

Web-based Supplementary Materials for “Estimation of the Optimal Regime in Treatment of Prostate Cancer Recurrence from Observational Data Using Flexible Weighting Models”

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Web Appendix A: The connection between counterfactual and observational data

Here, we demonstrate that following the causal inference assumptions made in Section 3 of the manuscript, we would be able to deduce the distribution for regime g^b specific counterfactuals $p_{\bar{\mathbf{R}}_K, \bar{\mathbf{L}}_{K-1}^b}(\bar{\mathbf{r}}_K, \bar{\mathbf{l}}_{K-1})$ from the distribution of the observed data. This can be written as

$$\begin{aligned} p_{\bar{\mathbf{R}}_K, \bar{\mathbf{L}}_{K-1}^b}(\bar{\mathbf{r}}_K, \bar{\mathbf{l}}_{K-1}) &= p_{R_K^b | \bar{\mathbf{L}}_{K-1}^b, \bar{\mathbf{R}}_{K-1}^b}(r_K | \bar{\mathbf{l}}_{K-1}, \bar{\mathbf{r}}_{K-1}) \times p_{L_0}(\mathbf{l}_0) \\ &\quad \times \prod_{j=1}^{K-1} p_{L_j^b | \bar{\mathbf{R}}_j^b, \bar{\mathbf{L}}_{j-1}^b}(l_j | \bar{\mathbf{r}}_j, \bar{\mathbf{l}}_{j-1}) \times p_{R_j^b | \bar{\mathbf{L}}_{j-1}^b, \bar{\mathbf{R}}_{j-1}^b}(r_j | \bar{\mathbf{l}}_{j-1}, \bar{\mathbf{r}}_{j-1}) \end{aligned}$$

First, we have for a fixed $\bar{\mathbf{g}}_{k-1}^b(\bar{\boldsymbol{\sigma}}_{k-1}, \bar{\mathbf{a}}_{k-2}) = \bar{\mathbf{a}}_{k-1} \in \bar{\mathcal{A}}_{k-1}$, $k = 1, \dots, K$,

$$\begin{aligned} p_{R_k^b | \bar{\mathbf{L}}_{k-1}, \bar{\mathbf{R}}_{k-1}}(r_k | \bar{\mathbf{l}}_{k-1}, \bar{\mathbf{r}}_{k-1}) &= p_{R_k^C(\bar{\mathbf{g}}_{k-1}) | \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{g}}_{k-2}), \bar{\mathbf{R}}_{k-1}^C(\bar{\mathbf{g}}_{k-2})}(r_k | \bar{\mathbf{l}}_{k-1}, \bar{\mathbf{r}}_{k-1}) \\ &= p_{R_k^C(\bar{\mathbf{a}}_{k-1}) | \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2}), \bar{\mathbf{R}}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(r_k | \bar{\mathbf{l}}_{k-1}, \bar{\mathbf{r}}_{k-1}) \end{aligned}$$

and for $k = 1, \dots, K - 1$,

$$\begin{aligned} p_{L_k^b | \bar{\mathbf{R}}_k^b, \bar{\mathbf{L}}_{k-1}^b}(l_k | \bar{\mathbf{r}}_k, \bar{\mathbf{l}}_{k-1}) &= p_{L_k^C(\bar{\mathbf{g}}_{k-1}) | \bar{\mathbf{R}}_k^C(\bar{\mathbf{g}}_{k-1}), \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{g}}_{k-2})}(l_k | \bar{\mathbf{r}}_k, \bar{\mathbf{l}}_{k-1}) \\ &= p_{L_k^C(\bar{\mathbf{a}}_{k-1}) | \bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1}), \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(l_k | \bar{\mathbf{r}}_k, \bar{\mathbf{l}}_{k-1}) \end{aligned}$$

Here we need to show that the three assumptions are sufficient to connect these to the distribution of observed data, i.e., we want to show

$$p_{R_k^C(\bar{\mathbf{a}}_{k-1}) | \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2}), \bar{\mathbf{R}}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(r_k | \bar{\mathbf{l}}_{k-1}, \bar{\mathbf{r}}_{k-1}) = p_{R_k | \bar{\mathbf{A}}_{k-1}, \bar{\mathbf{L}}_{k-1}, \bar{\mathbf{R}}_{k-1}}(r_k | \bar{\mathbf{a}}_{k-1}, \bar{\mathbf{l}}_{k-1}, \bar{\mathbf{r}}_{k-1}) \quad (1)$$

and

$$p_{L_k^C(\bar{\mathbf{a}}_{k-1}) | \bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1}), \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(l_k | \bar{\mathbf{r}}_k, \bar{\mathbf{l}}_{k-1}) = p_{L_k | \bar{\mathbf{R}}_k, \bar{\mathbf{A}}_{k-1}, \bar{\mathbf{L}}_{k-1}}(l_k | \bar{\mathbf{r}}_k, \bar{\mathbf{a}}_{k-1}, \bar{\mathbf{l}}_{k-1}) \quad (2)$$

Since SADT treatment will not start at baseline, $A_0 = 0$, thus for $k = 1$, we have

$$p_{R_1^C(a_0) | \mathbf{L}_0, R_0}(r_1 | \mathbf{l}_0, r_0) = p_{R_1 | \mathbf{L}_0}(r_1 | \mathbf{l}_0) = p_{R_1 | A_0, \mathbf{L}_0, R_0}(r_1 | a_0, \mathbf{l}_0, r_0)$$

and

$$p_{L_1^C(a_0) | \bar{\mathbf{R}}_1^C(a_0), \mathbf{L}_0}(l_1 | \bar{\mathbf{r}}_1, \mathbf{l}_0) = p_{L_1 | R_1, \mathbf{L}_0}(l_1 | r_1, \mathbf{l}_0) = p_{L_1 | \bar{\mathbf{R}}_1, A_0, \mathbf{L}_0}(l_1 | \bar{\mathbf{r}}_1, a_0, \mathbf{l}_0)$$

Next we want to show that equation (1) and (2) also held for $k > 1$ cases. Let $\mathbf{Z}_{R,k}^C = \{R_0, \mathbf{L}_0, R_1^C(a_0), \mathbf{L}_1^C(a_0), \dots, \mathbf{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2}), R_k^C(\bar{\mathbf{a}}_{k-1}), \forall \bar{\mathbf{a}}_{k-1} \in \bar{\mathcal{A}}_{k-1}\}$ and $\mathbf{Z}_{L,k}^C = \{R_0, \mathbf{L}_0, R_1^C(a_0), \mathbf{L}_1^C(a_0), \dots, \mathbf{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2}), R_k^C(\bar{\mathbf{a}}_{k-1}), \mathbf{L}_k^C(\bar{\mathbf{a}}_{k-1}), \forall \bar{\mathbf{a}}_{k-1} \in \bar{\mathcal{A}}_{k-1}\}$ denote the set of corresponding counterfactual variables for $k = 1, \dots, K$. Thus $\mathbf{Z}_{R,K}^C = \mathbf{Z}^C$ is the full set of counterfactuals up to t_K .

Then joint density of $(\mathbf{Z}_k^C, \bar{\mathbf{A}}_{k-1})$ can be linked to the observed variables as

$$\begin{aligned}
p_{\mathbf{Z}_{R,k}^C, \bar{\mathbf{A}}_{k-1}}(\mathbf{z}_{R,k}, \bar{\mathbf{a}}_{k-1}) &= p_{\mathbf{Z}_{R,k}^C}(\mathbf{z}_{R,k}) p_{\bar{\mathbf{A}}_{k-1} | \mathbf{Z}_{R,k}^C}(\bar{\mathbf{a}}_{k-1} | \mathbf{z}_{R,k}) \\
&= p_{\mathbf{Z}_{R,k}^C}(\mathbf{z}_{R,k}) \prod_{j=1}^{k-1} p_{A_j | \mathbf{Z}_{R,k}^C, \bar{\mathbf{A}}_{j-1}}(a_j | \mathbf{z}_{R,k}, \bar{\mathbf{a}}_{j-1}) \\
&= p_{\mathbf{Z}_{R,k}^C}(\mathbf{z}_{R,k}) \prod_{j=1}^{k-1} p_{A_j | \bar{\mathbf{L}}_j, \bar{\mathbf{R}}_j, \bar{\mathbf{A}}_{j-1}}(a_j | \bar{\mathbf{l}}_j, \bar{\mathbf{r}}_j, \bar{\mathbf{a}}_{j-1})
\end{aligned}$$

Notice the no unmeasured confounders and consistency assumptions are employed here. Similarly,

$$\begin{aligned}
p_{\mathbf{Z}_{L,k}^C, \bar{\mathbf{A}}_{k-1}}(\mathbf{z}_{L,k}, \bar{\mathbf{a}}_{k-1}) &= p_{\mathbf{Z}_{L,k}^C}(\mathbf{z}_{L,k}) p_{\bar{\mathbf{A}}_{k-1} | \mathbf{Z}_{L,k}^C}(\bar{\mathbf{a}}_{k-1} | \mathbf{z}_{L,k}) = p_{\mathbf{Z}_{L,k}^C}(\mathbf{z}_{L,k}) p_{\bar{\mathbf{A}}_{k-1} | \mathbf{Z}_{R,k}^C}(\bar{\mathbf{a}}_{k-1} | \mathbf{z}_{R,k}) \\
&= p_{\mathbf{Z}_{L,k}^C}(\mathbf{z}_{L,k}) \prod_{j=1}^{k-1} p_{A_j | \bar{\mathbf{L}}_j, \bar{\mathbf{R}}_j, \bar{\mathbf{A}}_{j-1}}(a_j | \bar{\mathbf{l}}_j, \bar{\mathbf{r}}_j, \bar{\mathbf{a}}_{j-1})
\end{aligned}$$

Furthermore, the observed data can be further linked to the treatment specific counterfactuals through $\mathbf{Z}_{R,k}^C$ and $\mathbf{Z}_{L,k}^C$.

$$\begin{aligned}
&p_{\bar{\mathbf{R}}_k, \bar{\mathbf{A}}_{k-1}, \bar{\mathbf{L}}_{k-1}}(\bar{\mathbf{r}}_k, \bar{\mathbf{a}}_{k-1}, \bar{\mathbf{l}}_{k-1}) \\
&= \int_{\{\mathbf{u}: \bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1}) = \bar{\mathbf{r}}_k, \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2}) = \bar{\mathbf{l}}_{k-1}\}} p_{\mathbf{Z}_{R,k}^C, \bar{\mathbf{A}}_{k-1}}(\mathbf{u}, \bar{\mathbf{a}}_{k-1}) d\mu_{\mathbf{Z}_{R,k}^C}(\mathbf{u}) \\
&= \int_{\{\mathbf{u}: \bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1}) = \bar{\mathbf{r}}_k, \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2}) = \bar{\mathbf{l}}_{k-1}\}} p_{\mathbf{Z}_{R,k}^C}(\mathbf{u}) \prod_{j=1}^{k-1} p_{A_j | \bar{\mathbf{L}}_j, \bar{\mathbf{R}}_j, \bar{\mathbf{A}}_{j-1}}(a_j | \bar{\mathbf{l}}_j, \bar{\mathbf{r}}_j, \bar{\mathbf{a}}_{j-1}) d\mu_{\mathbf{Z}_{R,k}^C}(\mathbf{u}) \\
&= \int_{\{\mathbf{u}: \bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1}) = \bar{\mathbf{r}}_k, \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2}) = \bar{\mathbf{l}}_{k-1}\}} p_{\mathbf{Z}_{R,k}^C}(\mathbf{u}) d\mu_{\mathbf{Z}_{R,k}^C}(\mathbf{u}) \cdot \prod_{j=1}^{k-1} p_{A_j | \bar{\mathbf{L}}_j, \bar{\mathbf{R}}_j, \bar{\mathbf{A}}_{j-1}}(a_j | \bar{\mathbf{l}}_j, \bar{\mathbf{r}}_j, \bar{\mathbf{a}}_{j-1}) \\
&= p_{\bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1}), \bar{\mathbf{L}}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(\bar{\mathbf{r}}_k, \bar{\mathbf{l}}_{k-1}) \cdot \prod_{j=1}^{k-1} p_{A_j | \bar{\mathbf{L}}_j, \bar{\mathbf{R}}_j, \bar{\mathbf{A}}_{j-1}}(a_j | \bar{\mathbf{l}}_j, \bar{\mathbf{r}}_j, \bar{\mathbf{a}}_{j-1})
\end{aligned}$$

Similarly,

$$p_{\bar{\mathbf{L}}_k, \bar{\mathbf{R}}_k, \bar{\mathbf{A}}_{k-1}}(\bar{\mathbf{l}}_k, \bar{\mathbf{r}}_k, \bar{\mathbf{a}}_{k-1}) = p_{\bar{\mathbf{L}}_k^C(\bar{\mathbf{a}}_{k-1}), \bar{\mathbf{R}}_k^C(\bar{\mathbf{a}}_{k-1})}(\bar{\mathbf{l}}_k, \bar{\mathbf{r}}_k) \cdot \prod_{j=1}^{k-1} p_{A_j | \bar{\mathbf{L}}_j, \bar{\mathbf{R}}_j, \bar{\mathbf{A}}_{j-1}}(a_j | \bar{\mathbf{l}}_j, \bar{\mathbf{r}}_j, \bar{\mathbf{a}}_{j-1})$$

Thus, for $k = 2, \dots, K$, we have

$$\begin{aligned}
p_{R_k^C(\bar{\mathbf{a}}_{k-1})|\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2}),\bar{R}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(r_k|\bar{\mathbf{l}}_{k-1},\bar{\mathbf{r}}_{k-1}) &= \frac{p_{\bar{R}_k^C(\bar{\mathbf{a}}_{k-1}),\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(\bar{\mathbf{r}}_k,\bar{\mathbf{l}}_{k-1})}{p_{\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2}),\bar{R}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(\bar{\mathbf{l}}_{k-1},\bar{\mathbf{r}}_{k-1})} \\
&= \frac{p_{\bar{R}_k^C(\bar{\mathbf{a}}_{k-1}),\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(\bar{\mathbf{r}}_k,\bar{\mathbf{l}}_{k-1}) \cdot \prod_{j=1}^{k-1} p_{A_j|\bar{L}_j,\bar{R}_j,\bar{A}_{j-1}}(a_j|\bar{\mathbf{l}}_j,\bar{\mathbf{r}}_j,\bar{\mathbf{a}}_{j-1})}{p_{\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2}),\bar{R}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(\bar{\mathbf{l}}_{k-1},\bar{\mathbf{r}}_{k-1}) \cdot \prod_{j=1}^{k-1} p_{A_j|\bar{L}_j,\bar{R}_j,\bar{A}_{j-1}}(a_j|\bar{\mathbf{l}}_j,\bar{\mathbf{r}}_j,\bar{\mathbf{a}}_{j-1})} \\
&= \frac{p_{\bar{R}_k,\bar{A}_{k-1},\bar{L}_{k-1}}(\bar{\mathbf{r}}_k,\bar{\mathbf{a}}_{k-1},\bar{\mathbf{l}}_{k-1})}{p_{\bar{L}_{k-1},\bar{R}_{k-1},\bar{A}_{k-2}}(\bar{\mathbf{l}}_{k-1},\bar{\mathbf{r}}_{k-1},\bar{\mathbf{a}}_{k-2})p_{A_{k-1}|\bar{L}_{k-1},\bar{R}_{k-1},\bar{A}_{k-2}}(a_{k-1}|\bar{\mathbf{l}}_{k-1},\bar{\mathbf{r}}_{k-1},\bar{\mathbf{a}}_{k-2})} \\
&= p_{R_k|\bar{A}_{k-1},\bar{L}_{k-1},\bar{R}_{k-1}}(r_k|\bar{\mathbf{a}}_{k-1},\bar{\mathbf{l}}_{k-1},\bar{\mathbf{r}}_{k-1})
\end{aligned}$$

Similarly, we can have for $k = 2, \dots, K - 1$

$$\begin{aligned}
& p_{L_k^C(\bar{\mathbf{a}}_{k-1})|\bar{R}_k^C(\bar{\mathbf{a}}_{k-1}),\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(l_k|\bar{\mathbf{r}}_{k-1},\bar{\mathbf{l}}_{k-1}) \\
&= \frac{p_{L_k^C(\bar{\mathbf{a}}_{k-1}),\bar{R}_k^C(\bar{\mathbf{a}}_{k-1})}(\bar{\mathbf{l}}_k,\bar{\mathbf{r}}_k)}{p_{\bar{R}_k^C(\bar{\mathbf{a}}_{k-1}),\bar{L}_{k-1}^C(\bar{\mathbf{a}}_{k-2})}(\bar{\mathbf{r}}_k,\bar{\mathbf{l}}_{k-1})} = \frac{p_{\bar{L}_k,\bar{R}_k,\bar{A}_{k-1}}(\bar{\mathbf{l}}_k,\bar{\mathbf{r}}_k,\bar{\mathbf{a}}_{k-1})}{p_{\bar{R}_k,\bar{A}_{k-1},\bar{L}_{k-1}}(\bar{\mathbf{r}}_k,\bar{\mathbf{a}}_{k-1},\bar{\mathbf{l}}_{k-1})} \\
&= p_{L_k|\bar{R}_k,\bar{A}_{k-1},\bar{L}_{k-1}}(l_k|\bar{\mathbf{r}}_k,\bar{\mathbf{a}}_{k-1},\bar{\mathbf{l}}_{k-1})
\end{aligned}$$

This completes the argument.

Web Appendix B: Proof of Property 1

For a given regime g , $C_k^b = A_k g_k^b(\bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{a}}_{k-1}) + (1 - A_k)\{1 - g_k^b(\bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{a}}_{k-1})\}$ for $k = 0, \dots, K - 1$, thus,

(i) For the case that $a_{k-1} = 0$ and thus $\bar{\mathbf{a}}_{k-1} = \mathbf{0}$

$$\begin{aligned}
& P(C_k^b = 1|\bar{C}_{k-1}^b = \bar{\mathbf{1}}, \bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{a}}_{k-1}) \\
&= E \left\{ I \left([A_k g_k^b(\bar{\mathbf{O}}_k, \bar{\mathbf{A}}_{k-1}) + (1 - A_k)\{1 - g_k^b(\bar{\mathbf{O}}_k, \bar{\mathbf{A}}_{k-1})\}] = 1 \right) |\bar{C}_{k-1}^b = \bar{\mathbf{1}}, \bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{0}} \right\} \\
&= E \left\{ I(A_k = 1) |\bar{C}_{k-1}^b = \bar{\mathbf{1}}, \bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{0}} \right\} I \{g^b(\bar{\mathbf{o}}_k, \bar{\mathbf{a}}_{k-1}) = 1\} \\
&\quad + E \left\{ I(A_k = 0) |\bar{C}_{k-1}^b = \bar{\mathbf{1}}, \bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{0}} \right\} I \{g^b(\bar{\mathbf{o}}_k, \bar{\mathbf{a}}_{k-1}) = 0\} \\
&= P(A_k = 1|\bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{a}}_{k-1}) I \{g^b(\bar{\mathbf{o}}_k, \bar{\mathbf{a}}_{k-1}) = 1\} \\
&\quad + P(A_k = 0|\bar{\mathbf{O}}_k = \bar{\mathbf{o}}_k, \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{a}}_{k-1}) I \{g^b(\bar{\mathbf{o}}_k, \bar{\mathbf{a}}_{k-1}) = 0\}
\end{aligned}$$

(ii) For the case that $a_{k-1} = 1$, the patient will stay on treatment after t_{k-1} by the setting, so we have $P(C_k^b = 1 | \bar{C}_{k-1}^b = \bar{\mathbf{1}}, \bar{O}_k = \bar{o}_k, \bar{A}_{k-1} = \bar{a}_{k-1}) = 1$, on the other hand,

$$\begin{aligned} P(A_k = 1 | \bar{O}_k = \bar{o}_k, \bar{A}_{k-1} = \bar{a}_{k-1}) &= I\{g^b(\bar{o}_k, \bar{a}_{k-1}) = 1\} = 1 \\ P(A_k = 0 | \bar{O}_k = \bar{o}_k, \bar{A}_{k-1} = \bar{a}_{k-1}) &= I\{g^b(\bar{o}_k, \bar{a}_{k-1}) = 0\} = 0 \end{aligned}$$

thus, we have

$$\begin{aligned} &P(C_k^b = 1 | \bar{C}_{k-1}^b = \bar{\mathbf{1}}, \bar{O}_k = \bar{o}_k, \bar{A}_{k-1} = \bar{a}_{k-1}) \\ &= P(A_k = 1 | \bar{O}_k = \bar{o}_k, \bar{A}_{k-1} = \bar{a}_{k-1}) I\{g^b(\bar{o}_k, \bar{a}_{k-1}) = 1\} \\ &\quad + P(A_k = 0 | \bar{O}_k = \bar{o}_k, \bar{A}_{k-1} = \bar{a}_{k-1}) I\{g^b(\bar{o}_k, \bar{a}_{k-1}) = 0\} \end{aligned}$$

Property 1 then follows by combining (i) and (ii).

Web Appendix C: Proof of Proposition 1

The consistency of $\hat{\mu}^b$ can be proved by first proving the consistency of $\hat{\Lambda}^b(t)$ for $t \in (0, t_K]$. For subject i , let T_i be the observed event time and D_i be the censoring time for subject i . Let T_i^b be the counterfactual event time if subject i follows regime g^b . For simplicity, here, we consider the setting we used in our simulation studies that D_i is unconditionally independent of T_i and T_i^b . The more general setting where D_i is conditionally independent of T_i and T_i^b can be proved in a very similar way. Let $X_i = \min\{T_i, D_i\}$ and $\delta_i = I(T_i \leq D_i)$. The observed event counting process is defined as $N_i(t) = \delta_i I(X_i \leq t)$, and denote the at risk indicator by $Y_i(t) = I(X_i \geq t)$. Let $\hat{w}_{A,k,i}^b$ and $w_{A,k,i}^b$ be the estimated and true weight for subject i at time t_k , respectively. Similarly, for the g^b specific outcome we will have $X_i^b = \min\{T_i^b, D_i\}$, $\delta_i = I(T_i^b \leq D_i)$ and $N_i^b(t) = \delta_i^b I(X_i^b \leq t)$, $Y_i^b(t) = I(X_i^b \geq t)$. If we denote $\hat{w}_{A,i}^b(t) = \hat{w}_{A,k,i}^b$ and $w_{A,0,i}^b(t) = w_{A,k,i}^b$ with $k = \max_j\{t_j \leq t\}$ for $t \in (0, t_K)$, then the weighted Nelson-Aalen estimator can be written as

$$\begin{aligned} \hat{\Lambda}^b(t) &= \frac{1}{n} \sum_{i=1}^n \int_0^t \frac{\hat{w}_{A,i}^b(s)}{n^{-1} \sum_{j=1}^n Y_j(s) \hat{w}_{A,j}^b(s)} dN_i(s) \\ &= \int_0^t \frac{n^{-1} \sum_{i=1}^n \hat{w}_{A,i}^b(s) dN_i(s)}{n^{-1} \sum_{j=1}^n Y_j(s) \hat{w}_{A,j}^b(s)} \end{aligned}$$

when the weight are consistently estimated, i.e. $\hat{w}_{A,i}^b(s) \rightarrow w_{A,0,i}^b(s)$ for $k = \max_j \{t_j \leq s\}$ as $n \rightarrow \infty$, by the Weak Law of Large Numbers (WLLN), one can obtain that $n^{-1} \sum_{j=1}^n Y_j(s) \hat{w}_{A,j}^b(s)$ converges to $E \{Y_i(s) w_{A,0,i}^b(s)\}$, while

$$\begin{aligned}
& E \{Y_i(s) w_{A,0,i}^b(s)\} = E [E \{Y_i(s) w_{A,0,i}^b(s) | \bar{\mathbf{O}}_{k,i}, \bar{\mathbf{A}}_{k-1,i}\}] \\
& = E \left[E \left\{ Y_i(s) \frac{I(\bar{\mathbf{C}}_{k,i}^b = \bar{\mathbf{1}} | \bar{\mathbf{O}}_{k,i}, \bar{\mathbf{A}}_{k-1,i})}{P(\bar{\mathbf{C}}_{k,i}^b = \bar{\mathbf{1}} | \bar{\mathbf{O}}_{k,i}, \bar{\mathbf{A}}_{k-1,i})} | \bar{\mathbf{O}}_{k,i}, \bar{\mathbf{A}}_{k-1,i} \right\} \right] \\
& = E \left[\frac{P(\bar{\mathbf{C}}_{k,i}^b = \bar{\mathbf{1}} | \bar{\mathbf{O}}_{k,i} = \bar{\mathbf{o}}_{k,i}, \bar{\mathbf{A}}_{k-1,i} = \bar{\mathbf{a}}_{k-1,i})}{P(\bar{\mathbf{C}}_{k,i}^b = \bar{\mathbf{1}} | \bar{\mathbf{O}}_{k,i} = \bar{\mathbf{o}}_{k,i}, \bar{\mathbf{A}}_{k-1,i} = \bar{\mathbf{a}}_{k-1,i})} E \{Y_i(s) | \bar{\mathbf{O}}_{k,i} = \bar{\mathbf{o}}_{k,i}, \bar{\mathbf{A}}_{k-1,i} = \bar{\mathbf{a}}_{k-1,i}\} \right] \\
& = E \{Y_i(s) | \bar{\mathbf{O}}_{k,i} = \bar{\mathbf{o}}_{k,i}, \bar{\mathbf{A}}_{k-1,i} = \bar{\mathbf{a}}_{k-1,i}\} \\
& = E \left[E \left\{ Y_i^b(s) | \bar{\mathbf{O}}_{k,i}^C(g^b) = \bar{\mathbf{o}}_{k,i} \right\} \right] \\
& = E \{Y_i^b(s)\} = P(D_i > s) S^b(s)
\end{aligned}$$

Notice here only the g^b adherent person-time pieces from observed data were included here, i.e. $a_{k,i} = g_k^b(\bar{\mathbf{o}}_{k,i}, \bar{\mathbf{a}}_{k-1,i})$ for $k = 1, \dots, K-1$. Thus, the second last equality holds by the results in Web Appendix A. Using similar techniques, one can show that $n^{-1} \sum_{i=1}^n \hat{w}_{A,i}^b(s) dN_i(s)$ converges to $P(D_i > s) dF^b(s)$ as $n \rightarrow \infty$. By combining these two parts, one can obtain that $\hat{\Lambda}^b(t) \rightarrow \Lambda_0^b(t)$. It is then straightforward to show that $\hat{\mu}^b$ converges to μ_0^b as $n \rightarrow \infty$ using the continuous mapping theorem.

Web Appendix D: The true weights in simulation study

In our setting, we consider the treatment regime when the number of decision making stages is relatively large, since $\bar{\mathcal{A}}_k$ grows very fast with the increase of k , a practical problem is then for certain regimes the positivity assumption may not always hold. Thus it is possible that, a regime we are interested in may not always be viable across all iterations of our simulations. To avoid this problem and make sure the regimes of interest are estimable, we set up the simulation to make sure that there is no very extreme values for the true weights among the regimes of interest. To better understand this point, here we briefly explain how the probabilities of observing different

regimes in our simulation are connected to the true weights, and how the weights are bounded away from extreme values.

In the simulation study, we generate the observational data by randomly assigning a patient to one treatment regime in a given set of finite number of regimes (10 for Scenario 1 and 100 for Scenario 2). This is trying to mimic the situation where patients may go to different physicians and/or different hospitals. Meanwhile, we will show below that, this also guaranteed that the true weights for each of these regimes involved are bounded.

First, it may not be obvious how such a mechanism is connected with time-dependent treatment assignment $P(A_k | \bar{\mathbf{A}}_{k-1}, \bar{\mathbf{O}}_k)$ at time t_k , $k = 1, \dots, K$. Let $\overline{\text{PSA}}_K^0$ denote the counterfactual SADT free PSA trajectory. As mentioned in the paper, for a given regime g^b , we can determine the time to initial SADT solely based on $\overline{\text{PSA}}_K^0$ as

$$U^b = \min\{t_k : \text{PSA}_k^0 \geq b, \text{PSA}_{k-1}^0 < b, \text{PSA}_k^0 > \text{PSA}_{k-1}^0, k = 1, \dots, K\}$$

For patients whose PSA does not go above the threshold b , i.e., will not be assigned to SADT within the time period of the study if they follow regime g^b , we denote the observed SADT initiation time $U^b = \infty$. Then for all J regimes that were used to simulate the observational data $g^{b_1}, g^{b_2}, \dots, g^{b_J}$, we can calculate the treatment time $U^{b_1}, U^{b_2}, \dots, U^{b_J}$. Let p_j denote the probability to assign to regime g^{b_j} , $j = 1, \dots, J$, then the probability to start treatment at t_k can be written as

$$P(A_k = 1 | \bar{\mathbf{A}}_{k-1} = \bar{\mathbf{0}}, \bar{\mathbf{O}}_k) = \sum_{j=1}^J I\{U^{b_j} = t_k\} \times p_j.$$

i.e. the probability to initiate SADT at t_k is the sum of probabilities of observing the regimes which would initiate SADT at t_k according to the patient's given SADT free PSA trajectory. Furthermore, we can calculate the true weight for regime g^b adherence as

$$w_{A,k}^b = \frac{I\{C_k^b = 1 | \bar{\mathbf{C}}_{k-1}^b = \bar{\mathbf{1}}, \bar{\mathbf{O}}_k\}}{P(C_k^b = 1 | \bar{\mathbf{C}}_{k-1}^b = \bar{\mathbf{1}}, \bar{\mathbf{O}}_k)}$$

where there are two cases:

- (i) If the observed treatment $\bar{\mathbf{a}}_k = \bar{\mathbf{0}}$, i.e. the patient did not receive

SADT up to time t_k , we have

$$P(C_k^b = 1 | \overline{C}_{k-1}^b = \overline{\mathbf{1}}, \overline{\mathbf{O}}_k) = 1 - \sum_{l=1}^k P(A_l = 1 | \overline{\mathbf{A}}_{l-1} = \overline{\mathbf{0}}, \overline{\mathbf{O}}_l),$$

(ii) If there exists $l \leq k$ such that $a_l = 1$ and $\overline{a}_{l-1} = \overline{\mathbf{0}}$, i.e. we observe the patient starts SADT at t_l before or at t_k , then

$$P(C_k^b = 1 | \overline{C}_{k-1}^b = \overline{\mathbf{1}}, \overline{\mathbf{O}}_k) = P(A_l = 1 | \overline{\mathbf{A}}_{l-1} = \overline{\mathbf{0}}, \overline{\mathbf{O}}_l).$$

Thus in both (i) and (ii) we can calculate $w_{A,k}^b$ from $\{p_j : j = 1, \dots, J\}$. Furthermore, since the regime of interest is within the set of regimes used to generate the observational data. and $p_j > 0$ for all $j = 1, \dots, J$. For case (i), there exists at least one regime g^{b_q} (the regime of interest) with $\overline{\mathbf{A}}_{k-1}^{b_q} = \overline{\mathbf{0}}$, thus we have $\sum_{l=1}^k P(A_l = 1 | \overline{\mathbf{A}}_{l-1} = \overline{\mathbf{0}}, \overline{\mathbf{O}}_l) < \sum_{j=1}^J p_j = 1$, i.e. $P(C_k^b = 1 | \overline{C}_{k-1}^b = \overline{\mathbf{1}}, \overline{\mathbf{O}}_k) > 0$. Similarly, for case (ii), there exists at least one regime g^{b_q} (the regime of interest) with $A_l^{b_q} = 1$ and $\overline{\mathbf{A}}_{l-1}^{b_q} = \overline{\mathbf{0}}$, thus $P(C_k^b = 1 | \overline{C}_{k-1}^b = \overline{\mathbf{1}}, \overline{\mathbf{O}}_k) = P(A_l = 1 | \overline{\mathbf{A}}_{l-1} = \overline{\mathbf{0}}, \overline{\mathbf{O}}_l) \geq p_q > 0$. Thus the positivity assumption holds in our simulation settings.