EXERCISE 8 - TIME-VARYING COVARIATES WITHIN COX MODEL

Data: $(X_i, \delta_i, Z_i = \{Z_i(t), t>0\})$ where X_i, δ_i as usual and Z_i is p-dimensional stochastic process

Cox model: $\lambda(t|Z) = \lim_{h\to 0+} \frac{1}{h} P[t \le T < t+h \mid T \ge t, Z(t)]$ ← conditioned on the value of Z at time t

$= \lambda_0(t) \cdot \exp\{\beta^T Z(t)\}$ in the following $\lambda_0(t)\exp\{\alpha \cdot Z(t) + \beta^T Z\}$

- $Z(t) = \mathbb{1}(E \le t)$ where E is time of some other event (transplantation, surgery, ...)

$$\frac{\lambda(t|Z_1)}{\lambda(t|Z_2)} = \frac{\lambda_0(t)}{\lambda_0(t)} \cdot \frac{\exp\{\alpha \cdot \mathbb{1}(E_1 \le t) + \beta^T Z_1\}}{\exp\{\alpha \cdot \mathbb{1}(E_2 \le t) + \beta \cdot Z_2\}} \overset{Z_1 = Z_2}{=} \exp\{\alpha \cdot (\mathbb{1}(E_1 \le t) - \mathbb{1}(E_2 \le t))\}$$

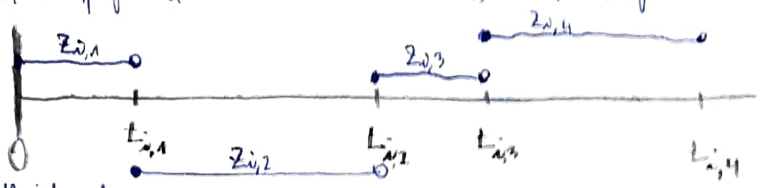
$$\overset{E_1 < E_2}{=} \exp\{\alpha \cdot \mathbb{1}(E_1 \le t < E_2)\}$$

$\Rightarrow \exp\{\alpha\}$ is the proportional increase in hazard limited to time span for which the processes differ

special case: $E_1 = 0$ „transplantation already performed prior entering to the study" } e^α refers to comparison of these two patients with fixed covariates (now they do not change in time)

$E_2 = \infty$ „transplantation was never performed"

- $Z_i(t) = \sum_{j=1}^{m_i} z_{ij} \mathbb{1}_{[t_{ij-1}, t_{ij})}(t)$



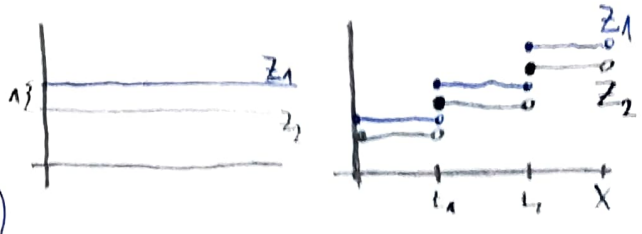
← times of visits

≈ piecewise constant process · z_{ij} value for j-th interval

$$\frac{\lambda(t|Z_1)}{\lambda(t|Z_2)} = \frac{\lambda_0(t)}{\lambda_0(t)} \cdot \frac{\exp\{\alpha \cdot \sum_{j=1}^{m_1} z_{1j} \mathbb{1}_{[t_{1j-1}, t_{1j})}(t) + \beta^T Z_1\}}{\exp\{\alpha \sum_{j=1}^{m_2} z_{1j} \mathbb{1}_{[t_{2j-1}, t_{2j})}(t) + \beta^T Z_2\}} \overset{Z_1 = Z_2}{=} \exp\{\alpha \cdot (Z_1(t) - Z_2(t))\}$$

e^α - can be interpreted not only with respect to two constant processes, but also with respect to processes $Z_1(t) = Z_2(t) + 1$

(which implies visits at the same times and measurement always higher by 1 unit)



in R:

	id	start	stop	event	age at entry	surgery	transplant	blood pressure	cholesterol
	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
i-th patient	i	0	t_{i1}	0	a_i	0	0	b_{i1}	c_{i1}
	i	t_{i1}	t_{i2}	0	a_i	0	0	b_{i2}	c_{i2}
	i	t_{i2}	t_{i3}	0	a_i	0	1	b_{i3}	c_{i3}
	i	t_{i3}	$t_{i3} = X_i$	δ_i	a_i	0	1	b_{i4}	c_{i4}
	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮

Surv(start, stop, event)

Constant covariates

indicates at which time transplanted in this case at time t_{i2}

piecewise constant covariates