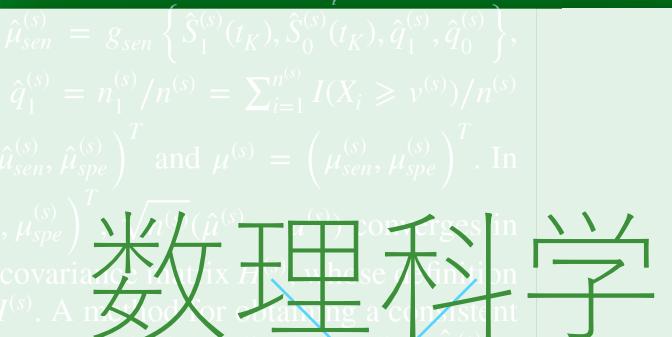


and $q_0^{(s)} = P(X \leq v^{(s)})$. The logit-transformed sensitivity $\mu_{sen}^{(s)} = \text{specificity } \mu_{spe}^{(s)} = \text{logit}\{\text{spe}(v^{(s)}, t_K)\}$ are given by $\mu_{sen}^{(s)} =$, and $\mu_{spe}^{(s)} = g_{spe}\left\{S_1^{(s)}(t_K), S_0^{(s)}(t_K), q_1^{(s)}, q_0^{(s)}\right\}$, respectively, where $g_{sen}(x, y, z, w) = \log\{(1-x)z\} - \log\{(1-y)w\}$ and $g_{spe}(x, y, z, w) =$ able to estimate $\mu_{sen}^{(s)}$ and $\mu_{spe}^{(s)}$ by $\hat{\mu}_{sen}^{(s)} = g_{sen}\left\{S_1^{(s)}(t_K), S_0^{(s)}(t_K), \hat{q}_1^{(s)}, \hat{q}_0^{(s)}\right\}$, $\hat{q}_1^{(s)} = n_1^{(s)}/n^{(s)} = \sum_{i=1}^{n^{(s)}} I(X_i \geq v^{(s)})/n^{(s)}$, $X_i < v^{(s)}/n^{(s)}$. Denote $\hat{\mu}^{(s)} = \left(\hat{\mu}_{sen}^{(s)}, \hat{\mu}_{spe}^{(s)}\right)^T$ and $\mu^{(s)} = \left(\mu_{sen}^{(s)}, \mu_{spe}^{(s)}\right)^T$. In $n^{(s)} \rightarrow \infty$, conditional on $\left(\mu_{sen}^{(s)}, \mu_{spe}^{(s)}\right)^T$ converges in distribution with a variance-covariance matrix $H^{(s)}$. Then, we can obtain $\hat{H}^{(s)}$ be a consistent estimator for $H^{(s)}$. A method for obtaining a consistent Appendix A. As is often carried out in meta-analysis studies, regarding $\hat{H}^{(s)}$ as the pair of logit-transformed time-dependent sensitivity and specificity;

on the other hand, allow dependence between $\alpha^{(s)}$ and $\delta^{(s)}$ in the model with $D_i^{(s)} = 1$ and with $D_i^{(s)} = 0$ are presented to demonstrate our interest. The location of the biomarker distribution for subjects of both $D_i^{(s)} = 1$, the distribution of $M_i^{(s)}$ with $D_i^{(s)} = 1$ and that with $D_i^{(s)} = 0$ would be correlation between $\theta^{(s)}$ and $\delta^{(s)}$ may affect likelihood and thus estimation affected. On the other hand, the parameter $\alpha^{(s)}$ is responsible for the distribution between the subjects of $D_i^{(s)} = 1$ and $D_i^{(s)} = 0$ and is likely to affect



3.3. Doubly Robust Estimator

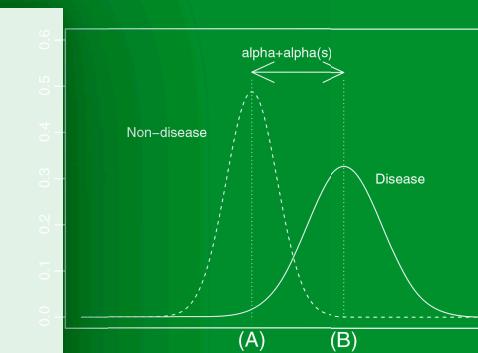
Finally, we propose a new estimator of double robustness by combining ideas of the *wPP* and *OR* estimators. The *DR* estimator is defined as

$$\hat{\Lambda}_E^{DR}(t) = \hat{\Lambda}_E^{wPP}(t) - \hat{\Gamma}(t) + \hat{\Lambda}_E^{OR}(t), \quad (8)$$

where

$$\hat{\Gamma}(t) = \int_0^t \frac{\sum_{i=1}^n \frac{I(G_i \geq u)}{S_G(u|Z_i)} \hat{S}_E(u|Z_i) d\hat{\Lambda}_E(u|Z_i)}{\sum_{j=1}^n \frac{I(G_j \geq u)}{S_G(u|Z_j)} \hat{S}_E(u|Z_j)}. \quad (9)$$

The first and third terms of the right-hand side of (8) are the



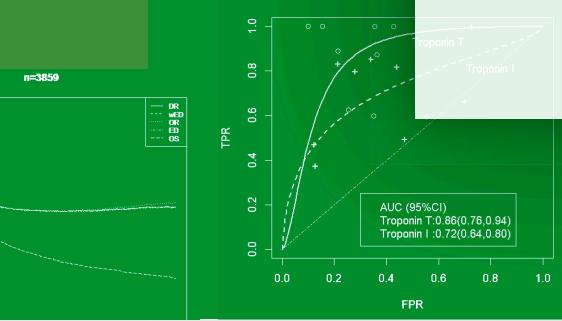
ture of the biomarker distributions of those with and without disease for explanatory variables of diseased and nondiseased, which are $\theta + \theta^{(s)} + 0.5(\alpha + \alpha^{(s)})$ and $\theta + \theta^{(s)}$

asymptotically, and its asymptotic variance can be consistently estimated by $n^{-1} \sum_{i=1}^n \hat{k}^{DR}(t_i, \hat{\theta})^2$, where the definition of $\hat{k}^{DR}(t, \hat{\theta})$ is given in Appendix. Due to the double robustness, $\Lambda_E^{DR}(t)$ agrees with $\Lambda_E(t)$ if at least one of $S_G(t|Z)$ and $S_G(t|Z)$ is correctly specified. Then, one can construct a pointwise confidence interval of $\Lambda_E(t)$ for a given t according to the asymptotic normality.

4. Simulation Study

We conducted a simulation study to examine the behavior of the proposed estimator. We considered three covariates, *age*, *gender*, and *year*, which were the age at diagnosis, the gender, and the year of diagnosis. *Age* and *gender* were generated from the normal distribution $N(60, 10^2)$ and the Bernoulli distribution $B(1/2)$, respectively. We generated the potential follow-up time G from the exponential distribution with hazard rate $\lambda_G(t|Z) = 0.12 \exp(-0.02 \times t(\text{age}) + \log 1.7 \times \text{gender} + \log 0.7 \times st(\text{age})^2)$, calculated by $e_f - G$, where $st(\text{age})$ was the date of the end of the follow-up. We considered three settings in generating T_E , generated from the exponential distribution with hazard rate $\lambda_E(t|Z) = 0.1 \exp(\beta^T Z)$, where β was as follows;

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The first and third terms of the right-hand side of (8) are the

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本研究室について

本研究室では、革新的な統計学的・数理科学的方法の開発と適用を通じて医学研究に貢献することを目指しています。我が国では医学統計学分野の研究は欧米に大きく遅れを取っており、多様な人材の参入を期待しています。関心のある方は気軽にお問合せください。

主な研究内容

- 1 生存時間解析法
- 2 観察研究の統計解析法
- 3 メタアナリシス
- 4 臨床試験における統計的方法論

卒業後の進路、キャリアパス

医学統計学分野の国内外の研究機関／大学病院等における臨床試験統計家／製薬企業やCRO

願書受付期間 ※社会人学生も受け入れ可能

修士課程 (年1回)

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第1回 2022年 8月10日 [水] – 8月17日 [水]

第2回 2022年 11月28日 [月] – 12月1日 [木]

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