MATH3085/6143 Survival Models – Worksheet 4 Solutions

1. i) The Kolmogorov forward equation has the form

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}{}_tp_x^{23} &= \sum_{k=1}^{3} {}_tp_x^{2k}\mu_{x+t}^{k3} \qquad \text{where we define } \mu_{x+t}^{33} = -\mu_{x+t}^{31} - \mu_{x+t}^{32} = 0 \\ &= {}_tp_x^{21}\mu_{x+t}^{13} + {}_tp_x^{22}\mu_{x+t}^{23}\end{aligned}$$

as $\mu_{x+t}^{31} = \mu_{x+t}^{32} = 0$ as state 3 is absorbing.

ii) The rate of change in the probability of moving from sick to death between time x and $x+t$ is a function of two elements:

a) The first term is the rate of death from the healthy state at time $x+t$ weighted by the probability that a person is healthy at $x+t$.

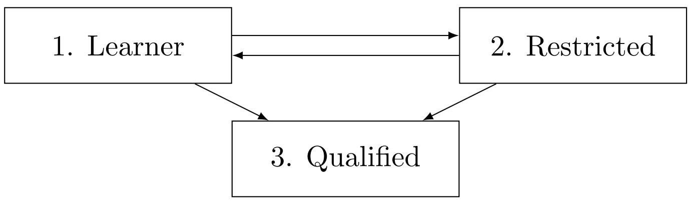
b) The second term is the rate of death from the sick state at time $x+t$ weighted by the probability a person is sick at $x+t$.

iii) The Kolmogorov forward equation has the form

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}{}_tp_x^{21} &= \sum_{k=1}^{3} {}_tp_x^{2k}\mu_{x+t}^{k1} \qquad \text{where we define } \mu_{x+t}^{11} = -\mu_{x+t}^{12} - \mu_{x+t}^{13} \\ &= {}_tp_x^{22}\mu_{x+t}^{21} + {}_tp_x^{23}\mu_{x+t}^{31} - {}_tp_x^{21}(\mu_{x+t}^{12} + \mu_{x+t}^{13}) \\ &= {}_tp_x^{22}\mu_{x+t}^{21} - {}_tp_x^{21}\mu_{x+t}^{12} - {}_tp_x^{21}\mu_{x+t}^{13}\end{aligned}$$

as $\mu_{x+t}^{31} = 0$ as state 3 is absorbing.

2. i)



ii) Using analogous notations defined in lecture notes, let

$$\begin{aligned}\mu_{12} &= \text{transition intensity from Learner to Restricted} \\ \mu_{13} &= \text{transition intensity from Learner to Qualified} \\ \mu_{21} &= \text{transition intensity from Restricted to Learner} \\ \mu_{23} &= \text{transition intensity from Restricted to Qualified} \\ t_1^+ &= \text{total observed holding (waiting) time in state Learner} \\ t_2^+ &= \text{total observed holding (waiting) time in state Restricted} \\ n_{12} &= \text{total observed number of transitions from state Learner to state Restricted} \\ n_{13} &= \text{total observed number of transitions from state Learner to state Qualified} \\ n_{21} &= \text{total observed number of transitions from state Resticted to state Learner} \\ n_{23} &= \text{total observed number of transitions from state Restricted to state Qualified.}\end{aligned}$$

Therefore, the likelihood function for $\boldsymbol{\mu} = \{\mu_{12}, \mu_{13}, \mu_{21}, \mu_{23}\}$ is given by

$$\begin{aligned}L(\boldsymbol{\mu}) &= \prod_{k,l:k\neq l} \mu_{kl}^{n_{kl}} \exp(-t_k^+\mu_{kl}) \\ &= \mu_{12}^{n_{12}} \exp(-t_1^+\mu_{12}) \times \mu_{13}^{n_{13}} \exp(-t_1^+\mu_{13}) \times \mu_{21}^{n_{21}} \exp(-t_2^+\mu_{21}) \times \mu_{23}^{n_{23}} \exp(-t_2^+\mu_{23}) \\ &= \mu_{12}^{n_{12}}\mu_{13}^{n_{13}}\mu_{21}^{n_{21}}\mu_{23}^{n_{23}} \exp[-t_1^+(\mu_{12}+\mu_{13})] \exp[-t_2^+(\mu_{21}+\mu_{23})].\end{aligned}$$

iii) (a) It is usually easier to work with log-likelihood,

$$\begin{aligned} l(\boldsymbol{\mu}) &= \log L(\boldsymbol{\mu}) \\ &= n_{12}\log\mu_{12} + n_{13}\log\mu_{13} + n_{21}\log\mu_{21} + n_{23}\log\mu_{23} - t_1^+(\mu_{12}+\mu_{13}) - t_2^+(\mu_{21}+\mu_{23}). \end{aligned}$$

The first order partial derivative of log-likelihood with respect to μ_{12} is then

$$\frac{\partial l(\boldsymbol{\mu})}{\partial \mu_{12}} = \frac{n_{12}}{\mu_{12}} - t_1^+.$$

Now set $\frac{\partial l(\boldsymbol{\mu})}{\partial \mu_{12}} = 0$ and solve for the MLE of the transition rate from Learner to Restricted

$$\frac{n_{12}}{\hat{\mu}_{12}} - t_1^+ = 0 \qquad \Rightarrow \qquad \hat{\mu}_{12} = \frac{n_{12}}{t_1^+}.$$

Also note that the second order partial derivative is given by

$$\frac{\partial^2 l(\boldsymbol{\mu})}{\partial \mu_{12}^2} = -\frac{n_{12}}{\mu_{12}^2},$$

which is always negative, confirming that the estimate is indeed a maximum.

(b) So from part (iii)(a), the estimated constant transition rate from Learner to Restricted is

$$\hat{\mu}_{12} = \frac{382}{1161} = 0.3290.$$

(c) Recall from lecture notes that the MLEs, $\hat{\mu}_{kl}$ are asymptotically independent, unbiased and normally distributed with $\mathrm{Var}(\hat{\mu}_{kl}) \approx \left[-\frac{\partial^2 l(\boldsymbol{\mu})}{\partial \mu_{kl}^2}\right]^{-1}$, thus we have

$$s.e.(\hat{\mu}_{12}) = \frac{\hat{\mu}_{12}}{n_{12}^{1/2}}.$$

Hence, the 95% confidence interval is given by

$$\hat{\mu}_{12} \pm 1.96 \times s.e.(\hat{\mu}_{12}) = 0.3290 \pm 1.96 \times \frac{0.3290}{382^{1/2}} = [0.296, 0.362].$$

3. i) Using the general expression of maximum likelihood estimate (MLE) of transition intensities in multiple state models, MLE of transition intensity from state 1 to 2, $\hat{\mu}_{12}$ is

$$\hat{\mu}_{12} = \frac{n_{12}}{t_1^+} = \frac{4330}{21650} = 0.2,$$

while the MLE of transition intensity from state 2 to 1, $\hat{\mu}_{21}$ is

$$\hat{\mu}_{21} = \frac{n_{21}}{t_2^+} = \frac{4160}{5200} = 0.8.$$

ii) Denoting $p_{ij}(x,t)$ as the probability that a person in state i at time x will be in state j at time $x+t$ and $\mu_{ij}(x+t)$ $(i \neq j)$ as the corresponding transition intensities, then we have from the Kolmogorov forward equations that

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}p_{12}(x,t) &= p_{11}(x,t)\mu_{12}(x+t) - p_{12}(x,t)\mu_{21}(x+t) \\ &= p_{11}(x,t)\mu_{12} - p_{12}(x,t)\mu_{21} \qquad \text{(for a time-homogeneous process)} \\ &= [1 - p_{12}(x,t)]\mu_{12} - p_{12}(x,t)\mu_{21} \\ &= \mu_{12} - (\mu_{12}+\mu_{21})p_{12}(x,t). \end{aligned}$$

Therefore,

$$\begin{aligned}
\int \frac{\mathrm{d}p_{12}(x,t)}{\mu_{12} - [\mu_{12}+\mu_{21}]p_{12}(x,t)} &= \int \mathrm{d}t \\
\Rightarrow \quad \frac{\log\{\mu_{12} - [\mu_{12}+\mu_{21}]p_{12}(x,t)\}}{-(\mu_{12}+\mu_{21})} &= t + C \\
\Rightarrow \quad \mu_{12} - [\mu_{12}+\mu_{21}]p_{12}(x,t) &= A\exp[-(\mu_{12}+\mu_{21})t] \\
\Rightarrow \quad p_{12}(x,t) &= \frac{\mu_{12} - A\exp[-(\mu_{12}+\mu_{21})t]}{\mu_{12}+\mu_{21}} \\
\Rightarrow \quad p_{12}(x,t) &= \frac{\mu_{12} - \mu_{12}\exp[-(\mu_{12}+\mu_{21})t]}{\mu_{12}+\mu_{21}}
\end{aligned}$$

because we have the boundary condition that $p_{12}(x,0) = 0$. By substituting the MLE of μ_{12} and μ_{21} obtained from part (i), the required probability is then computed as

$$p_{12}(x,3) = \frac{0.2 - 0.2\exp\{-(0.2+0.8)3\}}{0.2+0.8} = 0.1900.$$

4. i) Similar to question 2(ii), we let

$$\begin{aligned}
\mu_{12} &= \text{transition intensity from state Alive to Dead from heart disease} \\
\mu_{13} &= \text{transition intensity from state Alive to Dead from cancer} \\
\mu_{14} &= \text{transition intensity from state Alive to Dead from other causes} \\
t_1^+ &= \text{total observed waiting time in state Alive} \\
n_{12} &= \text{total observed number of transitions from state Alive to Dead from heart disease} \\
n_{13} &= \text{total observed number of transitions from state Alive to Dead from cancer} \\
n_{14} &= \text{total observed number of transitions from state Alive to Dead from other causes}
\end{aligned}$$

The likelihood for the transition intensities, $\boldsymbol{\mu} = \{\mu_{12}, \mu_{13}, \mu_{14}\}$ is given by

$$\begin{aligned}
L(\boldsymbol{\mu}) &= \prod_{k,l:k\neq l} \mu_{kl}^{n_{kl}} \exp(-t_k^+ \mu_{kl}) \\
&= \mu_{12}^{n_{12}} \mu_{13}^{n_{13}} \mu_{14}^{n_{14}} \exp[-t_1^+(\mu_{12}+\mu_{13}+\mu_{14})].
\end{aligned}$$

ii) The log-likelihood is

$$l(\boldsymbol{\mu}) = \log L(\boldsymbol{\mu}) = n_{12}\log\mu_{12} + n_{13}\log\mu_{13} + n_{14}\log\mu_{14} - t_1^+(\mu_{12}+\mu_{13}+\mu_{14}).$$

The first order partial derivative of log-likelihood with respect to μ_{12} is then

$$\frac{\partial}{\partial\mu_{12}} l(\boldsymbol{\mu}) = \frac{n_{12}}{\mu_{12}} - t_1^+.$$

Now set $\frac{\partial}{\partial\mu_{12}} l(\boldsymbol{\mu}) = 0$ to obtain the MLE of transition intensity from alive to dead from heart disease as

$$\hat{\mu}_{12} = \frac{n_{12}}{t_1^+}.$$

Also, a simple check shows that the second order partial derivative is

$$\frac{\partial^2}{\partial\mu_{12}^2} l(\boldsymbol{\mu}) = -\frac{n_{12}}{\mu_{12}^2},$$

which is always negative, confirming that the estimate is indeed a maximum.