Exercise Cox

1 Exercise 1, Partial likelihood

Consider survival times T_1 and T_2, and bounded covariates X_1 and X_2 that have density $f(x_1, x_2)$. Assume that T_1 and T_2 are independent given γ and X_1, X_2.

Given γ, X_1, X_2:
T_1 has hazard

$$\lambda_1(t, X, \gamma) = \lambda(t, \gamma) \exp(X_1^T \beta)$$

and T_2 has hazard

$$\lambda_2(t, X, \gamma) = \lambda(t, \gamma) \exp(X_2^T \beta).$$

1. Show that the hazard for $\min(T_1, T_2)$ given γ and X_1, X_2 is $\lambda_1(t, X, \gamma) + \lambda_2(t, X, \gamma)$.

2. Let j denote the index of the subject that dies first (among 1 and 2). Show that

$$P(j = 1 | \min(T_1, T_2) = t) = \frac{\lambda_1(t, X, \gamma)}{\lambda_1(t, X, \gamma) + \lambda_2(t, X, \gamma)}$$

3. With n subjects under risk at time t what is then the probability that it was the first subject that died given $\min(T_1, ..., T_n) = t$.

2 Exercise 2, Collapsability

Given X, Z we assume that T has Cox model $\lambda(t) \exp(X^T \beta + Z^T \gamma)$

1. Show that hazard for T given X is not a Cox model when $\gamma \neq 0$.
2. Assume now that X and Z are independent. Are X and Z independent among survivors if $\beta \neq 0$ and $\gamma \neq 0$.

Assume now that the hazard is additive $\alpha_0(t) + X^T \alpha(t) + Z^T \gamma(t)$

1. Find the hazard of T given X.
2. Assume now that X and Z are independent. Are X and Z independent among survivors.

3 Exercise 3

We consider a randomized clinical study with treatment A that is thus independent of additional covariates Z. Assume that a survival time T has hazard $\lambda(t, A, Z)$ and we wish to check if treatment matters by comparing $\lambda(t, 1, Z)$ and $\lambda(t, 0, Z)$. Assume that there is also independent right censoring given A and Z. We thus observe a right censored survival time. In addition we have i.i.d. replicates from this model.

1. Show that if $\lambda(s, 1, Z) = \lambda(s, 0, Z)$ for $s \in [0, \tau]$ then the marginals hazards satisfy $\lambda(s, 1) = \lambda(s, 0)$.
2. We now fit a Cox model $\lambda_0(t) \exp(\beta_1 A + \beta_2 Z^T)$ to the data. Using the results of Struthers-Kalbfleish (1986), Lin-Wei (1989): $\hat{\beta}$ that converge to the solution of

$$U(\beta) = \int_0^\tau \left[s_1(s) - \frac{s_1(s, \gamma, \beta)}{s_0(s, \gamma, \beta)} s_0(s) \right] ds$$
$$s_j(t) = \lim_p n^{-1} \sum Y_i(s) X^j \lambda(t, X)$$
$$s_j(t, \beta) = \lim_p n^{-1} \sum Y_i(s) X^j \exp(X\beta)$$

   and is asymptotically normal with standard errors estimated by the robust standard errors via sandwhich formula.

   Show that if

- i) $\lambda(s, 1, Z) = \lambda(s, 0, Z)$
- ii) the hazard of C is $\lambda_0(t) + A\lambda_1(t) + \lambda_2(t, Z)$,

then $\beta_1^* = 0$ will make the first equation 0 and therefore solve the joint set of equations.

Hint, simply compute the s's and their limits (means).

3. Now in a competintg risks setting with two causes\Show that if

   - i) $\lambda_j(s, 1, Z) = \lambda_j(s, 0, Z)$ for $j = 1, 2$
   - ii) the hazard of C is $\lambda_0(t) + A\lambda_1(t) + \lambda_2(t, Z)$, then $\beta_1^* = 0$ will make the first equation 0 and therefore solve the joint set of equations.

4 Exercise 4, TRACE data

Consider the TRACE data of the timereg package. Do help(TRACE) to get going.

1. Fit a Cox model with vf, diabetes and chf to describe their effects on the risk of dying.

   - You may consider using time-dependent covariates as a way of describing the risk over time.

2. Validate the model.

3. Do survival predictions.

4. Compute robust standard errors and compare with the martingale standard errors.