

Web-based Supplementary Materials for ”A log-rank type test to compare net survival distributions” by

Nathalie Grafféo^{1,2}, Fabienne Castell³, Aurélien Belot^{4,5,6}, and Roch Giorgi^{1,2,7,*}

¹INSERM, UMR912 ” Economics and Social Sciences Applied to Health & Analysis of Medical Information ” (SESSTIM), 13006 Marseille, France

²Aix Marseille University, UMR_S912, IRD, 13006, Marseille, France

³Aix Marseille University, CNRS, Centrale Marseille, I2M, UMR 7373, 13453 Marseille, France

⁴Hospices Civils de Lyon, Service de Biostatistique, Lyon, France

⁵University Lyon 1, UMR 5558 Laboratoire Biostatistique-Santé, , Villeurbanne, France

⁶Institut de Veille Sanitaire, DMCT, Saint-Maurice, France

⁷APHM, Hôpital Timone, BIOSTIC, Marseille, France

**email:* roch.giorgi@univ-amu.fr

Web Appendix A. Proof of $E \langle Z_h^w \rangle < \infty$

We have $\langle Z_h^w \rangle (T) = \sum_{l=1}^k \left\{ \int_0^T \mathbf{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right)^2 \sum_{i=1}^{n_l} \frac{d \langle M_{l,i} \rangle (s)}{\left(\tilde{S}_{P,l,i}(s) \right)^2} \right\}$.

Note that $\forall s \in [0, T] \mathbf{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right)^2 \leq 1$. Thus,

$$E \langle Z_h^w \rangle (T) \leq \sum_{l=1}^k n_l E \left\{ \int_0^T \frac{Y_{l,1}(s)}{\left(\tilde{S}_{P,l,1}(s) \right)^2} \left(\tilde{\lambda}_{P,l,1}(s) + \lambda_E(s) \right) ds \right\}.$$

As T_E , T_P and C are conditionally independent given \mathbf{X} , we can write

$$E(Y_{l,1}(s) \mid \mathbf{X}_{l,1}) = S_{C,l}(s) S_E(s) \tilde{S}_{P,l,1}(s).$$

Using that $0 \leq S_{C,l}$, $S_E \leq 1$, we get

$$E \langle Z_h^w \rangle (T) \leq \sum_{l=1}^k n_l E \left\{ \int_0^T \frac{\tilde{\lambda}_{P,l,1}(s)}{\tilde{S}_{P,l,1}(s)} ds + \int_0^T \frac{S_E(s) \lambda_E(s)}{\tilde{S}_{P,l,1}(s)} ds \right\}.$$

Note that $\int_0^T \frac{\tilde{\lambda}_{P,l,1}(s)}{\tilde{S}_{P,l,1}(s)} ds = \int_0^T \tilde{\lambda}_{P,l,1}(s) e^{\tilde{\Lambda}_{P,l,1}(s)} ds = \left[e^{\tilde{\Lambda}_{P,l,1}(s)} \right]_0^T = \frac{1}{\tilde{S}_{P,l,1}(T)} - 1$.

Moreover, for $0 \leq s \leq T$, $\tilde{S}_{P,l,1}(s) \geq \tilde{S}_{P,l,1}(T)$ and $\int_0^T S_E(s) \lambda_E(s) ds = 1 - S_E(T)$, we get $E \langle Z_h^w \rangle (T) \leq 2E \left(\sum_{l=1}^k \frac{n_l}{\tilde{S}_{P,l,1}(T)} \right)$, which is finite according to the second assumption in (1) in the main document.

Web Appendix B. Proof of the asymptotic distribution of the test statistic under the null

By law of large numbers: $\forall h \in \llbracket 1; k \rrbracket$, $\frac{Y_h^w(s)}{n} \xrightarrow[n \rightarrow \infty]{(a.s.)} \alpha_h S_{C,h}(s) S_E(s)$.

Let us define

$$\begin{aligned} y^w(s) &:= \left(\sum_{h=1}^k \alpha_h S_{C,h}(s) \right) S_E(s) \\ a_h(s) &:= \frac{\alpha_h S_{C,h}(s)}{\sum_{l=1}^k \alpha_l S_{C,l}(s)} \end{aligned}$$

We introduce

$$V_h = \sum_{l=1}^k \int_0^T \mathbf{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) \sum_{i=1}^{n_l} \frac{dM_{l,i}(s)}{\tilde{S}_{P,l,i}(s)}.$$

We can write under the null $Z_h^w(T) = V_h + R_T^h$, where

$$R_T^h = \sum_{l=1}^k \sum_{i=1}^{n_l} \int_0^T \left\{ \mathbb{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) - \mathbb{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) \right\} \frac{dM_{l,i}(s)}{\tilde{S}_{P,l,i}(s)}.$$

Let us denote

$$\Sigma_{hj}^2(T) = E \left\{ \sum_{l=1}^k \alpha_l \int_0^T \mathbb{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) (\delta_{jl} - a_j(s)) \frac{S_{C,l}(s) S_E(s)}{\tilde{S}_{P,l,1}(s)} \left(\tilde{\lambda}_{P,l,1}(s) + \lambda_E(s) \right) ds \right\}.$$

We are going to prove

LEMMA 1: $\frac{1}{\sqrt{n}}(V_1, \dots, V_k) \xrightarrow[n \rightarrow \infty]{(d)} \mathcal{N}(0, \Sigma^2(T))$, where $\Sigma^2(T)$ is the matrix whose entries are the $\Sigma_{hj}^2(T)$.

LEMMA 2: Under the null, $\frac{1}{\sqrt{n}} R_T^h \xrightarrow[n \rightarrow \infty]{L^2} 0$.

By Slutsky's lemma, these two lemmas imply that under the null,

$$\frac{1}{\sqrt{n}}(Z_1^w(T), \dots, Z_k^w(T)) \xrightarrow[n \rightarrow \infty]{(d)} \mathcal{N}(0, \Sigma^2(T)). \quad (1)$$

Proof of Lemma 1.

Let us denote, for $(h, j) \in \llbracket 1; k \rrbracket^2$

$$W_{h,j} := \sum_{i=1}^{n_j} \int_0^T \mathbb{1}(y^w(s) > 0) (\delta_{hj} - a_h(s)) \frac{dM_{j,i}(s)}{\tilde{S}_{P,j,i}(s)}.$$

We can prove that the vector

$$\frac{1}{\sqrt{n}} (W_{h,j})_{1 \leq h, j \leq k} \xrightarrow[n \rightarrow \infty]{(d)} \mathcal{N}(0, S^2(T)) \quad (*)$$

where $S^2(T)$ is a k^2 square symmetric matrix whose entries are given by

$$S_{(h,j),(h',j')}^2 = \delta_{jj'} \alpha_j E \left\{ \int_0^T \mathbb{1}(y^w(s) > 0) (\delta_{hj} - a_h(s)) (\delta_{h'j} - a_{h'}(s)) \frac{S_{C,j}(s) S_E(s)}{\tilde{S}_{P,j,1}(s)} \left(\tilde{\lambda}_{P,j,1}(s) + \lambda_E(s) \right) ds \right\}$$

Indeed, let $(\theta_{h,j})_{1 \leq h,j \leq k} \in \mathbb{R}^{k^2}$.

$$\begin{aligned} & E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{h,j} \theta_{h,j} W_{h,j} \right) \right\} \\ &= E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{h,j} \sum_{p=1}^{n_j} \int_0^T \mathbb{1}(y^w(s) > 0) \theta_{h,j} (\delta_{hj} - a_h(s)) \frac{dM_{j,p}(s)}{\tilde{S}_{P,j,p}(s)} \right) \right\} \\ &= \prod_{j=1}^k E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{p=1}^{n_j} \int_0^T \mathbb{1}(y^w(s) > 0) \sum_{h=1}^k \theta_{h,j} (\delta_{hj} - a_h(s)) \frac{dM_{j,p}(s)}{\tilde{S}_{P,j,p}(s)} \right) \right\}, \end{aligned}$$

by independence of the individuals between groups.

$$E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{h,j} \theta_{h,j} W_{h,j} \right) \right\} = \prod_{j=1}^k E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{p=1}^{n_j} \int_0^T \Theta_j(s) \frac{dM_{j,p}(s)}{\tilde{S}_{P,j,p}(s)} \right) \right\},$$

where $\Theta_j(s) = \sum_{h=1}^k \theta_{h,j} (\delta_{hj} - a_h(s)) \mathbb{1}(y^w(s) > 0)$.

j being fixed, the variables $\left(\int_0^T \Theta_j(s) \frac{dM_{j,p}(s)}{\tilde{S}_{P,j,p}(s)} \right)_{1 \leq p \leq n_j}$ are centered independent identically distributed, with common variance:

$$E \left\{ \int_0^T \Theta_j^2(s) \frac{d\langle M_{j,1} \rangle(s)}{\tilde{S}_{P,j,1}^2(s)} \right\} = E \left\{ \int_0^T \Theta_j^2(s) \frac{S_{C,j}(s) S_E(s)}{\tilde{S}_{P,j,1}(s)} (\tilde{\lambda}_{P,j,1}(s) + \lambda_E(s)) ds \right\}.$$

Hence, by central limit theorem, for all $j \in \llbracket 1; k \rrbracket$

$$\begin{aligned} & E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{p=1}^{n_j} \int_0^T \Theta_j(s) \frac{dM_{j,p}(s)}{\tilde{S}_{P,j,p}(s)} \right) \right\} \\ & \xrightarrow{n \rightarrow \infty} \exp \left[-\frac{\alpha_j}{2} E \left\{ \int_0^T \Theta_j^2(s) \frac{S_{C,j}(s) S_E(s)}{\tilde{S}_{P,j,1}(s)} (\tilde{\lambda}_{P,j,1}(s) + \lambda_E(s)) ds \right\} \right] \end{aligned}$$

Therefore,

$$\begin{aligned}
& E \left\{ \exp \left(\frac{i}{\sqrt{n}} \sum_{h,j} \theta_{h,j} W_{h,j} \right) \right\} \\
& \xrightarrow{n \rightarrow \infty} \exp \left[-\frac{1}{2} E \left\{ \sum_{j=1}^k \alpha_j \int_0^T \Theta_j^2(s) \frac{S_{C,j}(s) S_E(s)}{\tilde{S}_{P,j,1}(s)} \left(\tilde{\lambda}_{P,j,1}(s) + \lambda_E(s) \right) ds \right\} \right] \\
& = \exp \left[-\frac{1}{2} \sum_{j=1}^k \sum_{h,h'=1}^k \theta_{h',j} \theta_{h,j} \alpha_j E \left\{ \int_0^T (\delta_{hj} - a_h(s)) (\delta_{h'j} - a_{h'}(s)) \times \right. \right. \\
& \qquad \qquad \qquad \left. \left. \mathbb{1}(y^w(s) > 0) \frac{S_{C,j}(s) S_E(s)}{\tilde{S}_{P,j,1}(s)} \left(\tilde{\lambda}_{P,j,1}(s) + \lambda_E(s) \right) ds \right\} \right] \\
& = \exp \left\{ -\frac{1}{2} \sum_{h,h',j=1}^k \theta_{h',j} \theta_{h,j} S_{(hj),(h'j)}^2 \right\},
\end{aligned}$$

which proves (*).

Note that $\frac{1}{\sqrt{n}} (V_1, \dots, V_k) = \frac{1}{\sqrt{n}} \left(\sum_{l=1}^k W_{1,l}, \dots, \sum_{l=1}^k W_{k,l} \right)$.

Hence $\frac{1}{\sqrt{n}} (V_1, \dots, V_k) \xrightarrow[n \rightarrow \infty]{(d)} \mathcal{N}(0, \Sigma^2(T))$, where $\Sigma_{hj}^2(T) = \sum_{l,l'=1}^k S_{(hl),(jl')}^2 = \sum_{l=1}^k S_{(hl),(jl)}^2$. ■

Proof of Lemma 2.

Let us denote

$$R_T^{h,l} = \sum_{i=1}^{n_i} \int_0^T \left\{ \mathbb{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) - \mathbb{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) \right\} \frac{dM_{l,i}(s)}{\tilde{S}_{P,l,i}(s)},$$

so that $R_T^h = \sum_{l=1}^k R_T^{h,l}$. We have

$$E \left(\frac{1}{\sqrt{n}} R_T^{h,l} \right)^2 = E \left\{ \int_0^T f_n(s, \omega)^2 \left(\frac{1}{n} \sum_{i=1}^{n_i} Y_{l,i}(s) \frac{\tilde{\lambda}_{P,l,i}(s) + \lambda_E(s)}{\tilde{S}_{P,l,i}^2(s)} \right) ds \right\}$$

where $f_n : (s, \omega) \in (\mathbb{R} \times \Omega) \mapsto \mathbb{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) - \mathbb{1}(y^w(s) > 0) (\delta_{hl} - a_h(s))$.

Then by Cauchy-Schwarz inequality:

$$E \left(\frac{1}{\sqrt{n}} R_T^{h,l} \right)^2 \leq \sqrt{E \left\{ \int_0^T f_n(s, \omega)^4 ds \right\}} \sqrt{E \left\{ \int_0^T \left(\frac{1}{n} \sum_{i=1}^{n_i} Y_{l,i}(s) \frac{\tilde{\lambda}_{P,l,i}(s) + \lambda_E(s)}{\tilde{S}_{P,l,i}^2(s)} \right)^2 ds \right\}}.$$

By law of large numbers, under the null, $f_n(s, \omega) \xrightarrow[n \rightarrow \infty]{} 0$ a.s.. Moreover, $\forall (s, \omega) \in (\mathbb{R} \times \Omega)$, $|f_n(s, \omega)| \leq 2$. By Lebesgue's dominated convergence theorem, we get

$$E \left(\int_0^T f_n(s, \omega)^4 ds \right) \xrightarrow[n \rightarrow \infty]{} 0 \text{ under the null.}$$

On the other hand, since

$$\left(\frac{1}{n} \sum_{i=1}^{n_l} Y_{l,i}(s) \frac{\tilde{\lambda}_{P,l,i}(s) + \lambda_E(s)}{\tilde{S}_{P,l,i}^2(s)} \right)^2 \leq 2 \frac{n_l}{n^2} \sum_{i=1}^{n_l} \frac{Y_{l,i}^2(s)}{\tilde{S}_{P,l,i}^4(s)} \left(\tilde{\lambda}_{P,l,i}^2(s) + \lambda_E^2(s) \right)$$

we have:

$$\begin{aligned} & E \left\{ \int_0^T \left(\frac{1}{n} \sum_{i=1}^{n_l} Y_{l,i}(s) \frac{\tilde{\lambda}_{P,l,i}(s) + \lambda_E(s)}{\tilde{S}_{P,l,i}^2(s)} \right)^2 ds \right\} \\ & \leq 2 \frac{n_l^2}{n^2} \int_0^T E \left\{ \frac{S_{C,l}(s) S_E(s) \tilde{S}_{P,l,1}(s)}{\tilde{S}_{P,l,1}^4(s)} \left(\tilde{\lambda}_{P,l,1}^2(s) + \lambda_E^2(s) \right) \right\} ds \\ & \leq 2E \left(\frac{\int_0^T S_E(s) \lambda_E^2(s) ds}{\tilde{S}_{P,l,1}^3(T)} + \int_0^T \frac{\tilde{\lambda}_{P,l,1}^2(s)}{\tilde{S}_{P,l,1}^3(s)} ds \right) \\ & < \infty, \text{ according to assumptions (1) in the main document.} \end{aligned}$$

We deduce from this that under the null, $\left(\frac{1}{\sqrt{n}} R_T^{h,l} \right)_n \xrightarrow[n \rightarrow \infty]{L^2} 0$, $\forall (l, h) \in \llbracket 1; k \rrbracket^2$, which ends the proof of Lemma 2. ■

Using (1), to prove that the asymptotic distribution of the test statistic is χ_{k-1}^2 , it remains to prove

- LEMMA 3: (1) $\frac{1}{n} \hat{\sigma}_{h,j}^{2,w}(T) \xrightarrow[n \rightarrow \infty]{P} \Sigma_{h,j}^2(T)$.
(2) $\text{Ker}(\Sigma^2(T)) = \text{Vect}\{\mathbb{1}\}$ and hence the matrix $\Sigma_0^2(T) = (\Sigma_{h,j}^2(T))_{1 \leq h,j \leq k-1}$ is a symmetric positive definite matrix.

Point (2) of Lemma 3 ensures that we can delete the last row and the last column to use matrix $\hat{\Sigma}_0^{2,w}(T)$ in formula (5) in the main document.

Proof of Lemma 3.

(1)

$$\begin{aligned}
\hat{\sigma}_{h,j}^{2,w}(T) &= [Z_h^w, Z_j^w](T) \\
&= \sum_{l=1}^k \int_0^T \mathbf{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) \left(\delta_{jl} - \frac{Y_j^w(s)}{Y^w(s)} \right) \sum_{i=1}^{n_l} \frac{dN_{l,i}(s)}{\tilde{S}_{P,l,i}^2(s)} \\
&=: N_T - Q_T
\end{aligned}$$

with

$$N_T = \sum_{l=1}^k \int_0^T \mathbf{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) (\delta_{jl} - a_j(s)) \sum_{i=1}^{n_l} \frac{dN_{l,i}(s)}{\tilde{S}_{P,l,i}^2(s)}$$

and

$$\begin{aligned}
Q_T &= \sum_{l=1}^k \int_0^T \left\{ \mathbf{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) \left(\delta_{jl} - \frac{Y_j^w(s)}{Y^w(s)} \right) \right. \\
&\quad \left. - \mathbf{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) (\delta_{jl} - a_j(s)) \right\} \times \sum_{i=1}^{n_l} \frac{dN_{l,i}(s)}{\tilde{S}_{P,l,i}^2(s)}
\end{aligned}$$

Firstly, by the law of large numbers, we have for all $(h, j, l) \in \llbracket 1; k \rrbracket^3$

$$\frac{1}{n} \sum_{i=1}^{n_l} \int_0^T \mathbf{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) (\delta_{jl} - a_j(s)) \frac{dN_{l,i}(s)}{\tilde{S}_{P,l,i}^2(s)} \xrightarrow[n \rightarrow \infty]{(a.s.)} S_{(hl),(jl)}^2.$$

Thus $\frac{1}{n} N_T \xrightarrow[n \rightarrow \infty]{(a.s.)} \sum_{l=1}^k S_{(hl),(jl)}^2 = \Sigma_{hj}^2(T)$.

Secondly, we can show that $\frac{1}{n} Q_T \xrightarrow[n \rightarrow \infty]{L^1} 0$. Indeed,

$$\begin{aligned}
\frac{1}{n} E[|Q_T|] &\leq \sum_{l=1}^k \frac{1}{n} E \left\{ \sum_{i=1}^{n_l} \int_0^T \left| \mathbf{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) \left(\delta_{jl} - \frac{Y_j^w(s)}{Y^w(s)} \right) \right. \right. \\
&\quad \left. \left. - \mathbf{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) (\delta_{jl} - a_j(s)) \right| Y_{l,i}(s) \frac{\tilde{\lambda}_{P,l,i}(s) + \lambda_E(s)}{\tilde{S}_{P,l,i}^2(s)} ds \right\} \\
&\leq \sum_{l=1}^k \frac{n_l}{n} \sqrt{E(A_T)} \times \sqrt{E(B_T)}
\end{aligned}$$

with

$$\begin{aligned}
A_T &= \int_0^T \left| \mathbf{1}(Y^w(s) > 0) \left(\delta_{hl} - \frac{Y_h^w(s)}{Y^w(s)} \right) \left(\delta_{jl} - \frac{Y_j^w(s)}{Y^w(s)} \right) \right. \\
&\quad \left. - \mathbf{1}(y^w(s) > 0) (\delta_{hl} - a_h(s)) (\delta_{jl} - a_j(s)) \right|^2 ds \\
B_T &= \int_0^T \frac{S_{C,l}(s) S_E(s)}{\tilde{S}_{P,l,1}^3(s)} \left(\tilde{\lambda}_{P,l,1}(s) + \lambda_E(s) \right)^2 ds
\end{aligned}$$

We have $A_T \xrightarrow[n \rightarrow \infty]{L^1} 0$ and $E(B_T) < \infty$ (see the proof of Lemma 2). So we have shown that

$$\frac{1}{n} [Z_h^w, Z_j^w](T) \xrightarrow[n \rightarrow \infty]{P} \Sigma_{hj}^2(T)$$

(2) Let us denote by \mathbb{I} and $\vec{u}(s)$ the vectors of \mathbb{R}^k given by

$$\mathbb{I} := \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix}, \quad \vec{u}(s) := \begin{pmatrix} a_1(s) \\ \vdots \\ a_k(s) \end{pmatrix}.$$

Then

$$\begin{aligned}
\Sigma^2(T) &= E \left\{ \int_0^T (\text{Id} - \vec{u}(s)^t \mathbb{I}) D(s)^t (\text{Id} - \vec{u}(s)^t \mathbb{I}) ds \right\} \\
&= \int_0^T A(s) D(s)^t A(s) ds,
\end{aligned}$$

where

$$A(s) = \text{Id} - \vec{u}(s)^t \mathbb{I}, \text{ and}$$

$$\begin{aligned}
D(s) &= \text{diag}(d_l(s)) \\
&= \text{diag} \left[\alpha_l E \left\{ \mathbf{1}(y^w(s) > 0) \frac{S_{C,l}(s) S_E(s)}{\tilde{S}_{P,l,1}^3(s)} \left(\tilde{\lambda}_{P,l,1}(s) + \lambda_E(s) \right) \right\} \right].
\end{aligned}$$

Note that when $\vec{v} \in \text{Vect}(\mathbb{I})^\perp$, $A(s)\vec{v} = \vec{v} - \vec{u}(s) \langle \vec{v}, \mathbb{I} \rangle = \vec{v}$.

Hence $\forall s \in [0, T]$, $\text{Vect}(\mathbb{I})^\perp \subset \text{Im}(A(s))$.

On the other side,

$${}^t A(s) \mathbb{I} = \mathbb{I} - \mathbb{I} \langle \vec{u}(s), \mathbb{I} \rangle = \mathbb{I} - \mathbb{I} = \vec{0},$$

since $\langle \vec{u}(s), \mathbb{I} \rangle = \sum_{l=1}^k a_l(s) = 1$.

Hence $\text{Vect}(\mathbb{I}) \subset \text{Ker}({}^t A(s)) = \text{Im}(A(s))^\perp \subset \text{Vect}(\mathbb{I})$.

We thus get $\forall s \in [0, T]$, $\text{Ker}({}^t A(s)) = \text{Vect}(\mathbb{I})$.

Now let $\vec{v} \in \text{Ker}(\Sigma^2(T))$, then

$$\begin{aligned} \langle \vec{v}, \Sigma^2(T)\vec{v} \rangle &= 0 \\ \iff \int_0^T \sum_{l=1}^k d_l(s) ({}^t A(s)\vec{v})_l^2 ds &= 0 \\ \implies \text{ds a.e., } \forall l \in \llbracket 1; k \rrbracket \quad d_l(s) ({}^t A(s)\vec{v})_l^2 &= 0. \end{aligned}$$

Assume now that $\int_0^T d_l(s)ds > 0$. Then $\{s/d_l(s) > 0\}$ is a set of positive Lebesgue measure. On this set, we get $({}^t A(s)\vec{v})_l = 0$.

Therefore there exists a set of positive measure \mathcal{S} such that ${}^t A(s)\vec{v} = 0, \forall s \in \mathcal{S}$

$$\iff \vec{v} \in \text{Ker}({}^t A(s)) = \text{Vect}(\mathbb{I}), \forall s \in \mathcal{S}.$$

Hence $\text{Ker}(\Sigma^2(T)) \subset \text{Vect}(\mathbb{I})$ and it is clear that $\Sigma^2(T)\mathbb{I} = \int_0^T A(s)D(s){}^t A(s)\mathbb{I}ds = 0$, so that $\text{Ker}(\Sigma^2(T)) = \text{Vect}(\mathbb{I})$. ■

Web Table A

[Table 1 about here.]

Web Table B

[Table 2 about here.]

Web Table C

[Table 3 about here.]

Table 1

Comparison of 2 groups: percentage of rejection of the null hypothesis at the 5% level of significance for 2000 simulations of 1000 patients. Distribution of age specific to each scenario: Scenario 1: 25% aged [40 – 64], 35% aged [65 – 74], and 40% aged [75 – 85]; Scenario 2: $30 \leq \text{age} \leq 40$ (uniform); Scenario 3: $65 \leq \text{age} \leq 80$ (uniform).

HR^a	Percentage of rejection of the following tests (95%CI)			
	Proposed test		Usual log-rank on data from hypothetical world	
	<i>Scenario 1: unbalanced case^b</i>			
0.7	63.85	(61.74;65.96)	84.50	(82.91;86.09)
0.8	34.50	(32.42;36.58)	50.80	(48.61;52.99)
0.9	10.90	(9.53;12.27)	16.40	(14.78;18.02)
1	4.45	(3.55;5.35)	4.50	(3.59;5.41)
1.2	31.45	(29.42;33.48)	36.25	(34.14;38.36)
1.4	78.65	(76.85;80.45)	87.40	(85.95;88.85)
1.6	97.90	(97.27;98.53)	99.30	(98.93;99.67)
	<i>Scenario 2: unbalanced case^b</i>			
0.7	82.80	(81.15;84.45)	85.90	(84.37;87.43)
0.8	47.15	(44.96;49.34)	52.20	(50.01;54.39)
0.9	11.35	(9.96;12.74)	13.95	(12.43;15.47)
1	5.25	(4.27;6.23)	5.05	(4.09;6.01)
1.2	40.70	(38.55;42.85)	37.55	(35.43;39.67)
1.4	89.15	(87.79;90.51)	87.85	(86.42;89.28)
1.6	99.40	(99.06;99.74)	99.45	(99.13;99.77)
	<i>Scenario 3: unbalanced case^b</i>			
0.7	65.50	(63.42;67.58)	83.70	(82.08;85.32)
0.8	33.55	(31.48;35.62)	48.60	(46.41;50.79)
0.9	10.95	(9.58;12.32)	15.75	(14.15;17.35)
1	4.30	(3.41;5.19)	5.05	(4.09;6.01)
1.2	31.95	(29.91;33.99)	37.45	(35.33;39.57)
1.4	77.15	(75.31;78.99)	84.70	(83.12;86.28)
1.6	97.70	(97.04;98.36)	99.35	(99.00;99.70)

^a: Hazard Ratio of the level of G on excess mortality used in data generation, where G is the covariate representing the groups;

^b: Unbalanced cases correspond to the cases where groups are not similar in size with $P(G = 0) = 1/4$ and $P(G = 1) = 3/4$.

Table 2

Comparison of 3 groups: percentage of rejection of the null hypothesis at the 5% level of significance for 2000 simulations of 1000 patients. Distribution of age specific to each scenario: Scenario 2: $30 \leq \text{age} \leq 40$ (uniform); Scenario 3: $65 \leq \text{age} \leq 80$ (uniform).

$(HR_1, HR_2)^a$	Percentage of rejection of the following tests (95%CI)			
	Proposed test		Usual log-rank on data from hypothetical world	
	<i>Scenario 2: balanced case^b</i>			
(1, 0.7)	84.45	(82.86;86.04)	84.60	(83.02;86.18)
(1, 1)	4.70	(3.77;5.63)	4.90	(3.95;5.85)
(1, 1.2)	34.60	(32.52;36.68)	36.30	(34.19;38.41)
(1, 1.4)	88.00	(86.58;89.42)	89.80	(88.47;91.13)
(1, 1.6)	99.55	(99.26;99.84)	99.70	(99.46;99.94)
(0.9, 1.2)	56.40	(54.23;58.57)	57.10	(54.93;59.27)
(0.8, 1.4)	99.35	(99.00;99.70)	99.50	(99.19;99.81)
(0.7, 1.6)	100	(99.81;100)	100	(99.81;100)
	<i>Scenario 3: balanced case^b</i>			
(1, 0.7)	69.60	(67.58;71.62)	83.15	(81.51;84.79)
(1, 1)	4.50	(3.59;5.41)	4.20	(3.32;5.08)
(1, 1.2)	26.45	(24.52;28.38)	33.95	(31.87;36.03)
(1, 1.4)	76.90	(75.05;78.75)	88.50	(87.10;89.90)
(1, 1.6)	96.75	(95.97;97.53)	99.30	(98.93;99.67)
(0.9, 1.2)	47.70	(45.51;49.89)	60.45	(58.31;62.59)
(0.8, 1.4)	97.20	(96.48;97.92)	99.40	(99.06;99.74)
(0.7, 1.6)	100	(99.81;100)	100	(99.81;100)

^a: Hazard Ratio of the level of G on excess mortality used in data generation, where G is the covariate representing the groups;

^b: Balanced cases correspond to the cases where groups are similar in size with $P(G = 0) = P(G = 1) = P(G = 2)$.

Table 3*Description of the real dataset from the SEER made of patients diagnosed with colorectal cancer in 1998.*

Prognostic factors	Numbers	(%) ^a	Deaths at 5 years	(%) ^b
Age				
< 70 (age1)	4332	(47.5)	1552	(35.8)
70 – 79 (age2)	2757	(30.2)	1320	(47.9)
≥ 80 (age3)	2034	(22.3)	1349	(66.3)
Sex				
Man	4722	(51.8)	2137	(45.3)
Woman	4401	(48.2)	2084	(47.4)
Ethnicity				
Black	902	(9.9)	471	(52.2)
White	8221	(90.1)	3750	(45.6)
Tumor Stage at diagnosis				
Stage I	2132	(23.4)	501	(23.5)
Stage II	2880	(31.6)	1008	(35.0)
Stage III	2669	(29.2)	1385	(51.9)
Stage IV	1442	(15.8)	1327	(92.0)
Ethnicity × Tumor Stage at diagnosis × Age class				
Black × Stage I × age1	98	(1.1)	13	(13.3)
Black × Stage I × age2	44	(0.5)	19	(43.2)
Black × Stage I × age3	22	(0.2)	13	(59.1)
Black × Stage II × age1	140	(1.5)	34	(24.3)
Black × Stage II × age2	90	(1.0)	38	(42.2)
Black × Stage II × age3	32	(0.4)	22	(68.8)
Black × Stage III × age1	168	(1.8)	81	(48.2)
Black × Stage III × age2	75	(0.8)	42	(56.0)
Black × Stage III × age3	41	(0.5)	31	(75.6)
Black × Stage IV × age1	124	(1.4)	111	(89.5)
Black × Stage IV × age2	48	(0.5)	47	(97.9)
Black × Stage IV × age3	20	(0.2)	20	(100)
White × Stage I × age1	917	(10.1)	78	(8.5)
White × Stage I × age2	636	(7.0)	166	(26.1)
White × Stage I × age3	415	(4.5)	212	(51.1)
White × Stage II × age1	1052	(11.5)	189	(18.0)
White × Stage II × age2	822	(9.0)	302	(36.7)
White × Stage II × age3	744	(8.2)	423	(56.9)
White × Stage III × age1	1181	(12.9)	462	(39.1)
White × Stage III × age2	677	(7.4)	369	(54.5)
White × Stage III × age3	527	(5.8)	400	(75.9)
White × Stage IV × age1	652	(7.1)	584	(89.6)
White × Stage IV × age2	365	(4.0)	337	(92.3)
White × Stage IV × age3	233	(2.6)	228	(97.9)
Overall	9123	(100)	4221	(46.3)

^a: Percentage of all 9123 patients;^b: Percentage of patients in a given category who died within the first 5 years after diagnosis.