Trends and comparison in HR's

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Let us have a Cox model

$$\lambda(t|X) = \lambda_0(t)\exp\{-X\beta\}$$

and the estimate b of β with variance matrix V. Asymptotically, $b \sim \mathcal{N}(\beta, V)$.

Trend in immunities

Let $h_{t_1}, \ldots, h_{t_n}$ be a series of HR's corresponding to a certain source of immunity, where the index stands for the time since obtaining the immunity. Asymptotically, by Delta Theorem[1] and Continuous mapping theorem,

$$\operatorname{var}(h) \doteq W := T'V^\star T, \qquad T = \operatorname{diag}(\exp\{b_{(1)}\}, \ldots, \exp\{b_{(n)}\})$$

where $(b_{(1)}, \ldots, b_{(n)})'$ is the vector of b's corresponding to h and $V^\star$ is the corresponding sub-matrix of V.

We assume a linear trend in h, i.e.

$$h_{t_i} = \eta_0 + \delta t_i + \epsilon_i, \qquad i = 1, \ldots, n, \qquad \operatorname{var}(\epsilon) \doteq W.$$

Teh GLS estimate of (η_0, δ)' is given by

$$\begin{bmatrix} v \\ d \end{bmatrix} = (X'W^{-1}X)^{-1}X'W^{-1}h, \qquad X = \begin{bmatrix} 1 & t_1 \\ 1 & t_2 \\ \vdots & \vdots \\ 1 & t_n \end{bmatrix}$$

with

$$\operatorname{var}\begin{bmatrix} v \\ d \end{bmatrix} = (X'W^{-1}X)^{-1}$$

The estimate of the trend is then

$$\tau(t) = v + dt, \qquad t \geq 0.$$

[1]https://www.jepusto.com/multivariate-delta-method/)

Comparison of immunities

Say that we want to compare HR's $h = (h_{t_1}, \dots, h_{t_n})'$ with another vector of HR's, say $k = (k_{t_1}, \dots, k_{t_n})'$ and assume both to follow *the same* linear trend. This implies that

$$h_{t_i} - k_{t_i} = \rho + e_i, \qquad i = 1, \dots, n, \qquad \mathrm{var}(e) = U := SV^{\star\star}S',$$

$$S = \begin{bmatrix} \exp\{b_{[1]}\} & \cdots & 0 & -\exp\{b_{[n+1]}\} & \cdots & 0 \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ 0 & \cdots & \exp\{b_{[n]}\} & 0 & \cdots & -\exp\{b_{[2n]}\} \end{bmatrix}$$

where $(b_{[1]}, \dots, b_{[2n]})'$ is the vector of b's corresponding to $(h, k)'$ and $V^{\star\star}$is a corresponding sub-matrix of V.

The GLS estimator of ρ is

$$r = (1_n' U^{-1} 1_n)^{-1} 1_n' U^{-1}(h - k)$$

where 1_n is an n-vector of 1's. We have

$$\mathrm{var}(r) {=} (1_n' U^{-1} 1_n)^{-1}$$

The corresponding Z-score is

$$z = \frac{r}{\sqrt{\mathrm{var}(r)}}.$$