SOLUTIONS TO EXERCISES WEEK 44

Exercise 4.3

The counting processes $N_1(t), \ldots, N_n(t)$ have intensity processes $\lambda_i(t) = Y_i(t)\beta_0(t)$; $i=1,\ldots,n$. Here $Y_i(t) = 0,1$ is an at risk indicator.

This is a special case of the additive regression model with [cf. page 157 in ABG]

$N(t) = (N_1(t), \ldots, N_n(t))$, $B(t) = B_0(t) = \int_0^t \beta_0(u)du$,

and $X(t) = (Y_1(t), \ldots, Y_n(t))^T$. We note that (since $Y_i(t)$ only takes the values 0 and 1):

$$X(t)^T X(t) = \sum_{i=1}^n Y_i(t)^2 = \sum_{i=1}^n Y_i(t) = Y_\bullet(t)$$

Further $J(t) = I(\text{rank } X(t) = 1) = I(Y_\bullet(t) > 0)$.

Hence the estimator (4.59) takes the form

$$\hat{B}_0(t) = \int_0^t J(u)\,(X(u)^T X(u))^{-1} X(u)^T dN(u)$$

$$= \int_0^t J(u)\, Y_\bullet(u)^{-1} \left(\sum_{i=1}^n Y_i(u) dN_i(u) \right)$$

$$= \int_0^t \left(J(u) / Y_\bullet(u) \right) dN_\bullet(u)$$

which is the Nelson-Aalen estimator

Exercise 4.4

$N_i(t)$ has intensity process

$\lambda_i(t) = Y_i(t)\{\beta_0(t) + \beta_1(t)x_i\}$, where $Y_i(t)$ is an at risk indicator and $x_i = 0,1$ is a group indicator. The number at risk in group 0 (i.e. $x_i = 0$) is

$Y^{(0)}(t) = \sum_{i=1}^{n}(1-x_i)Y_i(t)$ and the number at risk in group 1 (i.e. $x_i = 1$) is

$Y^{(1)}(t) = \sum_{i=1}^{n} x_i Y_i(t)$. Thus $Y_\bullet(t) = Y^{(0)}(t) + Y^{(1)}(t)$

$= \sum_{i=1}^{n} Y_i(t)$.

a) We have that

$$X(t) = \begin{pmatrix} Y_1(t) & Y_1(t)x_1 \\ Y_2(t) & Y_2(t)x_2 \\ \vdots & \\ Y_n(t) & Y_n(t)x_n \end{pmatrix}$$

By a direct computation we get

$$X(t)^T X(t) = \begin{pmatrix} \sum_{i=1}^{n} Y_i(t)^2 & \sum_{i=1}^{n} Y_i(t)^2 x_i \\ \sum_{i=1}^{n} Y_i(t)^2 x_i & \sum_{i=1}^{n} Y_i(t)^2 x_i^2 \end{pmatrix}$$

$$= \begin{pmatrix} Y_\bullet(t) & Y^{(1)}(t) \\ Y^{(1)}(t) & Y^{(1)}(t) \end{pmatrix}$$

where the last equality follows since $Y_i(t)^2 = Y_i(t)$ and $x_i^2 = x_i$.

b) We have that

$$\mathrm{Det}\left(X(t)^T X(t)\right) = Y_\bullet(t)\, Y^{(1)}(t) - Y^{(1)}(t)^2$$

$$= Y^{(1)}(t)\left(Y_\bullet(t) - Y^{(1)}(t)\right)$$

$$= Y^{(0)}(t)\, Y^{(1)}(t)$$

It follows that (when $Y^{(0)}(t) > 0$ and $Y^{(1)}(t) > 0$):

$$\left(X(t)^T X(t)\right)^{-1} = \frac{1}{\operatorname{Det}\left(X(t)^T X(t)\right)} \begin{pmatrix} Y^{(1)}(t) & -Y^{(1)}(t) \\ -Y^{(1)}(t) & Y_{\cdot}(t) \end{pmatrix}$$

$$= \frac{1}{Y^{(0)}(t)\,Y^{(1)}(t)} \begin{pmatrix} Y^{(1)}(t) & -Y^{(1)}(t) \\ -Y^{(1)}(t) & Y^{(0)}(t)+Y^{(1)}(t) \end{pmatrix}$$

$$= \begin{pmatrix} \frac{1}{Y^{(0)}(t)} & -\frac{1}{Y^{(0)}(t)} \\ -\frac{1}{Y^{(0)}(t)} & \frac{1}{Y^{(0)}(t)} + \frac{1}{Y^{(1)}(t)} \end{pmatrix}$$

c) The estimator $\hat{B}(t) = (\hat{B}_0(t), \hat{B}_1(t))^T$ is given by [cf. (4.58) & (4.59) in ABG]:

$$\hat{B}(t) = \int_0^t J(u) \left(X(u)^T X(u)\right)^{-1} X(u)^T \, dN(u)$$

where $N(t) = (N_1(t), \dots, N_n(t))^T$.

Now we have that

$$(X(t)^T X(t))^{-1} X(t)^T$$

$$= \begin{pmatrix} \frac{Y_1(t)}{Y^{(0)}(t)} - \frac{Y_1(t)x_1}{Y^{(0)}(t)} & \cdots\cdots & \frac{Y_n(t)}{Y^{(0)}(t)} - \frac{Y_n(t)x_n}{Y^{(0)}(t)} \\ \frac{Y_1(t)x_1}{Y^{(0)}(t)} + \frac{Y_1(t)x_1}{Y^{(1)}(t)} - \frac{Y_1(t)}{Y^{(0)}(t)} & \cdots\cdots & \frac{Y_n(t)x_n}{Y^{(0)}(t)} + \frac{Y_n(t)x_n}{Y^{(1)}(t)} - \frac{Y_n(t)}{Y^{(0)}(t)} \end{pmatrix}$$

Hence we get

$$\hat{B}(t) = \int_0^t J(u) \begin{pmatrix} \sum_{i=1}^n \frac{(1-x_i)Y_i(u)}{Y^{(0)}(u)} dN_i(u) \\ \sum_{i=1}^n \frac{x_i Y_i(u)}{Y^{(1)}(u)} dN_i(u) - \sum_{i=1}^n \frac{(1-x_i)Y_i(u)}{Y^{(0)}(u)} dN_i(u) \end{pmatrix}$$

$$= \int_0^t J(u) \begin{pmatrix} dN^{(0)}(u)/Y^{(0)}(u) \\ dN^{(1)}(u)/Y^{(1)}(u) - dN^{(0)}(u)/Y^{(0)}(u) \end{pmatrix}$$

Where $N^{(0)}(t) = \sum_{i=1}^n (1-x_i) N_i(t)$ and $N^{(1)}(t) = \sum_{i=1}^n x_i N_i(t)$

Thus $\hat{B}_0(t) = \int_0^t (J(u)/Y^{(0)}(u))\, dN^{(0)}(u)$ is the Nelson-Aalen estimator for group 0 and $\hat{B}_1(t) = \int_0^t (J(u)/Y^{(1)}(u))\, dN^{(1)}(u) - \int_0^t (J(u)/Y^{(0)}(u))\, dN^{(0)}(u)$ is the difference between the Nelson-Aalen estimators in the two groups.

Exercise 4.5

We consider the situation of exercise 4.4. We want to test the null hypothesis $H_0: \beta_1(t) = 0$ for $0 \le t \le t_0$. The TST test statistic is given by

$$U_1(t_0) = \frac{Z_1(t_0)}{\sqrt{V_{11}(t_0)}}$$

where $Z_1(t_0)$ and $V_{11}(t_0)$ are given by (4.66) and (4.67) in the ABG-book, where the weight process $L_1(t)$ is given as described below (4.68).

a) By result b) in exercise 4.4, we have

$$\left(X(t)^T X(t)\right)^{-1} = \begin{pmatrix} \frac{1}{Y^{(0)}(t)} & -\frac{1}{Y^{(0)}(t)} \\ -\frac{1}{Y^{(0)}(t)} & \frac{1}{Y^{(0)}(t)} + \frac{1}{Y^{(1)}(t)} \end{pmatrix}$$

From this we obtain

$$\operatorname{diag}\left[(X(t)^T X(t))^{-1}\right] = \begin{pmatrix} \frac{1}{Y^{(0)}(t)} & 0 \\ 0 & \frac{1}{Y^{(0)}(t)} + \frac{1}{Y^{(1)}(t)} \end{pmatrix}$$

and hence

$$K(t) = \left\{\operatorname{diag}\left[(X(t)^T X(t))^{-1}\right]\right\}^{-1}$$

$$= \begin{pmatrix} Y^{(0)}(t) & 0 \\ 0 & \frac{Y^{(0)}(t)\, Y^{(1)}(t)}{Y_\bullet(t)} \end{pmatrix}$$

The weight process $L_1(t)$ is given as $K_{11}(t)$, i.e. the element in the lower right-hand corner of $K(t)$.

Thus

$$L_1(t) = \frac{Y^{(0)}(t)\, Y^{(1)}(t)}{Y_\bullet(t)}$$

Using (4.66) and the result in question c of exercise 4.4, we find that the test statistic $Z_1(t_0)$ takes the form

$$Z_1(t_0) = \int_0^{t_0} L_1(t)\, d\hat{B}_1(t)$$

$$= \int_0^{t_0} \frac{Y^{(0)}(t)\, Y^{(1)}(t)}{Y_\bullet(t)} \left(\frac{dN^{(1)}(t)}{Y^{(1)}(t)} - \frac{dN^{(0)}(t)}{Y^{(0)}(t)} \right)$$

which equals (3.52) when we use the log-rank weights (cf table 3.2 on page 107 in ABG)

b) The variance estimator is given as [cf (4.67)]

$$V_{11}(t_0) = \int_0^{t_0} L_1(t)^2\, d\hat{\sigma}_{11}(t)$$

$$= \sum_{T_j \le t_0} L_1(T_j)^2\, \Delta\hat{\sigma}_{11}(T_j)$$

As described on page 164 in ABG there are two options for computing $\hat{\sigma}_{11}(t)$. We may either use (4.63), which is obtained from (4.62) by replacing $\lambda(u)du$ in (4.62) by $dN(u)$. Or we may use (4.64), which is obtained by replacing $\lambda(u)du$ by the estimated intensity process under H_0. Then (4.64) takes the form

$$\Sigma_{mod}(t) = \sum_{T_j \le t} J(T_j) X^-(T_j) \operatorname{diag}\{X_0(T_j) \Delta \hat{B}_0(T_j)\} X^-(T_j)^T \quad (\#)$$

where $X^-(t) = (X(t)^T X(t))^{-1} X(t)^T$

is defined for the model of exercise 4.4, and an expression is given on the top of page 5 in the solution of exercise 4.4. Further $X_0(t)$ and $\hat{B}_0(t)$ are given under H_0, which corresponds to the situation in exercise 4.3.

Thus we have

$$X_0(t) = (Y_1(t), \ldots, Y_n(t))^T$$

and

$$\hat{B}_0(t) = \int_0^t \frac{dN_\cdot(u)}{Y_\cdot(u)}$$

By a direct matrix multiplication we then find after (quite some) algebra that

$$X^-(T_j)\,\mathrm{diag}\{X_0(T_j)\,\Delta \hat{B}_0(T_j)\}\,X^-(T_j)^T$$

$$= \begin{pmatrix} \frac{1}{Y^{(0)}(T_j)}\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)} & -\frac{1}{Y^{(0)}(T_j)}\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)} \\ -\frac{1}{Y^{(0)}(T_j)}\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)} & \left(\frac{1}{Y^{(1)}(T_j)}+\frac{1}{Y^{(0)}(T_j)}\right)\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)} \end{pmatrix}$$

Further we have that $J(T_j)$ in (#) is equal to 1 if there is at least one individual at risk in each group.

From this we obtain

$$\Delta\hat{\sigma}_{11}(T_j) = J(T_j)\left(\frac{1}{Y^{(1)}(T_j)} + \frac{1}{Y^{(0)}(T_j)}\right)\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)}$$

$$= J(T_j)\,\frac{Y_\cdot(T_j)}{Y^{(1)}(T_j)\,Y^{(0)}(T_j)}\,\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)}$$

and hence the variance estimator of the test statistic becomes

$$V_{11}(t_0) = \sum_{T_j \le t_0} L_1(T_j)^2\,\Delta\hat{\sigma}_{11}(T_j)$$

$$= \sum_{T_j \le t_0}\left(\frac{Y^{(0)}(T_j)\,Y^{(1)}(T_j)}{Y_\cdot(T_j)}\right)^2 \frac{Y_\cdot(T_j)}{Y^{(1)}(T_j)\,Y^{(0)}(T_j)}\,\frac{\Delta N_\cdot(T_j)}{Y_\cdot(T_j)}$$

$$= \sum_{T_j' \le t_0} \frac{Y^{(0)}(T_j')\, Y^{(1)}(T_j')}{Y_\bullet(T_j')} \, \Delta N_\bullet(T_j') \qquad (\#\#)$$

The variance estimator of the logrank test is given by [cf (3.55)]

$$\int_0^{t_0} \frac{L^2(t)}{Y_1(t)\, Y_2(t)} \, dN_\bullet(t)$$

$$= \int_0^{t_0} \left(\frac{Y_1(t)\, Y_2(t)}{Y_\bullet(t)} \right)^2 \frac{dN_\bullet(t)}{Y_1(t)\, Y_2(t)}$$

$$= \int_0^{t_0} \frac{Y_1(t)\, Y_2(t)}{Y_\bullet(t)^2} \, dN_\bullet(t)$$

Which is the same as (##).