

# 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  $\beta$  with variance matrix  $V$ . Asymptotically,  $b \sim \mathcal{N}(\beta, V)$ .

## Trend in immunities

Let  $h_{t_1}, \dots, h_{t_n}$  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<sup>1</sup> and Continuous mapping theorem,

$$\text{var}(h) \doteq W := T'V^*T, \quad T = \text{diag}(\exp\{b_{(1)}\}, \dots, \exp\{b_{(n)}\})$$

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

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

$$h_{t_i} = \eta_0 + \delta t_i + \epsilon_i, \quad i = 1, \dots, n, \quad \text{var}(\epsilon) \doteq W.$$

The GLS estimate of  $(\eta_0, \delta)'$  is given by

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

with

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

The estimate of the trend is then

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

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<sup>1</sup><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

$$h_{t_i} - k_{t_i} = \rho + e_i, \quad i = 1, \dots, n, \quad \text{var}(e) = U := S'V^{**}S,$$

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

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

The GLS estimator of  $\rho$  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

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

The corresponding  $Z$ -score is

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