Adapting TP statistic to DIC model

In DIC model the only choice for states j, l, and m, is $j = 1, l = 2$, and the only null hypothesis for testing the Markov property is

$$H_0 : \alpha_{23}(t|X(s) = 1) = \alpha_{23}(t|X(s) = 2), t > s.$$

Assuming that there are no right censored observations in state 1, we adapt TP statistic to DIC model using the following steps.

Proper and improper MI rectangles

Step 1) We divide MI rectangles obtained from M observation rectangles into two subsets according to whether the time of $2 \to 3$ transition is finite or is right censored in state 2:
$\{\mathcal{R}_u \equiv (l_u, r_u] \times (w_u, z_u], z_u < \infty, 1 \leq u \leq U_1\}$ and
$\{\mathcal{R}_u \equiv (l_u, r_u] \times (w_u, \infty], 1 \leq u \leq U_2\}$.

We refer to an MI rectangle in the first subset as proper and in the second as improper. Similarly an observation rectangle (OR) is proper or improper depending on whether its time of $2 \to 3$ transition is finite or right censored in state 2.

Reduction step after imputation

Step 2) (The main step): If $(l_u, r_u] \times (w_u, z_u]$ is the imputed MI rectangle for a proper OR, we reduce it to the proper pair (r_u, z_u), thus assuming that $1 \to 2$ and $2 \to 3$ transitions occur at the end points of their respective intervals.

If $(l_u, r_u] \times (w_u, \infty]$, is the imputed MI rectangle for an improper OR we reduce it to the improper pair (r_u, w_u), thus assuming that $1 \to 2$ transition occurs at the endpoint of its interval and keeping the censoring time w_u in state 2 as is.

In the k'th imputation for proper OR, reduce its imputed proper MI rectangle to proper pair (r_u^k, z_u^k), and for improper OR, reduce its imputed MI rectangle to improper pair (r_u^k, w_u^k).Among all proper pairs, (r_u^k, z_u^k), there will be V^k distinct z_u^k values, that is, distinct times of $2 \to 3$ transition; we denote these ordered distinct times by $(t_1^k, t_2^k, ..., t_{V^k}^k)$.

Then, the k'th imputation set of proper pairs is

$$\mathcal{P}^k = \cup_{v=1}^{V^k} \left\{ \cup_{d=1}^{D_v^k} (r_{v,d}^k, t_v^k) \right\},$$

where D_v^k is the number of times of $1 \to 2$ transitions, and $r_{v,d}^k$ is the d'th time of $1 \to 2$ transition.corresponding to a given t_v^k.

The k'th imputation set of improper pairs is

$$\mathcal{IP}^k = \{(r_u^k, w_u^k), 1 \leq u \leq U^k\},$$

where U^k is their number.

The test statistic for DIC data

Step 3 The k'th imputation test statistic $U_s^{k,(1)}(2,3)$ is

$$\sum_{v=1}^{V^k} \left\{ \sum_{i=1}^{M} \delta_i^{(1)}(s) dN_i(t_v^k) - \left(\sum_i \delta_i^{(1)}(s) Y_i(t_v^k) \right) \frac{\sum_{i=1}^M dN_i(t_v^k)}{\sum_i Y_i(t_v^k)} \right\},$$

where the integral with respect to t was replaced by the sum over t_v^k, $1 \leq v \leq V^k$.

Here s has to be chosen so that for some proper pairs, $\delta_i^{(1)}(s) = 1 \Leftrightarrow X(s) = 1$, and for remaining proper pairs, $X(s) = 2 \Leftrightarrow \delta_i^{(1)}(s) = 0$.

Otherwise, the above statistic would be equal to zero.

We next compute the quantities needed for evaluating $U_s^{k,(1)}(2,3)$.

For a given t_v^k,

$$\sum_{i=1}^{M} \delta_i^{(1)}(s) dN_i(t_v^k) = \sum_{i=1}^{M} I(s \leq r_{v,i}^k) dN_i(t_v^k)$$

is the k'th imputation number of subjects who were in state 1 at time s and made $2 \to 3$ transition at time t_v^k, while

$$\sum_{i=1}^{M} dN_i(t_v^k),$$

is the k'th imputation number of patients who made $2 \to 3$ transition at time t_v^k.

Next

$$\begin{aligned} \sum_{i=1}^{M} Y_i(t_v^k) &= \sum_{i=1}^{M} \left[\sum_{p=0}^{V^k - v} dN_i(t_{v+p}^k) \right]^{\Delta_i = 1} \\ &+ \sum_{i=1}^{M} \left[I(r_i^k < t_v^k < w_i^k) \right]^{\Delta_i = 2} \end{aligned}$$

is the k'th imputation total number of subjects who were at risk of $2 \to 3$ transition at time $t_v^k -$. Here $\Delta_i = 1$ indicates that the i'th patient made $2 \to 3$ transition at time $t_{v+p}^k \geq t_v^k$, $0 \leq p \leq V^k - v$,thus contributing to the risk set at time t_v^k-. And $\Delta_i = 2$ indicates that the i'th patient made $1 \to 2$ transition at time r_i^k before time t_v^k and was right censored in state 2 at time w_i^k greater than t_v^k thus again contributing to the risk set at time t_v^k-.

Finally

$$\sum_{i=1}^{M} \delta_i^{(1)}(s) Y_i(t_v^k) = \sum_{i=1}^{M} \left[\sum_{p=0}^{V^k-v} I(s \leq r_{v+p,i}^k) dN_i(t_{v+p}^k) \right]^{\Delta_i=1}$$
$$+ \sum_{i=1}^{M} \left[I(s \leq r_i^k < t_v^k < w_i^k \right]^{\Delta_i=2},$$

is the k'th imputation total number of subjects who were in state 1 at time s and later were at risk for $2 \to 3$ transition at time $t_v -$.

Distribution of the k'th imputation test statistic

Let $n_v^k = \sum_{i=1}^{M} \delta_i^{(1)}(s) Y_i(t_v^k)$ and $n_{v1}^k = \sum_{i=1}^{M} \delta_i^{(1)}(s) Y_i(t_v^k)$. Then, recalling that the times of $2 \to 3$ transition are ordered $t_1^k < t_2^k, < \ldots < t_{V_k}^k,$, the asymptotic variance of $U_s^{k,(1)}(2,3)$ is given by

$$\widehat{Var}(U_s^{k,(1)}) = \sum_{v: t_v^k \geq s} \frac{n_{v1}^k (n_v^k - n_{v1}^k)}{(n_v^k)^2},$$

and under H_0, the asymptotic distribution of standardized $U_s^{k,(1)}(2,3)$ is

$$\frac{U_s^{k,(1)}}{\sqrt{\widehat{Var}(U_s^{k,(1)})}} \sim N(0,1).$$