COMPOSITE LIKELIHOOD INFERENCE UNDER BOUNDARY CONDITIONS

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Supplementary Material

In this supplementary material, we provide the detailed proof of Lemma 1 and Theorem 1, show the analysis results of an illustrating example using data of a diagnostic review of imaging technologies for surveillance of melanoma from Xing *et al.* (2011), and provide the empirical type I error rates and power of testing positive associations in stratified case-control studies with sparse data as described in Section 5.1, using composite likelihood ratio statistic and its limiting distribution calculated from the m-out-n bootstrap method.

S1 Proof of Lemma 1

We first prove the consistency of $\hat{\theta}_c$ by applying Theorem 5.7 in Van der Vaart (2000). Since Ω is compact and $E\{\ell_c(\theta)\}$ is continuous, the maximum of $E\{\ell_c(\theta)\}$ over the space $\{\theta \in \Omega : \|\theta - \theta_0\| \geq \epsilon\}$ is achieved at some $\tilde{\theta}$. By the uniqueness of θ_0, we have $E\{\ell_c(\tilde{\theta})\} < E\{\ell_c(\theta_0)\}$. Thus, the second condition in equation (5.8) of Van der Vaart (2000) holds. The first condition in equation (5.8) of Van der Vaart (2000) is the uniform convergence of $\ell_c(\theta)$ to $E\{\ell_c(\theta)\}$ over $\theta \in \Omega$. This is equivalent to showing the class of function $\sum_{k=1}^{K} \omega_k \log L_i(\theta; \mathscr{A}_k)$ indexed by $\theta \in \Omega$ is Glivenko-Cantelli. This holds by applying Example 19.8 in Van der Vaart (2000), since Ω is compact, and the function is continuous with integrable envelop function by Condition R2. Thus, the first condition in equation (5.8) of Van der Vaart (2000) holds. This yields the consistency of $\hat{\theta}_c$.

Then we consider the expansion of CLRT,

$$2\left\{\ell_c(\hat{\theta}_c) - \ell_c(\theta_0)\right\} = 2(\sqrt{N}A)^T\left\{\sqrt{N}(\hat{\theta}_c - \theta_0)\right\} - \left\{\sqrt{N}(\hat{\theta}_c - \theta_0)^T\right\} B(\tilde{\theta}) \left\{\sqrt{N}(\hat{\theta}_c - \theta_0)\right\}$$

where $\tilde{\theta}$ is some intermediate value between $\hat{\theta}_c$ and θ_0, and

$$A = \frac{1}{N}\sum_{i=1}^{N}\sum_{k=1}^{K}\omega_i \frac{\partial \log L_i(\theta_0; \mathscr{A}_k)}{\partial \theta}, \quad B(\theta) \ = -\frac{1}{N}\sum_{i=1}^{N}\sum_{k=1}^{K}\omega_i \frac{\partial^2 \log L_i(\theta; \mathscr{A}_k)}{\partial \theta^T \partial \theta}.$$

Similar to the argument in the proof of consistency, we can show that $B(\theta)$ also converges uniformly to $H(\theta)$. By the consistency of $\hat{\theta}_c$ and Condition R3, the dominated convergence theorem implies $B(\tilde{\theta}) = H(\theta_0) + o_p(1)$.

Thus, we obtain

$$2\left\{\ell_c(\hat{\theta}_c)-\ell_c(\theta_0)\right\}=2(\sqrt{N}A)^T\left\{\sqrt{N}(\hat{\theta}_c-\theta_0)\right\}-\left\{\sqrt{N}(\hat{\theta}_c-\theta_0)^T\right\}$$
$$H(\theta_0)\left\{\sqrt{N}(\hat{\theta}_c-\theta_0)\right\}+o_p(N\|\hat{\theta}_c-\theta_0\|^2).$$

Denote $\hat{h}=\sqrt{N}(\hat{\theta}_c-\theta_0)$. Since $\ell_c(\hat{\theta}_c)-\ell_c(\theta_0)\geq 0$, we have

$$\begin{aligned}0\leq 2\left\{\ell_c(\hat{\theta}_c)-\ell_c(\theta_0)\right\}&=2(\sqrt{N}A)^T\hat{h}-\hat{h}^TH(\theta_0)\hat{h}+o_p(\|\hat{h}\|^2)\\&\leq C\|\hat{h}\|-C'\|\hat{h}\|^2+o_p(\|\hat{h}\|^2),\end{aligned}$$

for some positive constants C and C'. Note that the last step follows from the fact that $\sqrt{N}A=O_p(1)$ and $H(\theta_0)$ is positive definite. Thus, $\|\hat{h}\|\leq C(C')^{-1}+o_p(\|\hat{h}\|)$, which implies $\hat{h}=O_p(1)$. This completes the proof.

S2 Proof of Theorem 1

In the following, we first show that

$$\begin{aligned}2\big\{\ell_c(\hat{\theta}_c)-\ell_c(\theta_0)\big\}=&-\inf_{\theta\in C_\Omega}\big\{(U-(\theta-\theta_0))^TH(\theta_0)(U-(\theta-\theta_0))\big\}\\&+\inf_{\theta\in C_{\Omega_0}}\big\{(U-(\theta-\theta_0))^TH(\theta_0)(U-(\theta-\theta_0))\big\}+o_p(1),\end{aligned}\tag{S2.1}$$

where $U = H^{-1}(\theta_0)\sqrt{N}A$. Since $\theta \in C_{\Omega_0}$ implies $\theta = \theta_0$, it suffices to prove that

$$2\big\{\ell_c(\hat{\theta}_c) - \ell_c(\theta_0)\big\} = \sup_{h \in C_\Omega(0)} \big\{ - W_h^T H(\theta_0) W_h \big\} + U^T H(\theta_0) U + o_p(1), \tag{S2.2}$$

where $W_h = H^{-1}(\theta_0)\sqrt{N}A - h$, $h = \sqrt{N}(\theta - \theta_0)$ and $C_\Omega(0)$ is the translation of the cone C_Ω to the vertex 0.

Since $\hat{\theta}_c$ is root-N consistent by Lemma 1, the proof of Lemma 1 implies

$$2\big\{\ell_c(\hat{\theta}_c) - \ell_c(\theta_0)\big\} = \sup_{h \in \Omega_n} \{-W_h^T H(\theta_0) W_h\} + U^T H(\theta_0) U + o_p(1),$$

where $\Omega_n = \{n^{1/2}(\theta - \theta_0) : \theta \in \Omega\}$. Let $H = H(\theta_0)$. Comparing to (S2.2), we need to show $\inf_{h \in \Omega_n} W_h^T H W_h = \inf_{h \in C_\Omega(0)} W_h^T H W_h + o_p(1)$. Similar to the proof of root-n convergence of $\hat{\theta}_c$, it can be shown that $\arg\min_{h \in \Omega_n} W_h^T I_{11} W_h = O_p(1)$. By the definition of Ω_n, for any $h \in \Omega_n$ with $|h| = O(1)$, there exists $\theta \in \Omega$ such that $h = n^{1/2}(\theta - \theta_0)$. By the definition of the approximating cone, there exists a sequence $\bar{\theta} \in C_\Omega$ such that $|\bar{\theta} - \theta| = o(|\theta - \theta_0|) = o(n^{-1/2})$. Let $\bar{h} = n^{1/2}(\bar{\theta} - \theta_0)$. We have that $\bar{h}$ belongs to the cone $C_\Omega(0)$ and $|\bar{h} - h| = o(1)$. Then,

$$\begin{aligned}(U - h)^T H (U - h) &= (U - \bar{h} + \bar{h} - h)^T H (U - \bar{h} + \bar{h} - h)\\ &\geq (U - \bar{h})^T (U - \bar{h}) - O_p(\|\bar{h} - h\|) - O_p(\|\bar{h} - h\|^2)\\ &= (U - \bar{h})^T H (U - \bar{h}) + o_p(1).\end{aligned}$$

Thus,

$$\inf_{h\in\Omega_n}(U-h)^T H(U-h) \geq \inf_{h\in\Omega_n}(U-\bar{h})^T H(U-\bar{h}) + o_p(1)$$
$$= (U-\bar{h})^T H(U-\bar{h}) + o_p(1) \geq \inf_{\bar{h}\in C_\Omega(0)}(U-\bar{h})^T H(U-\bar{h}) + o_p(1).$$

Following similar arguments, we can also show that

$$\inf_{\bar{h}\in C_\Omega(0)}(U-\bar{h})^T H(U-\bar{h}) \geq \inf_{h\in\Omega_n}(U-h)^T H(U-h) + o_p(1).$$

These together imply that $\inf_{h\in\Omega_n} W_h^T H W_h = \inf_{h\in C_\Omega(0)} W_h^T H W_h + o_p(1)$, and therefore equation (S2.2) and (S2.1) hold. The Central limit theorem implies that $U = H^{-1}(\theta_0)\sqrt{N}A$ converges weakly to $MVN(0, G^{-1}(\theta_0))$, where $G(\theta_0) = H(\theta_0)J(\theta_0)^{-1}H(\theta_0)$. Let $Z \sim MVN(0, G^{-1}(\theta_0))$. The continuous mapping theorem implies that

$$\inf_{\theta\in\varphi}\left\{(U-(\theta-\theta_0))^T H(\theta_0)(U-(\theta-\theta_0))\right\} \rightarrow_d Q_\varphi(Z),$$

where $Q_\varphi(Z) = \inf_{\theta\in\varphi}\{Z-(\theta-\theta_0)\}^T H(\theta_0)\{Z-(\theta-\theta_0)\}$. This completes the proof.

S3 Supplementary results of application to a systematic review of modern imaging technologies for surveillance of melanoma

In this section, we show the results of applying the proposed composite likelihood model described in Section 2.3 and using the proposed composite likelihood ratio test described in Section 3.3 to test the heterogeneity of both sensitivity and specificity of the imaging technologies for different cancer types across multiple studies. Number of studies for 7 technology-cancer combinations are shown in Table S1. Figure S1 demonstrates the range of the sensitivities and specificities of the imaging technologies in diagnosis of different cancer types across studies.

Table S1: Numbers of studies studied by Xing *et al.* (2011) stratified by the type of metastasis (regional versus distant metastasis) and the type of imaging modalities

Type of imaging modalities	Number of studies
Regional metastasis	
Ultrasonography (US)	21
Computed Tomography (CT)	3
Positron Emission Tomography (PET)	22
Combination of both (PET-CT)	5
Distant metastasis	
Computed Tomography (CT)	9
Positron Emission Tomography (PET)	30
Combination of both (PET-CT)	8

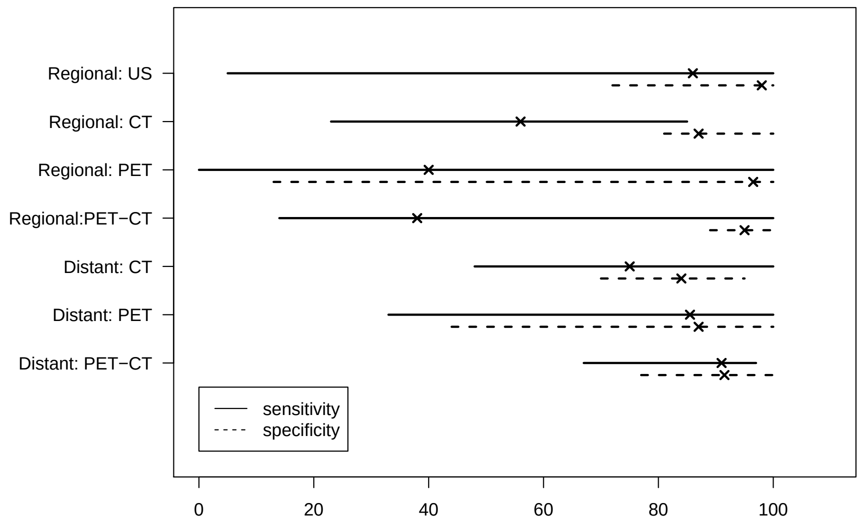

Figure S1: Summary of diagnosis accuracy of the imaging technologies for different cancer types across multiple studies. Star points represent median.

S4 M-out-of-n bootstrap

In this section, we show the empirical rejection rates, based on the limiting distribution of composite likelihood ratio statistic estimated using the m-out-of-n bootstrap method, in testing the positive associations in stratified case-control studies with sparse data using simulated data sets described in Section 5.1. We adopted the method proposed by Bickel & Sakov (2008) to make data-adaptive choice of resample size m, with tuning parameters

$q = 0.85$. The selected optimal resample size m and the empirical rejection rates of the over 5,000 simulations are shown in Table S2.

Table S2: Empirical rejection rates (%) in 5000 simulations of CLRT, based on limiting distribution estimated from m-out-of-n bootstrap, to test for two regression coefficients in stratified case-control study, in scenarios with different numbers of stratum K, stratum size N, and effect sizes.

			$\alpha = 0.10$	$\alpha = 0.05$	$\alpha = 0.01$
$(\beta_1, \beta_2, \beta_3)$	(K,N)	m	Rejection (%)	Rejection (%)	Rejection (%)
(0,0,0.1)	(25,10)	4	3.9	1.9	0.5
	(50,10)	6	3.2	1.5	0.3
	(100,10)	12	3.2	1.6	0.3
	(200,10)	46	3.5	2.0	0.3
(0.1,0,0.1)	(25,10)	4	10.8	6.5	2.0
	(50,10)	6	17.0	11.0	4.1
	(100,10)	12	30.1	20.0	7.7
	(200,10)	46	53.8	41.1	21.7
(0.1,0.1,0.1)	(25,10)	4	19.6	12.3	4.8
	(50,10)	6	33.5	23.3	9.7
	(100,10)	12	56.9	44.3	23.9
	(200,10)	46	83.1	74.2	53.2
(0.2,0.2,0.2)	(25,10)	4	56.7	45.2	24.6
	(50,10)	6	83.9	76.0	56.0
	(100,10)	12	99.0	97.6	91.1
	(200,10)	46	100.0	100.0	99.8

Bibliography

Bickel, Peter J, & Sakov, Anat. 2008. On the choice of m in the m out of n bootstrap and confidence bounds for extrema. *Statistica Sinica*, 967–985.

Van der Vaart, Aad W. 2000. *Asymptotic statistics*. Vol. 3. Cambridge university press.

Xing, Yan, Bronstein, Yulia, Ross, Merrick I, Askew, Robert L, Lee, Jeffrey E, Gershenwald, Jeffrey E, Royal, Richard, & Cormier, Janice N. 2011. Contemporary diagnostic imaging modalities for the staging and surveillance of melanoma patients: a meta-analysis. *Journal of the National Cancer Institute*, **103**(2), 129–142.