Supplement Appendix for "On Estimation of Optimal Treatment Regimes For Maximizing t-Year Survival Probability"

Runchao Jiang, Wenbin Lu, Rui Song and Marie Davidian

North Carolina State University, Raleigh, USA

A. Proof of Theorems

To establish the asymptotic results given in Theorems 1-2, we need to assume some regularity conditions. Recall that a working logistic model (3) is assumed for the propensity scores with parameters $\boldsymbol{\theta}$ for the IPSWKME and a working proportional hazards model (5) is further assumed for the survival time T for the AIPSWKME with parameters $\boldsymbol{\beta}$ and Λ_0. Let $\boldsymbol{\nu}_{Ai} = (\boldsymbol{X}_i^T, A_i, A_i\boldsymbol{X}_i^T)^T$ and $\boldsymbol{\nu}_{\boldsymbol{\eta}i} = (\boldsymbol{X}_i^T, g_{\boldsymbol{\eta}}(\boldsymbol{X}_i), g_{\boldsymbol{\eta}}(\boldsymbol{X}_i)\boldsymbol{X}_i^T)^T$. Define

$$K_1^I(\boldsymbol{X}, A, \tilde{T}, \delta; \boldsymbol{\eta}) = \int_0^t \frac{(2A-1)dN(u)}{\pi^* E\{w_{\boldsymbol{\eta}}^* Y(u)\}},$$

$$K_2^I(\boldsymbol{X}, A, \tilde{T}, \delta; \boldsymbol{\eta}) = \int_0^t \frac{(2A-1)Y(u)E[\{(2A-1)g_{\boldsymbol{\eta}}(\boldsymbol{X}) + (1-A)\}dN(u)]}{[\pi^* E\{w_{\boldsymbol{\eta}}^* Y(u)\}]^2},$$

where $w_{\boldsymbol{\eta}}^* = [Ag_{\boldsymbol{\eta}}(\boldsymbol{X}) + (1-A)\{1-g_{\boldsymbol{\eta}}(\boldsymbol{X})\}]/\pi^*$ and $\pi^* = \pi(\boldsymbol{X}; \boldsymbol{\theta}^*)A + \{1-\pi(\boldsymbol{X}; \boldsymbol{\theta}^*)\}(1-A)$. In addition, define

$$K_1^A(\boldsymbol{X}, A, \tilde{T}, \delta; \boldsymbol{\eta}) = \int_0^t \frac{J_1^A(u) - J_0^A(u)}{E\left[\{L_1^A(u) - L_0^A(u)\}g_{\boldsymbol{\eta}}(\boldsymbol{X}) + L_0^A(u)\right]},$$

$$K_2^A(\boldsymbol{X}, A, \tilde{T}, \delta; \boldsymbol{\eta}) = \int_0^t \frac{\{L_1^A(u) - L_0^A(u)\}E\left[\{J_1^A(u) - J_0^A(u)\}g_{\boldsymbol{\eta}}(\boldsymbol{X}) + J_0^A(u)\right]}{\left(E\left[\{L_1^A(u) - L_0^A(u)\}\ g_{\boldsymbol{\eta}}(\boldsymbol{X}) + L_0^A(u)\right]\right)^2},$$

where $J_k^A(u) = \frac{1-k-(-1)^k A}{\pi^*}dN(u) + e_k\left(1 - \frac{1-k-(-1)^k A}{\pi^*}\right)\exp\{-\Lambda_0^*(u)e_k\}\,S_C(u)d\Lambda_0^*(u)$, $L_k^A(u) = \frac{1-k-(-1)^k A}{\pi^*}Y(u) + \left(1 - \frac{1-k-(-1)^k A}{\pi^*}\right)\exp\{-\Lambda_0^*(u)e_k\}\,S_C(u)$, $e_k = \exp\left\{\boldsymbol{\beta}^{*T}(\boldsymbol{X}^T, k, k\boldsymbol{X}^T)^T\right\}$, $k = 0, 1$. We assume the following conditions.

A1. The covariates $\boldsymbol{X}$ are bounded.
A2. The propensity score $\pi(\boldsymbol{X})$ is bounded away from 0 and 1 for all possible values of $\boldsymbol{X}$.
A3. The equation $E\left[\left\{A - \frac{\exp(\boldsymbol{\theta}^T\tilde{\boldsymbol{X}})}{1+\exp(\boldsymbol{\theta}^T\tilde{\boldsymbol{X}})}\right\}\tilde{\boldsymbol{X}}\right] = 0$ has a unique solution $\boldsymbol{\theta}^*$.
A4. The equation

$$E\left(\int_0^\tau \left[\boldsymbol{\nu}_{Ai} - \frac{E\left\{Y_i(s)\exp(\boldsymbol{\beta}^T\boldsymbol{\nu}_{Ai})\boldsymbol{\nu}_{Ai}\right\}}{E\left\{Y_i(s)\exp(\boldsymbol{\beta}^T\boldsymbol{\nu}_{Ai})\right\}}\right] \times dN_i(s)\right) = 0.$$

has a unique solution $\boldsymbol{\beta}^*$, where $\tau > t$ is a prespecified time point satisfying $P(\tilde{T}_i \geq \tau) > 0$. Let $\Lambda_0^*(u) = E[\int_0^u dN_i(s)/E\{Y_i(s)\exp(\boldsymbol{\beta}^{*T}\boldsymbol{\nu}_{Ai})\}]$ and it satisfies $\Lambda_0^*(\tau) < \infty$.

A5. $\sup_{||\boldsymbol{\eta}||=1} E[\{K_j^I(\boldsymbol{X}, A, \tilde{T}, \delta; \boldsymbol{\eta})\}^2] < \infty$ and $\sup_{||\boldsymbol{\eta}||=1} E[\{K_j^A(\boldsymbol{X}, A, \tilde{T}, \delta; \boldsymbol{\eta})\}^2] < \infty$, $j = 1, 2$.

A6. $nh \to \infty$ and $nh^4 \to 0$ as $n \to \infty$.

Under assumed regularity conditions A1 - A4, we have the following asymptotic representations:

$$\sqrt{n}(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}^*) = \frac{1}{\sqrt{n}} \sum_{i=1}^n \phi_{1i} + o_p(1), \quad \sqrt{n}(\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}^*) = \frac{1}{\sqrt{n}} \sum_{i=1}^n \phi_{2i} + o_p(1),$$

$$\sqrt{n}\{\hat{\Lambda}_0(u) - \Lambda_0^*(u)\} = \frac{1}{\sqrt{n}} \sum_{i=1}^n \phi_{3i}(u) + o_p(1), \quad \sqrt{n}\{\hat{S}_C(u) - S_C(u)\} = \frac{1}{\sqrt{n}} \sum_{i=1}^n \phi_{4i}(u) + o_p(1),$$

where ϕ_{1i}'s and ϕ_{2i}'s are independently and identically distributed mean-zero vectors, and $\phi_{3i}(u)$ and $\phi_{4i}(u)$ are independent mean-zero processes. Moreover, consistent estimators $\hat{\phi}_{1i}$, $\hat{\phi}_{2i}$, $\hat{\phi}_{3i}(u)$ and $\hat{\phi}_{4i}(u)$ of ϕ_{1i}, ϕ_{2i}, $\phi_{3i}(u)$ and $\phi_{4i}(u)$ can be easily obtained.

A.1. Proof of Theorem 1

For any given regime $g_{\boldsymbol{\eta}}$, we first derive the asymptotic properties for the corresponding inverse propensity score weighted (IPSW) Nelson-Aalen estimator. Specifically,

$$\widehat{\Lambda}_I(u; \boldsymbol{\eta}) \equiv \widehat{\Lambda}_I(u; \boldsymbol{\eta}, \hat{\boldsymbol{\theta}}) = \int_0^u \frac{\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i} dN_i(s)}{\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i} Y_i(s)}. \tag{A.1}$$

It is easy to show that $\widehat{S}_I(u; \boldsymbol{\eta})$ and $\exp\{-\widehat{\Lambda}_I(u; \boldsymbol{\eta})\}$ are asymptotically equivalent for any given $\boldsymbol{\eta}$. Therefore, the asymptotic properties of $\widehat{S}_I(u; \boldsymbol{\eta})$ easily follows those of $\widehat{\Lambda}_I(u; \boldsymbol{\eta})$.

When the propensity score model is correctly specified, we have $\boldsymbol{\theta}^* = \boldsymbol{\theta}$ and $w_{\boldsymbol{\eta}i}^* = w_{\boldsymbol{\eta}i}$. Then $n^{-1}\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i} Y_i(s) \to_p E\{w_{\boldsymbol{\eta}i} Y_i(s)\} = E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X}); s\}]$ uniformly for $s \in [0, \tau]$ as $n \to \infty$. Similarly, we have $n^{-1}\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i} dN_i(s) \to_p E\{w_{\boldsymbol{\eta}i} dN_i(s)\} = E[dN^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X}); s\}]$ uniformly for $s \in [0, \tau]$ as $n \to \infty$. Therefore,

$$\begin{aligned} \widehat{\Lambda}_I(u; \boldsymbol{\eta}) \to_p \quad & \int_0^u \frac{E[dN^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X}); s\}]}{E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X}); s\}]} = \int_0^u \frac{S_C(s) dP[T^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X})\} \leq s]}{S_C(s) P[T^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X})\} \geq s]} \\ & = -\log\{S^*(u; \boldsymbol{\eta})\} \equiv \Lambda^*(u; \boldsymbol{\eta}), \end{aligned}$$

which establish the consistency given in (i) of Theorem 1.

Next, we derive the asymptotic distribution of $\widehat{\Lambda}_I(u; \boldsymbol{\eta})$. By applying the first-order Taylor expansion of $\widehat{\Lambda}_I(u; \boldsymbol{\eta})$ with respect to parameter $\boldsymbol{\theta}$, we have

$$\sqrt{n}\{\widehat{\Lambda}_I(u; \boldsymbol{\eta}) - \Lambda^*(u; \boldsymbol{\eta})\} = \sqrt{n}\{\widehat{\Lambda}_I(u; \boldsymbol{\eta}, \boldsymbol{\theta}) - \Lambda^*(u; \boldsymbol{\eta})\} + D_1(u)^T \sqrt{n}(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}) + o_p(1),$$

where $D_1(u) = \lim_{n\to\infty} \partial\widehat{\Lambda}_I(u;\boldsymbol{\eta},\boldsymbol{\theta})/\partial\boldsymbol{\theta}$. In addition,

$$\begin{aligned}
\sqrt{n}\{\widehat{\Lambda}_I(u;\boldsymbol{\eta},\boldsymbol{\theta}) - \Lambda^*(u;\boldsymbol{\eta})\} &= \sqrt{n}\int_0^u \frac{\sum_{i=1}^n w_{\boldsymbol{\eta}i}\{dN_i(s) - Y_i(s)d\Lambda^*(s;\boldsymbol{\eta})\}}{\sum_{i=1}^n w_{\boldsymbol{\eta}i}Y_i(s)} \\
= \quad n^{-1/2}\sum_{i=1}^n \int_0^u \frac{w_{\boldsymbol{\eta}i}[dN_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\} - Y_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}d\Lambda^*(s;\boldsymbol{\eta})]}{E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}]} + o_p(1) \\
= \quad n^{-1/2}\sum_{i=1}^n \int_0^u \frac{w_{\boldsymbol{\eta}i}dM_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}}{E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}]} + o_p(1),
\end{aligned}$$

where $M_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\} = N_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\} - \int_0^s Y_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});v\}d\Lambda^*(v;\boldsymbol{\eta})$ is a mean-zero martingale process. Therefore,

$$\begin{aligned}
\sqrt{n}\{\widehat{\Lambda}_I(u;\boldsymbol{\eta}) - \Lambda^*(u;\boldsymbol{\eta})\} &= n^{-1/2}\sum_{i=1}^n \left(\int_0^u \frac{w_{\boldsymbol{\eta}i}dM_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}}{E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}]} + D_1(u)^T\phi_{1i}\right) + o_p(1) \\
&\equiv n^{-1/2}\sum_{i=1}^n \zeta_i(u;\boldsymbol{\eta}) + o_p(1),
\end{aligned}$$

where $\zeta_i(u;\boldsymbol{\eta})$'s are independent mean-zero processes. By delta method, we have $\sqrt{n}\{\widehat{S}_I(u;\boldsymbol{\eta}) - S^*(u;\boldsymbol{\eta})\} = -S^*(u;\boldsymbol{\eta})n^{-1/2}\sum_{i=1}^n \zeta_i(u;\boldsymbol{\eta}) + o_p(1)$, which converges weakly to a mean-zero Gaussian process by applying the empirical process theory. This proves (ii) of Theorem 1.

Since $\hat{\boldsymbol{\eta}}_I^{\text{opt}}$ is the maximizer of $\widehat{S}_I(t;\boldsymbol{\eta})$ and $\boldsymbol{\eta}^{\text{opt}}$ is the maximizer of $S^*(t;\boldsymbol{\eta})$, following the similar arguments in Zhang et al. (2012), we have

$$\sqrt{n}\{\widehat{S}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}}) - S^*(t;\boldsymbol{\eta}^{\text{opt}})\} - \sqrt{n}\{\widehat{S}_I(t;\boldsymbol{\eta}^{\text{opt}}) - S^*(t;\boldsymbol{\eta}^{\text{opt}})\} = o_p(1).$$

It follows that $\sqrt{n}\{\widehat{S}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}}) - S^*(t;\boldsymbol{\eta}^{\text{opt}})\} \to^d N(0,\Sigma_I(t;\boldsymbol{\eta}^{\text{opt}}))$, where $\Sigma_I(t;\boldsymbol{\eta}^{\text{opt}}) = \{S^*(t;\boldsymbol{\eta}^{\text{opt}})\}^2 E\{\zeta_i^2(t;\boldsymbol{\eta}^{\text{opt}})\}$. This proves (iii) of Theorem 1. In addition, $\Sigma_I(t;\boldsymbol{\eta}^{\text{opt}})$ can be consistently estimated by $\{\widehat{S}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}})\}^2 n^{-1}\sum_{i=1}^n \hat{\zeta}_i^2(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}})$, where

$$\hat{\zeta}_i(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}}) = \int_0^t \frac{\hat{w}_{\boldsymbol{\eta}i}\{dN_i(s) - Y_i(s)d\widehat{\Lambda}_I(s;\hat{\boldsymbol{\eta}}_I^{\text{opt}})\}}{n^{-1}\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i}Y_i(s)} + \hat{D}_1(t)^T\hat{\phi}_{1i},$$

and $\hat{D}_1(t) = \partial\widehat{\Lambda}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}},\boldsymbol{\theta})/\partial\boldsymbol{\theta}|_{\boldsymbol{\theta}=\hat{\boldsymbol{\theta}}}$.

Finally, we show that $\widehat{S}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}})$ and $\widetilde{S}_I(t;\tilde{\boldsymbol{\eta}}_I^{\text{opt}})$ are asymptotically equivalent. For any given $\boldsymbol{\eta}$, we have

$$\begin{aligned}
&\sqrt{n}\left\{\widetilde{\Lambda}_I(t;\boldsymbol{\eta}) - \widehat{\Lambda}_I(t;\boldsymbol{\eta})\right\} \\
&= \sqrt{n} \times \frac{1}{n}\sum_{i=1}^n \left\{\Phi\left(\frac{\boldsymbol{\eta}^T\boldsymbol{X}_i}{h}\right) - I\left(\boldsymbol{\eta}^T\boldsymbol{X}_i \geq 0\right)\right\} \times K_1^I(\boldsymbol{X}_i, A_i, \tilde{T}_i, \delta;\boldsymbol{\eta}) \qquad \text{(A.2)} \\
&+ \sqrt{n} \times \frac{1}{n}\sum_{i=1}^n \left\{\Phi\left(\frac{\boldsymbol{\eta}^T\boldsymbol{X}_i}{h}\right) - I\left(\boldsymbol{\eta}^T\boldsymbol{X}_i \geq 0\right)\right\} \times K_2^I(\boldsymbol{X}_i, A_i, \tilde{T}_i, \delta;\boldsymbol{\eta}) \qquad \text{(A.3)} \\
&+ o_p(1).
\end{aligned}$$

For simplicity, define $\boldsymbol{q} = (\boldsymbol{X}_i, A_i, \tilde{T}_i, \delta)$ and $r^{\boldsymbol{\eta}} = \boldsymbol{\eta}^T \boldsymbol{X}$. Following the similar arguments in Heller (2007), we have

$$|(\text{A.2})| \leq M\sqrt{n}\, \sup_{||\boldsymbol{\eta}||=1} \left| \int_{\boldsymbol{q}} \int_{r^{\boldsymbol{\eta}}} \left\{ \Phi\left(\frac{r^{\boldsymbol{\eta}}}{h}\right) - I(r^{\boldsymbol{\eta}} \geq 0) \right\} K_1^I(\boldsymbol{q};\boldsymbol{\eta}) d\hat{F}(r^{\boldsymbol{\eta}}|\boldsymbol{q};\boldsymbol{\eta}) d\hat{G}(\boldsymbol{q};\boldsymbol{\eta}) \right|,$$

where M is a finite constant, $\hat{G}(\boldsymbol{q};\boldsymbol{\eta})$ and $\hat{F}(r^{\boldsymbol{\eta}}|\boldsymbol{q};\boldsymbol{\eta})$ are the marginal empirical cumulative distribution functions for $\boldsymbol{q}$ and the conditional empirical cumulative distribution function for $r^{\boldsymbol{\eta}}$, respectively. For simplicity, we omit the superscript $\boldsymbol{\eta}$ in $r^{\boldsymbol{\eta}}$, the condition $\boldsymbol{\eta}$ in $K_1^I(\boldsymbol{q};\boldsymbol{\eta})$, $\hat{F}(r|\boldsymbol{q};\boldsymbol{\eta})$ and $\hat{G}(\boldsymbol{q};\boldsymbol{\eta})$. Thus, the equation (A.2) is bounded by $M\sqrt{n}\sup_{||\boldsymbol{\eta}||=1}|\Upsilon|$, where

$$\Upsilon = \int_{\boldsymbol{q}} \int_{r} \left\{ \Phi\left(\frac{r}{h}\right) - I(r \geq 0) \right\} K_1^I(\boldsymbol{q}) d\hat{F}(r|\boldsymbol{q}) d\hat{G}(\boldsymbol{q}).$$

Write $\Upsilon = \Upsilon_1 + \Upsilon_2$, where

$$\Upsilon_1 = \int_{\boldsymbol{q}} \int_{r} \left\{ \Phi\left(\frac{r}{h}\right) - I(r \geq 0) \right\} K_1^I(\boldsymbol{q}) \left\{ d\hat{F}(r|\boldsymbol{q}) - dF(r|\boldsymbol{q}) \right\} d\hat{G}(\boldsymbol{q})$$
$$\Upsilon_2 = \int_{\boldsymbol{q}} \int_{r} \left\{ \Phi\left(\frac{r}{h}\right) - I(r \geq 0) \right\} K_1^I(\boldsymbol{q}) dF(r|\boldsymbol{q}) d\hat{G}(\boldsymbol{q})$$

with $F(r|\boldsymbol{q}) = \lim_{n\to+\infty} \hat{F}(r|\boldsymbol{q})$. By variable transformation $z = r/h$ and integration by parts, we have

$$\Upsilon_1 = \int_{\boldsymbol{q}} \int_{z} K_1^I(\boldsymbol{q})\varphi(z) \left\{ \left[\hat{F}(zh|\boldsymbol{q}) - F(zh|\boldsymbol{q})\right] - \left[\hat{F}(0|\boldsymbol{q}) - F(0|\boldsymbol{q}))\right] \right\} dz d\hat{G}(\boldsymbol{q}), \quad \text{(A.4)}$$

where $\varphi(z)$ is the probability density function of standard normal distribution. Under regularity condition A5, we apply the results on oscillations of empirical process (Shorack and Wellner, 2009, Theorem 1, p. 542) to equation (A.4) and have

$$\sqrt{n}|\Upsilon_1| = O_p\left(\sqrt{h \log n \log\left(\frac{1}{h \log n}\right)} \right).$$

In addition, by similar arguments and applying second order Taylor expansion of Υ_2 with respect to h around 0, we have

$$\Upsilon_2 = -\frac{h^2}{2} \int_{\boldsymbol{q}} \int_{z} K_1^I(\boldsymbol{q})\varphi(z) f'(zh^*|\boldsymbol{q}) z^2 dz d\hat{G}(\boldsymbol{q}),$$

where $f'(u|\boldsymbol{q}) = \partial^2 F(u|\boldsymbol{q})/\partial u^2$ and h^* lies between h and 0. Thus, we have $\sqrt{n}|\Upsilon_2| = O_p(\sqrt{n}h^2)$. Combine the above results, we have

$$|(\text{A.2})| \leq \sqrt{n}|\Upsilon_1| + \sqrt{n}|\Upsilon_2| = O_p\left(\sqrt{h \log n \log\left(\frac{1}{h \log n}\right)} + \sqrt{n}h^2 \right).$$

By condition A6, we have $\sup_{||\boldsymbol{\eta}||=1}|(\text{A.2})| = o_p(1)$. Similarly, we have $\sup_{||\boldsymbol{\eta}||=1}|(\text{A.3})| = o_p(1)$. Therefore, we have $\sqrt{n}\{\widetilde{\Lambda}_I(t;\boldsymbol{\eta}) - \widehat{\Lambda}_I(t;\boldsymbol{\eta})\} = o_p(1)$ uniformly in $\boldsymbol{\eta}$, which implies $\sqrt{n}\{\widetilde{S}_I(t;\boldsymbol{\eta}) - \widehat{S}_I(t;\boldsymbol{\eta})\} = o_p(1)$ uniformly in $\boldsymbol{\eta}$. In addition, it is easy to show that $\sqrt{n}\{\widetilde{S}_I(t;\tilde{\boldsymbol{\eta}}_I^{\text{opt}}) - \widetilde{S}_I(t;\boldsymbol{\eta}^{\text{opt}})\} = o_p(1)$ and $\sqrt{n}\{\widehat{S}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}}) - \widehat{S}_I(t;\boldsymbol{\eta}^{\text{opt}})\} = o_p(1)$. It follows that $\sqrt{n}\{\widetilde{S}_I(t;\tilde{\boldsymbol{\eta}}_I^{\text{opt}}) - \widehat{S}_I(t;\hat{\boldsymbol{\eta}}_I^{\text{opt}})\} = o_p(1)$, which proves (iv) of Theorem 1.

A.2. Proof of Theorem 2

For any given regime $g_{\boldsymbol{\eta}}$, we similarly introduce the augmented IPSW Nelson-Aalen estimator

$$\widehat{\Lambda}_A(u;\boldsymbol{\eta}) = \int_0^u \frac{\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i} dN_i(s) + (1-\hat{w}_{\boldsymbol{\eta}i})\hat{S}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)\hat{S}_C(s)d\hat{\Lambda}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)}{\sum_{i=1}^n \hat{w}_{\boldsymbol{\eta}i}Y_i(s) + (1-\hat{w}_{\boldsymbol{\eta}i})\hat{S}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)\hat{S}_C(s)}. \tag{A.5}$$

We will show that $\widehat{\Lambda}_A(u;\boldsymbol{\eta})$ is consistent when either the propensity score model is correctly specified or the survival model for T is correctly specified, i.e. having the doubly robustness property. First, assume that the propensity score model is correctly specified. Then, we have $\boldsymbol{\theta}^* = \boldsymbol{\theta}$ and $w^*_{\boldsymbol{\eta}i} = w_{\boldsymbol{\eta}i}$. In addition, the denominator of equation (A.5) converges in probability to $E\{w_{\boldsymbol{\eta}i}Y_i(s)\} + E\left[(1-w_{\boldsymbol{\eta}i})\exp\{-\Lambda^*_0(s)\exp(\boldsymbol{\beta^*}^T\nu_{\boldsymbol{\eta}i})\}S_C(s)\right]$ uniformly for $s\in[0,\tau]$. Note that the second term is zero since $E(w_{\boldsymbol{\eta}i}|\boldsymbol{X}_i)=0$. Similarly, the numerator of equation (A.5) converges in probability to

$$E\{w_{\boldsymbol{\eta}i}dN_i(u)\} + E\left[(1-w_{\boldsymbol{\eta}i})\exp\{-\Lambda^*_0(u)\exp(\boldsymbol{\beta^*}^T\nu_{\boldsymbol{\eta}i})\}S_C(u)\exp(\boldsymbol{\beta^*}^T\nu_{\boldsymbol{\eta}i})d\Lambda^*_0(u)\right]$$

uniformly for $s\in[0,\tau]$, where the second term is also zero. The proof of consistency then follows that for the IPSW Nelson-Aalen estimator.

On the other hand, when the survival model for T is correctly specified, we have $\boldsymbol{\beta}^*=\boldsymbol{\beta}$ and $\Lambda^*_0(s) = \Lambda_0(s)$. We can show that the denominator of equation (A.5) converges in probability to

$$E\left[\exp\{-\Lambda_0(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})\}S_C(s)\right] + E\left(w^*_{\boldsymbol{\eta}i}[Y_i(s) - \exp\{-\Lambda_0(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})\}S_C(s)]\right)$$

uniformly for $s\in[0,\tau]$, where the first term equals to $S^*(s;\boldsymbol{\eta})S_C(s)$ and the second term is zero since $E[Y_i(s) - \exp\{-\Lambda_0(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})\}S_C(s)|A_i,\boldsymbol{X}_i]=0$. In addition, the numerator of equation (A.5) converges in probability to

$$\begin{aligned}&E\left[\exp\{-\Lambda_0(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})\}S_C(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})d\Lambda_0(s)\right]\\ &+E\left(w^*_{\boldsymbol{\eta}i}[dN_i(u) - \exp\{-\Lambda_0(s)\exp(\boldsymbol{\beta}^T\nu_{gi})\}S_C(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})d\Lambda_0(u)]\right)\end{aligned}$$

uniformly for $s\in[0,\tau]$, where the first term equals to $-S_C(s)dS^*(s;\boldsymbol{\eta})$ and the second term is zero since $E[dN_i(u)-\exp\{-\Lambda_0(s)\exp(\boldsymbol{\beta}^T\nu_{gi})\}S_C(s)\exp(\boldsymbol{\beta}^T\nu_{\boldsymbol{\eta}i})d\Lambda_0(u)|A_i,\boldsymbol{X}_i]=0$. Therefore, the remaining proof follows that for the IPSW Nelson-Aalen estimator.

Next, we derive the asymptotic distribution for $\widehat{S}_A(u;\boldsymbol{\eta})$, assuming that either the propensity score model or the survival model for T is correctly specified. Note that $\widehat{\Lambda}_A(u;\boldsymbol{\eta}) = \widehat{\Lambda}_A(u;\boldsymbol{\eta},\hat{\boldsymbol{\theta}},\hat{\boldsymbol{\beta}},\hat{\Lambda}_0,\hat{S}_C)$. By Taylor expansion of $\widehat{\Lambda}_A(u;\boldsymbol{\eta},\hat{\boldsymbol{\theta}},\hat{\boldsymbol{\beta}},\hat{\Lambda}_0,\hat{S}_C)$ with respect to the estimators $\hat{\boldsymbol{\theta}}$, $\hat{\boldsymbol{\beta}}$, $\hat{\Lambda}_0$ and $\hat{S}_C$ around their population values, we have

$$\sqrt{n}\{\widehat{\Lambda}_A(u;\boldsymbol{\eta})-\Lambda^*(u;\boldsymbol{\eta})\} = \sqrt{n}\{\widehat{\Lambda}_A(u;\boldsymbol{\eta},\boldsymbol{\theta}^*,\boldsymbol{\beta}^*,\Lambda^*_0,S_C)-\Lambda^*(u;\boldsymbol{\eta})\}+n^{-1/2}\sum_{i=1}^n\psi_{2i}(u;\boldsymbol{\eta})+o_p(1),$$

where $\psi_{2i}(u;\boldsymbol{\eta})$'s are independent mean-zero processes due to the asymptotic expansions of the estimators $\hat{\boldsymbol{\theta}}$, $\hat{\boldsymbol{\beta}}$, $\hat{\Lambda}_0$ and $\hat{S}_C$, and are functions of ϕ_{1i}, ϕ_{2i}, $\phi_{3i}(u)$ and $\phi_{4i}(u)$. As in the proof of Theorem 1, $\psi_{2i}(u;\boldsymbol{\eta})$ can be consistently estimated by the usual plug-in method, and its estimator is denoted as $\hat{\psi}_{2i}(u;\boldsymbol{\eta})$. By simple algebra, we have

$$\sqrt{n}\{\widehat{\Lambda}_A(u;\boldsymbol{\eta},\boldsymbol{\theta}^*,\boldsymbol{\beta}^*,\Lambda_0^*,S_C)-\Lambda^*(u;\boldsymbol{\eta})\}=n^{-1/2}\sum_{i=1}^n\int_0^u\frac{dh_i(s)}{E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}]}+o_p(1),$$

where

$$\begin{aligned}dh_i(s)=&w_{\boldsymbol{\eta}i}^*\{dN_i(s)-Y_i(s)d\Lambda^*(s;\boldsymbol{\eta})\}\\&+(1-w_{\boldsymbol{\eta}i}^*)S_T^*(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)S_C(s)d\{\Lambda_T^*(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)-\Lambda^*(s;\boldsymbol{\eta})\}.\end{aligned}$$

Note that the first term in $dh_i(s)$ equals to $w_{\boldsymbol{\eta}i}^*dM_i^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}$ and the second term is zero if the propensity score model is correctly specified. If the survival model for T is correctly specified, we have $E\{\Lambda_T^*(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)\}-\Lambda^*(s;\boldsymbol{\eta})=0$. Define $\psi_{1i}(u;\boldsymbol{\eta})=\int_0^u\frac{dh_i(s)}{E[Y^*\{g_{\boldsymbol{\eta}}(\boldsymbol{X});s\}]}$. Then, $\psi_{1i}(u;\boldsymbol{\eta})$'s are independent mean-zero processes. In addition, $\psi_{1i}(u;\boldsymbol{\eta})$ can be consistently estimated by

$$\begin{aligned}\hat{\psi}_{1i}(u;\boldsymbol{\eta})=&\int_0^u\frac{\hat{w}_{\boldsymbol{\eta}i}\{dN_i(s)-Y_i(s)d\widehat{\Lambda}_A(s;\boldsymbol{\eta})\}}{n^{-1}\sum_{i=1}^n\{\hat{w}_{\boldsymbol{\eta}i}Y_i(s)+(1-\hat{w}_{\boldsymbol{\eta}i})\hat{S}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)\hat{S}_C(s)\}}\\&+\int_0^u\frac{(1-\hat{w}_{\boldsymbol{\eta}i})\hat{S}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)\hat{S}_C(s)d\{\widehat{\Lambda}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)-\widehat{\Lambda}_A(s;\boldsymbol{\eta})\}}{n^{-1}\sum_{i=1}^n\{\hat{w}_{\boldsymbol{\eta}i}Y_i(s)+(1-\hat{w}_{\boldsymbol{\eta}i})\hat{S}_T(s|g_{\boldsymbol{\eta}}(\boldsymbol{X}_i),\boldsymbol{X}_i)\hat{S}_C(s)\}}.\end{aligned}$$

Let $\psi_i(u;\boldsymbol{\eta})=\psi_{1i}(u;\boldsymbol{\eta})+\psi_{2i}(u;\boldsymbol{\eta})$. We have $\sqrt{n}\{\widehat{\Lambda}_A(u;\boldsymbol{\eta})-\Lambda^*(u;\boldsymbol{\eta})\}=n^{-1/2}\sum_{i=1}^n\psi_i(u;\boldsymbol{\eta})+o_p(1)$, which converges weakly to a mean-zero Gaussian process. By Delta method, $\sqrt{n}\{\widehat{S}_A(u;\boldsymbol{\eta})-S^*(u;\boldsymbol{\eta})\}$ also converges weakly to a mean-zero Gaussian process. Following the proof for Theorem 1, we have

$$\sqrt{n}\{\widehat{S}_A(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})-S^*(t;\boldsymbol{\eta}^{\rm opt})\}-\sqrt{n}\{\widehat{S}_A(t;\boldsymbol{\eta}^{\rm opt})-S^*(t;\boldsymbol{\eta}^{\rm opt})\}=o_p(1).$$

It follows that $\sqrt{n}\{\widehat{S}_A(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})-S^*(t;\boldsymbol{\eta}^{\rm opt})\}\to^d N(0,\Sigma_A(t;\boldsymbol{\eta}^{\rm opt}))$, where $\Sigma_A(t;\boldsymbol{\eta}^{\rm opt})=\{S^*(t;\boldsymbol{\eta}^{\rm opt})\}^2E\{\psi_i^2(t;\boldsymbol{\eta}^{\rm opt})\}$. Moreover, $\Sigma_A(t;\boldsymbol{\eta}^{\rm opt})$ can be consistently estimated by

$$\{\widehat{S}_A(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})\}^2n^{-1}\sum_{i=1}^n\{\hat{\psi}_{1i}(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})+\hat{\psi}_{2i}(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})\}^2.$$

Finally, for any given $\boldsymbol{\eta}$, we have

$$\begin{aligned}&\sqrt{n}\left\{\widetilde{\Lambda}_A(t;\boldsymbol{\eta})-\widehat{\Lambda}_A(t;\boldsymbol{\eta})\right\}\\&=\sqrt{n}\times\frac{1}{n}\sum_{i=1}^n\left\{\Phi\left(\frac{\boldsymbol{\eta}^T\boldsymbol{X}_i}{h}\right)-I\left(\boldsymbol{\eta}^T\boldsymbol{X}_i\geq 0\right)\right\}\times K_1^A(\boldsymbol{X}_i,A_i,\tilde{T}_i,\delta;\boldsymbol{\eta}) &\text{(A.6)}\\&+\sqrt{n}\times\frac{1}{n}\sum_{i=1}^n\left\{\Phi\left(\frac{\boldsymbol{\eta}^T\boldsymbol{X}_i}{h}\right)-I\left(\boldsymbol{\eta}^T\boldsymbol{X}_i\geq 0\right)\right\}\times K_2^A(\boldsymbol{X}_i,A_i,\tilde{T}_i,\delta;\boldsymbol{\eta}) &\text{(A.7)}\\&+o_p(1).\end{aligned}$$

Under conditions A5 and A6, following the similar arguments in the proof for (iv) of Theorem 1, (A.6) and (A.7) can be bounded uniformly in $\boldsymbol{\eta}$. Therefore, $\sqrt{n}\{\widetilde{S}_A(t;\boldsymbol{\eta})-\widehat{S}_A(t;\boldsymbol{\eta})\}=o_p(1)$ uniformly in $\boldsymbol{\eta}$. Since $\sqrt{n}\{\widetilde{S}_A(t;\tilde{\boldsymbol{\eta}}_A^{\rm opt})-\widetilde{S}_A(t;\boldsymbol{\eta}^{\rm opt})\}=o_p(1)$ and $\sqrt{n}\{\widehat{S}_A(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})-\widehat{S}_A(t;\boldsymbol{\eta}^{\rm opt})\}=o_p(1)$, it follows that $\sqrt{n}\{\widetilde{S}_A(t;\tilde{\boldsymbol{\eta}}_A^{\rm opt})-\widehat{S}_A(t;\hat{\boldsymbol{\eta}}_A^{\rm opt})\}=o_p(1)$.

A.3. Proof of Theorem 3

To establish the asymptotic results given in Theorem 3, the regularity conditions A1-A3 and A5-A6 need to be modified accordingly to incorporate the two-stage treatment regimes, and condition A4 is not needed. However, the proof of Theorem 3 can follow similar steps as for the proof of Theorem 1, and is omitted here.

References

Heller, G. (2007). Smoothed rank regression with censored data. *Journal of the American Statistical Association*, 102(478):552–559.

Shorack, G. R. and Wellner, J. A. (2009). *Empirical processes with applications to statistics*, volume 59. SIAM.

Zhang, B., Tsiatis, A. A., Laber, E. B., and Davidian, M. (2012). A robust method for estimating optimal treatment regimes. *Biometrics*, 68(4):1010–1018.