td>
<td>0.17</td>
</tr>
</tbody>
</table>

(a) Give a 95% confidence interval for the hazard ratio for each factor and interpret these intervals.

(b)  (i) Calculate the hazard ratio for a male with previous hip surgery compared to a female without previous hip surgery.
     (ii) Give a 95% confidence interval for this hazard ratio and interpret it.

(c) The data have been collected over three decades. Do you see any problems arising from this? Give a reason. If yes, how can you address them in the analysis?