**Additional file 1: The hazards ratio function inverts for a given time.**

The purpose is to show that, under certain conditions, the hazards ratio (HR) in equation (2),

\[ HR(t) = \frac{\lambda(t)Z_i^{(1)} = 1}{\lambda(t)Z_i^{(1)} = 0} = \left( \frac{p_{11}e^{\alpha+\gamma}S_0(t)e^{\alpha+\gamma} + p_{10}S_0(t)}{p_{11}S_0(t)e^{\alpha+\gamma} + p_{10}S_0(t)} \right) \times \left( \frac{p_{01}S_0(t)e^{\gamma} + p_{00}S_0(t)}{\left(p_{01}e^{\gamma}S_0(t)e^{\gamma} + p_{00}S_0(t)\right)} \right) \]

equals one at a given time \( t_0 \) in \((0; +\infty)\), being greater than one for \( t < t_0 \) and lesser than or equal to one for \( t > t_0 \).

In the sequel, it is assumed that \( p_{11} = p_{10} = p_{01} = p_{00} \) and that \( \alpha > 0 \), and \( \gamma > 0 \). The following notations will be used: \( k = \alpha/\gamma \), \( a = \exp(\gamma) \) with \( a > 1 \), and \( X = S_0(t) \) where \( X \) increases in \((0, 1)\) as \( t \) decreases from \(+\infty\) to 0. For \( X > 0 \), \( HR \) becomes:

\[
HR(X) = \frac{a^{k+1}X^{(a^{k+1}+1)} + 1}{X(a^{k+1}+1)} \left( \frac{X^{a-1} + 1}{aX^{a-1} + 1} \right)
\]

\[
= \frac{a^{k+1}X^{(a^{k+1}+2a-2)} + a^{k+1}X^{(a^{k+1}+1)} + X^{a-1} + 1}{aX^{(a^{k+1}+2a-2)} + X^{(a^{k+1}+1)} + aX^{a-1} + 1} = \frac{N(X)}{D(X)}
\]

Note that if \( X \) tends towards zero (i.e. if \( t \) tends towards infinity), \( HR(X) \) tends towards 1 (as does \( HR(t) \)). In order to prove the existence and uniqueness of \( 0 < X_0 < 1 \) such that \( HR(X_0) = 1 \), it is useful to consider the difference \( (N(X) - D(X)) \). More precisely, noting :

\[
N(X) - D(X) = f(X)X^{a-1}
\]

with \( f(X) = (a^{k+1} - a)X^{(a^{k+1}+1)} + (a^{k+1} - 1)X^{a^{k+1}+a} + (1 - a) = 0 \).

It is obvious that the searched \( X_0 \) is the solution, if any, of the equation \( f(X) = 0 \).

The first derivative of \( f \) relative to \( X \) is equal to

\[
\frac{\partial f(X)}{\partial X} = (a^{k+1} - a)(a^{k+1} - 1) \left[ X^{(a^{k+1}+2a-2)} + X^{a^{k+1}+a-1} \right]
\]

It is positive on \((0; 1)\) since \( a > 1 \) and \( k > 0 \), so that \( f \) is increasing on \((0; 1)\). As \( f(0) < 0 \) and \( f(1) > 0 \), the equation \( f(X) = 0 \) has a unique solution \( X_0 \) on \((0; 1)\). Moreover, it follows that, for \( 0 < X < X_0 \) (\( X > X_0 \), respectively), the function \( f(X) \) is negative (positive, respectively) so that \( (N(X) - D(X)) \) is negative (positive, respectively) as shown by formula (8) above. Noting that \( (N(X) - D(X)) \) negative (positive, respectively) is equivalent to \( HR(X) < 1 \) (> 1, respectively), the above results can be summarized as follows (See also Table 1).

As expected, it exists an unique time value \( t_0 = S_0^{-1}(X_0) \) with \( 0 < t_0 < +\infty \) such that \( HR(t) \) is greater than one for \( t < t_0 \), and lesser than one for \( t > t_0 \). Note that the function \( HR(t) \) is not monotone, since \( HR(t) \) tends towards one as \( t \) tends towards \(+\infty\), as already remarked.
Table 1: Summary of the signs of $f$ and $HR$

<table>
<thead>
<tr>
<th></th>
<th>$X$</th>
<th>0</th>
<th>$X_0$</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>$f(X)$</td>
<td>$1 - a &lt; 0$</td>
<td>$-$</td>
<td>0</td>
<td>$+$</td>
</tr>
<tr>
<td>$t$</td>
<td>0</td>
<td>$t_0$</td>
<td>$+\infty$</td>
<td></td>
</tr>
<tr>
<td>$HR(t)$</td>
<td>$\frac{e^{\gamma(k+1)}}{e^{\gamma} + 1} &gt; 1$</td>
<td>$&gt; 1$</td>
<td>1</td>
<td>$&lt; 1$</td>
</tr>
</tbody>
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