Marginal and conditional hazards for modeling co-infection in SIMPACT

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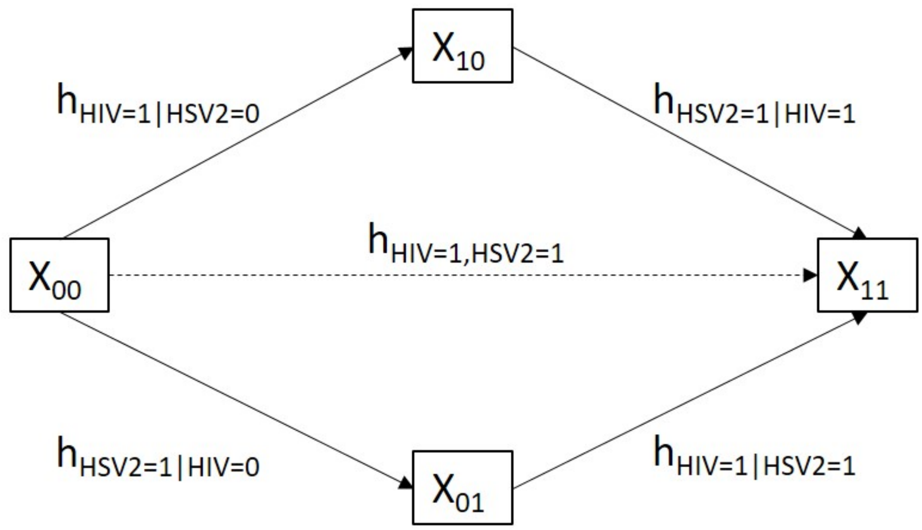

Figure 1: Schematic representation of HIV-HSV2 co-infection. X_{00}: number of persons not infected by HIV or HSV2; X_{10}: number of persons infected by HIV but not by HSV2; X_{01}: number of persons infected by HSV2 but not by HIV; X_{11}: number of persons infected by both HIV and HSV2.

Suppose we have the following hazard functions for HIV and HSV2 transmission:
hazard for HIV transmission: $h_1(t) = e^{A_1+B_1t}$
hazard for HSV2 transmission: $h_2(t) = e^{A_2+B_2t}$

1 Marginal hazards

The marginal hazards are $(i = 1, 2)$:

$$\begin{aligned}
\Lambda_i(t) &= \int_0^t h_i(u)\,du \\
&= \int_0^t e^{A_i+B_iu}du \\
&= \left[\frac{e^{A_i+B_iu}}{B_i}\right]_0^t \\
&= \frac{1}{B_i}\left[e^{A_i+B_it} - e^{A_i}\right]
\end{aligned}$$

$$\mathbf{\Lambda_i(t) = \frac{e^{A_i}}{B_i}\left[e^{B_it} - 1\right]}$$

2 Marginal probabilities

$$\boldsymbol{\pi_{1+} = 1 - e^{-\Lambda_1(t)}}$$

$$\boldsymbol{\pi_{+1} = 1 - e^{-\Lambda_2(t)}}$$

3 Joint probabilities

In the following formulas, θ is a heterogeneity parameter measuring the association between the two infections.

$$\boldsymbol{\pi_{00}(t) = \left(e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1\right)^{-\theta}}$$

$$\boldsymbol{\pi_{10}(t) = e^{-\Lambda_2(t)} - \pi_{00}(t)}$$

$$\boldsymbol{\pi_{01}(t) = e^{-\Lambda_1(t)} - \pi_{00}(t)}$$

$$\boldsymbol{\pi_{11}(t) = 1 - \pi_{00}(t) - \pi_{10}(t) - \pi_{01}(t)}$$

4 Conditional probabilities

$$\begin{aligned}
\pi_{HIV=1|HSV2=0}(t) &= \frac{\pi_{10}(t)}{1 - \pi_{+1}(t)} \\
&= \frac{e^{-\Lambda_2(t)} - \pi_{00}(t)}{1 - \left(1 - e^{-\Lambda_2(t)}\right)} \\
&= \frac{e^{-\Lambda_2(t)} - \left(e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1\right)^{-\theta}}{e^{-\Lambda_2(t)}} \\
&= 1 - \left(\frac{e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1}{e^{\frac{\Lambda_2(t)}{\theta}}}\right)^{-\theta}
\end{aligned}$$

$$\boldsymbol{\pi_{HIV=1|HSV2=0}(t) = 1 - \left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}} - e^{\frac{-\Lambda_2(t)}{\theta}} + 1\right)^{-\theta}}$$

In the same way we derive

$$\boldsymbol{\pi_{HSV2=1|HIV=0}\left(t\right)= 1-\left(e^{\frac{\Lambda_2(t)-\Lambda_1(t)}{\theta}}-e^{\frac{-\Lambda_1(t)}{\theta}}+1\right)^{-\theta}}$$

$$\begin{aligned}
\pi_{HIV=1|HSV2=1}\left(t\right) &= \frac{\pi_{11}\left(t\right)}{\pi_{+1}\left(t\right)} \\
&= \frac{1-\pi_{00}\left(t\right)-\pi_{10}\left(t\right)-\pi_{01}\left(t\right)}{1-e^{-\Lambda_2(t)}} \\
&= \frac{1-e^{-\Lambda_2(t)}-e^{-\Lambda_1(t)}+\pi_{00}\left(t\right)}{1-e^{-\Lambda_2(t)}} \\
&= \frac{1-e^{-\Lambda_2(t)}-e^{-\Lambda_1(t)}+\left(e^{\frac{\Lambda_1(t)}{\theta}}+e^{\frac{\Lambda_2(t)}{\theta}}-1\right)^{-\theta}}{e^{-\Lambda_1(t)}}
\end{aligned}$$

$$\boldsymbol{\pi_{HIV=1|HSV2=1}\left(t\right)= 1+\frac{\left(e^{\frac{\Lambda_1(t)}{\theta}}+e^{\frac{\Lambda_2(t)}{\theta}}-1\right)^{-\theta}-e^{-\Lambda_1(t)}}{1-e^{-\Lambda_2(t)}}}$$

In the same way we derive

$$\boldsymbol{\pi_{HSV2=1|HIV=1}\left(t\right)= 1+\frac{\left(e^{\frac{\Lambda_1(t)}{\theta}}+e^{\frac{\Lambda_2(t)}{\theta}}-1\right)^{-\theta}-e^{-\Lambda_2(t)}}{1-e^{-\Lambda_1(t)}}}$$

5 Conditional hazards

$$h_{HIV=1|HSV2=0}\left(t\right) = \frac{\pi'_{HIV=1|HSV2=0}\left(t\right)}{1-\pi_{HIV=1|HSV2=0}\left(t\right)}$$

$$\begin{aligned}
\pi'_{HIV=1|HSV2=0}\left(t\right) &= \theta\cdot\left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}-e^{\frac{-\Lambda_2(t)}{\theta}}+1\right)^{-\theta-1}\cdot\left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}-e^{\frac{-\Lambda_2(t)}{\theta}}+1\right)' \\
&= \theta\cdot\left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}-e^{\frac{-\Lambda_2(t)}{\theta}}+1\right)^{-\theta-1}\left[e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}\cdot\left(\frac{\Lambda_1\left(t\right)-\Lambda_2\left(t\right)}{\theta}\right)'-e^{\frac{-\Lambda_2(t)}{\theta}}\cdot\left(\frac{-\Lambda_2\left(t\right)}{\theta}\right)'\right] \\
&= \theta\cdot\left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}-e^{\frac{-\Lambda_2(t)}{\theta}}+1\right)^{-\theta-1}\left[e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}\cdot\left(\frac{h_1\left(t\right)-h_2\left(t\right)}{\theta}\right)+e^{\frac{-\Lambda_2(t)}{\theta}}\cdot\left(\frac{-h_2\left(t\right)}{\theta}\right)\right]
\end{aligned}$$

$$\begin{aligned}
h_{HIV=1|HSV2=0}\left(t\right) &= \left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}-e^{\frac{-\Lambda_2(t)}{\theta}}+1\right)^{-1}\cdot\left[e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}\cdot\left(h_1\left(t\right)-h_2\left(t\right)\right)+e^{\frac{-\Lambda_2(t)}{\theta}}\cdot h_2\left(t\right)\right] \\
&= \frac{e^{\frac{\Lambda_1(t)}{\theta}}\cdot\left(h_1\left(t\right)-h_2\left(t\right)\right)+h_2\left(t\right)}{e^{\frac{\Lambda_2(t)}{\theta}}\left(e^{\frac{\Lambda_1(t)-\Lambda_2(t)}{\theta}}-e^{\frac{-\Lambda_2(t)}{\theta}}+1\right)}
\end{aligned}$$

$$\boldsymbol{h_{HIV=1|HSV2=0}\left(t\right)= \frac{e^{\frac{\Lambda_1(t)}{\theta}}\cdot\left(h_1\left(t\right)-h_2\left(t\right)\right)+h_2\left(t\right)}{e^{\frac{\Lambda_1(t)}{\theta}}+e^{\frac{\Lambda_2(t)}{\theta}}-1}}$$

In the same way, we derive

$$\boldsymbol{h_{HSV2=1|HIV=0}\left(t\right)= \frac{e^{\frac{\Lambda_2(t)}{\theta}}\cdot\left(h_2\left(t\right)-h_1\left(t\right)\right)+h_1\left(t\right)}{e^{\frac{\Lambda_1(t)}{\theta}}+e^{\frac{\Lambda_2(t)}{\theta}}-1}}$$

$$h_{HIV=1|HSV2=1}\left(t\right) = \frac{\pi'_{HIV=1|HSV2=1}\left(t\right)}{1-\pi_{HIV=1|HSV2=1}\left(t\right)}$$

Nominator:

$$\pi'_{HIV=1|HSV2=1}(t) = \left(\frac{f}{g}\right)' = \frac{f'g - g'f}{g^2}$$

$$f = \left(e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1\right)^{-\theta} - e^{-\Lambda_1(t)}$$

$$g = 1 - e^{-\Lambda_2(t)}$$

$$f' = -\theta \cdot \left(e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1\right)^{-\theta-1} \cdot \left(e^{\frac{\Lambda_1(t)}{\theta}} \cdot \frac{h_1(t)}{\theta} + e^{\frac{\Lambda_2(t)}{\theta}} \cdot \frac{h_2(t)}{\theta}\right) + e^{-\Lambda_1(t)} \cdot h_1(t)$$

$$g' = e^{-\Lambda_2(t)} \cdot h_2(t)$$

Denominator:

$1 - \pi_{HIV=1|HSV2=1}(t) = \frac{f}{g}$

$$\begin{aligned} h_{HIV=1|HSV2=1}(t) &= \frac{\frac{f'g-g'f}{g^2}}{\frac{f}{g}} \\ &= \frac{f'g - g'f}{fg} \\ &= \frac{f'}{f} - \frac{g'}{g} \end{aligned}$$

$$\mathbf{h_{HIV=1|HSV2=1}(t)} = \frac{-\theta \cdot \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} - \mathbf{1}\right)^{-\theta-1} \cdot \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} \cdot \frac{\mathbf{h_1}(\mathbf{t})}{\theta} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} \cdot \frac{\mathbf{h_2}(\mathbf{t})}{\theta}\right) + \mathbf{e}^{-\boldsymbol{\Lambda_1}(\mathbf{t})} \cdot \mathbf{h_1}(\mathbf{t})}{\left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} - \mathbf{1}\right)^{-\theta} - \mathbf{e}^{-\boldsymbol{\Lambda_1}(\mathbf{t})}} - \frac{\mathbf{e}^{-\boldsymbol{\Lambda_2}(\mathbf{t})} \cdot \mathbf{h_2}(\mathbf{t})}{\mathbf{1} - \mathbf{e}^{-\boldsymbol{\Lambda_2}(\mathbf{t})}}$$

In the same way, we derive:

$$\mathbf{h_{HSV2=1|HIV=1}(t)} = \frac{-\theta \cdot \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} - \mathbf{1}\right)^{-\theta-1} \cdot \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} \cdot \frac{\mathbf{h_1}(\mathbf{t})}{\theta} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} \cdot \frac{\mathbf{h_2}(\mathbf{t})}{\theta}\right) + \mathbf{e}^{-\boldsymbol{\Lambda_2}(\mathbf{t})} \cdot \mathbf{h_2}(\mathbf{t})}{\left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} - \mathbf{1}\right)^{-\theta} - \mathbf{e}^{-\boldsymbol{\Lambda_2}(\mathbf{t})}} - \frac{\mathbf{e}^{-\boldsymbol{\Lambda_1}(\mathbf{t})} \cdot \mathbf{h_1}(\mathbf{t})}{\mathbf{1} - \mathbf{e}^{-\boldsymbol{\Lambda_1}(\mathbf{t})}}$$

6 Joint hazard

$$\begin{aligned} h_{HIV=1,HSV2=1}(t) &= \frac{\pi'_{11}(t)}{1 - \pi_{11}(t)} \\ &= \frac{-\pi'_{00}(t) - \pi'_{10}(t) - \pi'_{01}(t)}{\pi_{00}(t) + \pi_{10}(t) + \pi_{01}(t)} \end{aligned}$$

$$\pi'_{00}(t) = -\theta \cdot \left(e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1\right)^{-\theta-1} \cdot \left(e^{\frac{\Lambda_1(t)}{\theta}} \frac{h_1(t)}{\theta} + e^{\frac{\Lambda_2(t)}{\theta}} \frac{h_2(t)}{\theta}\right)$$

$$\pi'_{10}(t) = -e^{-\Lambda_2(t)} \cdot h_2(t)$$

$$\pi'_{01}(t) = -e^{-\Lambda_1(t)} \cdot h_1(t)$$

$$\begin{aligned} denominator &= e^{-\Lambda_1(t)} + e^{-\Lambda_2(t)} - \pi_{00}(t) \\ &= e^{-\Lambda_1(t)} + e^{-\Lambda_2(t)} - \left(e^{\frac{\Lambda_1(t)}{\theta}} + e^{\frac{\Lambda_2(t)}{\theta}} - 1\right)^{-\theta} \end{aligned}$$

$$\mathbf{h_{HIV=1,HSV2=1}(t)} = \frac{\theta \cdot \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} - \mathbf{1}\right)^{-\theta-1} \cdot \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} \frac{\mathbf{h_1}(\mathbf{t})}{\theta} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} \frac{\mathbf{h_2}(\mathbf{t})}{\theta}\right) + \mathbf{e}^{-\boldsymbol{\Lambda_1}(\mathbf{t})} \cdot \mathbf{h_1}(\mathbf{t}) + \mathbf{e}^{-\boldsymbol{\Lambda_2}(\mathbf{t})} \cdot \mathbf{h_2}(\mathbf{t})}{\mathbf{e}^{-\boldsymbol{\Lambda_1}(\mathbf{t})} + \mathbf{e}^{-\boldsymbol{\Lambda_2}(\mathbf{t})} - \left(\mathbf{e}^{\frac{\boldsymbol{\Lambda_1}(\mathbf{t})}{\theta}} + \mathbf{e}^{\frac{\boldsymbol{\Lambda_2}(\mathbf{t})}{\theta}} - \mathbf{1}\right)^{-\theta}}$$