Using a monotonic density ratio model to find the
asymptotically optimal combination of multiple diagnostic
tests: Supplementary document

Baojiang Chen¹, Pengfei Li², Jing Qin³, and Tao Yu⁴

¹Baojiang Chen is Assistant Professor, Department of Biostatistics, University of
Nebraska Medical Center, Omaha, Nebraska 68198, U.S.A.

(Email: *baojiang.chen@unmc.edu*)

²Pengfei Li is Associate Professor, Department of Statistics and Actuarial Sciences,
University of Waterloo, Waterloo, ON, Canada, N2L 3G1

(Email: *pengfei.li@uwaterloo.ca*)

³Jing Qin is Mathematical Statistician, National Institute of Allergy and Infectious
Diseases, National Institutes of Health, MD 20892, U.S.A.

(Email: *jingqin@niaid.nih.gov*)

⁴Tao Yu is Assistant Professor, Department of Statistics & Applied Probability, National
University of Singapore, Singapore, 117546

(Email: *stayt@nus.edu.sg*)

1. INTRODUCTION

This is a supplementary document to the corresponding paper submitted to the *Journal of the American Statistical Association*. It contains the simulation studies for the cases where $h(\cdot)$ and $v(\cdot)$ in model (2) in the main paper are misspecified (see Section 2); supplementary

technical details for the Appendix of the main paper (see Section 3); further simulation results, which are additional to those in Sections 4.1–4.3 of the main paper (see Cases I, II, and IV in Sections 4, 5, and 7) and Section 2 of this document (see Case III in Section 6); and simulation studies for combinations of more biomarkers (see Section 8).

For the simulation studies in Sections 4–8, we compare the following methods: (1) that based on the proposed semiparametric monotonic density ratio model (2) in the main paper (i.e., the *monotone density ratio* method); (2) the exponential tilting method by Qin and Zhang (2010) (i.e., the *exponential tilting* method); (3) that based on the nonparametric logistic regression type models by Ma and Huang (2005, 2007), in which, basically for all possible linear combinations of biomarkers, they maximize the area of the ROC (Huang et al. 2011) (i.e., the *MH* method); (4) the nonparametric method based on best linear combinations by Vexler et al. (2006) (i.e., the *nonparametric* method); (5) the min-max linear combination method by Liu et al. (2011) (i.e., the *min-max* method); (6) the linear combination based on the decision tree by Breiman et al. (1984) (i.e., the *tree* method); and (7) the smoothed empirical likelihood estimator by Chen et al. (2015) (i.e., the *smoothed EL* method). We consider several combinations of sample sizes (n_0, n_1) , namely $(30, 30)$, $(200, 100)$, $(300, 200)$, $(1000, 500)$, and $(1000, 1000)$. The other simulation parameters are as in Section 4 of the main paper. We observe that the min-max method and the tree method do not lead to β estimates comparable with those of the other methods; therefore, they do not appear in the tables of Sections 7 and 8. Furthermore, in Sections 4–6, in addition to the averaged ROC curve estimates, we also compute the corresponding averages of the integrated absolute errors (IAEs) of the ROC estimates over 2000 replicates, where the IAE of a ROC estimate is defined to be

$$\int_0^1 \left| \widehat{\text{ROC}}(s) - \text{ROC}^{\text{true}}(s) \right| ds.$$

This measurement evaluates the efficacy of the different methods in combining the biomarkers.

Based on our numerical studies, we observe that our method leads to very promising results. All the conclusions we have drawn in the main part of the paper and Section 2 are applicable in Sections 4–8; please refer to these sections for a more detailed discussion.

2. SIMULATION STUDY FOR MISSPECIFICATION OF $h(\cdot)$ AND $v(\cdot)$

In this section, we study the robustness of the proposed method to the misspecification of model (2) in the main paper. In particular, $h(\mathbf{x})$ and $v(\mathbf{x}; \boldsymbol{\beta})$ in this model are misspecified.

First, we consider the case where $h(\mathbf{x})$ is misspecified. The simulation setup is the same as that in Section 4.2 in the main paper except that when processing the data, we use $\log(X_1)$ and $\log(X_2)$ instead of X_1 and X_2 in the linear combination; here $\lambda_0 = \lambda_1 = 1$. Clearly, $h(\mathbf{x})$ in model (2) in the main paper is misspecified. Figure 1 demonstrates that the proposed and MH methods yield a much smaller bias in the ROC estimation than the exponential tilting method does. The corresponding AUCs, however, are very close: 0.88, 0.88, and 0.87 respectively. This indicates that AUC may not be a good criterion for deriving the optimal combinations of biomarkers.

Second, we consider the case where $v(\mathbf{x}; \boldsymbol{\beta})$ is misspecified. The model setup is the same as that in Section 4.1 in the main paper except that when processing the data, we use (X_1, X_2^2) instead of $(X_1, X_2, X_1^2, X_2^2, X_1 X_2)$ in the linear combination, so that $v(\mathbf{x}; \boldsymbol{\beta})$ in model (2) in the main paper is misspecified. Here $\lambda_0 = \lambda_1 = 1$. Figure 2 demonstrates that the proposed method leads to a much smaller bias in the ROC estimation than the MH and exponential tilting methods do.

3. SUPPLEMENTARY TECHNICAL DETAILS

In this section, we provide technical details for Lemmas 2 and 3, and Theorems A.1 and A.2 in the Appendix of the main paper.

Figure 1: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate exponential distribution.

3.1 Condition **A**, Lemmas, and Theorems to be Proved

The following set of conditions (Condition **A**) is needed for our technical development.

A1. $\beta \in \{1\} \times \mathbf{B}_{-1}$ and $\mathbf{B}_{-1}$ is a compact subspace of $\mathbf{R}^{p-1}$.

A2. There exists a constant C_0 independent of u such that

$$\int |I(\beta_1^\tau \mathbf{h}(\mathbf{x}) \leq u) - I(\beta_2^\tau \mathbf{h}(\mathbf{x}) \leq u)| dP(\mathbf{x}) \leq C_0 \|\beta_1 - \beta_2\|_1$$

for $P = F_0$ and G_0 . Here $\|\beta_1 - \beta_2\|_1$ is the L_1 norm of $\beta_1 - \beta_2$.

Figure 2: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate normal distribution

A3. $\theta(\cdot)$ is a monotonically increasing function such that if $\theta(v(\mathbf{x}; \boldsymbol{\beta})) = \theta_0(v(\mathbf{x}; \boldsymbol{\beta}_0))$ for all $\mathbf{x}$, then $\boldsymbol{\beta} = \boldsymbol{\beta}_0$ and $\theta(\cdot) = \theta_0(\cdot)$.

A4. $F_C(y)$ is Lipschitz continuous; $G_C(y)$ is second-order continuously differentiable with bounded second-order derivatives.

In this supplementary document, we shall prove the following lemmas and theorems. The first lemma below is Lemma 2 in the Appendix of the main paper; it establishes the δ -entropy with bracketing of the single-index class

$$\Lambda = \{\theta(v(\mathbf{x}; \boldsymbol{\beta})) : \theta(\cdot) \in \Theta, \boldsymbol{\beta} \in \mathbf{B}\},$$

where

$$\Theta = \{\theta(\cdot) : \theta(\cdot) \in [0, 1] \text{ and is monotonic increasing}\}.$$

The idea of the proof is close to that of Theorem 1.2.3 in Tanaka (2013).

Lemma S.1 *Suppose Conditions A1 and A2 are satisfied. For $P = F_0$, $P = G_0$, and $P = H_0$, any $\delta > 0$, and any integer $q > 0$, we have*

(a) if $\delta \leq 1$,

$$H_{q,B}(\delta, \Lambda, P) \lesssim 1/\delta$$

where “ $\lesssim$ ” is up to a universal constant depending only on p and q ;

(b) if $\delta > 1$, we have

$$H_{q,B}(\delta, \Lambda, P) = 0.$$

Furthermore, Λ is F_0 -G-C and G_0 -G-C.

Lemma S.2 below is Lemma 3 in the Appendix of the main paper.

Lemma S.2 *Let*

$$\gamma_1(\mathbf{x}; \theta, \beta) = 4\lambda \left\{ \sqrt{\frac{\theta(v(\mathbf{x}; \beta))}{\theta_0(v(\mathbf{x}; \beta_0))}} - 1 \right\} \quad (1)$$

and

$$\gamma_2(\mathbf{x}; \theta, \beta) = 4(1 - \lambda) \left\{ \sqrt{\frac{1 - \theta(v(\mathbf{x}; \beta))}{1 - \theta_0(v(\mathbf{x}; \beta_0))}} - 1 \right\}. \quad (2)$$

Further, let

$$F_{n_1}(\mathbf{x}) = \frac{1}{n_1} \sum_{i=1}^{n_1} I(\mathbf{Y}_i \leq \mathbf{x}), \quad G_{n_0}(\mathbf{x}) = \frac{1}{n_0} \sum_{j=1}^{n_0} I(\mathbf{X}_j \leq \mathbf{x}),$$

which are the empirical cumulative distribution functions of $\{\mathbf{Y}_1, \dots, \mathbf{Y}_{n_1}\}$ and $\{\mathbf{X}_1, \dots, \mathbf{X}_{n_0}\}$, respectively. Then we have

$$\begin{aligned} d^2(\hat{\theta}(v(\mathbf{x}; \hat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))) &\leq \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{F_{n_1}(\mathbf{x}) - F_0(\mathbf{x})\} \\ &\quad + \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{G_{n_0}(\mathbf{x}) - G_0(\mathbf{x})\}. \end{aligned} \quad (3)$$

Theorem S.1 below is Theorem A.1 in the Appendix of the main paper.

Theorem S.1 *Assume Condition A above. We have*

- (a) $d\left(\widehat{\theta}(v(\mathbf{x}; \widehat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))\right) = o_p(1);$
- (b) $\widehat{\beta} - \beta_0 = o_p(1).$

Theorem S.2 below is Theorem A.2 in the Appendix of the main paper.

Theorem S.2 *Assume Condition A above. We have*

- (a) $\sup_{u \in \mathbf{R}} |\widehat{F}_C(u) - F_C(u; \beta_0)| = o_p(1)$ and $\sup_{u \in \mathbf{R}} |\widehat{G}_C(u) - G_C(u; \beta_0)| = o_p(1);$
- (b) $\sup_{0 \leq s \leq 1} |\widehat{\text{ROC}}_C(s) - \text{ROC}_C(s)| = o_p(1);$
- (c) $\widehat{\text{AUC}}_C = \text{AUC}_C + o_p(1).$

3.2 Lemmas Adapted from the Empirical Process Literature

Our proof relies heavily on some results in empirical processes. We first review some results.

In the proofs of Theorems S.1 and S.2, we use the Glivenko–Cantelli theorem, which gives sufficient conditions for

$$\sup_{g \in \mathcal{G}} \left| \int g d(P_n - P) \right| = o_p(1),$$

i.e., Equation (A.1) in the main paper, to hold.

Lemma S.3 *If $H_{1,B}(\delta, \mathcal{G}, P) < \infty$ for any $\delta > 0$, then*

$$\sup_{g \in \mathcal{G}} \left| \int g d(P_n - P) \right| = o_p(1).$$

For the class $\mathcal{G}$, the function $G = \sup_{g \in \mathcal{G}}$ is called the envelope of $\mathcal{G}$. The following lemma provides useful results for building up G-C classes from other G-C classes (Kosorok 2008, p. 169).

Lemma S.4 *Let $\mathcal{F}$ and $\mathcal{G}$ be P -G-C classes with respective integrable envelopes F and G . Then the following are true:*

(i) $\mathcal{F} + \mathcal{G}$ is P -G-C.

(ii) $\mathcal{F} \cdot \mathcal{G}$ is P -G-C provided $\int F \cdot G dP < \infty$.

(iii) Let ϕ be a continuous function. Then $\phi(\mathcal{F})$ is P -G-C provided it has an integrable envelope.

3.3 Proof of Lemma S.1

Part (a). We consider only $P = F_0$; the proof can be similarly applied to $P = G_0$ and $P = H_0$. It suffices to show that for any given $\delta > 0$, we can find a set with a finite number of pairs of functions that covers Λ .

First, we construct a set that covers $\{\beta^\tau \mathbf{h}(\mathbf{x}) : \beta \in \mathbf{B}\}$. For any given $\delta > 0$, let $\delta_1 = \frac{1}{p2^p C_0} \cdot \left(\frac{\delta}{4}\right)^q$ with C_0 being defined in Condition A2. Since $\mathbf{B}$ is a compact subset of $\mathbf{R}^p$, we can find $\beta_1, \dots, \beta_N$ with $N \lesssim \frac{p^p}{\delta_1^p}$, such that

$$\mathbf{B} = \cup_{j=1}^N \{\beta : \|\beta - \beta_j\|_1 < \delta_1, \beta \in \mathbf{B}\}.$$

For $j = 1, \dots, N$, define

$$\beta_{j+} = \beta_j + (0, \delta_1, \dots, \delta_1)^\tau, \quad \beta_{j-} = \beta_j - (0, \delta_1, \dots, \delta_1)^\tau, \quad j = 1, \dots, N$$

and

$$l_j(\mathbf{x}) = \beta_{j-}^\tau \mathbf{h}^+(\mathbf{x}) - \beta_{j+}^\tau \mathbf{h}^-(\mathbf{x}), \quad u_j(\mathbf{x}) = \beta_{j+}^\tau \mathbf{h}^+(\mathbf{x}) - \beta_{j-}^\tau \mathbf{h}^-(\mathbf{x})$$

with $\mathbf{h}^+(\mathbf{x})$ and $\mathbf{h}^-(\mathbf{x})$ being the positive part and negative part of $\mathbf{h}(\mathbf{x})$, respectively.

Note that for any $\beta \in \mathbf{B}$, we can find a j such that $\|\beta - \beta_j\|_1 < \delta_1$. Since $\beta_{j-} < \beta < \beta_{j+}$, we have that

$$l_j(\mathbf{x}) \leq \beta^\tau \mathbf{h}(\mathbf{x}) = \beta^\tau \mathbf{h}^+(\mathbf{x}) - \beta^\tau \mathbf{h}^-(\mathbf{x}) \leq u_j(\mathbf{x}).$$

Then $\{(l_j(\mathbf{x}), u_j(\mathbf{x}))\}_{j=1}^N$ forms a set covering $\{\beta^\tau \mathbf{h}(\mathbf{x}) : \beta \in \mathbf{B}\}$.

Next, for each given j , we construct a set that covers the class Θ of monotonically increasing functions. Let $P_j(u) = F_C(u; \beta_j)$. For the previously given $\delta > 0$, let $\delta_2 = \delta/10$ and $M_j = N_{q,B}(\delta_2, \Theta, P_j)$. It is well known that $\log M_j \lesssim 1/\delta_2$; see for example Theorem 9.24 in Kosorok (2008). Thus, there exists a set $\{(L_{ij}(u), U_{ij}(u))\}_{i=1}^{M_j}$ satisfying (i)

$$\left\{ \int |L_{ij}(u) - U_{ij}(u)|^q dP_j(u) \right\}^{1/q} \leq \delta_2; \quad (4)$$

and (ii) for any given $\theta(u)$, there exists an i such that $L_{ij}(u) \leq \theta(u) \leq U_{ij}(u)$ for any u . Without loss of generality, we assume that $L_{ij}(u)$ and $U_{ij}(u)$ are monotonically increasing functions, $L_{ij}(u) \in [0, 1]$ and $U_{ij}(u) \in [0, 1]$.

Finally, we argue that

$$\left\{ (L_{ij}(l_j(\mathbf{x})), U_{ij}(u_j(\mathbf{x}))), i = 1, \dots, M_j, j = 1, \dots, N \right\}$$

forms a set satisfying (i)

$$\left\{ \int |U_{ij}(u_j(\mathbf{x})) - L_{ij}(l_j(\mathbf{x}))|^q dP(\mathbf{x}) \right\}^{1/q} \leq \delta; \quad (5)$$

and (ii) for any given $\theta(\beta^\tau \mathbf{h}(\mathbf{x}))$, there exist (j, i) such that

$$L_{ij}(l_j(\mathbf{x})) \leq \theta(\beta^\tau \mathbf{h}(\mathbf{x})) \leq U_{ij}(u_j(\mathbf{x})) \quad (6)$$

for any $\mathbf{x}$. Note that (5) and (6) together imply that

$$H_{q,B}(\delta, \Lambda, P) \leq \log \left(\sum_{j=1}^N M_j \right) \lesssim \log \left(N \max_j \{M_j\} \right) \lesssim -\log \delta_1 + 1/\delta_2 \lesssim 1/\delta,$$

which ensure that Λ is F_0 -G-C and G_0 -G-C by Lemma S.3.

We first show that (6) is correct. Recall that for any given β , there is a j such that $l_j(\mathbf{x}) \leq \beta^\tau \mathbf{h}(\mathbf{x}) \leq u_j(\mathbf{x})$. Further, for any given $\theta(u)$, there exists an i such that $L_{ij}(u) \leq \theta(u) \leq U_{ij}(u)$. Since both $L_{ij}(u)$ and $U_{ij}(u)$ are monotonically increasing functions, we can verify that (6) is correct.

We next argue that (5) is also correct. By the triangle inequality, we have

$$\begin{aligned} & \left\{ \int \left| U_{ij}(u_j(\mathbf{x})) - L_{ij}(l_j(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \\ & \leq \left\{ \int \left| U_{ij}(u_j(\mathbf{x})) - U_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \end{aligned} \quad (7)$$

$$+ \left\{ \int \left| U_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) - L_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \quad (8)$$

$$+ \left\{ \int \left| L_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) - L_{ij}(l_j(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q}. \quad (9)$$

Because of (4), the term in (8) satisfies

$$\left\{ \int \left| U_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) - L_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} = \left\{ \int \left| U_{ij}(u) - L_{ij}(u) \right|^q dP_j(u) \right\}^{1/q} \leq \delta_2. \quad (10)$$

We now consider the term in (7). Since $U_{ij}(u)$ is a monotonically increasing function such that $U_{ij}(u) \in [0, 1]$, we can find a monotonically increasing function $S(u) = \sum_l c_l I(a_l \leq u)$ such that $0 \leq c_l \leq 1$, $\sum_l c_l \leq 1$, and

$$\sup_u |S(u) - U_{ij}(u)| \leq \delta_2.$$

Then

$$\left\{ \int \left| U_{ij}(u_j(\mathbf{x})) - U_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \leq 2\delta_2 + \left\{ \int \left| S(u_j(\mathbf{x})) - S(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q}. \quad (11)$$

Note that

$$\left\{ \int \left| S(u_j(\mathbf{x})) - S(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \leq \sum_l c_l \left\{ \int I(\beta_j^\tau \mathbf{h}(\mathbf{x}) \leq a_l \leq u_j(\mathbf{x})) dP(\mathbf{x}) \right\}^{1/q}. \quad (12)$$

According to the signs of the p elements in $\mathbf{h}(\mathbf{x})$, we partition the integration region in (12) into 2^p subregions. For instance, when $p = 2$ and $\mathbf{h}(\mathbf{x}) = (h_1(\mathbf{x}), h_2(\mathbf{x}))^\tau$, the integration region is partitioned into four subregions:

$$\{\mathbf{x} : \mathbf{h}(\mathbf{x}) \geq 0\} = \{\mathbf{x} : h_1(\mathbf{x}) \geq 0, h_2(\mathbf{x}) \geq 0\}, \{\mathbf{x} : h_1(\mathbf{x}) \geq 0, h_2(\mathbf{x}) \leq 0\},$$

$$\{\mathbf{x} : \mathbf{h}(\mathbf{x}) \leq 0\} = \{\mathbf{x} : h_1(\mathbf{x}) \leq 0, h_2(\mathbf{x}) \leq 0\}, \{\mathbf{x} : h_1(\mathbf{x}) \leq 0, h_2(\mathbf{x}) \geq 0\}.$$

It can be proved that the integration on each of the 2^p subregions is bounded by $pC_0\delta_1$. To see this, consider the integration on the subregion $\{\mathbf{x} : \mathbf{h}(\mathbf{x}) \geq 0\}$:

$$\begin{aligned} & \int_{\mathbf{h}(\mathbf{x}) \geq 0} I(\beta_j^\tau \mathbf{h}(\mathbf{x}) \leq a_l \leq u_j(\mathbf{x})) dP(\mathbf{x}) \\ &= \int_{\mathbf{h}(\mathbf{x}) \geq 0} \left| I(a_l \leq \beta_{j+}^\tau \mathbf{h}(\mathbf{x})) - I(a_l \leq \beta_j^\tau \mathbf{h}(\mathbf{x})) \right| dP(\mathbf{x}) \\ &\leq \int \left| I(a_l \leq \beta_{j+}^\tau \mathbf{h}(\mathbf{x})) - I(a_l \leq \beta_j^\tau \mathbf{h}(\mathbf{x})) \right| dP(\mathbf{x}) \\ &\leq C_0 \|\beta_j - \beta_{j+}\|_1 \leq pC_0\delta_1, \end{aligned}$$

where we use Condition A2 in the last step. The integration on the other subregions can be similarly assessed. Hence,

$$\left\{ \int \left| S(u_j(\mathbf{x})) - S(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \leq (p2^p C_0 \delta_1)^{1/q}. \quad (13)$$

(11) and (13) together lead to

$$\left\{ \int \left| U_{ij}(u_j(\mathbf{x})) - U_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \leq 2\delta_2 + (p2^p C_0 \delta_1)^{1/q}. \quad (14)$$

Similarly,

$$\left\{ \int \left| L_{ij}(\beta_j^\tau \mathbf{h}(\mathbf{x})) - L_{ij}(l_j(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \leq 2\delta_2 + (p2^p C_0 \delta_1)^{1/q}. \quad (15)$$

Combining (7)–(10) and (14)–(15) gives

$$\left\{ \int \left| U_{ij}(u_j(\mathbf{x})) - L_{ij}(l_j(\mathbf{x})) \right|^q dP(\mathbf{x}) \right\}^{1/q} \leq 5\delta_2 + 2(p2^p C_0 \delta_1)^{1/q} = \delta,$$

where in the last step, we use the facts that $\delta_1 = \frac{1}{p2^p C_0} \cdot \left(\frac{\delta}{4}\right)^q$ and $\delta_2 = \delta/10$. Hence, (5) is verified. This completes the proof of Part (a).

Part (b). By the definition of Λ , $\{(0, 1)\}$ is a set of brackets that covers Λ . In addition, for any integer q , $\|1 - 0\|_q = 1 \leq \delta$. Therefore,

$$H_{q,B}(\delta, \mathcal{G}, P) = \log N_{q,B}(\delta, \mathcal{G}, P) = \log 1 = 0.$$

3.4 Proof of Lemma S.2

Since $(\hat{\theta}, \hat{\beta})$ minimizes $M_n(\theta, \beta)$, we have

$$\begin{aligned}
0 &\geq M_n(\hat{\theta}, \hat{\beta}) - M_n(\theta_0, \beta_0) \\
&= -\frac{1}{n} \sum_{i=1}^n \left\{ m_i \log \frac{\hat{\theta}(v(\mathbf{t}_i; \hat{\beta}))}{\theta_0(v(\mathbf{t}_i; \beta_0))} + r_i \log \frac{1 - \hat{\theta}(v(\mathbf{t}_i; \hat{\beta}))}{1 - \theta_0(v(\mathbf{t}_i; \beta_0))} \right\} \\
&= -\frac{1}{n} \left\{ \sum_{i=1}^{n_1} \log \frac{\hat{\theta}(v(\mathbf{Y}_i; \hat{\beta}))}{\theta_0(v(\mathbf{Y}_i; \beta_0))} + \sum_{j=1}^{n_0} \log \frac{1 - \hat{\theta}(v(\mathbf{X}_j; \hat{\beta}))}{1 - \theta_0(v(\mathbf{X}_j; \beta_0))} \right\} \\
&= -\left\{ \lambda \int \log \frac{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{\theta_0(v(\mathbf{x}; \beta_0))} dF_{n_1}(\mathbf{x}) + (1 - \lambda) \int \log \frac{1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{1 - \theta_0(v(\mathbf{x}; \beta_0))} dG_{n_0}(\mathbf{x}) \right\},
\end{aligned}$$

where in the last step, we have used the fact that $\lambda = n_1/n$.

Using the inequality $0.5 \log u \leq \sqrt{u} - 1$ for $u > 0$, we get

$$-\lambda \log \frac{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{\theta_0(v(\mathbf{x}; \beta_0))} \geq 2\lambda \left\{ 1 - \sqrt{\frac{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{\theta_0(v(\mathbf{x}; \beta_0))}} \right\} = -0.5\gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta})$$

and

$$-(1-\lambda) \log \frac{1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{1 - \theta_0(v(\mathbf{x}; \beta_0))} \geq 2(1-\lambda) \left\{ 1 - \sqrt{\frac{1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{1 - \theta_0(v(\mathbf{x}; \beta_0))}} \right\} = -0.5\gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}).$$

Hence,

$$\begin{aligned}
0 &\geq -0.5 \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_{n_1}(\mathbf{x}) - 0.5 \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) dG_{n_0}(\mathbf{x}) \\
&= -0.5 \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{F_{n_1}(\mathbf{x}) - F_0(\mathbf{x})\} - 0.5 \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{G_{n_0}(\mathbf{x}) - G_0(\mathbf{x})\} \\
&\quad -0.5 \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_0(\mathbf{x}) - 0.5 \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) dG_0(\mathbf{x}).
\end{aligned}$$

To finish the proof of Step 1, it suffices to show that

$$-\int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_0(\mathbf{x}) - \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) dG_0(\mathbf{x}) \geq d^2\left(\hat{\theta}(v(\mathbf{x}; \hat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))\right). \quad (16)$$

Using the facts that $dF_0(\mathbf{x}) = \psi_0(v(\mathbf{x}; \beta_0))dG_0(\mathbf{x})$ and (1), we get

$$-\int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_0(\mathbf{x}) = \int 4\lambda\psi_0(v(\mathbf{x}; \beta_0)) \left\{ 1 - \sqrt{\frac{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{\theta_0(v(\mathbf{x}; \beta_0))}} \right\} dG_0(\mathbf{x}).$$

Noting that

$$dH_0(\mathbf{x}) = \lambda dF_0(\mathbf{x}) + (1 - \lambda) dG_0(\mathbf{x}) = \{\lambda \psi_0(v(\mathbf{x}; \beta_0)) + (1 - \lambda)\} dG_0(\mathbf{x})$$

and

$$\theta_0(v(\mathbf{x}; \beta_0)) = \frac{\lambda \psi_0(v(\mathbf{x}; \beta_0))}{\lambda \psi_0(v(\mathbf{x}; \beta_0)) + (1 - \lambda)},$$

we further have

$$\begin{aligned} - \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_0(\mathbf{x}) &= \int 4\theta_0(v(\mathbf{x}; \beta_0)) \left\{ 1 - \sqrt{\frac{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))}{\theta_0(v(\mathbf{x}; \beta_0))}} \right\} dH_0(\mathbf{x}) \\ &= \int 4 \left\{ \theta_0(v(\mathbf{x}; \beta_0)) - \sqrt{\hat{\theta}(v(\mathbf{x}; \hat{\beta})) \theta_0(v(\mathbf{x}; \beta_0))} \right\} dH_0(\mathbf{x}). \end{aligned} \quad (17)$$

With (2) and the above techniques, we can similarly obtain

$$\begin{aligned} - \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) dG_0(\mathbf{x}) \\ = \int 4 \left[\left\{ 1 - \theta_0(v(\mathbf{x}; \beta_0)) \right\} - \sqrt{\left\{ 1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta})) \right\} \left\{ 1 - \theta_0(v(\mathbf{x}; \beta_0)) \right\}} \right] dH_0(\mathbf{x}). \end{aligned} \quad (18)$$

Combining (17) and (18) leads to

$$\begin{aligned} & - \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_0(\mathbf{x}) - \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) dG_0(\mathbf{x}) \\ &= \int 4 \left[1 - \sqrt{\hat{\theta}(v(\mathbf{x}; \hat{\beta})) \theta_0(v(\mathbf{x}; \beta_0))} - \sqrt{\left\{ 1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta})) \right\} \left\{ 1 - \theta_0(v(\mathbf{x}; \beta_0)) \right\}} \right] dH_0(\mathbf{x}) \\ &= 2 \int \left\{ \sqrt{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))} - \sqrt{\theta_0(v(\mathbf{x}; \beta_0))} \right\}^2 dH_0(\mathbf{x}) \\ &\quad + 2 \int \left\{ \sqrt{1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta}))} - \sqrt{1 - \theta_0(v(\mathbf{x}; \beta_0))} \right\}^2 dH_0(\mathbf{x}). \end{aligned}$$

Using the fact that $\theta(\cdot) \in [0, 1]$ and $\theta_0(\cdot) \in [0, 1]$, we further get

$$\left\{ \sqrt{\hat{\theta}(v(\mathbf{x}; \hat{\beta}))} - \sqrt{\theta_0(v(\mathbf{x}; \beta_0))} \right\}^2 \geq \frac{1}{4} \{\theta(v(\mathbf{x}; \beta)) - \theta_0(v(\mathbf{x}; \beta_0))\}^2$$

and

$$\left\{ \sqrt{1 - \hat{\theta}(v(\mathbf{x}; \hat{\beta}))} - \sqrt{1 - \theta_0(v(\mathbf{x}; \beta_0))} \right\}^2 \geq \frac{1}{4} \{\theta(v(\mathbf{x}; \beta)) - \theta_0(v(\mathbf{x}; \beta_0))\}^2.$$

Therefore,

$$\begin{aligned} - \int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) dF_0(\mathbf{x}) - \int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) dG_0(\mathbf{x}) &\geq \int \left\{ \hat{\theta}(v(\mathbf{x}; \hat{\beta})) - \theta_0(v(\mathbf{x}; \beta_0)) \right\}^2 dH_0(\mathbf{x}) \\ &= d^2\left(\hat{\theta}(v(\mathbf{x}; \hat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))\right) \end{aligned}$$

as claimed in (16). This completes the proof of this lemma.

3.5 Proof of Theorem S.1

Part (a). Based on Lemma S.2, we immediately have

$$d\left(\hat{\theta}(v(\mathbf{x}; \hat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))\right) = o_p(1)$$

if we can show

$$\int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{F_{n_1}(\mathbf{x}) - F_0(\mathbf{x})\} = o_p(1)$$

and

$$\int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{G_{n_0}(\mathbf{x}) - G_0(\mathbf{x})\} = o_p(1).$$

To this end, note that $|\gamma_1(\mathbf{x}; \theta, \beta)| \leq 4\lambda\{1 + 1/\theta_0(v(\mathbf{x}; \beta_0))\}$ and

$$\int 4\lambda\{1 + 1/\theta_0(v(\mathbf{x}; \beta_0))\} dF_0(\mathbf{x}) = 4\lambda + 4 \int dH_0(\mathbf{x}) = 4(\lambda + 1) < \infty.$$

That is, the class $\{\gamma_1(\mathbf{x}; \theta, \beta) : \theta(v(\mathbf{x}; \beta)) \in \Lambda\}$ has an integrable envelope. Using Lemmas S.4 and S.1, we have that $\{\gamma_1(\mathbf{x}; \theta, \beta) : \theta(v(\mathbf{x}; \beta)) \in \Lambda\}$ is F_0 -G-C, i.e.,

$$\sup_{\theta(v(\mathbf{x}; \beta)) \in \Lambda} \left| \int \gamma_1(\mathbf{x}; \theta, \beta) d\{F_{n_1}(\mathbf{x}) - F_0(\mathbf{x})\} \right| = o_p(1),$$

which implies that

$$\int \gamma_1(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{F_{n_1}(\mathbf{x}) - F_0(\mathbf{x})\} = o_p(1).$$

Similarly,

$$\int \gamma_2(\mathbf{x}; \hat{\theta}, \hat{\beta}) d\{G_{n_0}(\mathbf{x}) - G_0(\mathbf{x})\} = o_p(1).$$

This completes our proof of Part (a).

Part (b). Let

$$M^*(\beta) = \min_{\theta(\cdot) \in \Theta} d\left(\theta(v(\mathbf{x}; \beta)), \theta_0(v(\mathbf{x}; \beta_0))\right).$$

From the arguments in Wald (1949), to prove that $\widehat{\beta} = \beta_0 + o_p(1)$ it suffices to show that

(b.1) $M^*(\widehat{\beta}) = o_p(1);$

(b.2) $M^*(\beta) = 0$ implies that $\beta = \beta_0;$

(b.3) $M^*(\beta)$ is continuous on $\mathbf{B}.$

Part (b.1) is obvious since

$$0 \leq M^*(\widehat{\beta}) \leq d\left(\widehat{\theta}(v(\mathbf{x}; \widehat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))\right) = o_p(1).$$

Part (b.2) is due to the identifiability condition in Condition A3.

We now show that Part (b.3) is also true. For any given $\epsilon > 0$ and $\beta^* \in \mathbf{B}$, let $\delta_1 = \epsilon^2/(4p2^p C_0)$ and $\delta_2 = \epsilon^2/10$. Following the arguments in the proof of Lemma S.1, we can find a set with a finite number M^* of pairs of functions $\left\{ \left(b_j^L(\mathbf{x}), b_j^U(\mathbf{x}) \right) \right\}_{j=1}^{M^*}$ satisfying
(i)

$$\int |b_j^U(\mathbf{x}) - b_j^L(\mathbf{x})| dH_0(\mathbf{x}) \leq 5\delta_2 + 2p2^p C_0 \delta_1 = \epsilon^2; \quad (19)$$

and (ii) for any given $\theta(u) \in \Theta$, there exists a j such that

$$0 \leq b_j^L(\mathbf{x}) \leq \theta(v(\mathbf{x}; \beta)) \leq b_j^U(\mathbf{x}) \leq 1 \quad (20)$$

whenever $\|\beta - \beta^*\| < \delta_1$ and $\beta \in \mathbf{B}.$

Note that (19) and (20) together imply that

$$d(b_j^U(\mathbf{x}), b_j^L(\mathbf{x})) \leq \left\{ \int |b_j^U(\mathbf{x}) - b_j^L(\mathbf{x})| dH_0(\mathbf{x}) \right\}^{1/2} \leq \epsilon.$$

By the triangle inequality,

$$d\left(\theta(v(\mathbf{x}; \beta)), \theta_0(v(\mathbf{x}; \beta_0))\right) \geq d\left(\theta(v(\mathbf{x}; \beta^*)), \theta_0(v(\mathbf{x}; \beta_0))\right) - d\left(\theta(v(\mathbf{x}; \beta)), \theta(v(\mathbf{x}; \beta^*))\right).$$

Further, from (20), we have

$$|\theta(v(\mathbf{x}; \boldsymbol{\beta})) - \theta(v(\mathbf{x}; \boldsymbol{\beta}^*))| \leq b_j^U(\mathbf{x}) - b_j^L(\mathbf{x}).$$

Hence,

$$d(\theta(v(\mathbf{x}; \boldsymbol{\beta})), \theta(v(\mathbf{x}; \boldsymbol{\beta}^*))) \leq d(b_j^U(\mathbf{x}), b_j^L(\mathbf{x})) \leq \epsilon.$$

Therefore,

$$d(\theta(v(\mathbf{x}; \boldsymbol{\beta})), \theta_0(v(\mathbf{x}; \boldsymbol{\beta}_0))) \geq d(\theta(v(\mathbf{x}; \boldsymbol{\beta}^*)), \theta_0(v(\mathbf{x}; \boldsymbol{\beta}_0))) - \epsilon. \quad (21)$$

Taking the minimum over $\theta(\cdot)$ on both sides of (21) gives $M^*(\boldsymbol{\beta}) \geq M^*(\boldsymbol{\beta}^*) - \epsilon$. Similarly, we can show that $M^*(\boldsymbol{\beta}) \leq M^*(\boldsymbol{\beta}^*) + \epsilon$. Hence, for any given $\epsilon > 0$, when $\|\boldsymbol{\beta} - \boldsymbol{\beta}^*\| < \delta_1$, we have that $|M^*(\boldsymbol{\beta}) - M^*(\boldsymbol{\beta}^*)| \leq \epsilon$, which implies that $M^*(\boldsymbol{\beta})$ is continuous at $\boldsymbol{\beta} = \boldsymbol{\beta}^*$. Because of the arbitrariness of $\boldsymbol{\beta}^*$, we conclude that $M^*(\boldsymbol{\beta})$ is a continuous function on $\mathbf{B}$. This completes the proof of Part (b.3) and hence that of Theorem S.1.

3.6 Proof of Theorem S.2

Part (a). We consider only the consistency of $\hat{F}_C(u)$; the consistency of $\hat{G}_C(u)$ follows similarly.

Let

$$H_n(\mathbf{x}) = \sum_{i=1}^n \frac{m_i + r_i}{n} I(\mathbf{t}_i \leq \mathbf{x}).$$

Note that for any u ,

$$\hat{F}_C(u) = \int I(v(\mathbf{x}; \hat{\boldsymbol{\beta}}) \leq u) \hat{\theta}(v(\mathbf{x}; \hat{\boldsymbol{\beta}})) dH_n(\mathbf{x})$$

and

$$F_C(u; \boldsymbol{\beta}_0) = \int I(v(\mathbf{x}; \boldsymbol{\beta}_0) \leq u) \theta_0(v(\mathbf{x}; \boldsymbol{\beta}_0)) H_0(\mathbf{x}).$$

Then

$$\widehat{F}_C(u) - F_C(u; \beta_0) = \int I(v(\mathbf{x}; \widehat{\beta}) \leq u) \widehat{\theta}(v(\mathbf{x}; \widehat{\beta})) d\{H_n(\mathbf{x}) - H_0(\mathbf{x})\} \quad (22)$$

$$+ \int I(v(\mathbf{x}; \widehat{\beta}) \leq u) \left\{ \widehat{\theta}(v(\mathbf{x}; \widehat{\beta})) - \theta_0(v(\mathbf{x}; \beta_0)) \right\} dH_0(\mathbf{x}) \quad (23)$$

$$+ \int \left\{ I(v(\mathbf{x}; \widehat{\beta}) \leq u) - I(v(\mathbf{x}; \beta_0) \leq u) \right\} \theta_0(v(\mathbf{x}; \beta_0)) dH_0(\mathbf{x}). \quad (24)$$

Next we assess the orders of the three terms in (22)–(24). We first consider the term in (23). Note that

$$\begin{aligned} & \left| \int I(v(\mathbf{x}; \widehat{\beta}) \leq u) \left\{ \widehat{\theta}(v(\mathbf{x}; \widehat{\beta})) - \theta_0(v(\mathbf{x}; \beta_0)) \right\} dH_0(\mathbf{x}) \right| \\ & \leq \int \left| \left\{ \widehat{\theta}(v(\mathbf{x}; \widehat{\beta})) - \theta_0(v(\mathbf{x}; \beta_0)) \right\} \right| dH_0(\mathbf{x}) \\ & \leq \left[\int \left\{ \widehat{\theta}(v(\mathbf{x}; \widehat{\beta})) - \theta_0(v(\mathbf{x}; \beta_0)) \right\}^2 dH_0(\mathbf{x}) \right]^{1/2} \\ & = d\left(\widehat{\theta}(v(\mathbf{x}; \widehat{\beta})), \theta_0(v(\mathbf{x}; \beta_0))\right) = o_p(1), \end{aligned} \quad (25)$$

as shown in Theorem S.1.

We next consider the term in (24). Condition A2 implies that

$$\begin{aligned} & \left| \int \left\{ I(v(\mathbf{x}; \widehat{\beta}) \leq u) - I(v(\mathbf{x}; \beta_0) \leq u) \right\} \theta_0(v(\mathbf{x}; \beta_0)) dH_0(\mathbf{x}) \right| \\ & = \lambda \left| \int \left\{ I(v(\mathbf{x}; \widehat{\beta}) \leq u) - I(v(\mathbf{x}; \beta_0) \leq u) \right\} dF_0(\mathbf{x}) \right| \\ & \leq \int \left| I(\widehat{\beta}^\tau \mathbf{h}(\mathbf{x}) \leq u) - I(\beta_0^\tau \mathbf{h}(\mathbf{x}) \leq u) \right| dF_0(\mathbf{x}) \\ & \leq C_0 \|\widehat{\beta} - \beta_0\|_1 = o_p(1), \end{aligned} \quad (26)$$

as shown in Theorem S.1.

Finally, we consider the term in (22). We first argue that

$$\{I(v(\mathbf{x}; \beta) \leq u) : \beta \in \mathbf{B}, u \in \mathbf{R}\}$$

is F_0 -G-C and G_0 -G-C. According to Lemma 9.8 and Lemma 9.12 of Kosorok (2008),

$$\{I(v(\mathbf{x}; \beta) \leq u) : \beta \in \mathbf{B}, u \in \mathbf{R}\}$$

is a Vapnik–Chervonenkis subgraph class with the bounded envelope 1. Hence, it is F_0 -G-C and G_0 -G-C by Corollary 3.12 of van de Geer (2000).

By Lemma S.4, the class

$$\{I(v(\mathbf{x}; \boldsymbol{\beta}) \leq u)\theta(v(\mathbf{x}; \boldsymbol{\beta})) : \theta \in \boldsymbol{\Theta}, \boldsymbol{\beta} \in \mathbf{B}, u \in \mathbf{R}\}$$

is also F_0 -G-C and G_0 -G-C. That is,

$$\sup_{\theta \in \boldsymbol{\Theta}, \boldsymbol{\beta} \in \mathbf{B}, u \in \mathbf{R}} \left| \int I(v(\mathbf{x}; \boldsymbol{\beta}) \leq u)\theta(v(\mathbf{x}; \boldsymbol{\beta})) d\{F_{n_1}(\mathbf{x}) - F_0(\mathbf{x})\} \right| = o_p(1)$$

and

$$\sup_{\theta \in \boldsymbol{\Theta}, \boldsymbol{\beta} \in \mathbf{B}, u \in \mathbf{R}} \left| \int I(v(\mathbf{x}; \boldsymbol{\beta}) \leq u)\theta(v(\mathbf{x}; \boldsymbol{\beta})) d\{G_{n_0}(\mathbf{x}) - G_0(\mathbf{x})\} \right| = o_p(1),$$

which together imply that

$$\sup_{\theta \in \boldsymbol{\Theta}, \boldsymbol{\beta} \in \mathbf{B}, u \in \mathbf{R}} \left| \int I(v(\mathbf{x}; \boldsymbol{\beta}) \leq u)\theta(v(\mathbf{x}; \boldsymbol{\beta})) d\{H_n(\mathbf{x}) - H_0(\mathbf{x})\} \right| = o_p(1).$$

Hence,

$$\sup_{u \in \mathbf{R}} \left| \int I(v(\mathbf{x}; \hat{\boldsymbol{\beta}}) \leq u)\hat{\theta}(v(\mathbf{x}; \hat{\boldsymbol{\beta}})) d\{H_n(\mathbf{x}) - H_0(\mathbf{x})\} \right| = o_p(1). \quad (27)$$

Combining (22)–(27) gives

$$\sup_{u \in \mathbf{R}} |\hat{F}_C(u) - F_C(u; \beta_0)| = o_p(1)$$

as required.

Part (b). The proof is essentially similar to the proof of Theorem 1 in Jokiel-Rokita and Pulit (2013) and is therefore omitted.

Part (c). Note that

$$\begin{aligned} |\widehat{\text{AUC}}_C - \text{AUC}_C| &= \left| \int_0^1 \widehat{\text{ROC}}_C(s) - \text{ROC}_C(s) ds \right| \leq \int_0^1 |\widehat{\text{ROC}}_C(s) - \text{ROC}_C(s)| ds \\ &\leq \sup_{0 \leq s \leq 1} |\widehat{\text{ROC}}_C(s) - \text{ROC}_C(s)| = o_p(1). \end{aligned}$$

This completes the proof.

4. CASE I: SIMULATION STUDIES ADDITIONAL TO SECTION 4.1 OF THE MAIN PAPER

In this section, we consider the same simulation setups as those in Section 4.1 of the main paper with different sample sizes n_0 and n_1 . Note that in this section, the biomarkers in both the healthy and diseased groups follow multivariate normal distributions. As in Section 4.1, we consider the following two subcases: (I) $\lambda_0 = \lambda_1 = 1$, so that both the exponential tilting model (1) (i.e., Model I) and the monotonic density ratio model (2) (i.e., Model II) in the main paper are correctly specified; (II) $\lambda_0 = \lambda_1 = 0.8$, so that Model I is misspecified, but Model II is correctly specified. In this study, we compare our method with all the other methods given in Section 1. We emphasize that the ROC curve estimates from the proposed method are highlighted in red in Sections 4–8.

4.1 Case I; Subcase I: Models I and II are correctly specified; i.e., $\lambda_0 = \lambda_1 = 1$

- $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 3.
- $n_0 = 200, n_1 = 100$. The constructed ROC curves for all the methods are given in Figure 4.
- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 5.
- $n_0 = 1000, n_1 = 500$. The constructed ROC curves for all the methods are given in Figure 6.
- $n_0 = 1000, n_1 = 1000$. The constructed ROC curves for all the methods are given in Figure 7.
- The averages of the corresponding IAEs of the ROC estimates over 2000 replicates are given in Table 1.

Observations: The figures show that the averages of the ROC curve estimates from all the methods, except the min-max and tree methods, are very close to the true ROC curve. The table shows that the averages of the IAEs of the ROC estimates from the min-max and tree methods are larger than those from other methods. In summary, in this simulation setup, the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods perform similarly, and they are better than the min-max and tree methods.

Table 1: Comparison of the averages of the IAEs of the ROC estimates over 2000 replicates when the biomarkers follow a normal distribution; both the monotonic density ratio and exponential tilting models are correctly specified, i.e., $\lambda_0 = \lambda_1 = 1$.

Method	(n_0, n_1)				
	(30, 30)	(200, 100)	(300, 200)	(1000, 500)	(1000, 1000)
Exponential tilting model is correctly specified: $\lambda_0 = \lambda_1 = 1$					
Proposed	0.031	0.017	0.012	0.007	0.006
Exponential tilting	0.031	0.017	0.012	0.007	0.006
MH	0.035	0.023	0.013	0.007	0.006
Nonparametric	0.033	0.018	0.012	0.007	0.006
Min-max	0.034	0.020	0.016	0.016	0.015
Smoothed EL	0.031	0.018	0.012	0.007	0.006
Tree	0.040	0.050	0.063	0.069	0.057

Figure 3: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 30$, $n_1 = 30$.

Figure 4: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 200$, $n_1 = 100$.

Figure 5: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 300$, $n_1 = 200$.

Figure 6: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 1000$, $n_1 = 500$.

Figure 7: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 1000$, $n_1 = 1000$.

4.2 Case I; Subcase II: Model I is misspecified but Model II is correctly specified; i.e.,

$$\lambda_0 = \lambda_1 = 0.8$$

- $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 8.
- $n_0 = 200, n_1 = 100$. The constructed ROC curves for all the methods are given in Figure 9.
- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 10.
- $n_0 = 1000, n_1 = 500$. The constructed ROC curves for all the methods are given in Figure 11.
- $n_0 = 1000, n_1 = 1000$. The constructed ROC curves for all the methods are given in Figure 12.
- The averages of the corresponding IAEs of ROC estimates over 2000 replicates are given in Table 2.

Observations: The figures show that the averages of the ROC curve estimates from all the methods, except the exponential tilting and tree methods, are very close to the true ROC curve. The table shows that the averages of the IAEs of the ROC estimates from our method are slightly smaller than those from the exponential tilting, MH, nonparametric, min-max, and smoothed EL methods, and they are much smaller than those from the tree method.

Table 2: Comparison of the averages of the IAEs of the ROC estimates over 2000 replicates when the biomarkers follow a normal distribution; the monotonic density ratio model is correctly specified, but the exponential tilting model is misspecified, i.e., $\lambda_0 = \lambda_1 = 0.8$.

Method	(n_0, n_1)				
	(30, 30)	(200, 100)	(300, 200)	(1000, 500)	(1000, 1000)
Exponential tilting model is misspecified: $\lambda_0 = \lambda_1 = 0.8$					
Proposed	0.067	0.043	0.035	0.027	0.024
Exponential tilting	0.067	0.045	0.039	0.031	0.029
MH	0.081	0.046	0.042	0.030	0.028
Nonparametric	0.078	0.046	0.039	0.029	0.027
Min-max	0.078	0.049	0.040	0.032	0.030
Smoothed EL	0.080	0.045	0.039	0.029	0.027
Tree	0.136	0.114	0.119	0.134	0.127

Figure 8: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate normal distribution: $n_0 = 30, n_1 = 30$.

Figure 9: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate normal distribution: $n_0 = 200$, $n_1 = 100$.

Figure 10: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate normal distribution: $n_0 = 300$, $n_1 = 200$.

Figure 11: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate normal distribution: $n_0 = 1000$, $n_1 = 500$.

Figure 12: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate normal distribution: $n_0 = 1000$, $n_1 = 1000$

5. CASE II: SIMULATION STUDIES ADDITIONAL TO SECTION 4.2 OF THE MAIN PAPER

In this section, we consider the same simulation setups as those in Section 4.2 of the main paper with different sample sizes n_0 and n_1 . Note that in this section, the biomarkers in both the healthy and diseased groups follow multivariate exponential distributions. We also consider the following two subcases: (I) $\lambda_0 = \lambda_1 = 1$, so that Models I and II are both correctly specified; (II) $\lambda_0 = \lambda_1 = 0.8$, so that Model I is misspecified, but Model II is correctly specified. In this study, we compare our method with all the other methods given in Section 1.

5.1 Case II; Subcase I: Models I and II are correctly specified; i.e., $\lambda_0 = \lambda_1 = 1$

- $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 13.
- $n_0 = 200, n_1 = 100$. The constructed ROC curves for all the methods are given in Figure 14.
- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 15.
- $n_0 = 1000, n_1 = 500$. The constructed ROC curves for all the methods are given in Figure 16.
- $n_0 = 1000, n_1 = 1000$. The constructed ROC curves for all the methods are given in Figure 17.
- The averages of the corresponding IAEs of the ROC estimates over 2000 replicates are given in Table 3.

Observations: The figures show that the averages of the ROC curve estimates from all the methods, except the min-max and tree methods, are very close to the true ROC curve. The table shows that the averages of the IAEs of the ROC estimates from the tree method are much larger than those from other methods, whereas the proposed, MH, nonparametric, min-max, and smoothed EL methods have comparable averaged IAEs of the ROC estimates for all the sample sizes. The exponential method leads to slightly smaller averaged IAEs than the proposed, MH, nonparametric, min-max, and smoothed EL methods when n_0 and n_1 are relatively small (i.e., $n_0 = n_1 = 30$); it has similar averaged IAEs when n_0 and n_1 are large.

Table 3: Comparison of the averages of the IAEs of the ROC estimates over 2000 replicates when the biomarkers follow an exponential distribution; both the monotonic density ratio and the exponential tilting models are correctly specified, i.e., $\lambda_0 = \lambda_1 = 1$.

Method	(n_0, n_1)				
	(30, 30)	(200, 100)	(300, 200)	(1000, 500)	(1000, 1000)
Exponential tilting model is correctly specified: $\lambda_0 = \lambda_1 = 1$					
Proposed	0.045	0.025	0.018	0.010	0.008
Exponential tilting	0.038	0.024	0.018	0.010	0.008
MH	0.048	0.025	0.018	0.011	0.009
Nonparametric	0.048	0.025	0.018	0.011	0.009
Min-max	0.049	0.027	0.021	0.013	0.013
Smoothed EL	0.048	0.025	0.018	0.011	0.009
Tree	0.082	0.079	0.072	0.066	0.059

Figure 13: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 30$, $n_1 = 30$.

Figure 14: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 200$, $n_1 = 100$.

Figure 15: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 300$, $n_1 = 200$.

Figure 16: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 1000$, $n_1 = 500$.

Figure 17: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio and exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 1000$, $n_1 = 1000$.

5.2 Case II; Subcase II: Model I is misspecified but Model II is correctly specified; i.e.,

$$\lambda_0 = \lambda_1 = 0.8$$

- $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 18.
- $n_0 = 200, n_1 = 100$. The constructed ROC curves for all the methods are given in Figure 19.
- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 20.
- $n_0 = 1000, n_1 = 500$. The constructed ROC curves for all the methods are given in Figure 21.
- $n_0 = 1000, n_1 = 1000$. The constructed ROC curves for all the methods are given in Figure 22.
- The averages of the corresponding IAEs of the ROC estimates over 2000 replicates are given in Table 4.

Observations: The figures show that the averages of the ROC curve estimates from all the methods, except the exponential tilting and tree methods, are very close to the true ROC curve. The table shows that the proposed, MH, nonparametric, min-max, and smoothed EL methods lead to comparable averaged IAEs, which are smaller than those from the exponential tilting and tree methods.

Table 4: Comparison of the averages of the IAEs of the ROC estimates over 2000 replicates when the biomarkers follow an exponential distribution; the monotonic density ratio model is correctly specified, but the exponential tilting model is misspecified, i.e., $\lambda_0 = \lambda_1 = 0.8$.

Method	(n_1, n_0)				
	(30, 30)	(200, 100)	(300, 200)	(1000, 500)	(1000, 1000)
Exponential tilting model is misspecified: $\lambda_0 = \lambda_1 = 0.8$					
Proposed	0.070	0.038	0.029	0.020	0.017
Exponential tilting	0.072	0.069	0.061	0.065	0.055
MH	0.072	0.039	0.031	0.022	0.019
Nonparametric	0.074	0.039	0.031	0.022	0.020
Min-max	0.074	0.039	0.031	0.023	0.019
Smoothed EL	0.073	0.039	0.031	0.022	0.020
Tree	0.171	0.136	0.135	0.140	0.129

Figure 18: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate exponential distribution: $n_0 = 30$, $n_1 = 30$.

Figure 19: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate exponential distribution: $n_0 = 200$, $n_1 = 100$.

Figure 20: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate exponential distribution: $n_0 = 300$, $n_1 = 200$.

Figure 21: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate exponential distribution: $n_0 = 1000$, $n_1 = 500$.

Figure 22: Plot of the ROC curves of the optimal combinations of two biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the two biomarkers follow a bivariate exponential distribution: $n_0 = 1000$, $n_1 = 1000$.

6. CASE III: SIMULATION STUDIES ADDITIONAL TO SECTION 2

In this section, we consider the same simulation setups as those in Section 2 with different sample sizes n_0 and n_1 . As in Section 2, we consider the following two subcases: (I) using the simulation setup of Section 4.2 in the main paper but in the processing of the data $h(\mathbf{x})$ is misspecified; (II) using the simulation setup of Section 4.1 in the main paper but in the processing of the data $v(\mathbf{x}, \boldsymbol{\beta})$ is misspecified. For both subcases, we set $\lambda_0 = \lambda_1 = 1$. In this study, we compare our method with all the other methods given in Section 1.

6.1 Case III; Subcase I: $h(\mathbf{x})$ is misspecified

- $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 23.
- $n_0 = 200, n_1 = 100$. The constructed ROC curves for all the methods are given in Figure 24.
- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 25.
- $n_0 = 1000, n_1 = 500$. The constructed ROC curves for all the methods are given in Figure 26.
- $n_0 = 1000, n_1 = 1000$. The constructed ROC curves for all the methods are given in Figure 27.
- The averages of the corresponding IAEs of the ROC estimates over 2000 replicates are given in Table 5.

Observations: The figures show that the averages of the ROC curve estimates from all the methods, except the exponential tilting and tree methods, are very close to the true ROC curve. The table shows that the proposed, MH, nonparametric, min-max, and smoothed EL

methods have comparable averaged IAEs of the ROC estimates, which are smaller than those from the tree and exponential tilting methods.

Table 5: Comparison of the averages of the IAEs of the ROC estimates over 2000 replicates when the biomarkers follow an exponential distribution; both the monotonic density ratio and the exponential tilting models are correctly specified, i.e., $\lambda_0 = \lambda_1 = 1$, but $h(\mathbf{x})$ is misspecified in the processing of the data.

Method	(n_1, n_0)				
	(30, 30)	(200, 100)	(300, 200)	(1000, 500)	(1000, 1000)
$h(x)$ is misspecified					
Proposed	0.048	0.027	0.021	0.014	0.011
Exponential tilting	0.069	0.056	0.052	0.051	0.052
MH	0.050	0.027	0.020	0.013	0.010
Nonparametric	0.050	0.027	0.020	0.013	0.010
Min-max	0.050	0.027	0.020	0.013	0.010
Smoothed EL	0.050	0.027	0.020	0.013	0.010
Tree	0.064	0.059	0.057	0.075	0.062

Figure 23: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 30, n_1 = 30$.

Figure 24: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 200, n_1 = 100$.

Figure 25: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 300$, $n_1 = 200$.

Figure 26: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 1000$, $n_1 = 500$.

Figure 27: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate exponential distribution: $n_0 = 1000$, $n_1 = 1000$.

6.2 Case III; Subcase II: $v(\mathbf{x}, \beta)$ is misspecified

- $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 28.
- $n_0 = 200, n_1 = 100$. The constructed ROC curves for all the methods are given in Figure 29.
- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 30.
- $n_0 = 1000, n_1 = 500$. The constructed ROC curves for all the methods are given in Figure 31.
- $n_0 = 1000, n_1 = 1000$. The constructed ROC curves for all the methods are given in Figure 32.
- The averages of the corresponding IAEs of the ROC estimates over 2000 replicates are given in Table 6.

Observations: The figures show that all the methods lead to biased ROC curve estimates. However, the proposed method leads to a much smaller bias in the ROC estimation than those of the other methods. The table shows that our method leads to much smaller averaged IAEs of the ROC estimates.

Table 6: Comparison of the averages of the IAEs of the ROC estimates over 2000 replicates when the biomarkers follow a normal distribution; both the monotonic density ratio and the exponential tilting model are correctly specified, i.e., $\lambda_0 = \lambda_1 = 1$, but $v(\mathbf{x}, \boldsymbol{\beta})$ is misspecified in the processing of the data.

Method	(n_0, n_1)				
	(30, 30)	(200, 100)	(300, 200)	(1000, 500)	(1000, 1000)
$v(x)$ is misspecified					
Proposed	0.025	0.019	0.019	0.024	0.024
Exponential tilting	0.077	0.073	0.077	0.074	0.074
MH	0.077	0.073	0.075	0.074	0.074
Nonparametric	0.045	0.031	0.030	0.030	0.030
Min-max	0.046	0.036	0.035	0.034	0.034
Smoothed EL	0.042	0.035	0.034	0.031	0.031
Tree	0.035	0.034	0.032	0.043	0.037

Figure 28: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 30, n_1 = 30$.

Figure 29: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 200$, $n_1 = 100$.

Figure 30: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 300$, $n_1 = 200$.

Figure 31: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 1000$, $n_1 = 500$.

Figure 32: Plot of the ROC curves of the optimal combinations of two biomarkers based on misspecified monotonic density ratio and misspecified exponential tilting models when the two biomarkers follow a bivariate normal distribution: $n_0 = 1000$, $n_1 = 1000$.

7. CASE IV: SIMULATION STUDIES ADDITIONAL TO SECTION 4.3 OF THE MAIN PAPER

In this section, we present simulation results complementary to those of Section 4.3 in the main paper, where different sample sizes n_0 and n_1 are considered. As in Section 4.3, we consider the following two subcases: (I) β estimates based on the simulation setup of Section 4.1 in the main paper; (II) β estimates based on the simulation setup of Section 4.2 in the main paper. In this study, we compare our method with the exponential tilting method, the MH method, and the nonparametric method.

7.1 Case IV; Subcase I: Simulation setup of Section 4.1 in the main paper is used

- $n_0 = 30, n_1 = 30$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 7.
- $n_0 = 200, n_1 = 100$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 8.
- $n_0 = 300, n_1 = 200$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 9.
- $n_0 = 1000, n_1 = 500$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 10.
- $n_0 = 1000, n_1 = 1000$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 11.

Observations: Tables 7–11 show that when $\lambda_0 = \lambda_1 = 1$, all the methods produce very small and comparable biases. When $\lambda_0 < 1$ and $\lambda_1 < 1$, our model has the smallest biases; the MH, nonparametric, and smoothed EL methods lead to medium biases; and the exponential tilting method yields the largest biases. Moreover, when $\lambda_0 = \lambda_1 = 1$, our

method and the exponential tilting method lead to comparable MSEs, whereas those for the MH, nonparametric, and smoothed EL methods are larger; when $\lambda_0 < 1$ and $\lambda_1 < 1$, our method leads to much smaller MSEs for β than the other methods give.

Table 7: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow normal distribution; $n_0 = 30, n_1 = 30$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1	1	β_1	-0.115	0.369	0.149	-0.100	0.349	0.132	-0.233	0.384	0.202	-0.216	0.405	0.211	-0.291	0.336	0.198
1	1	β_2	0.104	0.529	0.291	0.140	0.507	0.277	0.120	0.543	0.309	0.055	0.609	0.374	0.364	0.445	0.330
1	1	β_3	-0.045	0.174	0.032	-0.048	0.156	0.027	-0.058	0.181	0.036	0.043	0.217	0.049	-0.023	0.205	0.043
1	1	β_4	-0.036	0.209	0.045	-0.055	0.198	0.042	-0.071	0.208	0.048	0.057	0.212	0.048	0.020	0.247	0.061
1	1	β_5	0.046	0.226	0.053	0.053	0.218	0.050	0.087	0.247	0.069	0.176	0.286	0.113	0.267	0.358	0.199
0.9	0.9	β_1	-0.132	0.401	0.178	-0.194	0.365	0.171	-0.119	0.468	0.233	-0.236	0.509	0.315	-0.352	0.378	0.267
0.9	0.9	β_2	0.104	0.585	0.353	0.397	0.561	0.472	0.101	0.604	0.375	0.060	0.623	0.392	0.445	0.471	0.420
0.9	0.9	β_3	-0.077	0.177	0.037	-0.187	0.157	0.060	-0.106	0.192	0.048	0.049	0.220	0.051	-0.049	0.207	0.045
0.9	0.9	β_4	-0.053	0.228	0.055	-0.144	0.196	0.059	-0.093	0.242	0.067	0.006	0.266	0.071	0.015	0.251	0.063
0.9	0.9	β_5	0.049	0.271	0.076	0.057	0.229	0.056	0.151	0.318	0.124	0.178	0.317	0.132	0.331	0.358	0.238
0.8	0.8	β_1	-0.127	0.419	0.192	-0.236	0.437	0.247	-0.185	0.555	0.342	-0.218	0.600	0.408	-0.444	0.444	0.395
0.8	0.8	β_2	0.086	0.544	0.303	0.539	0.552	0.595	0.160	0.550	0.328	0.101	0.610	0.382	0.452	0.478	0.433
0.8	0.8	β_3	-0.101	0.179	0.042	-0.245	0.132	0.077	-0.142	0.179	0.052	0.006	0.260	0.068	-0.064	0.235	0.059
0.8	0.8	β_4	-0.057	0.242	0.062	-0.187	0.186	0.070	-0.104	0.251	0.074	-0.005	0.313	0.098	-0.012	0.266	0.071
0.8	0.8	β_5	0.022	0.296	0.088	0.069	0.241	0.063	0.138	0.325	0.125	0.134	0.312	0.115	0.343	0.377	0.259
0.7	0.7	β_1	-0.133	0.429	0.202	-0.332	0.509	0.369	-0.114	0.555	0.321	-0.182	0.618	0.415	-0.530	0.443	0.477
0.7	0.7	β_2	0.076	0.568	0.328	0.443	0.599	0.555	0.151	0.588	0.369	0.083	0.584	0.348	0.485	0.478	0.465
0.7	0.7	β_3	-0.111	0.190	0.048	-0.256	0.161	0.091	-0.166	0.228	0.080	-0.019	0.263	0.070	-0.051	0.257	0.068
0.7	0.7	β_4	-0.080	0.245	0.066	-0.239	0.179	0.089	-0.057	0.259	0.070	-0.011	0.272	0.074	-0.032	0.298	0.090
0.7	0.7	β_5	0.025	0.299	0.090	0.106	0.284	0.092	0.140	0.332	0.130	0.105	0.326	0.117	0.400	0.380	0.305
0.6	0.6	β_1	-0.125	0.469	0.236	-0.469	0.579	0.555	-0.144	0.618	0.403	-0.196	0.673	0.491	-0.568	0.453	0.529
0.6	0.6	β_2	0.069	0.553	0.311	0.469	0.636	0.624	0.088	0.589	0.355	0.106	0.599	0.370	0.473	0.473	0.448
0.6	0.6	β_3	-0.133	0.213	0.063	-0.302	0.163	0.118	-0.193	0.242	0.096	-0.015	0.291	0.085	-0.128	0.292	0.102
0.6	0.6	β_4	-0.135	0.253	0.082	-0.264	0.193	0.107	-0.178	0.268	0.104	-0.065	0.313	0.102	-0.064	0.326	0.110
0.6	0.6	β_5	-0.041	0.271	0.075	0.146	0.265	0.092	0.171	0.349	0.151	0.091	0.353	0.133	0.424	0.415	0.352

Table 8: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow normal distribution; $n_0 = 200, n_1 = 100$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1	1	β_1	-0.021	0.130	0.017	-0.044	0.115	0.015	-0.062	0.321	0.107	-0.073	0.315	0.104	-0.099	0.212	0.055
1	1	β_2	0.019	0.289	0.084	0.056	0.284	0.084	0.088	0.365	0.141	0.035	0.373	0.140	0.200	0.363	0.172
1	1	β_3	-0.022	0.081	0.007	-0.031	0.078	0.007	-0.060	0.126	0.019	0.045	0.135	0.020	-0.017	0.123	0.015
1	1	β_4	-0.009	0.127	0.016	-0.026	0.120	0.015	-0.076	0.159	0.031	0.014	0.168	0.028	0.027	0.186	0.035
1	1	β_5	0.000	0.112	0.012	0.015	0.104	0.011	0.063	0.177	0.035	0.097	0.206	0.052	0.060	0.180	0.036
0.9	0.9	β_1	-0.005	0.142	0.020	0.062	0.123	0.019	-0.093	0.352	0.133	-0.132	0.353	0.142	-0.179	0.299	0.121
0.9	0.9	β_2	0.016	0.318	0.101	0.627	0.297	0.482	0.093	0.428	0.192	0.057	0.422	0.182	0.251	0.415	0.235
0.9	0.9	β_3	-0.015	0.103	0.011	-0.254	0.063	0.069	-0.096	0.249	0.071	0.048	0.255	0.067	-0.031	0.156	0.025
0.9	0.9	β_4	-0.015	0.162	0.026	-0.231	0.083	0.060	-0.110	0.225	0.063	0.054	0.230	0.056	0.029	0.219	0.049
0.9	0.9	β_5	-0.001	0.111	0.012	0.065	0.094	0.013	0.038	0.304	0.094	0.131	0.309	0.113	0.132	0.260	0.085
0.8	0.8	β_1	-0.039	0.164	0.029	0.006	0.205	0.042	-0.131	0.351	0.141	-0.087	0.352	0.131	-0.279	0.355	0.203
0.8	0.8	β_2	0.022	0.361	0.131	0.709	0.343	0.621	0.122	0.486	0.252	0.058	0.452	0.208	0.281	0.452	0.283
0.8	0.8	β_3	-0.018	0.143	0.021	-0.283	0.057	0.083	-0.058	0.215	0.050	0.022	0.211	0.045	-0.040	0.175	0.032
0.8	0.8	β_4	-0.020	0.189	0.036	-0.261	0.082	0.075	-0.080	0.300	0.096	0.084	0.319	0.109	0.051	0.244	0.062
0.8	0.8	β_5	-0.002	0.121	0.015	0.068	0.108	0.016	0.092	0.354	0.134	0.165	0.363	0.159	0.170	0.304	0.121
0.7	0.7	β_1	-0.016	0.168	0.029	-0.063	0.305	0.097	-0.238	0.409	0.224	-0.191	0.447	0.236	-0.367	0.409	0.301
0.7	0.7	β_2	0.012	0.373	0.139	0.683	0.428	0.650	0.126	0.570	0.341	0.074	0.579	0.341	0.322	0.491	0.345
0.7	0.7	β_3	-0.012	0.169	0.029	-0.286	0.079	0.088	-0.015	0.300	0.090	0.030	0.333	0.112	-0.064	0.210	0.048
0.7	0.7	β_4	-0.004	0.212	0.045	-0.265	0.097	0.080	-0.066	0.308	0.099	-0.018	0.320	0.102	-0.001	0.261	0.068
0.7	0.7	β_5	-0.002	0.129	0.017	0.081	0.127	0.023	0.091	0.366	0.142	0.159	0.365	0.159	0.277	0.360	0.206
0.6	0.6	β_1	-0.031	0.173	0.031	-0.283	0.488	0.319	-0.128	0.513	0.280	-0.089	0.528	0.287	-0.518	0.465	0.484
0.6	0.6	β_2	0.018	0.387	0.150	0.635	0.560	0.717	0.157	0.621	0.410	0.108	0.593	0.363	0.435	0.504	0.444
0.6	0.6	β_3	-0.005	0.186	0.035	-0.303	0.109	0.104	-0.079	0.366	0.140	-0.017	0.385	0.149	-0.109	0.256	0.078
0.6	0.6	β_4	-0.020	0.270	0.074	-0.266	0.153	0.094	-0.138	0.431	0.205	-0.078	0.421	0.183	-0.050	0.299	0.092
0.6	0.6	β_5	0.005	0.187	0.035	0.124	0.204	0.057	0.144	0.410	0.188	0.163	0.418	0.201	0.371	0.393	0.292

Table 9: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow normal distribution; $n_0 = 300, n_1 = 200$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1	1	β_1	-0.032	0.097	0.010	-0.017	0.081	0.007	0.030	0.249	0.063	0.022	0.260	0.068	-0.040	0.151	0.024
1	1	β_2	0.026	0.223	0.051	0.034	0.195	0.039	-0.038	0.269	0.074	-0.012	0.280	0.079	0.112	0.264	0.082
1	1	β_3	0.002	0.062	0.004	-0.017	0.059	0.004	-0.028	0.068	0.005	-0.012	0.076	0.006	-0.014	0.093	0.009
1	1	β_4	0.002	0.103	0.011	-0.012	0.089	0.008	-0.027	0.126	0.017	0.003	0.135	0.018	0.013	0.148	0.022
1	1	β_5	-0.001	0.077	0.006	0.002	0.066	0.004	0.027	0.117	0.014	0.032	0.113	0.014	0.029	0.121	0.015
0.9	0.9	β_1	-0.015	0.127	0.016	0.088	0.096	0.017	0.054	0.455	0.210	0.026	0.482	0.233	-0.110	0.214	0.058
0.9	0.9	β_2	0.016	0.273	0.075	0.625	0.235	0.446	-0.083	0.283	0.087	-0.107	0.285	0.092	0.135	0.348	0.139
0.9	0.9	β_3	0.000	0.092	0.008	-0.248	0.049	0.064	-0.120	0.146	0.036	0.009	0.155	0.024	-0.010	0.131	0.017
0.9	0.9	β_4	0.001	0.134	0.018	-0.226	0.057	0.054	-0.126	0.192	0.053	-0.002	0.205	0.042	0.029	0.178	0.033
0.9	0.9	β_5	-0.005	0.072	0.005	0.012	0.068	0.005	0.053	0.181	0.035	0.042	0.182	0.035	0.071	0.185	0.039
0.8	0.8	β_1	-0.020	0.139	0.020	0.059	0.129	0.020	0.084	0.425	0.188	0.023	0.429	0.185	-0.186	0.278	0.112
0.8	0.8	β_2	0.031	0.313	0.099	0.684	0.274	0.543	-0.098	0.314	0.109	-0.126	0.315	0.115	0.211	0.409	0.212
0.8	0.8	β_3	-0.002	0.113	0.013	-0.269	0.052	0.075	-0.104	0.137	0.030	0.004	0.146	0.021	-0.018	0.154	0.024
0.8	0.8	β_4	-0.004	0.164	0.027	-0.248	0.050	0.064	-0.136	0.209	0.062	0.022	0.208	0.044	0.053	0.211	0.047
0.8	0.8	β_5	-0.006	0.081	0.007	0.044	0.068	0.007	0.063	0.220	0.053	0.064	0.215	0.050	0.119	0.247	0.075
0.7	0.7	β_1	-0.013	0.143	0.021	-0.006	0.231	0.054	0.087	0.542	0.301	0.052	0.584	0.344	-0.273	0.363	0.207
0.7	0.7	β_2	0.025	0.314	0.099	0.708	0.364	0.634	-0.206	0.442	0.238	-0.186	0.461	0.247	0.266	0.461	0.283
0.7	0.7	β_3	-0.019	0.133	0.018	-0.283	0.069	0.085	-0.033	0.145	0.022	-0.028	0.177	0.032	-0.058	0.177	0.035
0.7	0.7	β_4	0.009	0.168	0.028	-0.256	0.087	0.073	-0.061	0.201	0.044	-0.014	0.259	0.067	0.024	0.235	0.056
0.7	0.7	β_5	-0.002	0.106	0.011	0.075	0.117	0.019	0.084	0.233	0.061	0.081	0.283	0.086	0.197	0.329	0.147
0.6	0.6	β_1	-0.036	0.150	0.024	-0.177	0.396	0.188	0.050	0.582	0.341	0.067	0.589	0.352	-0.443	0.439	0.389
0.6	0.6	β_2	0.025	0.328	0.108	0.675	0.505	0.711	-0.341	0.468	0.335	-0.311	0.469	0.317	0.328	0.494	0.352
0.6	0.6	β_3	-0.022	0.151	0.023	-0.292	0.109	0.097	-0.274	0.153	0.098	0.004	0.242	0.059	-0.096	0.228	0.061
0.6	0.6	β_4	-0.008	0.230	0.053	-0.269	0.115	0.085	-0.219	0.225	0.098	-0.040	0.271	0.075	-0.015	0.285	0.082
0.6	0.6	β_5	0.005	0.141	0.020	0.115	0.183	0.047	0.114	0.273	0.088	0.106	0.353	0.136	0.264	0.407	0.235

Table 10: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow normal distribution; $n_0 = 1000, n_1 = 500$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1	1	β_1	-0.023	0.062	0.004	-0.007	0.045	0.002	0.016	0.138	0.019	0.014	0.140	0.020	-0.011	0.069	0.005
1	1	β_2	0.012	0.146	0.022	0.025	0.126	0.016	-0.010	0.164	0.027	-0.004	0.170	0.029	0.031	0.155	0.025
1	1	β_3	0.002	0.039	0.001	-0.003	0.036	0.001	-0.011	0.043	0.002	-0.002	0.050	0.002	-0.006	0.049	0.002
1	1	β_4	0.001	0.071	0.005	0.001	0.056	0.003	-0.012	0.088	0.008	0.001	0.090	0.008	0.003	0.079	0.006
1	1	β_5	0.004	0.046	0.002	-0.011	0.042	0.002	0.009	0.061	0.004	-0.002	0.063	0.004	0.005	0.064	0.004
0.9	0.9	β_1	-0.025	0.075	0.006	0.098	0.062	0.013	0.051	0.245	0.063	0.022	0.249	0.062	-0.033	0.113	0.014
0.9	0.9	β_2	0.018	0.156	0.025	0.695	0.145	0.504	-0.029	0.169	0.029	-0.031	0.174	0.031	0.078	0.240	0.063
0.9	0.9	β_3	0.007	0.056	0.003	-0.258	0.029	0.067	-0.019	0.076	0.006	0.003	0.088	0.008	-0.015	0.076	0.006
0.9	0.9	β_4	0.009	0.082	0.007	-0.244	0.027	0.060	-0.032	0.130	0.018	0.020	0.131	0.018	0.020	0.129	0.017
0.9	0.9	β_5	0.006	0.050	0.002	0.025	0.040	0.002	0.012	0.109	0.012	0.012	0.108	0.012	0.018	0.097	0.010
0.8	0.8	β_1	-0.012	0.083	0.007	0.088	0.074	0.013	0.139	0.330	0.128	0.016	0.336	0.113	-0.106	0.213	0.057
0.8	0.8	β_2	0.007	0.202	0.041	0.735	0.152	0.563	-0.019	0.225	0.051	-0.051	0.226	0.054	0.099	0.314	0.108
0.8	0.8	β_3	0.000	0.072	0.005	-0.285	0.024	0.082	-0.072	0.129	0.022	-0.003	0.129	0.017	-0.002	0.116	0.013
0.8	0.8	β_4	0.004	0.100	0.010	-0.266	0.031	0.072	-0.102	0.161	0.036	0.006	0.165	0.027	0.032	0.175	0.032
0.8	0.8	β_5	0.002	0.043	0.002	0.069	0.041	0.006	0.010	0.122	0.015	0.018	0.128	0.017	0.050	0.161	0.028
0.7	0.7	β_1	-0.006	0.095	0.009	0.055	0.126	0.019	0.029	0.444	0.198	0.024	0.396	0.157	-0.195	0.311	0.135
0.7	0.7	β_2	0.075	0.223	0.055	0.757	0.228	0.625	-0.069	0.273	0.079	-0.127	0.286	0.098	0.153	0.405	0.187
0.7	0.7	β_3	-0.010	0.080	0.007	-0.291	0.036	0.086	-0.026	0.155	0.025	0.004	0.160	0.026	-0.022	0.143	0.021
0.7	0.7	β_4	0.016	0.111	0.013	-0.273	0.044	0.076	-0.047	0.187	0.037	0.017	0.192	0.037	0.037	0.216	0.048
0.7	0.7	β_5	-0.001	0.056	0.003	0.081	0.065	0.011	0.045	0.195	0.040	0.068	0.240	0.063	0.116	0.227	0.065
0.6	0.6	β_1	-0.033	0.101	0.011	-0.044	0.262	0.071	0.040	0.561	0.316	0.053	0.566	0.324	-0.351	0.414	0.294
0.6	0.6	β_2	0.017	0.229	0.053	0.755	0.387	0.720	-0.231	0.410	0.221	-0.277	0.444	0.274	0.286	0.489	0.321
0.6	0.6	β_3	-0.011	0.100	0.010	-0.297	0.060	0.092	-0.044	0.190	0.038	-0.014	0.202	0.041	-0.066	0.201	0.045
0.6	0.6	β_4	-0.002	0.141	0.020	-0.274	0.073	0.081	-0.083	0.194	0.044	0.009	0.248	0.061	0.005	0.248	0.061
0.6	0.6	β_5	-0.001	0.092	0.009	0.106	0.107	0.023	0.064	0.236	0.060	0.129	0.337	0.130	0.215	0.346	0.166

Table 11: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow normal distribution; $n_0 = 1000, n_1 = 1000$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1	1	β_1	-0.002	0.056	0.003	-0.007	0.043	0.002	0.003	0.100	0.010	0.024	0.104	0.011	-0.005	0.052	0.003
1	1	β_2	0.003	0.124	0.015	0.019	0.092	0.009	-0.004	0.143	0.020	0.005	0.149	0.022	0.022	0.118	0.015
1	1	β_3	0.007	0.037	0.001	0.000	0.031	0.001	-0.009	0.046	0.002	-0.007	0.048	0.002	-0.004	0.037	0.001
1	1	β_4	0.003	0.058	0.003	0.003	0.046	0.002	-0.006	0.061	0.004	0.004	0.068	0.005	0.003	0.064	0.004
1	1	β_5	-0.002	0.039	0.002	-0.003	0.037	0.001	0.006	0.054	0.003	0.008	0.056	0.003	0.004	0.047	0.002
0.9	0.9	β_1	-0.014	0.068	0.005	0.125	0.037	0.017	0.017	0.183	0.034	-0.003	0.187	0.035	-0.017	0.081	0.007
0.9	0.9	β_2	0.005	0.139	0.019	0.593	0.127	0.368	-0.024	0.144	0.021	-0.019	0.152	0.023	0.047	0.166	0.030
0.9	0.9	β_3	0.001	0.053	0.003	-0.227	0.025	0.052	0.003	0.064	0.004	0.015	0.065	0.004	-0.003	0.060	0.004
0.9	0.9	β_4	0.000	0.076	0.006	-0.215	0.032	0.047	-0.013	0.085	0.007	0.005	0.087	0.008	0.018	0.092	0.009
0.9	0.9	β_5	-0.003	0.039	0.002	0.002	0.038	0.001	0.019	0.088	0.008	0.029	0.088	0.009	0.012	0.076	0.006
0.8	0.8	β_1	-0.015	0.074	0.006	0.099	0.067	0.014	0.117	0.290	0.098	0.018	0.291	0.085	-0.054	0.145	0.024
0.8	0.8	β_2	0.011	0.170	0.029	0.695	0.155	0.507	-0.016	0.185	0.035	-0.041	0.186	0.036	0.059	0.246	0.064
0.8	0.8	β_3	0.008	0.064	0.004	-0.260	0.026	0.068	-0.047	0.108	0.014	0.008	0.111	0.012	-0.012	0.079	0.006
0.8	0.8	β_4	0.001	0.090	0.008	-0.244	0.032	0.061	-0.060	0.155	0.028	0.015	0.159	0.026	0.021	0.140	0.020
0.8	0.8	β_5	0.000	0.040	0.002	0.040	0.043	0.003	0.013	0.121	0.015	0.028	0.123	0.016	0.020	0.118	0.014
0.7	0.7	β_1	-0.010	0.079	0.006	0.098	0.076	0.015	0.029	0.409	0.168	0.022	0.416	0.173	-0.142	0.251	0.083
0.7	0.7	β_2	0.003	0.174	0.030	0.704	0.180	0.528	-0.057	0.256	0.069	-0.093	0.256	0.074	0.138	0.350	0.142
0.7	0.7	β_3	-0.003	0.077	0.006	-0.273	0.033	0.076	-0.110	0.145	0.033	0.001	0.148	0.022	-0.013	0.139	0.020
0.7	0.7	β_4	0.001	0.093	0.009	-0.257	0.040	0.068	-0.110	0.190	0.048	0.035	0.194	0.039	0.041	0.197	0.040
0.7	0.7	β_5	0.002	0.045	0.002	0.064	0.056	0.007	0.030	0.151	0.024	0.046	0.168	0.030	0.052	0.189	0.038
0.6	0.6	β_1	-0.013	0.087	0.008	0.018	0.198	0.040	0.023	0.450	0.203	0.039	0.465	0.218	-0.326	0.394	0.262
0.6	0.6	β_2	0.008	0.186	0.035	0.721	0.333	0.630	-0.120	0.310	0.110	-0.225	0.401	0.212	0.235	0.476	0.282
0.6	0.6	β_3	0.011	0.085	0.007	-0.276	0.064	0.080	-0.020	0.169	0.029	-0.006	0.181	0.033	-0.052	0.182	0.036
0.6	0.6	β_4	-0.001	0.126	0.016	-0.255	0.066	0.070	-0.109	0.213	0.057	0.031	0.232	0.055	0.038	0.231	0.055
0.6	0.6	β_5	0.002	0.079	0.006	0.071	0.095	0.014	0.067	0.215	0.051	0.091	0.289	0.092	0.177	0.319	0.133

7.2 Case IV; Subcase II: Simulation setup of Section 4.2 in the main paper is used

- $n_0 = 30, n_1 = 30$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 12.
- $n_0 = 200, n_1 = 100$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 13.
- $n_0 = 300, n_1 = 200$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 14.
- $n_0 = 1000, n_1 = 500$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 15.
- $n_0 = 1000, n_1 = 1000$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 16.

Observations: Scenarios similar to those in Section 7.1 are observed, and therefore the discussion is similar; we omit it for brevity.

Table 12: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow exponential distribution; $n_0 = 30$, $n_1 = 30$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

ξ	λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
				Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
3	1.0	1.0	β_1	-0.012	0.485	0.235	0.151	0.441	0.217	0.257	0.520	0.336	0.164	0.526	0.303	-0.200	0.512	0.302
3	1.0	1.0	β_2	0.180	0.473	0.256	0.166	0.452	0.232	0.215	0.485	0.281	0.195	0.486	0.274	-0.207	0.480	0.274
3	0.9	0.9	β_1	-0.006	0.490	0.240	0.237	0.535	0.342	0.315	0.566	0.419	0.211	0.592	0.395	-0.268	0.569	0.395
3	0.9	0.9	β_2	0.180	0.481	0.264	0.209	0.496	0.290	0.296	0.571	0.414	0.191	0.616	0.416	-0.303	0.567	0.413
3	0.8	0.8	β_1	-0.022	0.495	0.245	0.338	0.602	0.477	0.411	0.640	0.578	0.213	0.644	0.460	-0.348	0.630	0.518
3	0.8	0.8	β_2	0.213	0.481	0.277	0.312	0.589	0.444	0.386	0.634	0.551	0.239	0.647	0.476	-0.366	0.600	0.493
3	0.7	0.7	β_1	-0.050	0.524	0.277	0.427	0.659	0.617	0.457	0.643	0.622	0.271	0.676	0.530	-0.443	0.649	0.617
3	0.7	0.7	β_2	0.267	0.528	0.350	0.442	0.647	0.614	0.511	0.665	0.703	0.300	0.690	0.566	-0.479	0.678	0.690
3	0.6	0.6	β_1	-0.059	0.531	0.285	0.551	0.702	0.796	0.631	0.701	0.890	0.320	0.720	0.621	-0.585	0.705	0.840
3	0.6	0.6	β_2	0.256	0.541	0.358	0.576	0.684	0.800	0.581	0.689	0.812	0.329	0.710	0.612	-0.591	0.690	0.826
5	1.0	1.0	β_1	-0.001	0.260	0.068	0.047	0.244	0.062	0.059	0.323	0.108	0.074	0.337	0.119	-0.075	0.329	0.114
5	1.0	1.0	β_2	0.081	0.258	0.073	0.041	0.247	0.063	0.049	0.348	0.123	0.071	0.347	0.125	-0.094	0.342	0.126
5	0.9	0.9	β_1	0.001	0.319	0.102	0.111	0.342	0.129	0.107	0.396	0.168	0.115	0.403	0.176	-0.118	0.397	0.172
5	0.9	0.9	β_2	0.109	0.309	0.107	0.063	0.337	0.118	0.089	0.383	0.155	0.100	0.408	0.176	-0.118	0.385	0.162
5	0.8	0.8	β_1	-0.042	0.320	0.104	0.102	0.393	0.165	0.126	0.461	0.228	0.137	0.460	0.230	-0.168	0.458	0.238
5	0.8	0.8	β_2	0.192	0.323	0.141	0.169	0.438	0.220	0.188	0.445	0.233	0.159	0.447	0.225	-0.158	0.445	0.223
5	0.7	0.7	β_1	-0.020	0.327	0.107	0.255	0.543	0.360	0.276	0.545	0.373	0.211	0.587	0.389	-0.256	0.548	0.366
5	0.7	0.7	β_2	0.205	0.330	0.151	0.247	0.539	0.351	0.252	0.588	0.409	0.161	0.599	0.385	-0.312	0.584	0.438
5	0.6	0.6	β_1	-0.026	0.428	0.184	0.478	0.656	0.659	0.492	0.655	0.671	0.284	0.677	0.539	-0.480	0.657	0.663
5	0.6	0.6	β_2	0.240	0.439	0.250	0.406	0.654	0.592	0.482	0.640	0.642	0.253	0.693	0.544	-0.401	0.651	0.585
10	1.0	1.0	β_1	0.010	0.205	0.042	0.033	0.198	0.040	0.049	0.267	0.074	0.071	0.271	0.078	-0.056	0.271	0.077
10	1.0	1.0	β_2	0.053	0.223	0.053	0.023	0.197	0.039	0.026	0.268	0.072	0.036	0.267	0.073	-0.050	0.266	0.073
10	0.9	0.9	β_1	0.002	0.282	0.080	0.074	0.304	0.098	0.080	0.311	0.103	0.081	0.318	0.108	-0.071	0.313	0.103
10	0.9	0.9	β_2	0.090	0.289	0.092	0.065	0.308	0.099	0.059	0.320	0.106	0.077	0.332	0.116	-0.079	0.321	0.110
10	0.8	0.8	β_1	-0.023	0.327	0.107	0.108	0.383	0.158	0.113	0.372	0.151	0.110	0.372	0.150	-0.109	0.378	0.155
10	0.8	0.8	β_2	0.150	0.324	0.127	0.125	0.394	0.171	0.112	0.374	0.152	0.110	0.386	0.161	-0.106	0.373	0.151
10	0.7	0.7	β_1	-0.012	0.343	0.118	0.261	0.523	0.342	0.242	0.476	0.285	0.185	0.496	0.280	-0.145	0.481	0.253
10	0.7	0.7	β_2	0.170	0.368	0.164	0.180	0.501	0.283	0.184	0.485	0.269	0.145	0.502	0.273	-0.255	0.498	0.313
10	0.6	0.6	β_1	-0.038	0.431	0.187	0.445	0.631	0.596	0.418	0.607	0.543	0.277	0.620	0.461	-0.374	0.612	0.513
10	0.6	0.6	β_2	0.249	0.427	0.244	0.380	0.654	0.572	0.369	0.640	0.546	0.204	0.641	0.452	-0.383	0.642	0.558

Table 13: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow exponential distribution; $n_0 = 200$, $n_1 = 100$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

ξ	λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
				Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
3	1.0	1.0	β_1	0.014	0.302	0.091	-0.019	0.283	0.080	-0.077	0.299	0.095	-0.050	0.317	0.103	-0.060	0.312	0.101
3	1.0	1.0	β_2	-0.017	0.301	0.091	-0.091	0.286	0.090	-0.081	0.299	0.096	-0.088	0.326	0.114	-0.090	0.322	0.112
3	0.9	0.9	β_1	0.015	0.311	0.097	-0.055	0.274	0.078	-0.088	0.366	0.142	-0.100	0.387	0.160	-0.118	0.372	0.153
3	0.9	0.9	β_2	-0.020	0.310	0.096	-0.134	0.403	0.180	-0.048	0.363	0.134	-0.088	0.376	0.149	-0.091	0.368	0.144
3	0.8	0.8	β_1	0.002	0.322	0.104	-0.073	0.305	0.098	-0.035	0.444	0.198	-0.071	0.484	0.239	-0.156	0.447	0.224
3	0.8	0.8	β_2	-0.067	0.321	0.107	-0.261	0.539	0.359	-0.076	0.452	0.210	-0.031	0.476	0.228	-0.163	0.450	0.229
3	0.7	0.7	β_1	-0.013	0.332	0.110	-0.075	0.318	0.107	-0.030	0.552	0.306	-0.059	0.578	0.337	-0.251	0.543	0.358
3	0.7	0.7	β_2	-0.022	0.335	0.113	-0.449	0.646	0.619	-0.085	0.575	0.338	-0.083	0.550	0.309	-0.246	0.535	0.346
3	0.6	0.6	β_1	-0.032	0.338	0.115	-0.092	0.301	0.099	-0.114	0.726	0.540	-0.140	0.677	0.478	-0.451	0.655	0.632
3	0.6	0.6	β_2	-0.076	0.338	0.120	-0.772	0.718	1.111	-0.131	0.713	0.525	-0.184	0.681	0.498	-0.458	0.667	0.654
5	1.0	1.0	β_1	0.007	0.143	0.020	-0.020	0.135	0.019	-0.034	0.180	0.034	-0.018	0.184	0.034	-0.030	0.183	0.034
5	1.0	1.0	β_2	-0.010	0.147	0.022	-0.017	0.141	0.020	-0.030	0.173	0.031	-0.040	0.179	0.034	-0.016	0.177	0.031
5	0.9	0.9	β_1	0.025	0.144	0.021	-0.020	0.173	0.030	-0.097	0.212	0.054	-0.034	0.225	0.052	-0.033	0.215	0.047
5	0.9	0.9	β_2	-0.016	0.148	0.022	-0.030	0.175	0.032	-0.024	0.213	0.046	-0.065	0.228	0.056	-0.034	0.215	0.047
5	0.8	0.8	β_1	0.017	0.160	0.026	-0.039	0.236	0.057	-0.086	0.274	0.082	-0.054	0.285	0.084	-0.067	0.277	0.081
5	0.8	0.8	β_2	-0.095	0.164	0.036	-0.080	0.296	0.094	-0.052	0.275	0.078	-0.039	0.308	0.096	-0.041	0.264	0.071
5	0.7	0.7	β_1	0.018	0.190	0.036	-0.059	0.291	0.088	-0.025	0.366	0.135	-0.086	0.394	0.163	-0.092	0.366	0.143
5	0.7	0.7	β_2	-0.040	0.191	0.038	-0.202	0.481	0.272	-0.052	0.358	0.131	-0.111	0.392	0.166	-0.102	0.349	0.132
5	0.6	0.6	β_1	-0.003	0.232	0.054	-0.067	0.312	0.102	-0.116	0.511	0.275	-0.107	0.509	0.270	-0.194	0.501	0.288
5	0.6	0.6	β_2	-0.090	0.238	0.065	-0.593	0.686	0.822	-0.104	0.565	0.330	-0.109	0.537	0.300	-0.287	0.557	0.393
10	1.0	1.0	β_1	0.003	0.116	0.013	-0.017	0.113	0.013	-0.103	0.144	0.031	-0.032	0.149	0.023	-0.014	0.148	0.022
10	1.0	1.0	β_2	-0.014	0.120	0.015	-0.008	0.110	0.012	-0.008	0.150	0.023	-0.012	0.150	0.023	-0.017	0.147	0.022
10	0.9	0.9	β_1	0.015	0.139	0.020	-0.018	0.165	0.028	-0.075	0.179	0.038	-0.053	0.183	0.036	-0.037	0.181	0.034
10	0.9	0.9	β_2	-0.007	0.140	0.020	-0.035	0.173	0.031	-0.004	0.171	0.029	-0.006	0.177	0.031	-0.009	0.177	0.032
10	0.8	0.8	β_1	0.031	0.148	0.023	-0.034	0.215	0.047	-0.055	0.246	0.064	-0.083	0.256	0.072	-0.049	0.252	0.066
10	0.8	0.8	β_2	-0.088	0.155	0.032	-0.050	0.240	0.060	-0.017	0.253	0.064	-0.037	0.258	0.068	-0.045	0.255	0.067
10	0.7	0.7	β_1	0.026	0.178	0.032	-0.077	0.289	0.089	-0.019	0.320	0.103	-0.105	0.329	0.119	-0.074	0.324	0.111
10	0.7	0.7	β_2	-0.042	0.187	0.037	-0.114	0.401	0.174	-0.059	0.305	0.096	-0.020	0.334	0.112	-0.075	0.309	0.101
10	0.6	0.6	β_1	-0.018	0.216	0.047	-0.077	0.330	0.115	-0.033	0.458	0.211	-0.054	0.471	0.225	-0.156	0.459	0.235
10	0.6	0.6	β_2	-0.091	0.213	0.054	-0.509	0.662	0.697	-0.046	0.452	0.206	-0.088	0.461	0.220	-0.175	0.451	0.234

Table 14: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow exponential distribution; $n_0 = 300$, $n_1 = 200$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

ξ	λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
				Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
3	1.0	1.0	β_1	0.005	0.205	0.042	-0.030	0.173	0.031	-0.039	0.249	0.063	-0.048	0.259	0.069	-0.045	0.263	0.071
3	1.0	1.0	β_2	-0.009	0.204	0.042	-0.029	0.171	0.030	-0.060	0.255	0.069	-0.099	0.265	0.080	-0.054	0.258	0.070
3	0.9	0.9	β_1	-0.006	0.221	0.049	-0.072	0.232	0.059	-0.076	0.323	0.110	-0.083	0.324	0.112	-0.073	0.308	0.100
3	0.9	0.9	β_2	-0.107	0.224	0.062	-0.058	0.306	0.097	-0.076	0.308	0.100	-0.098	0.309	0.105	-0.069	0.309	0.100
3	0.8	0.8	β_1	0.003	0.232	0.054	-0.068	0.270	0.078	-0.072	0.386	0.154	-0.057	0.389	0.154	-0.117	0.379	0.157
3	0.8	0.8	β_2	-0.042	0.234	0.057	-0.149	0.415	0.194	-0.087	0.386	0.157	-0.060	0.395	0.160	-0.100	0.375	0.151
3	0.7	0.7	β_1	-0.008	0.230	0.053	-0.080	0.307	0.101	-0.105	0.501	0.262	-0.074	0.510	0.266	-0.217	0.508	0.305
3	0.7	0.7	β_2	-0.075	0.239	0.063	-0.365	0.593	0.485	-0.097	0.466	0.226	-0.102	0.489	0.250	-0.183	0.478	0.262
3	0.6	0.6	β_1	0.009	0.235	0.055	-0.041	0.310	0.098	-0.113	0.586	0.356	-0.155	0.610	0.396	-0.343	0.592	0.468
3	0.6	0.6	β_2	-0.074	0.236	0.061	-0.694	0.906	1.302	-0.113	0.612	0.387	-0.115	0.648	0.433	-0.340	0.620	0.500
5	1.0	1.0	β_1	0.014	0.102	0.011	-0.022	0.091	0.009	-0.009	0.139	0.019	-0.010	0.137	0.019	-0.009	0.140	0.020
5	1.0	1.0	β_2	-0.016	0.103	0.011	-0.008	0.089	0.008	-0.041	0.137	0.020	-0.037	0.147	0.023	-0.019	0.141	0.020
5	0.9	0.9	β_1	0.019	0.105	0.011	-0.040	0.144	0.022	-0.011	0.161	0.026	-0.034	0.162	0.028	-0.012	0.165	0.027
5	0.9	0.9	β_2	-0.007	0.104	0.011	-0.005	0.132	0.017	-0.006	0.165	0.027	-0.026	0.163	0.027	-0.027	0.167	0.029
5	0.8	0.8	β_1	0.022	0.129	0.017	-0.041	0.187	0.037	-0.040	0.214	0.048	-0.043	0.228	0.054	-0.052	0.226	0.054
5	0.8	0.8	β_2	-0.101	0.136	0.029	-0.034	0.189	0.037	-0.038	0.206	0.044	-0.082	0.211	0.051	-0.019	0.215	0.047
5	0.7	0.7	β_1	-0.001	0.149	0.022	-0.055	0.246	0.063	-0.075	0.296	0.093	-0.079	0.294	0.093	-0.061	0.292	0.089
5	0.7	0.7	β_2	-0.047	0.155	0.026	-0.103	0.344	0.129	-0.056	0.293	0.089	-0.024	0.295	0.088	-0.063	0.289	0.087
5	0.6	0.6	β_1	-0.003	0.177	0.031	-0.089	0.307	0.102	-0.080	0.464	0.222	-0.110	0.474	0.237	-0.201	0.473	0.264
5	0.6	0.6	β_2	-0.014	0.184	0.034	-0.411	0.627	0.562	-0.089	0.472	0.231	-0.115	0.474	0.238	-0.160	0.470	0.247
10	1.0	1.0	β_1	-0.009	0.086	0.008	-0.016	0.070	0.005	-0.011	0.095	0.009	-0.028	0.101	0.011	-0.014	0.111	0.013
10	1.0	1.0	β_2	-0.006	0.082	0.007	-0.019	0.073	0.006	-0.007	0.108	0.012	-0.015	0.110	0.012	-0.003	0.111	0.012
10	0.9	0.9	β_1	0.012	0.115	0.013	-0.024	0.139	0.020	-0.016	0.153	0.024	-0.022	0.169	0.029	-0.023	0.165	0.028
10	0.9	0.9	β_2	-0.012	0.112	0.013	-0.022	0.142	0.021	-0.024	0.154	0.024	-0.031	0.158	0.026	-0.015	0.161	0.026
10	0.8	0.8	β_1	0.013	0.121	0.015	-0.029	0.156	0.025	-0.032	0.191	0.037	-0.022	0.200	0.041	-0.033	0.202	0.042
10	0.8	0.8	β_2	-0.017	0.125	0.016	-0.033	0.174	0.031	-0.035	0.191	0.038	-0.058	0.195	0.041	-0.025	0.198	0.040
10	0.7	0.7	β_1	0.010	0.148	0.022	-0.053	0.221	0.052	-0.070	0.263	0.074	-0.065	0.273	0.079	-0.061	0.271	0.077
10	0.7	0.7	β_2	-0.103	0.152	0.034	-0.050	0.264	0.072	-0.044	0.265	0.072	-0.029	0.282	0.080	-0.049	0.277	0.079
10	0.6	0.6	β_1	-0.009	0.178	0.032	-0.077	0.305	0.099	-0.090	0.394	0.163	-0.080	0.412	0.176	-0.135	0.408	0.184
10	0.6	0.6	β_2	-0.058	0.180	0.036	-0.309	0.573	0.423	-0.074	0.407	0.171	-0.078	0.408	0.173	-0.099	0.401	0.171

Table 15: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow exponential distribution; $n_0 = 1000$, $n_1 = 500$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

ξ	λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
				Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
3	1.0	1.0	β_1	0.011	0.120	0.014	-0.006	0.113	0.013	-0.026	0.168	0.029	-0.029	0.167	0.029	-0.011	0.162	0.026
3	1.0	1.0	β_2	-0.008	0.119	0.014	-0.012	0.113	0.013	-0.009	0.169	0.029	-0.021	0.170	0.029	-0.028	0.167	0.029
3	0.9	0.9	β_1	0.018	0.132	0.018	-0.017	0.140	0.020	-0.007	0.213	0.045	-0.012	0.218	0.048	-0.057	0.226	0.054
3	0.9	0.9	β_2	-0.013	0.130	0.017	-0.014	0.141	0.020	-0.035	0.208	0.044	-0.048	0.203	0.044	-0.012	0.210	0.044
3	0.8	0.8	β_1	-0.002	0.134	0.018	-0.033	0.192	0.038	-0.065	0.274	0.080	-0.082	0.271	0.080	-0.058	0.271	0.077
3	0.8	0.8	β_2	-0.020	0.132	0.018	-0.020	0.188	0.036	-0.039	0.286	0.083	-0.030	0.289	0.084	-0.054	0.282	0.082
3	0.7	0.7	β_1	-0.026	0.144	0.021	-0.062	0.254	0.069	-0.023	0.359	0.130	-0.073	0.357	0.133	-0.089	0.351	0.131
3	0.7	0.7	β_2	-0.020	0.143	0.021	-0.099	0.383	0.156	-0.028	0.355	0.127	-0.035	0.352	0.125	-0.098	0.352	0.134
3	0.6	0.6	β_1	-0.013	0.167	0.028	-0.076	0.317	0.106	-0.108	0.521	0.283	-0.151	0.527	0.300	-0.248	0.522	0.334
3	0.6	0.6	β_2	-0.055	0.163	0.030	-0.431	0.652	0.610	-0.127	0.544	0.312	-0.168	0.555	0.337	-0.241	0.548	0.358
5	1.0	1.0	β_1	0.007	0.068	0.005	-0.001	0.064	0.004	-0.010	0.087	0.008	-0.013	0.086	0.008	-0.008	0.084	0.007
5	1.0	1.0	β_2	-0.007	0.066	0.004	-0.005	0.063	0.004	0.001	0.087	0.008	0.000	0.087	0.008	-0.002	0.085	0.007
5	0.9	0.9	β_1	0.018	0.083	0.007	-0.008	0.082	0.007	-0.009	0.104	0.011	-0.008	0.106	0.011	-0.011	0.108	0.012
5	0.9	0.9	β_2	-0.003	0.085	0.007	-0.003	0.086	0.007	-0.006	0.106	0.011	-0.013	0.108	0.012	-0.006	0.106	0.011
5	0.8	0.8	β_1	0.019	0.086	0.008	-0.012	0.112	0.013	0.010	0.139	0.020	0.010	0.137	0.019	-0.017	0.137	0.019
5	0.8	0.8	β_2	-0.019	0.086	0.008	-0.008	0.113	0.013	-0.028	0.140	0.020	-0.040	0.143	0.022	-0.010	0.140	0.020
5	0.7	0.7	β_1	0.004	0.105	0.011	-0.017	0.168	0.029	-0.020	0.214	0.046	-0.024	0.216	0.047	-0.033	0.210	0.045
5	0.7	0.7	β_2	-0.004	0.104	0.011	-0.027	0.171	0.030	-0.027	0.203	0.042	-0.043	0.209	0.045	-0.030	0.205	0.043
5	0.6	0.6	β_1	-0.010	0.142	0.020	-0.056	0.272	0.077	-0.048	0.350	0.125	-0.034	0.345	0.121	-0.081	0.342	0.123
5	0.6	0.6	β_2	-0.020	0.143	0.021	-0.130	0.410	0.185	-0.026	0.352	0.124	-0.035	0.345	0.120	-0.102	0.354	0.136
10	1.0	1.0	β_1	0.012	0.050	0.003	-0.004	0.049	0.002	-0.006	0.063	0.004	-0.008	0.066	0.004	-0.009	0.066	0.004
10	1.0	1.0	β_2	-0.008	0.055	0.003	-0.001	0.049	0.002	0.001	0.066	0.004	-0.001	0.066	0.004	0.003	0.065	0.004
10	0.9	0.9	β_1	0.003	0.064	0.004	-0.016	0.092	0.009	0.004	0.097	0.010	0.002	0.100	0.010	-0.001	0.097	0.009
10	0.9	0.9	β_2	-0.008	0.070	0.005	0.002	0.089	0.008	-0.015	0.097	0.010	-0.020	0.099	0.010	-0.012	0.096	0.009
10	0.8	0.8	β_1	0.017	0.088	0.008	-0.009	0.114	0.013	0.001	0.139	0.019	-0.004	0.136	0.018	-0.015	0.137	0.019
10	0.8	0.8	β_2	-0.093	0.084	0.016	-0.011	0.116	0.013	-0.019	0.141	0.020	-0.024	0.142	0.021	-0.011	0.134	0.018
10	0.7	0.7	β_1	0.009	0.090	0.008	-0.021	0.155	0.024	-0.002	0.190	0.036	-0.013	0.188	0.035	-0.027	0.187	0.036
10	0.7	0.7	β_2	-0.009	0.095	0.009	-0.014	0.149	0.022	-0.041	0.184	0.036	-0.046	0.183	0.036	-0.023	0.184	0.034
10	0.6	0.6	β_1	-0.029	0.109	0.013	-0.056	0.264	0.073	-0.045	0.298	0.091	-0.080	0.299	0.096	-0.055	0.300	0.093
10	0.6	0.6	β_2	-0.032	0.108	0.013	-0.106	0.377	0.154	-0.076	0.305	0.099	-0.062	0.302	0.095	-0.082	0.307	0.101

Table 16: Comparison of coefficient estimation for different choices of λ_0 and λ_1 when biomarkers follow exponential distribution; $n_0 = 1000$, $n_1 = 1000$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

ξ	λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
				Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
3	1.0	1.0	β_1	0.025	0.101	0.011	-0.003	0.089	0.008	-0.020	0.114	0.013	-0.021	0.149	0.023	-0.012	0.135	0.018
3	1.0	1.0	β_2	-0.005	0.103	0.011	-0.010	0.090	0.008	-0.003	0.114	0.013	-0.010	0.145	0.021	-0.015	0.137	0.019
3	0.9	0.9	β_1	0.021	0.109	0.012	-0.009	0.113	0.013	0.012	0.164	0.027	0.010	0.164	0.027	-0.020	0.171	0.030
3	0.9	0.9	β_2	-0.012	0.107	0.012	-0.013	0.112	0.013	-0.047	0.169	0.031	-0.058	0.171	0.033	-0.020	0.165	0.028
3	0.8	0.8	β_1	-0.005	0.113	0.013	-0.023	0.158	0.025	-0.023	0.230	0.053	-0.047	0.228	0.054	-0.031	0.228	0.053
3	0.8	0.8	β_2	-0.006	0.120	0.014	-0.012	0.147	0.022	-0.023	0.234	0.055	-0.082	0.237	0.063	-0.046	0.231	0.055
3	0.7	0.7	β_1	-0.012	0.117	0.014	-0.027	0.209	0.044	-0.097	0.307	0.104	-0.093	0.303	0.100	-0.059	0.303	0.096
3	0.7	0.7	β_2	-0.019	0.121	0.015	-0.050	0.240	0.060	-0.078	0.303	0.098	-0.094	0.306	0.102	-0.080	0.309	0.102
3	0.6	0.6	β_1	-0.016	0.124	0.016	-0.080	0.309	0.102	-0.103	0.487	0.248	-0.146	0.494	0.265	-0.183	0.485	0.269
3	0.6	0.6	β_2	-0.027	0.126	0.017	-0.319	0.599	0.460	-0.174	0.483	0.264	-0.166	0.494	0.271	-0.202	0.486	0.277
5	1.0	1.0	β_1	0.004	0.055	0.003	-0.001	0.048	0.002	0.001	0.060	0.004	-0.001	0.061	0.004	-0.008	0.069	0.005
5	1.0	1.0	β_2	-0.008	0.061	0.004	-0.004	0.048	0.002	-0.005	0.061	0.004	-0.006	0.061	0.004	0.001	0.068	0.005
5	0.9	0.9	β_1	0.005	0.064	0.004	-0.004	0.069	0.005	-0.005	0.074	0.006	-0.006	0.085	0.007	-0.001	0.085	0.007
5	0.9	0.9	β_2	-0.007	0.066	0.004	-0.004	0.066	0.004	-0.005	0.074	0.006	-0.008	0.084	0.007	-0.009	0.085	0.007
5	0.8	0.8	β_1	0.011	0.076	0.006	-0.009	0.095	0.009	-0.021	0.103	0.011	-0.028	0.117	0.015	-0.010	0.115	0.013
5	0.8	0.8	β_2	-0.004	0.075	0.006	-0.007	0.093	0.009	0.006	0.106	0.011	0.003	0.120	0.014	-0.010	0.119	0.014
5	0.7	0.7	β_1	-0.006	0.090	0.008	-0.014	0.130	0.017	-0.027	0.168	0.029	-0.037	0.176	0.032	-0.026	0.171	0.030
5	0.7	0.7	β_2	-0.019	0.091	0.009	-0.011	0.130	0.017	-0.009	0.172	0.030	-0.019	0.172	0.030	-0.016	0.170	0.029
5	0.6	0.6	β_1	-0.037	0.113	0.014	-0.029	0.239	0.058	-0.094	0.303	0.101	-0.040	0.307	0.096	-0.059	0.300	0.093
5	0.6	0.6	β_2	-0.019	0.113	0.013	-0.096	0.329	0.117	-0.067	0.315	0.104	-0.087	0.312	0.105	-0.079	0.310	0.102
10	1.0	1.0	β_1	0.004	0.040	0.002	0.001	0.038	0.001	-0.003	0.051	0.003	-0.007	0.058	0.003	-0.004	0.056	0.003
10	1.0	1.0	β_2	-0.008	0.040	0.002	-0.005	0.038	0.001	-0.002	0.051	0.003	0.003	0.058	0.003	-0.001	0.056	0.003
10	0.9	0.9	β_1	0.015	0.052	0.003	-0.001	0.073	0.005	-0.003	0.071	0.005	-0.003	0.079	0.006	-0.001	0.082	0.007
10	0.9	0.9	β_2	-0.005	0.052	0.003	-0.006	0.073	0.005	-0.003	0.075	0.006	-0.009	0.083	0.007	-0.008	0.084	0.007
10	0.8	0.8	β_1	0.024	0.069	0.005	-0.003	0.096	0.009	-0.027	0.078	0.007	-0.028	0.112	0.013	-0.016	0.116	0.014
10	0.8	0.8	β_2	-0.011	0.069	0.005	-0.011	0.099	0.010	0.016	0.082	0.007	0.009	0.104	0.011	-0.003	0.115	0.013
10	0.7	0.7	β_1	0.006	0.074	0.006	-0.015	0.130	0.017	0.012	0.127	0.016	-0.001	0.126	0.016	-0.016	0.160	0.026
10	0.7	0.7	β_2	-0.013	0.074	0.006	-0.012	0.128	0.017	-0.038	0.131	0.019	-0.047	0.167	0.030	-0.022	0.165	0.028
10	0.6	0.6	β_1	-0.018	0.087	0.008	-0.048	0.224	0.053	-0.038	0.275	0.077	-0.032	0.281	0.080	-0.055	0.265	0.073
10	0.6	0.6	β_2	-0.016	0.088	0.008	-0.048	0.281	0.081	-0.049	0.281	0.081	-0.054	0.327	0.110	-0.049	0.266	0.073

8. CASE V: SIMULATION STUDIES FOR COMBINATIONS OF MORE BIOMARKERS

In this simulation study, we consider four biomarkers and posit that $X_j|D = 1 \sim \exp(\xi_{1j})$ and $X_j|D = 0 \sim \exp(\xi_{0j})$ with $\xi_{1j} = j$ and $\xi_{0j} = j + 1$ for $j = 1, \dots, 4$. Let $f(\mathbf{x})$ and $g(\mathbf{x})$ be the density functions for $\mathbf{X}|D = 1$ and $\mathbf{X}|D = 0$. It is easy to verify that

$$\log \frac{f(\mathbf{x})}{g(\mathbf{x})} = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4,$$

with $\alpha = -\log(5)$, $\beta_1 = 1$, $\beta_2 = 2$, $\beta_3 = 1$, and $\beta_4 = 1$.

8.1 Case V; Subcase I: Comparison of the ROC curves

1. The exponential tilting model is correctly specified; i.e., $\lambda_0 = \lambda_1 = 1$.
 - $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 33.
 - $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 34.
2. The exponential tilting model is misspecified; i.e., $\lambda_0 = \lambda_1 = 0.8$.
 - $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 35.
 - $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 36.
3. $h(\mathbf{x})$ is misspecified; i.e., instead of using $\mathbf{x}$, we use $\log(\mathbf{x})$ when processing the data.
 - $n_0 = 30, n_1 = 30$. The constructed ROC curves for all the methods are given in Figure 37.

- $n_0 = 300, n_1 = 200$. The constructed ROC curves for all the methods are given in Figure 38.

Observations: The observations are similar to those in Sections 5 and 6.2; we omit them for brevity.

Figure 33: Plot of the ROC curves of the optimal combinations of four biomarkers based on correctly specified monotonic density ratio model and exponential tilting model when the four biomarkers follow exponential distributions: $n_0 = 30, n_1 = 30$.

Figure 34: Plot of the ROC curves of the optimal combinations of four biomarkers based on correctly specified monotonic density ratio model and exponential tilting model when the four biomarkers follow exponential distributions: $n_0 = 300$, $n_1 = 200$.

Figure 35: Plot of the ROC curves of the optimal combinations of four biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the four biomarkers follow exponential distributions: $n_0 = 30$, $n_1 = 30$.

Figure 36: Plot of the ROC curves of the optimal combinations of four biomarkers based on correctly specified monotonic density ratio model and misspecified exponential tilting model when the four biomarkers follow exponential distributions: $n_0 = 300$, $n_1 = 200$.

Figure 37: Plot of the ROC curves of the optimal combinations of four biomarkers based on correctly specified monotonic density ratio model and exponential tilting model when the four biomarkers follow exponential distributions: $n_0 = 30$, $n_1 = 30$; $h(\mathbf{x})$ is misspecified.

Figure 38: Plot of the ROC curves of the optimal combinations of four biomarkers based on correctly specified monotonic density ratio model and exponential tilting model when the four biomarkers follow exponential distributions: $n_0 = 300$, $n_1 = 200$; $h(\mathbf{x})$ is misspecified.

8.2 Case V; subcase II: Comparison of the coefficient estimates

- $n_0 = 30$, $n_1 = 30$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 17.
- $n_0 = 300$, $n_1 = 200$. The β estimates based on the proposed, exponential tilting, MH, nonparametric, and smoothed EL methods are summarized in Table 18.

Observations: The observations are similar to those in Section 7.2; we omit them for brevity.

Table 17: Comparison of coefficient estimation for multivariate biomarkers; $n_0 = 30$, $n_1 = 30$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1.0	1.0	β_1	-0.072	0.203	0.046	-0.080	0.197	0.045	-0.080	0.210	0.050	-0.083	0.224	0.057	-0.077	0.223	0.056
		β_2	-0.105	0.302	0.102	-0.120	0.294	0.100	-0.128	0.306	0.110	-0.123	0.312	0.112	-0.125	0.324	0.121
		β_3	-0.107	0.374	0.151	-0.144	0.359	0.150	-0.160	0.365	0.158	-0.153	0.364	0.156	-0.178	0.374	0.171
		β_4	-0.120	0.447	0.214	-0.181	0.445	0.230	-0.205	0.462	0.255	-0.188	0.433	0.223	-0.228	0.457	0.261
0.9	0.9	β_1	-0.099	0.203	0.051	-0.137	0.221	0.068	-0.141	0.239	0.077	-0.123	0.243	0.074	-0.116	0.264	0.083
		β_2	-0.111	0.314	0.111	-0.179	0.348	0.153	-0.160	0.336	0.139	-0.181	0.369	0.168	-0.149	0.348	0.143
		β_3	-0.140	0.376	0.161	-0.204	0.417	0.215	-0.190	0.415	0.208	-0.195	0.417	0.212	-0.203	0.412	0.211
		β_4	-0.129	0.452	0.221	-0.225	0.509	0.310	-0.241	0.501	0.309	-0.229	0.471	0.274	-0.262	0.475	0.294
0.8	0.8	β_1	-0.116	0.212	0.058	-0.202	0.214	0.087	-0.212	0.261	0.113	-0.147	0.311	0.118	-0.169	0.303	0.120
		β_2	-0.154	0.379	0.167	-0.288	0.418	0.258	-0.240	0.378	0.201	-0.266	0.415	0.243	-0.231	0.407	0.219
		β_3	-0.142	0.390	0.172	-0.302	0.504	0.345	-0.250	0.477	0.290	-0.275	0.490	0.316	-0.262	0.462	0.282
		β_4	-0.170	0.477	0.256	-0.319	0.567	0.423	-0.326	0.565	0.426	-0.301	0.506	0.347	-0.343	0.517	0.385
0.7	0.7	β_1	-0.145	0.267	0.092	-0.245	0.204	0.102	-0.302	0.271	0.165	-0.194	0.338	0.152	-0.267	0.333	0.182
		β_2	-0.191	0.400	0.196	-0.395	0.429	0.340	-0.329	0.400	0.268	-0.379	0.437	0.334	-0.313	0.421	0.276
		β_3	-0.164	0.410	0.195	-0.417	0.536	0.461	-0.337	0.514	0.377	-0.359	0.517	0.396	-0.319	0.498	0.350
		β_4	-0.161	0.546	0.324	-0.414	0.632	0.571	-0.306	0.609	0.465	-0.380	0.587	0.489	-0.318	0.557	0.411
0.6	0.6	β_1	-0.148	0.264	0.092	-0.276	0.194	0.113	-0.400	0.301	0.250	-0.203	0.440	0.235	-0.381	0.384	0.293
		β_2	-0.213	0.425	0.226	-0.495	0.427	0.427	-0.384	0.419	0.323	-0.485	0.479	0.465	-0.391	0.456	0.361
		β_3	-0.209	0.449	0.246	-0.488	0.557	0.548	-0.404	0.549	0.465	-0.485	0.545	0.533	-0.407	0.535	0.451
		β_4	-0.164	0.534	0.312	-0.494	0.649	0.666	-0.406	0.627	0.558	-0.497	0.573	0.576	-0.411	0.564	0.487

Table 18: Comparison of coefficient estimation for multivariate biomarkers; $n_0 = 300$, $n_1 = 200$; $\lambda_0 = \lambda_1 = 1$ indicates correctly specified monotonic density ratio and exponential tilting models; $\lambda_0 < 1$ or $\lambda_1 < 1$ indicates correctly specified monotonic density ratio model but misspecified exponential tilting model

λ_0	λ_1	Par.	Proposed			Exponential tilting			MH			Nonparametric			Smoothed EL		
			Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE	Bias	SD	MSE
1.0	1.0	β_1	-0.021	0.092	0.009	-0.016	0.091	0.008	-0.004	0.101	0.010	-0.017	0.109	0.012	-0.014	0.109	0.012
		β_2	-0.023	0.134	0.019	-0.015	0.116	0.014	-0.019	0.127	0.016	-0.021	0.137	0.019	-0.022	0.135	0.019
		β_3	-0.013	0.154	0.024	-0.015	0.138	0.019	-0.024	0.147	0.022	-0.027	0.160	0.026	-0.027	0.160	0.026
		β_4	-0.026	0.184	0.034	-0.030	0.184	0.035	-0.038	0.189	0.037	-0.033	0.200	0.041	-0.035	0.201	0.041
0.9	0.9	β_1	-0.030	0.099	0.011	-0.044	0.115	0.015	-0.017	0.132	0.018	-0.029	0.139	0.020	-0.026	0.137	0.019
		β_2	-0.022	0.146	0.022	-0.017	0.140	0.020	-0.020	0.151	0.023	-0.024	0.161	0.026	-0.023	0.158	0.026
		β_3	-0.033	0.180	0.033	-0.028	0.194	0.038	-0.034	0.196	0.040	-0.032	0.205	0.043	-0.031	0.207	0.044
		β_4	-0.045	0.214	0.048	-0.042	0.237	0.058	-0.071	0.241	0.063	-0.075	0.255	0.071	-0.080	0.255	0.072
0.8	0.8	β_1	-0.045	0.100	0.012	-0.066	0.147	0.026	-0.027	0.159	0.026	-0.032	0.170	0.030	-0.031	0.172	0.030
		β_2	-0.031	0.212	0.046	-0.047	0.208	0.045	-0.053	0.211	0.047	-0.057	0.225	0.054	-0.055	0.224	0.053
		β_3	-0.067	0.253	0.069	-0.079	0.263	0.075	-0.092	0.264	0.078	-0.102	0.275	0.086	-0.099	0.273	0.084
		β_4	-0.051	0.255	0.068	-0.047	0.300	0.093	-0.069	0.291	0.089	-0.070	0.294	0.091	-0.078	0.297	0.094
0.7	0.7	β_1	-0.058	0.107	0.015	-0.114	0.185	0.047	-0.079	0.209	0.050	-0.079	0.223	0.056	-0.078	0.221	0.055
		β_2	-0.060	0.252	0.067	-0.108	0.285	0.093	-0.118	0.281	0.093	-0.145	0.311	0.118	-0.123	0.294	0.101
		β_3	-0.068	0.289	0.088	-0.112	0.364	0.145	-0.118	0.365	0.147	-0.124	0.364	0.148	-0.125	0.361	0.146
		β_4	-0.074	0.292	0.091	-0.163	0.432	0.213	-0.181	0.418	0.207	-0.178	0.418	0.206	-0.186	0.419	0.210
0.6	0.6	β_1	-0.076	0.117	0.020	-0.213	0.203	0.086	-0.213	0.273	0.120	-0.164	0.254	0.091	-0.194	0.297	0.126
		β_2	-0.104	0.312	0.108	-0.320	0.400	0.262	-0.234	0.385	0.203	-0.344	0.445	0.316	-0.247	0.405	0.225
		β_3	-0.101	0.334	0.122	-0.286	0.501	0.333	-0.244	0.455	0.267	-0.314	0.477	0.326	-0.247	0.449	0.263
		β_4	-0.077	0.322	0.110	-0.289	0.587	0.428	-0.260	0.544	0.363	-0.319	0.555	0.410	-0.248	0.512	0.323

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