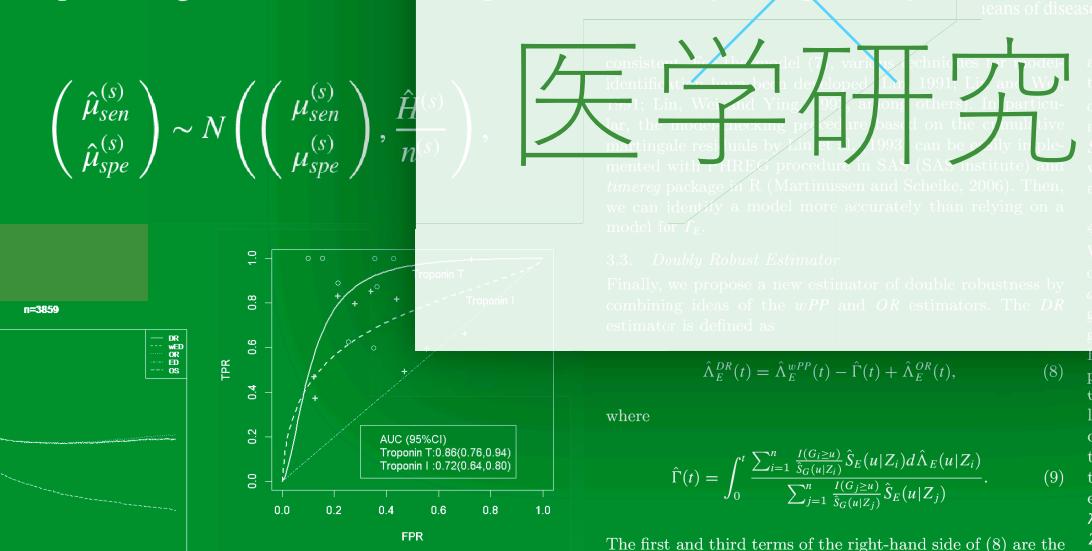


and $q_0^{(s)} = P(X \leq v^{(s)})$. The logit-transformed sensitivity $\mu_{sen}^{(s)} = \text{specificity } \mu_{spe}^{(s)} = \text{logit} \{spe(v^{(s)}, t_K)\}$ are given by $\mu_{sen}^{(s)} =$, and $\mu_{spe}^{(s)} = g_{spe} \{S_1^{(s)}(t_K), S_0^{(s)}(t_K), q_1^{(s)}, q_0^{(s)}\}$, respectively, 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 $\hat{\mu}_{sen}^{(s)} = g_{sen} \{S_1^{(s)}(t_K), S_0^{(s)}(t_K), \hat{q}_1^{(s)}, \hat{q}_0^{(s)}\}$, $\hat{\mu}_{spe}^{(s)} = g_{spe} \{S_1^{(s)}(t_K), S_0^{(s)}(t_K), \hat{q}_1^{(s)}, \hat{q}_0^{(s)}\}$, respectively, where $\hat{q}_1^{(s)} = n_1^{(s)} / n^{(s)} = \sum_{i=1}^{n^{(s)}} I(X_i \geq v^{(s)}) / n^{(s)}$, $X_i < v^{(s)} / n^{(s)}$. Denote $\hat{\mu}^{(s)} = (\hat{\mu}_{sen}^{(s)}, \hat{\mu}_{spe}^{(s)})^T$ and $\mu^{(s)} = (\mu_{sen}^{(s)}, \mu_{spe}^{(s)})^T$. In $n^{(s)} \rightarrow \infty$, conditional on $\hat{\mu}^{(s)}$ converges in distribution with a variance-covariance matrix $H^{(s)}$. Then, $\hat{\mu}^{(s)}$ is a consistent estimator for $H^{(s)}$. A method for obtaining a consistent estimator for $H^{(s)}$ is given in 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,;



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consistent for the model ℓ_E via the technique of local linearization to identify it. It was developed by Li (1991), Li and Wang (1994), Lin, Wei, and Ying (1999), and others. In particular, the model ℓ_E can be specified based on the cumulative residuals by a single step function. It can be easily implemented with a PHREG procedure in SAS (SAS institute) and *timereg* package in R (Martinussen and Scheike, 2006). Then, we can identify a model more accurately than relying on a model for ℓ_E .

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

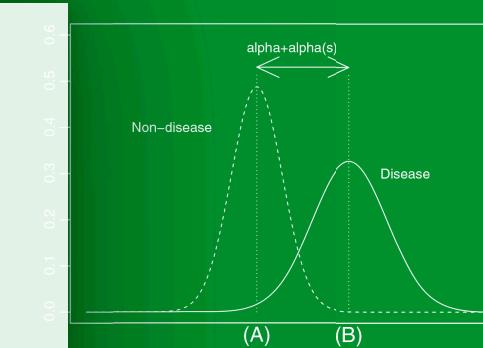
$$\hat{\Lambda}_E^{DR}(t) = \hat{\Lambda}_E^{wPP}(t) - \hat{\Gamma}(t) + \hat{\Lambda}_E^{OR}(t), \quad (8)$$

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

asymptotically, and its asymptotic variance can be consistently estimated by $n^{-1} \sum_{i=1}^n \hat{k}^{DR}(t, \hat{\theta})^2$, 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.



ure 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 $\theta + \theta^{(s)}$.

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 $\lambda_G(t|Z) = 0.12 \exp(0.02 \times t \times \text{age} + \log 1.7 \times \text{gender} + \log 0.7 \times \text{st}(\text{age})^2)$, where $\text{st}(\text{age})$ 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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大学院生募集

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

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博士課程

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第2回 2022年 11月28日 [月] – 12月1日 [木]

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