1. A clinical trial of chemotherapy against chemotherapy combined with radiotherapy in the treatment of locally unresectable gastric cancer was conducted. In this trial, forty-five patients were randomized to each of the two arms and followed for about eight years. The survival or censoring time in days are as follows:

Chemotherapy Only

1, 63, 105, 129, 182, 216, 250, 262, 301, 301, 342, 354, 356, 358, 380, 383, 383, 388, 394, 408, 460, 489, 499, 523, 524, 535, 562, 569, 675, 676, 748, 778, 786, 797, 955, 968, 1000, 1245, 1271, 1420, 1551, 1694, 2363, 2754*, 2950*.

Chemotherapy Plus Radiotherapy


where * denotes censored observations. Of interest in this study is a comparison of the efficacy of the two treatments on overall survival.

(i) Using an appropriate proportional hazards model, test the hypothesis of difference in survival between the two treatment regimes. Find a 95% confidence interval for the relative risk of death for patients treated only with chemotherapy compared to patients treated with chemotherapy plus radiation.

(ii) Check the assumption of proportional hazard rates. State what approach you used and the conclusion.

(iii) Instead of the covariate which represents the treatment type, consider a model with two time-dependent covariates defined as follows:

\[ x_1(t) = \begin{cases} 
1 & \text{if chemotherapy only and } t \leq 254, \\
0 & \text{otherwise.} 
\end{cases} \]

\[ x_2(t) = \begin{cases} 
1 & \text{if chemotherapy only and } t > 254, \\
0 & \text{otherwise.} 
\end{cases} \]
What is the relative risk of death for patients treated only with chemotherapy compared to patients treated with chemotherapy plus radiation when $t \leq 254$? What is this relative risk when $t > 254$? Compare the relative risks obtained from this model with those obtained in part (i).

2. Refer to the Bone Marrow Transplant data. The graft-versus-host disease is considered to have an antileukemic effect. Consider four time-varying GVHD groups: patients yet to develop any GVHD, patients who have aGVHD, cGVHD or have both aGVHD and cGVHD. Fit a proportional hazard model with appropriate time-dependent covariates which can be used to determine which of the above four groups has the lowest relapse risk. Note that the time to event of concern is the time to relapse, patients who died prior to relapse are considered as censored observations.

(i) Give explicit definitions for the time-dependent covariates to be used in the proportional hazard model.

(ii) Estimate model parameters and test the significance of the parameters.

(iii) Provide point estimate and 95% confidence intervals for the relative risk of relapse for the GVHD groups compared to the group with no GVHD at time $t$. 