Log-Rank Tests

1.1 Statistic

Discussion 1.1.1. Consider testing for equality of two survival curves across all times $t \in [0, \tau]$, that is $H_0 : S_1(t) = S_0(t)$. An equivalent null hypothesis is equivalence of the underlying hazard curves $H_0 : \alpha_1(t) = \alpha_0(t)$. Consider the statistic:

$$\begin{aligned} Z(\tau) &= \int_0^\tau \omega(t)\big\{d\hat{A}_1(t) - d\hat{A}_0(t)\big\} \\ &= \int_0^\tau \omega(t)\frac{1}{Y_1(t)}dN_1(t) - \int_0^\tau \omega(t)\frac{1}{Y_0(t)}dN_0(t). \end{aligned} \tag{1.1.1}$$

which aggregated the weighted difference of increments in the cumulative hazard. The weight process $\omega(t)$ is assumed non-negative, predictable, and equal to zero whenever $Y_1(t)$ or $Y_2(t)$ is zero. ♠

1.2 Weightings

Discussion 1.2.1. The standard log-rank test uses the weights:

$$\omega(t) = \frac{Y_1(t)Y_0(t)}{Y(t)}.$$

The test statistic becomes:

$$Z(\tau) = \int_0^\tau \frac{Y_0(t)}{Y(t)}dN_1(t) - \int_0^\tau \frac{Y_1(t)}{Y(t)}dN_0(t).$$

The Gehan-Breslow weights are:

$$\omega(t) = Y_1(t)Y_0(t),$$

for the test statistic:

$$Z(\tau) = \int_0^\tau Y_0(t)N_1(t) - \int_0^\tau Y_1(t)N_0(t).$$

The Harrington-Fleming family of weights take the form:

$$\omega(t) = \hat{S}^\rho(t-)\frac{Y_1(t)Y_0(t)}{Y(t)},$$

for $\rho \in [0, 1]$. The test statistic takes the form:

$$Z(\tau) = \int_0^\tau \hat{S}^\rho(t)\frac{Y_0(t)}{Y(t)}dN_1(t) - \int_0^\tau \hat{S}^\rho(t)\frac{Y_1(t)}{Y(t)}dN_0(t).$$

$\rho = 0$ recovers the standard log-rank test, while $\rho = 1$ is a Wilcoxon-type test, which places more weight on earlier time points, at which the survival is higher. ♠

1.3 Asymptotics

Proposition 1.3.1. Under the null hypothesis $H_0 : \alpha_1(t) = \alpha_0(t)$:

$$Z(\tau) = \int_0^\tau \omega(t)\frac{1}{Y_1(t)}dM_1(t) - \int_0^\tau \omega(t)\frac{1}{Y_0(t)}dM_0(t)$$

♦

Proof. Substituting $dN_j(t) = dM_j(t) + \alpha(t)Y_j(t)dt$:

$$\begin{aligned} Z(\tau) = & \int_0^\tau \omega(t)\frac{1}{Y_1(t)}dM_1(t) + \int_0^\tau \omega(t)\alpha(t)dt \\ & - \int_0^\tau \omega(t)\frac{1}{Y_0(t)}dM_0(t) - \int_0^\tau \omega(t)\alpha(t)dt \end{aligned}$$

■

Proposition 1.3.2. Consider the standard log-rank statistic:

$$Z(\tau) = \int_0^\tau \frac{Y_0(t)}{Y(t)}dN_1(t) - \int_0^\tau \frac{Y_1(t)}{Y(t)}dN_0(t),$$

which under the null hypothesis $H_0 : \alpha_1(t) = \alpha_0(t)$:

$$Z(\tau) = \int_0^\tau \frac{Y_0(t)}{Y(t)}dM_1(t) - \int_0^\tau \frac{Y_1(t)}{Y(t)}dM_0(t).$$

Suppose $n^{-1}Y_1(t) \xrightarrow{p} y_1(t)$ and $n^{-1}Y_0(t) \xrightarrow{p} y_0(t)$, then:

$$\frac{1}{\sqrt{n}}Z(\tau) \rightsquigarrow W\big\{\sigma^2_{\text{LR}}(\tau)\big\},$$

where:

$$\sigma^2_{\text{LR}}(\tau) = \int_0^\tau \frac{y_1(t)y_0(t)}{y(t)}\alpha(t)dt.$$

♦

Proof. The predictable variation is:

$$\begin{aligned} \left\langle \frac{1}{\sqrt{n}}Z(\tau)\right\rangle &= \int_0^\tau \frac{Y_0^2(t)}{nY^2(t)}d\langle M_1(t)\rangle + \int_0^\tau \frac{Y_1^2(t)}{nY^2(t)}d\langle M_0(t)\rangle \\ &= \int_0^\tau \frac{Y_0^2(t)}{nY^2(t)}Y_1(t)\alpha(t)dt + \int_0^\tau \frac{Y_1^2(t)}{nY^2(t)}Y_0(t)\alpha(t)dt \\ &= \int_0^\tau \frac{Y_0(t)Y_1(t)}{nY^2(t)}\big\{Y_0(t) + Y_1(t)\big\}\alpha(t)dt \\ &= \int_0^\tau \frac{Y_0(t)Y_1(t)}{nY(t)}\alpha(t)dt = \int_0^\tau \frac{n^{-1}Y_0(t)n^{-1}Y_1(t)}{n^{-1}Y(t)}\alpha(t)dt \\ &\xrightarrow{p} \int_0^\tau \frac{y_0(t)y_1(t)}{y(t)}dt. \end{aligned}$$

■

Discussion 1.3.1. From the equality:

$$\left\langle \frac{1}{\sqrt{n}} Z(\tau) \right\rangle = \int_0^\tau \frac{Y_0(t)Y_1(t)}{nY(t)} \alpha(t)dt,$$

and estimator for the asymptotic variance of the standard log-rank statistic is obtained by substituting $d\hat{A}(t)$, the Nelson-Aalen increment, for $\alpha(t)dt$:

$$\hat{\sigma}^2_{\text{LR}}(\tau) = \int_0^\tau \frac{Y_0(t)Y_1(t)}{nY(t)} d\hat{A}(t) = \int_0^\tau \frac{Y_0(t)Y_1(t)}{nY^2(t)} dN(t)$$

♠

1.4 Multi-sample Extension

Proposition 1.4.3. The log-rank type statistic (1.1.1) is expressible as:

$$Z(\tau) = \int_0^\tau \omega^*(t)dN_1(t) - \int_0^\tau \omega^*(t)\frac{Y_1(t)}{Y(t)}dN(t), \tag{1.4.2}$$

for $N(t) = N_1(t)+N_2(t)$, $Y(t) = Y_1(t)+Y_0(t)$, and a particular weight function $\omega^*(t)$. ♦

Proof. Writing $N_0(t) = N(t) - N_1(t)$:

$$\begin{aligned} Z(\tau) &= \int_0^\tau \omega(t)\frac{1}{Y_1(t)}dN_1(t) - \int_0^\tau \omega(t)\frac{1}{Y_0(t)}d\{N(t) - N_1(t)\} \\ &= \int_0^\tau \omega(t)\left\{\frac{1}{Y_1(t)} + \frac{1}{Y_0(t)}\right\}dN_1(t) - \int_0^\tau \omega(t)\frac{1}{Y_0(t)}dN_1(t) \\ &= \int_0^\tau \omega(t)\left\{\frac{Y_0(t)+Y_1(t)}{Y_1(t)Y_0(t)}\right\}dN_1(t) - \int_0^\tau \omega(t)\frac{1}{Y_0(t)}dN_1(t) \end{aligned}$$

Let:

$$\omega^*(t) = \omega(t)\left\{\frac{Y_0(t)+Y_1(t)}{Y_1(t)Y_0(t)}\right\} = \omega(t)Y(t)\{Y_1(t)Y_0(t)\}^{-1},$$

such that $\omega(t)\{Y_0(t)\}^{-1} = \omega^*(t)Y_1(t)\{Y(t)\}^{-1}$, then:

$$Z(\tau) = \int_0^\tau \omega^*(t)dN_1(t) - \int_0^\tau \omega^*(t)\frac{Y_1(t)}{Y(t)}dN(t).$$

■

Discussion 1.4.1. Consider the log-rank test, for which $\omega(t) = Y_1(t)Y_0(t)\{Y(t)\}^{-1}$, such that $\omega^*(t) = 1$, then:

$$Z(\tau) = \int_0^\tau dN_1(t) - \int_0^\tau \frac{Y_1(t)}{Y(t)}dN(t) = N_1(t) - E_1(t).$$

Here $N_1(t)$ is the observed number of events in arm 1 by time t, and $E_1(t)$ is the expected number of events under the null hypothesis $H_0 : \alpha_1(t) = \alpha_0(t)$. The representation in (1.4.2) may be extended to allow for multiple samples. In particular, consider testing:

$$H_0 : \alpha_1(t) = \alpha_2(t) = \cdots = \alpha_J(t) \text{ for } \forall t \in [0, \tau].$$

For $j \in \{1, \cdots, J\}$, define the process:

$$Z_j(\tau) = \int_0^\tau \omega^*(t) dN_j(t) - \int_0^\tau \omega^*(t) \frac{Y_j(t)}{Y(t)} dN(t), \tag{1.4.3}$$

where now $N(t) = \sum_{j=1}^J N_j(t)$. ♠

Proposition 1.4.4. Under the null hypothesis $H_0 : \alpha_1(t) = \alpha_2(t) = \cdots = \alpha_J(t) \equiv \alpha(t)$, the multi-sample statistic in (1.4.3) is expressible as:

$$Z_j(\tau) = \sum_{j^*=1}^J \int_0^\tau \omega^*(t) \left\{ \delta_{jj^*} - \frac{Y_j(t)}{Y(t)} \right\} dM_{j^*}(t),$$

where δ_{jj^*} is the Kronecker delta and $M_{j^*}(t) = N_{j^*}(t) - \int_0^\tau \alpha(t) Y_{j^*}(t)$. ♦

Proof. Substituting $dN_j(t) = dM_j(t) + \alpha(t)Y_j(t)dt$ into (1.4.3) gives:

$$Z_j(\tau) = \int_0^\tau \omega^*(t) dM_j(t) - \int_0^\tau \omega^*(t) \frac{Y_j(t)}{Y(t)} dM(t),$$

Writing $dM_j(t) = \sum_{j^*=1}^J \delta_{jj^*} dM_{j^*}(t)$ and $dM(t) = \sum_{j^*=1}^J dM_{j^*}(t)$:

$$\begin{aligned} Z_j(\tau) &= \int_0^\tau \omega^*(t) \left\{ \sum_{j^*=1}^J \delta_{jj^*} dM_{j^*}(t) \right\} - \int_0^\tau \omega^*(t) \frac{Y_j(t)}{Y(t)} \left\{ \sum_{j^*=1}^J dM_{j^*}(t) \right\} \\ &= \sum_{j^*=1}^J \int_0^\tau \omega^*(t) \left\{ \delta_{jj^*} - \frac{Y_j(t)}{Y(t)} \right\} dM_{j^*}(t). \end{aligned}$$

■

Proposition 1.4.5. The predictable covaraition of $Z_j(t)(\tau)$ and $Z_{j^*}(\tau)$ is:

$$\langle Z_j, Z_{j^*} \rangle(\tau) = \int_0^\tau \{\omega^*(t)\}^2 \frac{Y_j(t)}{Y(t)} \left\{ \delta_{jj^*} - \frac{Y_{j^*}(t)}{Y(t)} \right\} d\Lambda(t),$$

where $d\Lambda(t) = \alpha(t)Y(t)dt$. ♦

Proof. Since the predictable covariation is bilinear:

$$\langle Z_j, Z_{j^*} \rangle(\tau) = \sum_{k=1}^J \sum_{k^*=1}^J \int_0^\tau \{\omega^*(t)\}^2 \left\{ \delta_{jk} - \frac{Y_j(t)}{Y(t)} \right\} \left\{ \delta_{j^*k^*} - \frac{Y_{j^*}(t)}{Y(t)} \right\} d\langle M_k, M_{k^*} \rangle(t)$$

Since $dM_k(t)$ and $dM_{k^*}(t)$ are orthogonal for $k \neq k^*$:

$$\langle Z_j, Z_{j^*}\rangle(\tau) = \sum_{k=1}^{J}\int_0^\tau \{\omega^*(t)\}^2 \left\{\delta_{jk} - \frac{Y_j(t)}{Y(t)}\right\}\left\{\delta_{j^*k} - \frac{Y_{j^*}(t)}{Y(t)}\right\}\alpha(t)Y_k(t)dt.$$

Suppressing dependence on t and expanding the binomials:

$$\begin{aligned}\langle Z_j, Z_{j^*}\rangle(\tau) &= \int_0^\tau \{\omega^*\}^2\alpha\left\{\sum_{k=1}^{J}\delta_{jk}\delta_{j^*k}Y_k - \delta_{j^*k}\frac{Y_jY_k}{Y} - \delta_{jk}\frac{Y_{j^*}Y_k}{Y} + \frac{Y_jY_{j^*}Y_k}{Y^2}\right\}dt \\ &= \int_0^\tau \{\omega^*\}^2\alpha\left\{\delta_{jj^*}Y_j - \frac{Y_jY_{j^*}}{Y} - \frac{Y_jY_{j^*}}{Y} + \frac{Y_jY_{j^*}}{Y}\right\}dt \\ &= \int_0^\tau \{\omega^*\}^2\alpha Y_j\left\{\delta_{jj^*} - \frac{Y_{j^*}}{Y}\right\}dt\end{aligned}$$

Multiplying and dividing by $Y(t)$ and rearranging gives:

$$\langle Z_j, Z_{j^*}\rangle(\tau) = \int_0^\tau \{\omega^*(t)\}^2\frac{Y_j(t)}{Y(t)}\left\{\delta_{jj^*} - \frac{Y_{j^*}(t)}{Y(t)}\right\}\alpha(t)Y(t)dt.$$

■

Corollary 1.4.1. The optional covariation is:

$$\hat{\sigma}_{jj^*}(\tau) \equiv [Z_j, Z_{j^*}](\tau) = \int_0^\tau \{\omega^*(t)\}^2\frac{Y_j(t)}{Y(t)}\left\{\delta_{jj^*} - \frac{Y_{j^*}(t)}{Y(t)}\right\}dN(t). \tag{1.4.4}$$

♣

Discussion 1.4.2. Consider testing the null hypothesis:

$$H_0 : \alpha_1(t) = \alpha_2(t) = \cdots = \alpha_J(t) \equiv \alpha(t).$$

A Wald-type statistic evaluating this hypothesis is:

$$T_W = \boldsymbol{z}'\boldsymbol{\Sigma}^\dagger\boldsymbol{z},$$

where $\boldsymbol{z}_j = Z_j(\tau)$ from (1.4.3) and $\boldsymbol{\Sigma}_{jj^*} = \hat{\sigma}_{jj^*}(\tau)$ from (1.4.4). A pseudo-inverse is required since the (Z_j) satisfy the linear constraint:

$$\sum_{j=1}^{J} Z_j(\tau) = 0.$$

Alternatively, the Wald statistic may be modified, without loss of information, by omission of a single row, for instance the first or last. T_W follows an asymptotic χ^2 distribution with $(k-1)$ degrees of freedom. ♠

Difference of Survival Curves

2.1 Restricted Mean Survival Time

2.1.1 1 Sample Setting

Definition 2.1.1. The **restricted mean survival time** (RMST) $U(\tau)$ is the area under the survival curve up to time τ:

$$U(\tau) = \int_0^\tau S(t)dt.$$

An estimator for $U(\tau)$ is given by:

$$\hat{U}(\tau) = \int_0^\tau \hat{S}(t)dt,$$

where $\hat{S}(t)$ is the Kaplan-Meier (KM) estimator of the survival function. ■

Proposition 2.1.1. Define:

$$\mu_\tau(t) = \int_t^\tau S(u)du.$$

The standardized process $\sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\}$ converges weakly to a Gaussian martingale:

$$\sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\} \rightsquigarrow W\big\{\sigma^2_{\text{RMST}}(\tau)\big\},$$

where:

$$\sigma^2_{\text{RMST}}(\tau) = \int_0^\tau \frac{\mu_\tau^2(t)\alpha(t)}{y(t)}dt$$

and $y(t)$ is the probability limit of $n^{-1}Y(t)$. ♦

Proof. Noting that $d\mu_\tau(t) = -S(t)dt$,

$$\begin{aligned}
\sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\} &= \int_0^\tau \sqrt{n}\big\{\hat{S}(u) - S(u)\big\}du \\
&= \int_0^\tau \frac{\sqrt{n}\big\{\hat{S}(u) - S(u)\big\}}{-S(u)} \cdot \{-S(u)du\} \\
&= \int_0^\tau \sqrt{n}\big\{\hat{A}(u) - A(u)\big\}d\mu_\tau(t) + o_p(1).
\end{aligned}$$

Integrating by parts:

$$\begin{aligned}
\int_0^\tau \sqrt{n}\big\{\hat{A}(u) - A(u)\big\}d\mu_\tau(t) =& \Big[\sqrt{n}\big\{\hat{A}(u) - A(u)\big\}\mu_\tau(t)\Big]_{t=0}^{t=\tau} \\
&- \int_0^\tau \mu_\tau(t) \cdot \sqrt{n}d\big\{\hat{A}(u) - A(u)\big\}
\end{aligned}$$

The first term on the RHS vanishes since $\hat{A}(0) = A(0) = 0$ and $\mu_\tau(\tau) = 0$. Using the martingale representation of $\sqrt{n}\big\{\hat{A}(u) - A(u)\big\}$:

$$\sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\} = -\int_0^\tau \frac{\mu_\tau(t)\sqrt{n}}{Y(u)} dM(u) + o_p(1).$$

The predictable variation is:

$$\begin{aligned}
\Big\langle \sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\}\Big\rangle &= \int_0^\tau \frac{n\mu_\tau^2(t)}{Y^2(t)} d\langle M(t)\rangle + o_p(1) \\
&= \int_0^\tau \frac{n\mu_\tau^2(t)}{Y^2(t)} Y(t)\alpha(t)dt + o_p(1) \\
&= \int_0^\tau \frac{\mu_\tau^2(t)\alpha(t)}{n^{-1}Y(t)} dt + o_p(1) \\
&\xrightarrow{p} \int_0^\tau \frac{\mu_\tau^2(t)\alpha(t)}{y(t)} dt,
\end{aligned}$$

where $\alpha(t)$ is the hazard and $y(t)$ is the limit in probability of $n^{-1}Y(t)$. For additional details, see [2]. ■

Discussion 2.1.1. The optional variation of $\sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\}$ is:

$$\begin{aligned}
\Big[\sqrt{n}\big\{\hat{U}(\tau) - U(\tau)\big\}\Big] &= \int_0^\tau \frac{n\mu_\tau^2(t)}{Y^2(t)} d[M(t)] \\
&= \int_0^\tau \frac{\mu_\tau^2(t)}{n^{-1}Y^2(t)} dN(t).
\end{aligned}$$

The estimated variance:

$$\hat{\sigma}^2_{\text{RMST}}(\tau) = \int_0^\tau \frac{\hat{\mu}_\tau^2(t)}{n^{-1}Y^2(t)} dN(t),$$

where:

$$\hat{\mu}_\tau(t) = \int_t^\tau \hat{S}(u)du.$$

The variance estimator is expressible as:

$$\hat{\sigma}^2_{\text{RMST}}(\tau) = \int_0^\tau \frac{\hat{\mu}_\tau^2(t)}{n^{-1}Y(t)} d\hat{A}(t),$$

where $\hat{A}(t)$ is the Nelson-Aalen estimator.

♠

2.1.2 2 Sample Setting

Example 2.1.1. Let $\hat{S}_1(t)$ and $\hat{S}_0(t)$ denote the estimated survival functions for the treatment and reference groups. The treatment difference may be assessed using the difference of RMSTs:

$$\Delta(\tau) = \hat{U}_1(\tau) - \hat{U}_0(\tau) = \int_0^\tau \hat{S}_1(t)dt - \int_0^\tau \hat{S}_0(t)dt = \int_0^\tau \big\{\hat{S}_1(t) - \hat{S}_0(t)\big\}dt.$$

The estimated variance of the difference is:

$$\hat{\sigma}_{10}^2(\tau) = \int_0^\tau \frac{\hat{\mu}_1^2(t)}{n^{-1}Y_1(t)}d\hat{A}_1(t) + \int_0^\tau \frac{\hat{\mu}_0^2(t)}{n^{-1}Y_0(t)}d\hat{A}_0(t)$$

where $Y_j(t)$ is the number at risk for group j, $\hat{A}_j(u)$ is the corresponding Nelson-Aalen estimator, and:

$$\hat{\mu}_j(t) = \int_t^\tau \hat{S}_j(u)du.$$

A Wald-type statistic for assessing $H_0 : U_1(\tau) = U_0(\tau)$ is:

$$T_W = \frac{\Delta^2(\tau)}{\hat{\sigma}_{10}^2(\tau)} \dot{\sim} \chi_1^2(0).$$

♠

2.2 Difference of Survival Curves

Example 2.2.2. Let $\hat{S}_1(t)$ and $\hat{S}_0(t)$ denote the estimated survival functions for the treatment and reference groups, and suppose $g(x, y)$ is a continuously differentiable measure of the between-group difference, such as $g(x, y) = y - x$, such that:

$$g(\hat{S}_1, \hat{S}_0) = \hat{S}_1(t) - \hat{S}_0(t).$$

Consider generating confidence bands for the following process:

$$\Delta(t) = \sqrt{n}\omega(t)\big\{g(\hat{S}_1, \hat{S}_0) - g(S_1, S_0)\big\}, \tag{2.2.5}$$

where $n = n_1 + n_0$ is the overall sample size and $\omega(t)$ is a weight function. Let $t_{L,j}$ denote the the first time that $\hat{S}_j(t)$ jumps, and let $t_{U,j}$ denote the last time that $\hat{S}_j(t)$ jumps. Define $t_L = \max(t_{L,1}, t_{L,0})$ and $t_U = \min(t_{U,1}, t_{U,0})$. The confidence band for $\Delta(t)$ is sought over the interval $[t_L, t_U]$.

The difference process (2.2.5) is asymptotically equivalent to:

$$\dot{\Delta}(t) = \sqrt{n}\omega(t)\big\{g_2(\hat{S}_1, \hat{S}_0) \cdot (\hat{S}_1 - S_1) + g_1(\hat{S}_1, \hat{S}_0) \cdot (\hat{S}_0 - S_0)\big\},$$

which is expressible as:

$$\dot{\Delta}(t) = g_2(\hat{S}_1, \hat{S}_0)U_1(t) + g_1(\hat{S}_1, \hat{S}_0)U_0(t),$$

where:

$$U_j(t) = \sqrt{n} \cdot \omega(t)\big\{\hat{S}_j(t) - S_j(t)\big\}$$

$U_j(t)$ is asymptotically equivalent to the process:

$$\begin{aligned} U_j(t) &= -\omega(t)\hat{S}_j(t) \cdot \sqrt{n}\big\{\hat{A}_j(t) - A_j(t)\big\} + o_p(1) \\ &= -\omega(t)\hat{S}_j(t)\sum_{i=1}^{n_j}\int_0^t H_j(s)dM_{ij}(s) + o_p(1), \end{aligned}$$

with $H_j(s) = \sqrt{n}/Y_j(s)$ and $M_{ij}(s) = N_{ij}(s) - \int_0^t \alpha_j(s)Y_{ij}(s)ds$. Let $Z_{ij}^{(b)}$ denote IID $(0,1)$ perturbation weights, then sample paths from $U_j(t)$ may be simulated via:

$$U_j^{(b)}(t) = -\omega(t)\hat{S}_j(t)\sum_{i=1}^{n_j} Z_{ij}^{(b)} \int_0^t H_j(s)dN_{ij}(s).$$

The confidence band for $\Delta(t)$ may be generated as follows. For each of B iterations,

i. Generate the perturbation weights $Z_{ij}^{(b)}$.

ii. Approximate a sample path of $\Delta(t)$ via:

$$\dot{\Delta}^{(b)}(t) = g_2(\hat{S}_1, \hat{S}_0)U_1^{(b)}(t) + g_1(\hat{S}_1, \hat{S}_0)U_0^{(b)}(t).$$

iii. Compute and store $M^{(b)} = \sup_{t\in[t_L,t_U]}\big|\dot{\Delta}^{(b)}(t)\big|$

Let $\gamma_{1-\alpha}$ denote the upper $(1-\alpha)$th percentile of the $(M^{(b)})$, then:

$$g(\hat{S}_1, \hat{S}_0) \pm \frac{\gamma_{1-\alpha}}{\sqrt{n}\omega(t)}$$

is an asymptotic confidence band for $g(S_1, S_0)$.

Finally, let:

$$T_{\text{KS}} = \sqrt{n}\sup_{t\in[t_L,t_U]}\omega(t)\big|g(\hat{S}_1, \hat{S}_0)\big|$$

denote a KS-type statistics of $H_0 : S_1(t) = S_0(t)$. An approximate p-value is given by:

$$\hat{p} = \frac{1}{B}\sum_{b=1}^{B}\mathbb{I}\big\{M^{(b)} \geq T_{\text{KS}}\big\}.$$

See [1]. ♠

Example 2.2.3. The null hypothesis $H_0 : S_1(t) = S_0(t)$ may also be examined using an integrated difference of the form:

$$\Delta = \frac{\int_0^\tau \omega(t) \cdot \sqrt{n}\big\{\hat{S}_1(t) - \hat{S}_0(t)\big\}dt}{\int_0^\tau \omega(t)dt}$$

The integrand is expressible as:

$$\omega(t) \cdot \sqrt{n}\big\{\hat{S}_1(t) - \hat{S}_0(t)\big\} = U_1(t) - U_0(t),$$

where:

$$U_j(t) = -\omega(t)\hat{S}_j(t)\sum_{i=1}^{n_j}\int_0^t \frac{\sqrt{n}}{Y_j(s)}dM_{ij}(s) + o_p(1)$$

For each of B iterations:

1. Generate IID $(0, 1)$ perturbation weights $Z_{ij}^{(b)}$.
2. Calculate:

$$\Delta^{(b)} = \frac{\int_0^\tau \{U_1(t) - U_0(t)\}dt}{\int_0^\tau \omega(t)dt}.$$

A confidence interval may be generated by finding the $\alpha/2$ and $1-\alpha/2$ percentiles of the $(\Delta^{(b)})$. An approximate 2-sided p-value is given by twice the proportion of $(\Delta^{(b)})$ that have the opposite sign of the observed Δ. ♠

References

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