

# **TMA4275 Life time analysis**

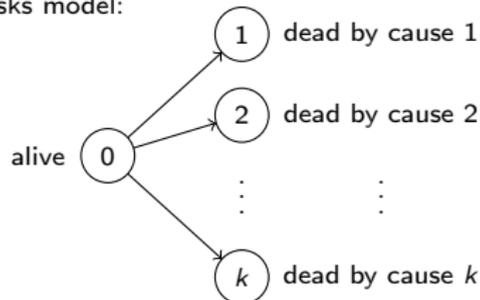
Håkon Tjelmeland

Department of Mathematical Sciences  
Norwegian University of Science and Technology

# Competing risks

(Reference: Section 3.4.1 in Aalen, Borgan and Gjessing, 2008)

★ Competing risks model:

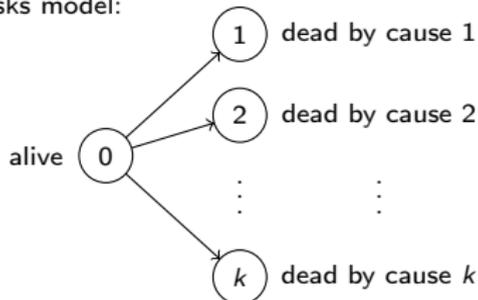


$$\begin{aligned}\hat{P}(s, t) &= \prod_{(s, t]} (\mathbb{I} + d\hat{A}(u)) \\ &= \prod_{j: s < T_j \leq t} (\mathbb{I} + \Delta\hat{A}(T_j))\end{aligned}$$

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★  $P(s, t)$  has the following structure

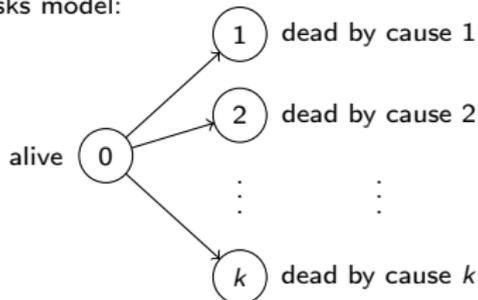
$$P(s, t) = \begin{bmatrix} P_{00}(s, t) & P_{01}(s, t) & P_{02}(s, t) & \dots & P_{0,k}(s, t) \\ 0 & 1 & 0 & \dots & 0 \\ 0 & 0 & 1 & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & 0 \\ 0 & 0 & 0 & \dots & 1 \end{bmatrix}$$

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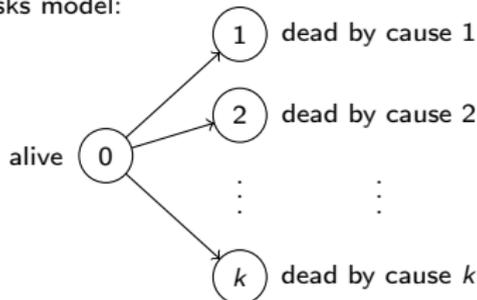
- ★ Want to find formulas for  $\widehat{P}_{00}(s, t)$  and  $\widehat{P}_{0h}(s, t)$

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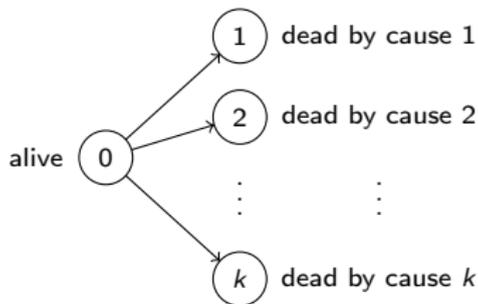
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- ★ Want to find formulas for  $\widehat{P}_{00}(s, t)$  and  $\widehat{P}_{0h}(s, t)$

- consider  $k = 3$
- the factor  $(\mathbb{I} + \Delta\widehat{A}(T_j))$
- product of two  $(\mathbb{I} + \Delta\widehat{A}(T_j))$  factors
- product of three  $(\mathbb{I} + \Delta\widehat{A}(T_j))$  factors
- “guess” on general formula
- general formula can be proved by induction

The factor  $(\mathbb{I} + \Delta\hat{A}(T_j))$

★ Competing risks model



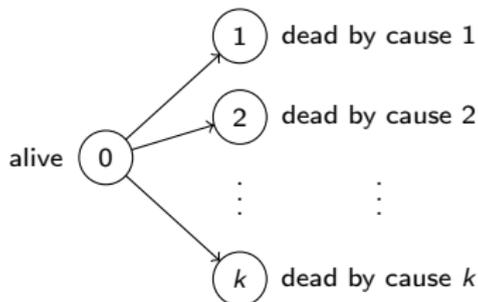
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$$\begin{aligned}\hat{A}_{gh}(t) &= \int_0^t \frac{J_g(s)}{Y_g(s)} dN_{gh}(s) \\ &= \sum_{j: T_j^{gh} \leq t} \frac{\mathbf{1}}{Y_g(T_j^{gh})}\end{aligned}$$

$$\hat{A}_{gg}(t) = - \sum_{h \neq g} \hat{A}_{gh}(t)$$

The factor  $(\mathbb{I} + \Delta\hat{A}(T_j))$

- ★ Competing risks model



- ★ Recall: Observe  $n$  individuals following the competing risks model

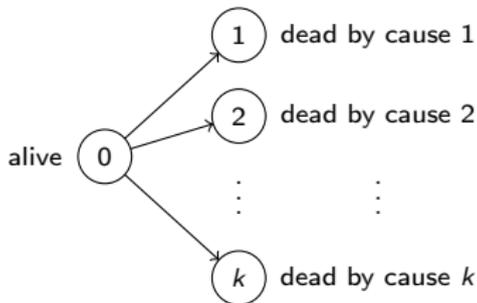
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# The factor $(\mathbb{I} + \Delta\hat{A}(T_j))$

- ★ Competing risks model



- ★ Recall: Observe  $n$  individuals following the competing risks model
- ★ Notation:  $0 < T_1 < T_2 < \dots$



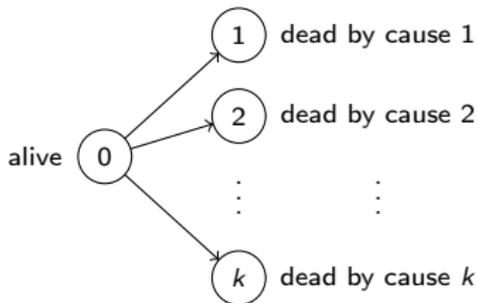
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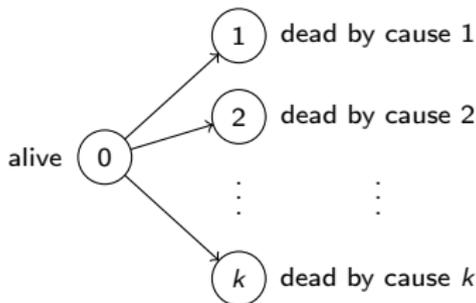


- ★ For  $k = 3$ , if we at time  $T_j$  observe a transition from state 0 to state 2 we have

$$\Delta\hat{A}(T_j) = \begin{bmatrix} -\frac{1}{Y_0(T_j)} & 0 & \frac{1}{Y_0(T_j)} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

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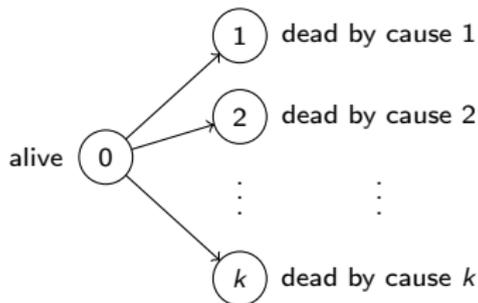


- ★ For  $k = 3$ , if we at time  $T_j$  observe a transition from state 0 to **some other state**, we have

$$\Delta\hat{A}(T_j) = \begin{bmatrix} -\frac{\mathbf{1}}{Y_0(T_j)} & \frac{\Delta N_{01}(T_j)}{Y_0(T_j)} & \frac{\Delta N_{02}(T_j)}{Y_0(T_j)} & \frac{\Delta N_{03}(T_j)}{Y_0(T_j)} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

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- ★ For  $k = 3$ , if we at time  $T_j$  observe a transition from state 0 to **some other state**, we have

$$\mathbb{I} + \Delta\hat{A}(T_j) = \begin{bmatrix} 1 - \frac{\mathbf{1}}{Y_0(T_j)} & \frac{\Delta N_{01}(T_j)}{Y_0(T_j)} & \frac{\Delta N_{02}(T_j)}{Y_0(T_j)} & \frac{\Delta N_{03}(T_j)}{Y_0(T_j)} \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

## Product of two factors

$$\left(\mathbb{I} + \Delta\widehat{A}(T_j)\right) \times \left(\mathbb{I} + \Delta\widehat{A}(T_k)\right)$$

$$= \begin{bmatrix} 1 - \frac{\mathbf{1}}{Y_{\mathbf{0}}(T_j)} & \frac{\Delta N_{\mathbf{01}}(T_j)}{Y_{\mathbf{0}}(T_j)} & \frac{\Delta N_{\mathbf{02}}(T_j)}{Y_{\mathbf{0}}(T_j)} & \frac{\Delta N_{\mathbf{03}}(T_j)}{Y_{\mathbf{0}}(T_j)} \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 1 - \frac{\mathbf{1}}{Y_{\mathbf{0}}(T_k)} & \frac{\Delta N_{\mathbf{01}}(T_k)}{Y_{\mathbf{0}}(T_k)} & \frac{\Delta N_{\mathbf{02}}(T_k)}{Y_{\mathbf{0}}(T_k)} & \frac{\Delta N_{\mathbf{03}}(T_k)}{Y_{\mathbf{0}}(T_k)} \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

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$$= \begin{bmatrix} a(T_j) & b_1(T_j) & b_2(T_j) & b_3(T_j) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} a(T_k) & b_1(T_k) & b_2(T_k) & b_3(T_k) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

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$$= \begin{bmatrix} a(T_j)a(T_k) & a(T_j)b_1(T_k) + b_1(T_j) & a(T_j)b_2(T_k) + b_2(T_j) & a(T_j)b_3(T_k) + b_3(T_j) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

## Product of three factors

$$a(T_j) = 1 - \frac{1}{Y_0(T_j)}$$

$$b_h(T_j) = \frac{\Delta N_{0h}(T_j)}{Y_0(T_j)}$$

$$\left(\mathbb{I} + \Delta \hat{A}(T_j)\right) \times \left(\mathbb{I} + \Delta \hat{A}(T_k)\right) \times \left(\mathbb{I} + \Delta \hat{A}(T_l)\right)$$

$$= \begin{bmatrix} a(T_j)a(T_k) & a(T_j)b_1(T_k) + b_1(T_j) & a(T_j)b_2(T_k) + b_2(T_j) & a(T_j)b_3(T_k) + b_3(T_j) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

$$\times \begin{bmatrix} 1 - \frac{1}{Y_0(T_l)} & \frac{\Delta N_{01}(T_l)}{Y_0(T_l)} & \frac{\Delta N_{02}(T_l)}{Y_0(T_l)} & \frac{\Delta N_{03}(T_l)}{Y_0(T_l)} \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

## Product of three factors

$$a(T_j) = 1 - \frac{1}{y_{\mathbf{0}}(T_j)}$$

$$b_h(T_j) = \frac{\Delta N_{\mathbf{0}h}(T_j)}{y_{\mathbf{0}}(T_j)}$$

$$\left(\mathbb{I} + \Delta \hat{A}(T_j)\right) \times \left(\mathbb{I} + \Delta \hat{A}(T_k)\right) \times \left(\mathbb{I} + \Delta \hat{A}(T_l)\right)$$

$$= \begin{bmatrix} a(T_j)a(T_k) & a(T_j)b_1(T_k) + b_1(T_j) & a(T_j)b_2(T_k) + b_2(T_j) & a(T_j)b_3(T_k) + b_3(T_j) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \\ \times \begin{bmatrix} a(T_l) & b_1(T_l) & b_2(T_l) & b_3(T_l) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

## Product of three factors

$$a(T_j) = 1 - \frac{1}{\gamma_{\mathbf{0}}(T_j)}$$

$$b_h(T_j) = \frac{\Delta N_{\mathbf{0}h}(T_j)}{\gamma_{\mathbf{0}}(T_j)}$$

$$\left(\mathbb{I} + \Delta \hat{A}(T_j)\right) \times \left(\mathbb{I} + \Delta \hat{A}(T_k)\right) \times \left(\mathbb{I} + \Delta \hat{A}(T_l)\right)$$

$$= \begin{bmatrix} a(T_j)a(T_k) & a(T_j)b_1(T_k) + b_1(T_j) & a(T_j)b_2(T_k) + b_2(T_j) & a(T_j)b_3(T_k) + b_3(T_j) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

$$\times \begin{bmatrix} a(T_l) & b_1(T_l) & b_2(T_l) & b_3(T_l) \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

$$= \begin{bmatrix} a(T_j)a(T_k)a(T_l) & a(T_j)a(T_k)b_1(T_l) + a(T_j)b_1(T_k) + b_1(T_j) \\ 0 & 1 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\begin{bmatrix} a(T_j)a(T_k)b_2(T_l) + a(T_j)b_2(T_k) + b_2(T_j) & a(T_j)a(T_k)b_3(T_l) + a(T_j)b_3(T_k) + b_3(T_j) \\ 0 & 0 \\ 1 & 0 \\ 0 & 1 \end{bmatrix}$$





## Product of three factors

$$a(T_j) = 1 - \frac{1}{Y_{\mathbf{0}}(T_j)}$$

$$b_h(T_j) = \frac{\Delta N_{\mathbf{0}h}(T_j)}{Y_{\mathbf{0}}(T_j)}$$

$$\left(\mathbb{I} + \Delta \widehat{A}(T_j)\right) \times \left(\mathbb{I} + \Delta \widehat{A}(T_k)\right) \times \left(\mathbb{I} + \Delta \widehat{A}(T_l)\right)$$

$$= \begin{bmatrix} a(T_j)a(T_k)a(T_l) & a(T_j)a(T_k)b_1(T_l) + a(T_j)b_1(T_k) + b_1(T_j) & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ a(T_j)a(T_k)b_2(T_l) + a(T_j)b_2(T_k) + b_2(T_j) & a(T_j)a(T_k)b_3(T_l) + a(T_j)b_3(T_k) + b_3(T_j) & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 \end{bmatrix}$$

★ From this we see that



$$\widehat{P}_{\mathbf{0}\mathbf{0}}(s, t) = \left[ \prod_{j:s < T_j \leq t} \left(\mathbb{I} + \Delta \widehat{A}(T_j)\right) \right]_{\mathbf{1}\mathbf{1}} = \prod_{j:s < T_j \leq t} a(T_j)$$











## Proof for the formulas

- ★ Want to prove the formulas

$$\hat{P}_{00}(s, t) = \prod_{j:s < T_j \leq t} \left(1 - \frac{1}{Y_0(T_j)}\right)$$

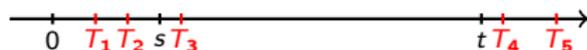
$$\hat{P}_{0h}(s, t) = \sum_{j:s < T_j \leq t} \hat{P}_{00}(s, T_{j-1}) \cdot \frac{\Delta N_{0h}(T_j)}{Y_0(T_j)}$$

- ★ Given

$$\hat{P}(s, t) = \prod_{j:s < T_j \leq t} (\mathbb{I} + \Delta \hat{A}(T_j))$$

- ★ Proof by induction

- proof formulas when only one observed transition in  $(s, t]$



- assume formulas correct for  $k$  observed transition in  $(s, t]$ ,

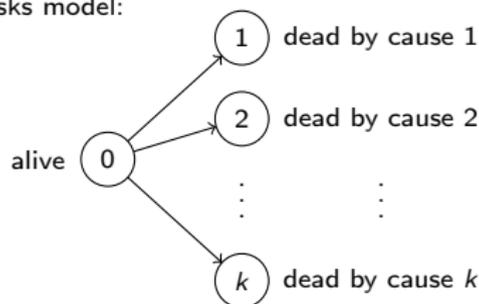


and show that then it is also correct with  $k + 1$  observed transitions in  $(s, t]$



# Summary

- ★ Competing risks model:



- ★ Used Kaplan–Meier estimator for general Markov chain

$$\hat{P}(s, t) = \prod_{(s, t]} (\mathbb{I} + d\hat{A}(u)) = \prod_{j: s < T_j \leq t} (\mathbb{I} + \Delta\hat{A}(T_j))$$

- ★ Showed that

$$\hat{P}_{00}(s, t) = \prod_{j: s < T_j \leq t} \left( 1 - \frac{1}{Y_0(T_j)} \right)$$

$$\hat{P}_{0h}(s, t) = \sum_{j: s < T_j \leq t} \hat{P}_{00}(s, T_{j-1}) \cdot \frac{\Delta N_{0h}(T_j)}{Y_0(T_j)}$$