

Supplement to “Efficient estimation in semivarying coefficient models for longitudinal/clustered data”

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S.1. Proofs of Propositions 1-3 and Lemma 1. In this section, we outline the proofs of Propositions 1-3 and present the proof of Lemma 1. When m_i is uniformly bounded, we have the same results for general link functions by just following closely the arguments of [3]. We outline the results at the end of this supplement. Note that the sub-Gaussian error assumption is necessary in that case. We outline the proofs of Propositions 1-3 since we allow some of the m_i 's to diverge as in Assumptions A1 and A2.

Proof of Proposition 1. First we consider the properties of $\Gamma_{\mathbf{V}}$. The (k, l) th element of $n^{-1}\mathbf{H}_{11.2}$ is given by

$$\langle X_k - \mathbf{Z}^T \hat{\boldsymbol{\varphi}}_{\mathbf{V}k}, X_l - \mathbf{Z}^T \hat{\boldsymbol{\varphi}}_{\mathbf{V}l} \rangle_n^V.$$

From Lemma 1 (v)-(vii), we have

$$\begin{aligned} \langle X_k - \mathbf{Z}^T \hat{\boldsymbol{\varphi}}_{\mathbf{V}k}, X_l - \mathbf{Z}^T \hat{\boldsymbol{\varphi}}_{\mathbf{V}l} \rangle_n^V &= \langle X_k - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}k}^*, X_l - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}l}^* \rangle_n^V + o_p(1) \\ &= \langle X_k - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}k}^*, X_l - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}l}^* \rangle^V + o_p(1). \end{aligned}$$

This and (2.5) imply that for some positive constants C_1 and C_2 , we have

$$C_1 \leq \lambda_{\min}(n^{-1}\mathbf{H}_{11.2}) \leq \lambda_{\max}(n^{-1}\mathbf{H}_{11.2}) \leq C_2$$

and hence

$$(S.1) \quad \frac{1}{nC_2} \leq \lambda_{\min}(\mathbf{H}^{11}) \leq \lambda_{\max}(\mathbf{H}^{11}) \leq \frac{1}{nC_1}$$

with probability tending to 1. Note that

$$\text{Var}(\hat{\boldsymbol{\beta}}_{\mathbf{V}} | \{\mathbf{X}_{ij}\}, \{\mathbf{Z}_{ij}\}, \{T_{ij}\}) = \Gamma_{\mathbf{V}}$$

and Theorem 1 of [13] implies that $\Gamma_{\mathbf{V}} - \mathbf{H}^{11}$ is nonnegative definite when \mathbf{H}^{11} is defined with $\mathbf{V}_i = \boldsymbol{\Sigma}_i$. Hence for some positive constant C_3 , we have

$$\lambda_{\min}(\Gamma_{\mathbf{V}}) \geq \frac{C_3}{n}$$

with probability tending to 1.

Now we prove the asymptotic normality of

$$\begin{aligned} & \widehat{\beta}_{\mathbf{V}} - \mathbb{E}\{\widehat{\beta}_{\mathbf{V}} \mid \{\mathbf{X}_{ij}\}, \{\mathbf{Z}_{ij}\}, \{T_{ij}\}\} \\ &= \mathbf{H}^{11} \left(\sum_{i=1}^n \mathbf{X}_i^T \mathbf{V}_i^{-1} \underline{\epsilon}_i - \mathbf{H}_{12} \mathbf{H}_{22}^{-1} \sum_{i=1}^n \mathbf{W}_i^T \mathbf{V}_i^{-1} \underline{\epsilon}_i \right). \end{aligned}$$

As in the proof of Theorem 2 of [13], we take $c \in \mathbb{R}^p$ such that $|c| = 1$ and write

$$c^T (\widehat{\beta}_{\mathbf{V}} - \mathbb{E}\{\widehat{\beta}_{\mathbf{V}} \mid \{\mathbf{X}_{ij}\}, \{\mathbf{Z}_{ij}\}, \{T_{ij}\}\}) = \sum_{i=1}^n a_i \eta_i \quad (\text{say}),$$

where

$$a_i^2 = c^T \mathbf{H}^{11} (\underline{\mathbf{X}}_i - \underline{\mathbf{W}}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21})^T \mathbf{V}_i^{-1} \Sigma_i \mathbf{V}_i^{-1} (\underline{\mathbf{X}}_i - \underline{\mathbf{W}}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21}) \mathbf{H}^{11} c$$

and $\{\eta_i\}$ is a sequence of conditionally independent random variables with

$$\mathbb{E}\{\eta_i \mid \{\mathbf{X}_{ij}\}, \{\mathbf{Z}_{ij}\}, \{T_{ij}\}\} = 0 \quad \text{and} \quad \text{Var}(\eta_i \mid \{\mathbf{X}_{ij}\}, \{\mathbf{Z}_{ij}\}, \{T_{ij}\}) = 1.$$

We have from (S.1) and Lemma 1 (vii) that

$$\max_{1 \leq i \leq n} a_i^2 = O_p \left(\frac{m_{\max}^2}{n^2} \sum_{k=1}^p \|X_k - \mathbf{Z}^T \widehat{\varphi}_{\mathbf{V}k}\|_{\infty}^2 \right) = O_p \left(\frac{m_{\max}^2}{n^2} \right).$$

On the other hand, we have for some positive constant C_4 ,

$$\sum_{i=1}^n a_i^2 = c^T \Gamma_{\mathbf{V}} c \geq \frac{C_4}{n}$$

with probability tending to 1. Hence we have established

$$\frac{\max_{1 \leq i \leq n} a_i^2}{\sum_{i=1}^n a_i^2} = O_p(n^{-1} m_{\max}^2) = o_p(1)$$

and it follows from the standard argument that

$$(S.2) \quad \left(\sum_{i=1}^n a_i^2 \right)^{-1/2} \sum_{i=1}^n a_i \eta_i \xrightarrow{d} \mathbf{N}(0, 1).$$

Finally we evaluate the conditional bias:

$$\text{Bias}_{\beta} = \mathbb{E}\{\widehat{\beta}_{\mathbf{V}} \mid \{\mathbf{X}_{ij}\}, \{\mathbf{Z}_{ij}\}, \{T_{ij}\}\} - \beta_0$$

Take $\tilde{\mathbf{g}} \in \mathbf{G}_B$ such that $\|\mathbf{g}_0 - \tilde{\mathbf{g}}\|_{G,\infty} = O(K_n^{-2})$ and set

$$\boldsymbol{\delta}_0 = \mathbf{g}_0 - \tilde{\mathbf{g}} \quad \text{and} \quad \delta_0 = \mathbf{Z}^T \boldsymbol{\delta}_0.$$

Note that

$$\|\delta_0\|_\infty = O(K_n^{-2}) \quad \text{and} \quad \|\delta_0\|^V = O(K_n^{-2}).$$

We also take $\tilde{\boldsymbol{\varphi}}_{\mathbf{V}k} \in \mathbf{G}_B$ such that $\|\boldsymbol{\varphi}_{\mathbf{V}k}^* - \tilde{\boldsymbol{\varphi}}_{\mathbf{V}k}\|_{G,\infty} = O(K_n^{-2})$. Then we have the following expression for the conditional bias:

$$\text{Bias}_\beta = n\mathbf{H}^{11}(S_1, \dots, S_p)^T,$$

where

$$\begin{aligned} S_k &= \langle X_k, \delta_0 - \mathbf{Z}^T \hat{\Pi}_{\mathbf{V}n} \delta_0 \rangle_n^V = \langle X_k - \mathbf{Z}^T \tilde{\boldsymbol{\varphi}}_{\mathbf{V}k}, \delta_0 - \mathbf{Z}^T \hat{\Pi}_{\mathbf{V}n} \delta_0 \rangle_n^V \\ &= \langle X_k - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}k}^*, \delta_0 - \mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0 \rangle_n^V \\ &\quad + \langle X_k - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}k}^*, \mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0 - \mathbf{Z}^T \hat{\Pi}_{\mathbf{V}n} \delta_0 \rangle_n^V \\ &\quad + \langle \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}k}^* - \mathbf{Z}^T \tilde{\boldsymbol{\varphi}}_{\mathbf{V}k}, \delta_0 - \mathbf{Z}^T \hat{\Pi}_{\mathbf{V}n} \delta_0 \rangle_n^V \\ &= S_{1k} + S_{2k} + S_{3k} \quad (\text{say}). \end{aligned}$$

Note that

$$\mathbb{E}\{S_{1k}\} = 0 \quad \text{and} \quad \mathbb{E}\{S_{1k}^2\} = O\left(\frac{(\|X_k - \mathbf{Z}^T \boldsymbol{\varphi}_{\mathbf{V}k}^*\|^V)^2}{K_n^3 n}\right)$$

since S_{1k} is a sum of independent random variables, $\boldsymbol{\varphi}_{\mathbf{V}k}^* = \Pi_{\mathbf{V}} X_k$, $\delta_0 = \mathbf{Z}^T \boldsymbol{\delta}_0$, and

$$\begin{aligned} \|\delta_0 - \mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0\|_\infty &\leq \|\delta_0\|_\infty + CK_n^{1/2} \|\mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0\|^V \\ &\leq \|\delta_0\|_\infty + CK_n^{1/2} \|\delta_0\|^V = O(K_n^{-3/2}). \end{aligned}$$

Hence we have

$$S_{1k} = O_p(1/(nK_n^3)^{1/2}) = o_p(n^{-1/2}).$$

Now we deal with S_{2k} . From Lemma 1 (vi) and the fact that $\|\delta_0 - \mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0\|_\infty = O(K_n^{-3/2})$, we have

$$\begin{aligned} &\|\mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0 - \mathbf{Z}^T \hat{\Pi}_{\mathbf{V}n} \delta_0\|_n^V \\ &= \sup_{\mathbf{g} \in \mathbf{G}_B} \frac{|\langle \delta_0 - \mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0, \mathbf{Z}^T \mathbf{g} \rangle_n^V - \langle \delta_0 - \mathbf{Z}^T \Pi_{\mathbf{V}n} \delta_0, \mathbf{Z}^T \mathbf{g} \rangle_n^V|}{\|\mathbf{Z}^T \mathbf{g}\|_n^V} \\ &= O_p\left(K_n^{-3/2} \sqrt{\frac{K_n}{n}}\right) = O_p(K_n^{-1} n^{-1/2}). \end{aligned}$$

Thus we have

$$|S_{2k}| = o_p(n^{-1/2}).$$

We also have

$$|S_{3k}| \leq \|\delta_0\|_n^V \|\mathbf{Z}^T(\boldsymbol{\varphi}_{\mathbf{V}k}^* - \tilde{\boldsymbol{\varphi}}_{\mathbf{V}k})\|_n^V = O_p(K_n^{-4}) = o_p(n^{-1/2})$$

since $\|\delta_0 - \mathbf{Z}^T \widehat{\boldsymbol{\Pi}}_{\mathbf{V}n} \delta_0\|_n^V \leq \|\delta_0\|_n^V$. Hence we have

$$\text{Bias}_\beta = o_p(n^{-1/2}).$$

The desired result follows from (S.2) and the above equality.

As for Proposition 2, there is almost no change in calculation of the score functions in [13] and [4] and we omit the outline. This is because m_i is bounded for any fixed n .

Proof of Proposition 3. When $\mathbf{V}_i = \boldsymbol{\Sigma}_i$, we have

$$\Gamma_{\mathbf{V}} = \mathbf{H}^{11} = (\mathbf{H}_{11.2})^{-1} \quad \text{and} \quad \boldsymbol{\varphi}_{\boldsymbol{\Sigma}k}^* = \boldsymbol{\varphi}_{eff,k}^*.$$

Lemma 1 (vii) implies that

$$\frac{1}{n} \Gamma_{\mathbf{V}}^{-1} = \frac{1}{n} \mathbf{H}_{11.2} = \frac{1}{n} \mathbf{E}\{\mathbf{l}_\beta^* (\mathbf{l}_\beta^*)^T\} + o_p(1) = \Omega_{\boldsymbol{\Sigma}} + o_p(1).$$

The desired result follows from the above result and Proposition 1.

Proof of Lemma 1. The proof consists of seven parts.

(i) Recall that

$$(\|\mathbf{Z}^T \mathbf{g}\|^V)^2 = \frac{1}{n} \mathbf{E}\left\{ \sum_{i=1}^n \frac{(\mathbf{Z}^T \mathbf{g})_i^T}{\mathbf{V}_i^{-1}} (\mathbf{Z}^T \mathbf{g})_i \right\}.$$

We have from Assumptions A4 and A5 that

$$\begin{aligned} \text{(S.3)} \quad & \frac{C_1}{n} \mathbf{E}\left\{ \sum_{i=1}^n \frac{1}{m_i} \sum_{j=1}^{m_i} \mathbf{g}^T(T_{ij}) \mathbf{Z}_{ij} \mathbf{Z}_{ij}^T \mathbf{g}(T_{ij}) \right\} \\ & \leq (\|\mathbf{Z}^T \mathbf{g}\|^V)^2 \leq \frac{C_2}{n} \mathbf{E}\left\{ \sum_{i=1}^n \sum_{j=1}^{m_i} \mathbf{g}^T(T_{ij}) \mathbf{Z}_{ij} \mathbf{Z}_{ij}^T \mathbf{g}(T_{ij}) \right\} \end{aligned}$$

for some positive constants C_1 and C_2 . Assumptions A2 and A3 imply that for some positive constants C_3 and C_4 ,

$$(S.4) \quad \begin{aligned} C_3 \sum_{l=1}^q \int g_l^2(t) dt &\leq \frac{1}{n} \mathbb{E} \left\{ \sum_{i=1}^n \frac{1}{m_i} \sum_{j=1}^{m_i} \mathbf{g}^T(T_{ij}) \mathbf{Z}_{ij} \mathbf{Z}_{ij}^T \mathbf{g}(T_{ij}) \right\} \\ &\leq \frac{1}{n} \mathbb{E} \left\{ \sum_{i=1}^n \sum_{j=1}^{m_i} \mathbf{g}^T(T_{ij}) \mathbf{Z}_{ij} \mathbf{Z}_{ij}^T \mathbf{g}(T_{ij}) \right\} \leq C_4 \sum_{l=1}^q \int g_l^2(t) dt. \end{aligned}$$

The desired result follows from (S.3) and (S.4).

(ii) This is a well-known result in the literature of spline regression. See for example A.2 of [S2].

(iii) The result in (ii) implies

$$\|\mathbf{X}^T \boldsymbol{\beta} + \mathbf{Z}^T \mathbf{g}\|_{\infty}^2 \leq CK_n \left(|\boldsymbol{\beta}|^2 + \|\mathbf{g}\|_{G,2}^2 \right)$$

for some positive constant C . Recall that p and q are fixed in this paper. On the other hand, we have from Assumptions A1-3 and A5 that for some positive constants C_1 , C_2 , and C_3 ,

$$\begin{aligned} &(\|\mathbf{X}^T \boldsymbol{\beta} + \mathbf{Z}^T \mathbf{g}\|_V)^2 \\ &\geq \frac{C_1}{n} \mathbb{E} \left\{ \sum_{i=1}^n \frac{1}{m_i} \sum_{j=1}^{m_i} (\boldsymbol{\beta}^T \mathbf{g}^T(T_{ij})) \begin{pmatrix} \mathbf{X}_{ij} \mathbf{X}_{ij}^T & \mathbf{X}_{ij} \mathbf{Z}_{ij}^T \\ \mathbf{Z}_{ij} \mathbf{X}_{ij}^T & \mathbf{Z}_{ij} \mathbf{Z}_{ij}^T \end{pmatrix} \begin{pmatrix} \boldsymbol{\beta} \\ \mathbf{g}(T_{ij}) \end{pmatrix} \right\} \\ &\geq \frac{C_2}{n} \mathbb{E} \left\{ \sum_{i=1}^n \frac{1}{m_i} \sum_{j=1}^{m_i} (\boldsymbol{\beta}^T \mathbf{g}^T(T_{ij})) \begin{pmatrix} \boldsymbol{\beta} \\ \mathbf{g}(T_{ij}) \end{pmatrix} \right\} \geq C_3 |\boldsymbol{\beta}|^2 + \|\mathbf{g}\|_{G,2}^2. \end{aligned}$$

Besides, we have for some positive constants C_1 and C_2 ,

$$(\|v\|_V)^2 \leq \frac{C_1}{n} \sum_{i=1}^n \sum_{j=1}^{m_i} |v_{ij}|^2 \leq C_2 \|v\|_{\infty}.$$

Hence the desired results are established.

(iv) For $\mathbf{g}_1 \in \mathbf{G}_B$ and $\mathbf{g}_2 \in \mathbf{G}_B$, we have

$$\langle \mathbf{Z}^T \mathbf{g}_1, \mathbf{Z}^T \mathbf{g}_2 \rangle_n^V = \boldsymbol{\gamma}_1^T \left\{ \frac{1}{n} \sum_{i=1}^n \mathbf{W}_i^T \mathbf{V}_i^{-1} \mathbf{W}_i \right\} \boldsymbol{\gamma}_2 = \boldsymbol{\gamma}_1^T \bar{\Delta}_{\mathbf{V}_n} \boldsymbol{\gamma}_2 \quad (\text{say}),$$

where $\bar{\Delta}_{\mathbf{V}_n}$ is a $qK_n \times qK_n$ matrix and $\boldsymbol{\gamma}_1$ and $\boldsymbol{\gamma}_2$ correspond to \mathbf{g}_1 and \mathbf{g}_2 , respectively. Elements of $\frac{1}{n} \sum_{i=1}^n \mathbf{W}_i^T \mathbf{V}_i^{-1} \mathbf{W}_i$ are written as

$$(S.5) \quad \frac{1}{n} \sum_{i=1}^n \sum_{j_1, j_2} v_i^{j_1 j_2} B_{k_1}(T_{ij_1}) B_{k_2}(T_{ij_2}) Z_{ij_1 l_1} Z_{ij_2 l_2} = \bar{\Delta}_{\mathbf{V}_n}^{(k_1, l_1, k_2, l_2)} \quad (\text{say}),$$

where $v_i^{j_1 j_2}$ is defined in (5.3), $1 \leq k_1, k_2 \leq K_n$, and $1 \leq l_1, l_2 \leq q$. By evaluating the variance of (S.5) and using the Bernstein inequality for independent bounded random variables, and Assumptions A1 and A2, we have uniformly in k_1, k_2, l_1 , and l_2 ,

$$(S.6) \quad \overline{\Delta}_{\mathbf{V}_n}^{(k_1, l_1, k_2, l_2)} - \mathbb{E}(\overline{\Delta}_{\mathbf{V}_n}^{(k_1, l_1, k_2, l_2)}) = O_p\left(\sqrt{\frac{\log n}{nK_n^2}}\right) \quad \text{if } B_{k_1}(t)B_{k_2}(t) \equiv 0$$

and

$$(S.7) \quad \overline{\Delta}_{\mathbf{V}_n}^{(k_1, l_1, k_2, l_2)} - \mathbb{E}(\overline{\Delta}_{\mathbf{V}_n}^{(k_1, l_1, k_2, l_2)}) = O_p\left(\sqrt{\frac{\log n}{nK_n}}\right) \quad \text{if } B_{k_1}(t)B_{k_2}(t) \not\equiv 0.$$

By exploiting (S.6), (S.7), and the local property of the B-spline basis, we obtain

$$(S.8) \quad \max\{|\lambda_{\min}(\overline{\Delta}_{\mathbf{V}_n} - \mathbb{E}(\overline{\Delta}_{\mathbf{V}_n}))|, |\lambda_{\max}(\overline{\Delta}_{\mathbf{V}_n} - \mathbb{E}(\overline{\Delta}_{\mathbf{V}_n}))|\} = O_p\left(\sqrt{\frac{\log n}{n}}\right).$$

We also have

$$(S.9) \quad \frac{C_1}{K_n} \leq \lambda_{\min}(\mathbb{E}(\overline{\Delta}_{\mathbf{V}_n})) \leq \lambda_{\max}(\mathbb{E}(\overline{\Delta}_{\mathbf{V}_n})) \leq \frac{C_2}{K_n}$$

since Assumptions A2 and A3 yields

$$\begin{aligned} & \frac{C_3}{n} \sum_{i=1}^n \frac{1}{m_i} \sum_{j=1}^{m_i} (\mathbf{Z}_{ij} \otimes \mathbf{B}(T_{ij}))^T (\mathbf{Z}_{ij} \otimes \mathbf{B}(T_{ij})) \\ & \leq \overline{\Delta}_{\mathbf{V}_n} \leq \frac{C_4}{n} \sum_{i=1}^n \sum_{j=1}^{m_i} (\mathbf{Z}_{ij} \otimes \mathbf{B}(T_{ij}))^T (\mathbf{Z}_{ij} \otimes \mathbf{B}(T_{ij})) \end{aligned}$$

for some positive constants C_3 and C_4 . See the proof of Lemma A.3 of [S2]. Hence the desired result follows from (S.8) and (S.9).

(v) This follows from (iv) and (vi).

(vi) Using Assumptions A1 and A2 we have

$$\langle \delta_n, Z_l B_k \rangle_n^V = \frac{1}{n} \sum_{i=1}^n \sum_{j_1, j_2} \delta_{n, ij_1} v_i^{j_1 j_2} Z_{ij_2 l} B_k(T_{ij_2})$$

and

$$\text{Var}(\langle \delta_n, Z_l B_k \rangle_n^V) \leq \frac{C_1 \|\delta_n\|_\infty^2}{n^2} \sum_{i=1}^n m_i^2 \sum_{j_1, j_2} \mathbb{E}\{B_k^2(T_{ij_1}) B_k^2(T_{ij_2})\} \leq \frac{C_2 \|\delta_n\|_\infty^2}{nK_n}$$

for some positive constants C_1 and C_2 . Hence we have

$$\sum_{l=1}^q \sum_{k=1}^{K_n} \text{Var}(\langle \delta_n, Z_l B_k \rangle_n^V) \leq \frac{C}{n} \|\delta_n\|_\infty^2$$

for some positive constant C and the desired result follows from (S.9).

(vii) Take $\tilde{\varphi}_{\mathbf{V}_k} \in \mathbf{G}_B$ such that $\|\tilde{\varphi}_{\mathbf{V}_k} - \varphi_{\mathbf{V}_k}^*\|_{G, \infty} = O(K_n^{-2})$. Then we have for some positive C ,

$$\begin{aligned} \text{(S.10)} \quad & \|\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \varphi_{\mathbf{V}_k}^*)\|_\infty \\ & \leq \|\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \tilde{\varphi}_{\mathbf{V}_k})\|_\infty + \|\mathbf{Z}^T(\tilde{\varphi}_{\mathbf{V}_k} - \varphi_{\mathbf{V}_k}^*)\|_\infty \\ & \leq C\sqrt{K_n} \|\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \tilde{\varphi}_{\mathbf{V}_k})\|^V + \|\mathbf{Z}^T(\tilde{\varphi}_{\mathbf{V}_k} - \varphi_{\mathbf{V}_k}^*)\|_\infty \\ & \leq C\sqrt{K_n} \|\mathbf{Z}^T(\varphi_{\mathbf{V}_k}^* - \tilde{\varphi}_{\mathbf{V}_k})\|^V + \|\mathbf{Z}^T(\tilde{\varphi}_{\mathbf{V}_k} - \varphi_{\mathbf{V}_k}^*)\|_\infty \\ & = O(K_n^{-3/2}). \end{aligned}$$

Here we used the fact that $\bar{\varphi}_{\mathbf{V}_k} = \Pi_{\mathbf{V}_n} X_k \in \mathbf{G}_B$ and $\varphi_{\mathbf{V}_k}^* = \Pi_{\mathbf{V}} X_k$. Inequality (S.10) implies $\|\mathbf{Z}^T \bar{\varphi}_{\mathbf{V}_k}\|_\infty = O(1)$ and we have only to evaluate $\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \hat{\varphi}_{\mathbf{V}_k})$. We should just follow the arguments on p.16 of [3] by replacing $\varphi_{k,n}^*$ and $\hat{\varphi}_{k,n}$ with $\mathbf{Z}^T \bar{\varphi}_{\mathbf{V}_k}$ and $\mathbf{Z}^T \hat{\varphi}_{\mathbf{V}_k}$ since the arguments employ (iv) and (vi) and don't depend on m_i . Then we have

$$\begin{aligned} \|\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \hat{\varphi}_{\mathbf{V}_k})\|_\infty &= o_p(1), \quad \|\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \hat{\varphi}_{\mathbf{V}_k})\|_n^V = O_p(\sqrt{K_n/n}), \\ \text{and} \quad \|\mathbf{Z}^T(\bar{\varphi}_{\mathbf{V}_k} - \hat{\varphi}_{\mathbf{V}_k})\|^V &= O_p(\sqrt{K_n/n}). \end{aligned}$$

The desired results follow from the above equations and (S.10).

S.2. Proof of Proposition 4. In the proof, we repeatedly use arguments based on exponential inequalities, truncation, and division of regions into small rectangles to prove uniform convergence results as in [S3]. We do not give the details of these arguments since they are standard ones in non-parametric kernel methods. Since we impose Assumption A2 and we do not use Σ_i or \mathbf{V}_i in the construction of $\hat{\mathbf{g}}(t)$, $\hat{\sigma}^2(t)$, and $\hat{\sigma}(s, t)$, we see the effects of diverging m_i explicitly only when applying the exponential inequality for generalized U-statistics. Recall that we assume three times continuous differentiability of the relevant functions in this proposition.

The proof consists of four parts: (i) representation of $\hat{\mathbf{g}}(t)$, (ii) representation of $\hat{\epsilon}_{ij}$, (iii) representation of $\hat{\sigma}^2(t)$, and (iv) representation of $\hat{\sigma}(s, t)$.

(i) Representation of $\widehat{\mathbf{g}}(t)$. Applying the third order Taylor series expansion to $\mathbf{g}_0(t)$, we have

(S.11)

$$\mathbf{Z}_{ij}^T \mathbf{g}_0(T_{ij}) = \mathbf{Z}_{ij}^T \left\{ \mathbf{g}_0(t) + h_1 \frac{T_{ij} - t}{h_1} \mathbf{g}'_0(t) + \frac{h_1^2}{2} \left(\frac{T_{ij} - t}{h_1} \right)^2 \mathbf{g}''_0(t) \right\} + O(h_1^3),$$

where $\mathbf{g}'_0(t) = (g'_{01}(t), \dots, g'_{0q}(t))^T$ and $\mathbf{g}''_0(t) = (g''_{01}(t), \dots, g''_{0q}(t))^T$. By plugging (S.11) into (3.2), we have uniformly in t ,

$$(S.12) \quad \widehat{\mathbf{g}}(t) = \mathbf{g}_0(t) + D_q(\widehat{L}_1(t))^{-1} \widehat{L}_2(t)(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) \\ + \frac{h_1^2}{2} D_q(\widehat{L}_1(t))^{-1} \widehat{L}_3(t) \mathbf{g}''_0(t) + D_q(\widehat{L}_1(t))^{-1} E_0(t) + O_p(h_1^3),$$

where $\widehat{L}_1(t) = A_{1n}(t)$ defined after (3.2),

$$\widehat{L}_2(t) = \frac{1}{N_1 h_1} \sum_{i=1}^n \sum_{j=1}^{m_i} \mathbf{Z}_{ij} \otimes \left(\frac{1}{\frac{T_{ij}-t}{h_1}} \right) K\left(\frac{T_{ij}-t}{h_1}\right) \mathbf{X}_{ij}^T, \\ \widehat{L}_3(t) = \frac{1}{N_1 h_1} \sum_{i=1}^n \sum_{j=1}^{m_i} (\mathbf{Z}_{ij} \mathbf{Z}_{ij}^T) \otimes \left(\frac{\left(\frac{T_{ij}-t}{h_1}\right)^2}{\left(\frac{T_{ij}-t}{h_1}\right)^3} \right) K\left(\frac{T_{ij}-t}{h_1}\right), \\ E_0(t) = \frac{1}{N_1 h_1} \sum_{i=1}^n \sum_{j=1}^{m_i} \mathbf{Z}_{ij} \otimes \left(\frac{1}{\frac{T_{ij}-t}{h_1}} \right) K\left(\frac{T_{ij}-t}{h_1}\right) \boldsymbol{\epsilon}_{ij}.$$

By following standard arguments such as those in [S3], we obtain for $j = 1, 2, 3$,

$$(S.13) \quad \widehat{L}_j(t) = L_j(t) + O_p\left(\sqrt{\frac{\log n}{nh_1}}\right) \quad \text{uniformly in } t,$$

where $L_j = E\{\widehat{L}_j(t)\}$, and

$$(S.14) \quad E_0(t) = O_p\left(\sqrt{\frac{\log n}{nh_1}}\right) \quad \text{uniformly in } t.$$

Assumption A2 implies that

$$(S.15) \quad C_1 \mathbf{I}_{2q} \leq L_1(t) \leq C_2 \mathbf{I}_{2q}$$

for some positive constants C_1 and C_2 . From (S.12)-(S.15), we have uni-

formly in t ,

(S.16)

$$\begin{aligned}\widehat{\mathbf{g}}(t) &= \mathbf{g}_0(t) + D_q(L_1(t))^{-1}L_2(t)(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) + \frac{h_1^2}{2}D_q(L_1(t))^{-1}L_3(t)\mathbf{g}_0''(t) \\ &\quad + D_q(L_1(t))^{-1}E_0(t) + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right) \\ &= \mathbf{g}_0(t) + L_4(t)(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) + h_1^2L_5(t)\mathbf{g}_0''(t) + L_6(t)E_0(t) \\ &\quad + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right) \quad (\text{say}).\end{aligned}$$

Note that all the elements of $L_j(t)$, $j = 4, 5, 6$, are bounded functions of t .

(ii) Representation of $\widehat{\epsilon}_{ij}$. We have

$$\widehat{\epsilon}_{ij} = \epsilon_{ij} + \mathbf{X}_{ij}^T(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) + \mathbf{Z}_{ij}^T(\mathbf{g}_0(T_{ij}) - \widehat{\mathbf{g}}(T_{ij})).$$

By plugging (S.16) into the above equality, we obtain uniformly in i and j ,

(S.17)

$$\begin{aligned}\widehat{\epsilon}_{ij} &= \epsilon_{ij} + (\mathbf{X}_{ij}^T - \mathbf{Z}_{ij}^T L_4(T_{ij}))(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) - h_1^2 \mathbf{Z}_{ij}^T L_5(T_{ij}) \mathbf{g}''(T_{ij}) \\ &\quad - \mathbf{Z}_{ij}^T L_6(T_{ij}) E_0(T_{ij}) + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right) \\ &= \epsilon_{ij} + M_{ij}^{(1)}(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) + h_1^2 M_{ij}^{(2)} \mathbf{g}''(T_{ij}) + M_{ij}^{(3)} E_0(T_{ij}) \\ &\quad + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right) \quad (\text{say}).\end{aligned}$$

Note that all the elements of $M_{ij}^{(1)}$, $M_{ij}^{(2)}$, and $M_{ij}^{(3)}$ are uniformly bounded functions of \mathbf{X}_{ij} , \mathbf{Z}_{ij} , and T_{ij} .

(iii) Representation of $\widehat{\sigma}^2(t)$. We have uniformly in i and j ,

$$\begin{aligned}(\widehat{\epsilon}_{ij})^2 &= \epsilon_{ij}^2 - \sigma^2(T_{ij}) + \sigma^2(T_{ij}) + 2\epsilon_{ij}M_{ij}^{(3)}E_0(T_{ij}) \\ &\quad + 2\epsilon_{ij}M_{ij}^{(1)}(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I) + 2\epsilon_{ij}h_1^2M_{ij}^{(2)}\mathbf{g}_0''(T_{ij}) \\ &\quad + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right).\end{aligned}$$

Recall that $M_{ij}^{(l)}$, $l = 1, 2, 3$, are defined in (S.17). It is easy to see that the contributions of $2\epsilon_{ij}M_{ij}^{(1)}(\boldsymbol{\beta}_0 - \widehat{\boldsymbol{\beta}}_I)$ and $2\epsilon_{ij}h_1^2M_{ij}^{(2)}\mathbf{g}_0''(T_{ij})$ to $\widehat{\sigma}^2(t)$ are

$$O_p\left(\frac{1}{\sqrt{n}}\sqrt{\frac{\log n}{nh_2}}\right) \quad \text{and} \quad O_p\left(h_1^2\sqrt{\frac{\log n}{nh_2}}\right)$$

uniformly in t , respectively. Thus we have only to consider $\epsilon_{ij}^2 - \sigma^2(T_{ij})$, $\sigma^2(T_{ij})$, and $2\epsilon_{ij}M_{ij}^{(3)}E_0(T_{ij})$ in (S.18).

Setting $\widehat{L}_7(t) = A_{2n}(t)$, which is defined after (3.3), we have for some positive constants C_1 and C_2 ,

$$(S.19) \quad \widehat{L}_7(t) = L_7(t) + O_p\left(\sqrt{\frac{\log n}{nh_2}}\right) \quad \text{and} \quad C_1\mathbf{I}_2 \leq L_7(t) \leq C_2\mathbf{I}_2$$

uniformly in t , where $L_7(t) = \mathbb{E}\{\widehat{L}_7(t)\}$. Now we have uniformly in t ,

$$(S.20) \quad \widehat{\sigma}^2(t) = (10)(\widehat{L}_7(t))^{-1}(E_1(t) + \text{Bias}_1(t) + R_1(t)) \\ + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right),$$

where $E_1(t)$ is defined in Proposition 4, $\text{Bias}_1(t)$ is the term of $\sigma^2(T_{ij})$, and $R_1(t)$ is the term of $2\epsilon_{ij}M_{ij}^{(3)}E_0(T_{ij})$. It is easy to see that uniformly in t ,

$$(S.21) \quad E_1(t) = O_p\left(\sqrt{\frac{\log n}{nh_2}}\right).$$

By applying the Taylor series expansion, we have

$$\sigma^2(T_{ij}) = \sigma^2(t) + h_2(\sigma^2)'(t)\frac{T_{ij} - t}{h_2} + \frac{h_2^2}{2}(\sigma^2)''(t)\left(\frac{T_{ij} - t}{h_2}\right)^2 + O(h_2^3).$$

Therefore $\text{Bias}_1(t)$ can be represented as

$$\text{Bias}_1(t) = \widehat{L}_7(t) \left(\frac{\sigma^2(t)}{h_2(\sigma^2)'(t)} \right) + \frac{h_2^2(\sigma^2)''(t)}{2N_1h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \left(\frac{(T_{ij}-t)^2}{\left(\frac{T_{ij}-t}{h_2}\right)^3} \right) K\left(\frac{T_{ij}-t}{h_2}\right) \\ + O_p(h_2^3).$$

uniformly in t . Setting

$$\widehat{L}_8(t) = \frac{1}{N_1h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \left(\frac{\left(\frac{T_{ij}-t}{h_2}\right)^2}{\left(\frac{T_{ij}-t}{h_2}\right)^3} \right) K\left(\frac{T_{ij}-t}{h_2}\right),$$

we have uniformly in t ,

$$\widehat{L}_8(t) = L_8(t) + O_p\left(\sqrt{\frac{\log n}{nh_2}}\right),$$

where $L_8(t) = E\{\widehat{L}_8(t)\}$ and $L_8(t)$ is a bounded vector function of t . Hence we have uniformly in t ,

$$(S.22) \quad \text{Bias}_1(t) = \widehat{L}_7(t) \begin{pmatrix} \sigma^2(t) \\ h_2(\sigma^2)'(t) \end{pmatrix} + \frac{h_2^2(\sigma^2)''(t)}{2} L_8(t) + O_p(h_2^3) + O_p\left(h_2^2 \sqrt{\frac{\log n}{nh_2}}\right).$$

Next we deal with $R_1(t)$, which can be written as

$$(S.23) \quad \frac{1}{N_1^2 h_1 h_2} \sum_{a,b} \sum_{i=1}^n \sum_{j=1}^{m_i} \sum_{i'=1}^n \sum_{j'=1}^{m_{i'}} \epsilon_{ij} \epsilon_{i'j'} A_{ab,ij} B_{ab,i'j'} K_a\left(\frac{T_{ij} - t}{h_2}\right) K_b\left(\frac{T_{i'j'} - T_{ij}}{h_1}\right),$$

where $K_l(t) = t^l K(t)$, $a = 0, 1$, and $b = 0, 1$. Note that $A_{ab,ij}$ and $B_{ab,ij}$ are uniformly bounded functions of \mathbf{X}_{ij} , \mathbf{Z}_{ij} , and T_{ij} . We evaluate

$$(S.24) \quad \begin{aligned} & \frac{1}{N_1^2 h_1 h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \sum_{i'=1}^n \sum_{j'=1}^{m_{i'}} \epsilon_{ij} \epsilon_{i'j'} A_{ab,ij} B_{ab,i'j'} K_a\left(\frac{T_{ij} - t}{h_2}\right) K_b\left(\frac{T_{i'j'} - T_{ij}}{h_1}\right) \\ &= \frac{1}{N_1^2 h_1 h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \epsilon_{ij}^2 A_{ab,ij} B_{ab,ij} K_a\left(\frac{T_{ij} - t}{h_2}\right) K_b(0) \\ & \quad + \frac{1}{N_1^2 h_1 h_2} \sum_{i=1}^n \sum_{j \neq j'} \epsilon_{ij} \epsilon_{ij'} A_{ab,ij} B_{ab,ij'} K_a\left(\frac{T_{ij} - t}{h_2}\right) K_b\left(\frac{T_{ij'} - T_{ij}}{h_1}\right) \\ & \quad + \frac{1}{N_1^2 h_1 h_2} \sum_{i \neq i'} \sum_{j, j'} \epsilon_{ij} \epsilon_{i'j'} A_{ab,ij} B_{ab,i'j'} K_a\left(\frac{T_{ij} - t}{h_2}\right) K_b\left(\frac{T_{i'j'} - T_{ij}}{h_1}\right) \\ &= R_{1ab}^{(1)}(t) + R_{1ab}^{(2)}(t) + R_{1ab}^{(3)}(t) \quad (\text{say}). \end{aligned}$$

Note that we cannot apply classical exponential inequalities for U-statistics since kernel functions depend on i and i' and observations are not identical. It is easy to see that uniformly in t ,

$$(S.25) \quad R_{1ab}^{(1)}(t) = O_p((nh_1)^{-1}) \quad \text{and} \quad R_{1ab}^{(2)}(t) = O_p(n^{-1}).$$

We evaluate $R_{1ab}^{(3)}(t)$ by using an exponential inequality as the one given in (3.5) of [S1] with $A = C_1(\log n)^k m_{\max}^2 / (n^2 h_1 h_2)$,

$$B^2 = C_2 \frac{(\log n)^{2k} m_{\max}^2}{n^3 h_1 h_2} (h_1^{-1} + h_2^{-1}),$$

$C = C_3 / (nh_1^{1/2} h_2^{1/2})$, and $x = M \log n / (nh_1^{1/2} h_2^{1/2})$ in the inequality and standard arguments in nonparametric regression as in [S3]. Note that we

used a kind of truncation technique to handle ϵ_{ij} and that we have to take sufficiently large k and M here. Hence we have

$$R_{1ab}^{(3)}(t) = O_p\left(\frac{\log n}{n(h_1 h_2)^{1/2}}\right).$$

The above equation and (S.23)-(S.25) imply that

$$(S.26) \quad R_1(t) = O_p\left(\frac{\log n}{n(h_1 h_2)^{1/2}}\right) + O_p\left(\frac{1}{nh_1}\right)$$

uniformly in t . It follows from (S.19)-(S.22) and (S.26) that

$$\begin{aligned} \widehat{\sigma}^2(t) &= \sigma^2(t) + (10)(L_7(t))^{-1}E_1(t) + \frac{h_2^2}{2}(10)(L_7(t))^{-1}L_8(t)(\sigma^2)''(t) \\ &\quad + O_p(h_1^3) + O_p(h_2^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(\frac{\log n}{nh_2}\right). \end{aligned}$$

The expression of $\widehat{\sigma}^2(t)$ in Proposition 4 also follows from the above expression.

(iv) Representation of $\widehat{\sigma}(s, t)$. We can proceed almost in the same way as when we deal with $\widehat{\sigma}^2(t)$. First we examine $\widehat{\epsilon}_{ij}\widehat{\epsilon}_{ij'}$ closely. Then we have uniformly in i, j , and j' ,

$$\begin{aligned} \widehat{\epsilon}_{ij}\widehat{\epsilon}_{ij'} &= \epsilon_{ij}\epsilon_{ij'} - \sigma(T_{ij}, T_{ij'}) + \sigma(T_{ij}, T_{ij'}) \\ &\quad + \epsilon_{ij}M_{ij'}^{(3)}E_0(T_{ij'}) + \epsilon_{ij'}M_{ij}^{(3)}E_0(T_{ij}) \\ (S.27) \quad &\quad + \epsilon_{ij}M_{ij'}^{(1)}(\beta_0 - \widehat{\beta}_I) + \epsilon_{ij'}M_{ij}^{(1)}(\beta_0 - \widehat{\beta}_I) \\ (S.28) \quad &\quad + \epsilon_{ij}h_1^2M_{ij'}^{(2)}\mathbf{g}_0''(T_{ij'}) + \epsilon_{ij'}h_1^2M_{ij}^{(2)}\mathbf{g}_0''(T_{ij}) \\ &\quad + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right). \end{aligned}$$

It is easy to see that the contributions of (S.27) and (S.28) to $\widehat{\sigma}(s, t)$ are

$$O_p\left(\frac{1}{\sqrt{n}}\sqrt{\frac{\log n}{nh_3^2}}\right) \quad \text{and} \quad O_p\left(h_1^2\sqrt{\frac{\log n}{nh_3^2}}\right)$$

uniformly in s and t , respectively. Therefore we have only to consider $\epsilon_{ij}\epsilon_{ij'} - \sigma(T_{ij}, T_{ij'})$, $\sigma(T_{ij}, T_{ij'})$, and $\epsilon_{ij}M_{ij'}^{(3)}E_0(T_{ij'}) + \epsilon_{ij'}M_{ij}^{(3)}E_0(T_{ij})$ in $\widehat{\epsilon}_{ij}\widehat{\epsilon}_{ij'}$.

Setting $\widehat{L}_9(s, t) = A_{3n}(s, t)$, which is defined after (3.4), we have for some positive constants C_1 and C_2 ,

$$(S.29) \quad \widehat{L}_9(s, t) = L_9(s, t) + O_p\left(\sqrt{\frac{\log n}{nh_3^2}}\right) \quad \text{and} \quad C_1\mathbf{I}_3 \leq L_9(s, t) \leq C_2\mathbf{I}_3$$

uniformly in s and t , where $L_9(s, t) = \mathbb{E}\{\widehat{L}_9(s, t)\}$. Now we have uniformly in s and t ,

$$(S.30) \quad \widehat{\sigma}(s, t) = (100)(\widehat{L}_9(s, t))^{-1}(E_2(s, t) + \text{Bias}_2(s, t) + R_2(s, t)) \\ + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(h_1^2\sqrt{\frac{\log n}{nh_1}}\right),$$

where $E_2(s, t)$ is defined in Proposition 4, $\text{Bias}_2(s, t)$ is the term of $\sigma(T_{ij}, T_{ij'})$, and $R_2(s, t)$ is the term of $\epsilon_{ij}M_{ij'}^{(3)}E_0(T_{ij'}) + \epsilon_{ij'}M_{ij}^{(3)}E_0(T_{ij})$. It is easy to see that uniformly in s and t ,

$$(S.31) \quad E_2(s, t) = O_p\left(\sqrt{\frac{\log n}{nh_3^2}}\right).$$

Setting

$$\widehat{L}_{10}(s, t) \\ = \frac{1}{N_2 h_3^2} \sum_{i=1}^n \sum_{j \neq j'} \left(\frac{1}{\frac{T_{ij}-s}{h_3} \frac{T_{ij'}-t}{h_3}} \right) \left(\left(\frac{T_{ij}-s}{h_3} \right)^2 \frac{2(T_{ij}-s)(T_{ij'}-t)}{h_3^2} \left(\frac{T_{ij'}-t}{h_3} \right)^2 \right) \\ \times K\left(\frac{T_{ij}-s}{h_3}\right) K\left(\frac{T_{ij'}-t}{h_3}\right),$$

we have uniformly in s and t ,

$$\widehat{L}_{10}(s, t) = L_{10}(s, t) + O_p\left(\sqrt{\frac{\log n}{nh_3^2}}\right),$$

where $L_{10}(s, t) = \mathbb{E}\{\widehat{L}_{10}(s, t)\}$ and $L_{10}(s, t)$ is a bounded matrix function of (s, t) . Then we have, as in the proof of the representation of $\widehat{\sigma}^2(t)$, uniformly in s and t

$$(S.32) \quad \text{Bias}_2(s, t) = \widehat{L}_9(s, t) \begin{pmatrix} \sigma(s, t) \\ h_3 \frac{\partial \sigma}{\partial s}(s, t) \\ h_3 \frac{\partial \sigma}{\partial t}(s, t) \end{pmatrix} + \frac{h_3^2}{2} L_{10}(s, t) \begin{pmatrix} \frac{\partial^2 \sigma}{\partial s^2}(s, t) \\ \frac{\partial^2 \sigma}{\partial s \partial t}(s, t) \\ \frac{\partial^2 \sigma}{\partial t^2}(s, t) \end{pmatrix} \\ + O_p(h_3^3) + O_p\left(h_3^2\sqrt{\frac{\log n}{nh_3^2}}\right).$$

Finally we deal with $R_2(s, t)$ in the same way as in the proof of the representation of $\widehat{\sigma}^2(t)$. We use the same exponential inequality for U-statistics.

We should consider

$$(S.33) \quad \frac{1}{N_1 N_2 h_1 h_3^2} \sum_{i_1=1}^n \sum_{i_2=1}^n \sum_{j_1 \neq j_2} \sum_{j_3} \epsilon_{i_1 j_1} \epsilon_{i_2 j_3} A_{abc, i_1 j_2} B_{abc, i_2 j_3} \\ \times K_a \left(\frac{T_{i_2 j_3} - T_{i_1 j_2}}{h_1} \right) K_b \left(\frac{T_{i_1 j_1} - t}{h_3} \right) K_c \left(\frac{T_{i_1 j_2} - s}{h_3} \right),$$

where $K_l(t) = t^l K(t)$, $a = 0, 1$, $b = 0, 1$, and $c = 0, 1$. Note that $A_{abc, ij}$ and $B_{abc, ij}$ are uniformly bounded functions of \mathbf{X}_{ij} , \mathbf{Z}_{ij} , and T_{ij} . This is a generalized U-statistics when we remove the summands of $i_1 = i_2$ and we recall (1.1) when we evaluate (S.33). It is easy to see that uniformly in s and t ,

$$(S.34) \quad \frac{1}{N_1 N_2 h_1 h_3^2} \sum_{i_1=1}^n \sum_{j_1 \neq j_2} \sum_{j_3} \epsilon_{i_1 j_1} \epsilon_{i_1 j_3} A_{abc, i_1 j_2} B_{abc, i_1 j_3} \\ \times K_a \left(\frac{T_{i_1 j_3} - T_{i_1 j_2}}{h_1} \right) K_b \left(\frac{T_{i_1 j_1} - t}{h_3} \right) K_c \left(\frac{T_{i_1 j_2} - s}{h_3} \right) = O_p \left(\frac{1}{n h_1} \right).$$

In the same way as when dealing with $R_{1ab}^{(3)}(t)$, we obtain

$$(S.35) \quad \frac{1}{N_1 N_2 h_1 h_3^2} \sum_{i_1 \neq i_2} \sum_{j_1 \neq j_2} \sum_{j_3} \epsilon_{i_1 j_1} \epsilon_{i_2 j_3} A_{abc, i_1 j_2} B_{abc, i_2 j_3} \\ \times K_a \left(\frac{T_{i_2 j_3} - T_{i_1 j_2}}{h_1} \right) K_b \left(\frac{T_{i_1 j_1} - t}{h_3} \right) K_c \left(\frac{T_{i_1 j_2} - s}{h_3} \right) = O_p \left(\frac{\log n}{n h_1^{1/2} h_3} \right)$$

with $A = C_1 (\log n)^k m_{\max}^3 / (n^2 h_1 h_3^2)$, $B = C_2 (\log n)^k m_{\max}^2 / (n^{3/2} h_1^{1/2} h_3^2)$, $C = C_3 / (n h_1^{1/2} h_3)$, and $x = M \log n / (n h_1^{1/2} h_3)$ in the exponential inequality. Note that we should choose sufficiently large k and M . It follows from (S.34) and (S.35) that uniformly in s and t ,

$$(S.36) \quad R_2(s, t) = O_p \left(\frac{\log n}{n h_1^{1/2} h_3} \right).$$

Note that we cannot relax the assumption of $m_{\max} = O(n^{1/8})$ in Assumption A1 when we derive (S.36). It follows from (S.29)- (S.32) and (S.36) that

uniformly in s and t ,

$$\begin{aligned} & \widehat{\sigma}(s, t) - \sigma(s, t) \\ &= (100)(L_9(s, t))^{-1}E_2(s, t) + \frac{h_3^2}{2}(100)(L_9(s, t))^{-1}L_{10}(s, t) \begin{pmatrix} \frac{\partial^2 \sigma}{\partial s^2}(s, t) \\ \frac{\partial^2 \sigma}{\partial s \partial t}(s, t) \\ \frac{\partial^2 \sigma}{\partial t^2}(s, t) \end{pmatrix} \\ & \quad + O_p(h_1^3) + O_p(h_3^3) + O_p\left(\frac{\log n}{nh_1}\right) + O_p\left(\frac{\log n}{nh_3^2}\right). \end{aligned}$$

The expression in Proposition 4 follows from the above expression. The proof of Proposition 4 is complete.

S.3. Proofs of Lemmas 2-8. First we state some results on $\widehat{\Sigma}_i$. Set

$$(S.37) \quad \bar{\delta}_n = h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}.$$

Then we have from Proposition 4 that uniformly in i ,

$$\max\{|\lambda_{\min}(\Sigma_i - \widehat{\Sigma}_i)|, |\lambda_{\max}(\Sigma_i - \widehat{\Sigma}_i)|\} = O_p(m_i \bar{\delta}_n).$$

Recall that

$$\begin{aligned} \widehat{\Sigma}_i^{-1} - \Sigma_i^{-1} &= \widehat{\Sigma}_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1} \\ &= \Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1} + \widehat{\Sigma}_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}. \end{aligned}$$

We have from Assumption A4 and Proposition 4 that uniformly in i ,

$$(S.38) \quad |\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}|_{\max} = O_p(m_i \bar{\delta}_n),$$

$$(S.39) \quad |\widehat{\Sigma}_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}|_{\max} = O_p(m_i^2 \bar{\delta}_n^2),$$

where $|A|_{\max} = \max_{i,j} |a_{ij}|$ for any matrix $A = (a_{ij})$. Besides, it follows from Assumption A4 that we have uniformly in i ,

$$(S.40) \quad \max\{|\lambda_{\min}(\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1})|, |\lambda_{\max}(\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1})|\} = O_p(m_i \bar{\delta}_n).$$

We also have the same result for $\widehat{\Sigma}_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}$ as in (S.40) with $m_i \bar{\delta}_n$ replaced by $(m_i \bar{\delta}_n)^2$. Proposition 4 also implies each element of $\Sigma_i^{-1}(\Sigma_i - \widehat{\Sigma}_i)\Sigma_i^{-1}$ has the form of

$$(S.41) \quad D_i^{(1)}(\underline{T}_i)h_2^2 + D_i^{(2)}(\underline{T}_i)h_3^2 + \sum_{j=1}^{m_i} D_{ij}^{(3)}(\underline{T}_i)E_1(T_{ij}) + \sum_{j \neq j'} D_{ijj'}^{(4)}(\underline{T}_i)E_2(T_{ij}, T_{ij'}) + D_i^{(5)},$$

where

$$D_i^{(5)} = m_i O_p \left(h_1^3 + h_2^3 + h_3^3 + \frac{\log n}{nh_1} + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2} \right)$$

uniformly in i .

We state the following two useful facts before we start proving Lemmas 2-8, both hold uniformly in l :

$$(S.42) \quad \frac{1}{n} \sum_{i=1}^n m_i^3 \sum_{j=1}^{m_i} |W_{ijl}| = O_p(K_n^{-1}),$$

$$(S.43) \quad \text{and} \quad \frac{1}{n} \sum_{i=1}^n m_i^2 \sum_{j_1=1}^{m_i} \sum_{j_2=1}^{m_i} |W_{ij_1 l}| |\epsilon_{ij_2}| = O_p(K_n^{-1}),$$

where W_{ijl} denotes the l th element of \mathbf{W}_{ij} . We can prove them in the same way, except that we need a kind of truncation argument when showing (S.43), and we outline the proof of (S.42) in the following. To prove (S.42), we evaluate the expectation and variance and apply the Bernstein inequality. First note that we have uniformly in l ,

$$\mathbb{E} \left\{ n^{-1} \sum_{i=1}^n m_i^3 \sum_{j=1}^{m_i} |W_{ijl}| \right\} = O(K_n^{-1}).$$

This follows from the local property of the B-spline basis and Assumption A2. In addition, since we have from Assumption A2 that

$$\begin{aligned} & \mathbb{E} \left\{ \frac{m_{\max}^2}{n^2} \sum_{i=1}^n m_i^4 \sum_{j=1}^{m_i} |W_{ijl}|^2 + \frac{m_{\max}^3}{n^2} \sum_{i=1}^n m_i^3 \sum_{j_1 \neq j_2} |W_{ij_1 l}| |W_{ij_2 l}| \right\} \\ &= O \left(\frac{m_{\max}^2}{nK_n} + \frac{m_{\max}^3}{nK_n^2} \right), \end{aligned}$$

the variance is bounded from above by $C_1 n^{-19/20}$ uniformly in l . Each summand is bounded from above by $C_2 m_{\max}^4/n = O(n^{-1/2})$. Hence (S.42) and the uniformity in l follow from the Bernstein inequality.

Proof of Lemma 2. We can verify the result on $n^{-1}h_{12,kl}$ by using the local property of the B-spline basis and the Bernstein inequality for independent

bounded random variables. Since

$$\begin{aligned} \frac{1}{n}(\widehat{\mathbf{H}}_{12} - \mathbf{H}_{12}) &= \frac{1}{n} \sum_{i=1}^n \underline{\mathbf{X}}_i^T \{ \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \underline{\mathbf{W}}_i \\ &\quad + \frac{1}{n} \sum_{i=1}^n \underline{\mathbf{X}}_i^T \{ \widehat{\boldsymbol{\Sigma}}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \underline{\mathbf{W}}_i, \end{aligned}$$

the desired result on $n^{-1}(\widehat{h}_{12,kl} - h_{12,kl})$ follows from (S.38), (S.39), and (S.42). The results on the Euclidean norm follow from those on the elements. Hence the proof is complete.

Proof of Lemma 3. We have from Assumption A4 that

$$(S.44) \quad \frac{C_1}{n} \sum_{i=1}^n \frac{1}{m_i} \underline{\mathbf{W}}_i^T \underline{\mathbf{W}}_i \leq \frac{1}{n} \mathbf{H}_{22} \leq \frac{C_2}{n} \sum_{i=1}^n \underline{\mathbf{W}}_i^T \underline{\mathbf{W}}_i$$

for some positive constants C_1 and C_2 and for $k = 0, 1$,

$$\frac{1}{n} \sum_{i=1}^n \frac{1}{m_i^k} \underline{\mathbf{W}}_i^T \underline{\mathbf{W}}_i = \frac{1}{n} \sum_{i=1}^n \frac{1}{m_i^k} \sum_{j=1}^{m_i} (\mathbf{Z}_{ij} \mathbf{Z}_{ij}^T) \otimes (\mathbf{B}(T_{ij}) \mathbf{B}^T(T_{ij})).$$

Thus the first result follows from Assumptions A2 and A3 and the standard arguments on B-spline bases as in the proofs of Lemmas A.1 and A.2 of [S2].

Since we have

$$\begin{aligned} \frac{1}{n}(\widehat{\mathbf{H}}_{22} - \mathbf{H}_{22}) &= \frac{1}{n} \sum_{i=1}^n \underline{\mathbf{W}}_i^T \{ \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \underline{\mathbf{W}}_i \\ &\quad + \frac{1}{n} \sum_{i=1}^n \underline{\mathbf{W}}_i^T \{ \widehat{\boldsymbol{\Sigma}}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \underline{\mathbf{W}}_i, \end{aligned}$$

the second result follows from (S.40), the inequalities similar to (S.44), and Assumptions A2 and A3. The third result follows from the first and second results. Finally we deal with the fourth result. Note that

$$\begin{aligned} (S.45) \quad &(n^{-1} \widehat{\mathbf{H}}_{22})^{-1} - (n^{-1} \mathbf{H}_{22})^{-1} \\ &= (n^{-1} \mathbf{H}_{22})^{-1} (n^{-1} \mathbf{H}_{22} - n^{-1} \widehat{\mathbf{H}}_{22}) (n^{-1} \mathbf{H}_{22})^{-1} \\ &\quad + (n^{-1} \widehat{\mathbf{H}}_{22})^{-1} (n^{-1} \mathbf{H}_{22} - n^{-1} \widehat{\mathbf{H}}_{22}) \\ &\quad \times (n^{-1} \mathbf{H}_{22})^{-1} (n^{-1} \mathbf{H}_{22} - n^{-1} \widehat{\mathbf{H}}_{22}) (n^{-1} \mathbf{H}_{22})^{-1}. \end{aligned}$$

By using the first, second, and third results and (S.45), we obtain the fourth one. Hence the proof is complete.

Proof of Lemma 4. The first result follows from (S.40). The second one follows from Lemmas 2 and 3. The last one follows from the first two.

Proof of Lemma 5. The first result follows from the fact

$$\frac{C_1}{n} \sum_{i=1}^n \frac{1}{m_i} \mathbf{W}_i^T \mathbf{W}_i \leq \frac{1}{n} \sum_{i=1}^n \mathbf{W}_i^T \boldsymbol{\Sigma}_i^{-1} \mathbf{W}_i \leq \frac{C_2}{n} \sum_{i=1}^n \mathbf{W}_i^T \mathbf{W}_i$$

for some positive constants C_1 and C_2 . Next note that

$$\begin{aligned} \text{(S.46)} \quad & \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T \{ \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \boldsymbol{\epsilon}_i \\ &= \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T \{ \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \boldsymbol{\epsilon}_i \\ & \quad + \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T \{ \widehat{\boldsymbol{\Sigma}}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \} \boldsymbol{\epsilon}_i. \end{aligned}$$

By employing (S.39) and (S.43), we can prove the stochastic order of the elements of the second term of the right-hand side is uniformly

$$O_p(\sqrt{n} K_n^{-1} (h_2^4 + h_3^4 + \log n / (nh_2) + \log n / (nh_3^2))).$$

Thus the norm of this qK_n -dimensional vector has the stochastic order of

$$\text{(S.47)} \quad \sqrt{\frac{n}{K_n}} O_p\left(h_2^4 + h_3^4 + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2}\right).$$

According to Proposition 4, the first term of the right-hand side of (S.46) can be decomposed into

$$\text{(S.48)} \quad \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T Q_{1i} \boldsymbol{\epsilon}_i + \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T Q_{2i} \boldsymbol{\epsilon}_i + \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T Q_{3i} \boldsymbol{\epsilon}_i,$$

where Q_{1i} corresponds to the first and second terms in (S.41), Q_{2i} corresponds to the third and fourth terms in (S.41), and Q_{3i} corresponds to the fifth term in (S.41). Proposition 4 implies

$$Q_{1i} = Q_{1i}^{(2)} h_2^2 + Q_{1i}^{(3)} h_3^2,$$

where we have for $s = 2, 3$,

$$\max\{|\lambda_{\min}(Q_{1i}^{(s)})|, |\lambda_{\max}(Q_{1i}^{(s)})|\} = O(m_i)$$

uniformly in i . Besides $Q_{1i}^{(s)}$ depends only on \underline{T}_i for $s = 2, 3$. The (k, l) element of Q_{2i} has the form of

$$\sum_{j=1}^{m_i} \sigma_i^{kj} \sigma_i^{lj} E_1(T_{ij}) + \sum_{j \neq j'} \sigma_i^{kj} \sigma_i^{lj'} E_2(T_{ij}, T_{ij'}),$$

where $\Sigma_i^{-1} = (\sigma_i^{kl})$. Note that uniformly in l and i ,

$$\sum_{k=1}^{m_i} (\sigma_i^{kl})^2 = O(1).$$

Uniformly in i , the elements of Q_{3i} , $D_i^{(5)}$ in (S.41), have the order of

$$m_i O_p\left(h_1^3 + h_2^3 + h_3^3 + \frac{\log n}{nh_1} + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2}\right).$$

We can prove as in the proof of Lemma 3 that for $s = 2, 3$,

$$\frac{C_1}{K_n} \mathbf{I}_{qK_n} \leq \text{Cov}\left(n^{-1/2} \sum_{i=1}^n \mathbf{W}_i^T Q_{1i}^{(s)} \boldsymbol{\varepsilon}_i\right) \leq \frac{C_2}{K_n} \mathbf{I}_{qK_n}$$

for some positive constants C_1 and C_2 . Hence we have

$$(S.49) \quad \left|n^{-1/2} \sum_{i=1}^n \mathbf{W}_i^T Q_{1i} \boldsymbol{\varepsilon}_i\right| = O_p(h_2^2 + h_3^2).$$

Similarly to the second term in the right-hand side of (S.46), we can demonstrate by using (S.43) that

$$(S.50) \quad \left|n^{-1/2} \sum_{i=1}^n \mathbf{W}_i^T Q_{3i} \boldsymbol{\varepsilon}_i\right| = \sqrt{\frac{n}{K_n}} O_p\left(h_1^3 + h_2^3 + h_3^3 + \frac{\log n}{nh_1} + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2}\right).$$

Finally we evaluate the second term of (S.48) and it has a structure of V-statistics. By exploiting the structure, we evaluate the expectations and the variances of the elements by using Assumption A2. Then we have

$$\left|n^{-1/2} \sum_{i=1}^n \mathbf{W}_i^T Q_{2i} \boldsymbol{\varepsilon}_i\right| = O_p\left(\frac{1}{\sqrt{nh_2}} + \frac{1}{\sqrt{nh_3^2}} + \frac{1}{\sqrt{nK_n h_2}} + \frac{1}{\sqrt{nK_n h_3^2}}\right).$$

The second result follows from (S.47), (S.49), (S.50), and the above equality.

Proof of Lemma 6. This lemma can be proved in the same way as Lemma 5 and the details are omitted.

Proof of Lemma 7. From the definition of γ^* given after (5.6), we have

$$\max_{1 \leq j \leq m_i} |\mathbf{W}_{ij}^T \gamma^* - \mathbf{Z}_{ij}^T \mathbf{g}_0(T_{ij})| = O_p(K_n^{-2})$$

uniformly in i . The above equality and (S.42) imply that the elements of

$$\frac{1}{n} \sum_{i=1}^n \mathbf{W}_i^T \Sigma_i^{-1} (\mathbf{W}_i \gamma^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)}_i)$$

is uniformly $O_p(K_n^{-3})$ and the first result follows from this. As for the second result, first we note that

$$|\widehat{\Sigma}_i^{-1} - \Sigma_i^{-1}|_{\max} = O_p(m_i \bar{\delta}_n)$$

uniformly in i from (S.38) and (S.39). Recall that $\bar{\delta}_n$ is defined in (S.37). Thus the elements of $\mathbf{W}_i^T (\widehat{\Sigma}_i^{-1} - \Sigma_i^{-1}) (\mathbf{W}_i \gamma^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)}_i)$ are bounded uniformly in l by

$$CK_n^{-2} \bar{\delta}_n m_i^2 \sum_{j=1}^{m_i} |W_{ijl}|$$

with probability tending to 1 for some positive constant C . Hence the second result follows from (S.42).

Proof of Lemma 8. This lemma can be proved in the same way as Lemma 7 and the details are omitted.

S.4. Results for general link functions. We state the results of Section 2 for general link functions when m_i is uniformly bounded and $\underline{\epsilon}_i$ satisfies the sub-Gaussian assumption, Assumption A6' here. Note that we have no counterpart of Theorem 1 for general link functions even when m_i is uniformly bounded.

Let v_1 and v_2 be two processes each taking a scalar stochastic value at T_{ij} , $i = 1, \dots, n$, $j = 1, \dots, m_i$. Then we define two inner products of v_1 and v_2 by

$$\langle v_1, v_2 \rangle_n^\Delta = \frac{1}{n} \sum_{i=1}^n \underline{v}_{1i}^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} v_{2i} \text{ and } \langle v_1, v_2 \rangle^\Delta = \mathbb{E}\{\langle v_1, v_2 \rangle_n^\Delta\},$$

where \underline{v}_{1i} and \underline{v}_{2i} are defined in the same way as \underline{T}_i and

$$\Delta_{0i} = \text{diag}(\mu'(\mathbf{X}_{i1}^T \boldsymbol{\beta}_0 + \mathbf{Z}_{i1}^T \mathbf{g}_0(T_{i1})), \dots, \mu'(\mathbf{X}_{im_i}^T \boldsymbol{\beta}_0 + \mathbf{Z}_{im_i}^T \mathbf{g}_0(T_{im_i}))).$$

The associated norms are then defined by

$$\|v\|_n^\Delta = (\langle v, v \rangle_n^\Delta)^{1/2} \text{ and } \|v\|^\Delta = (\langle v, v \rangle^\Delta)^{1/2}.$$

We now define the projections, with respect to $\|\cdot\|^\Delta$, of the k th element of \mathbf{X} onto $\mathbf{Z}^T \mathbf{G}$ and $\mathbf{Z}^T \mathbf{G}_B$ by

$$\Pi_\Delta X_k = \underset{\mathbf{g} \in \mathbf{G}}{\text{argmin}} \|X_k - \mathbf{Z}^T \mathbf{g}\|^\Delta \text{ and } \Pi_{\Delta n} X_k = \underset{\mathbf{g} \in \mathbf{G}_B}{\text{argmin}} \|X_k - \mathbf{Z}^T \mathbf{g}\|^\Delta,$$

where

$$\|X_k - \mathbf{Z}^T \mathbf{g}\|^\Delta = \frac{1}{n} \mathbb{E} \left\{ \sum_{i=1}^n (\underline{X}_{ik} - (\mathbf{Z}^T \mathbf{g})_i)^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} (\underline{X}_{ik} - (\mathbf{Z}^T \mathbf{g})_i) \right\},$$

with $\underline{X}_{ik} = (X_{i1k}, \dots, X_{im_ik})^T$ and $(\mathbf{Z}^T \mathbf{g})_i = (\mathbf{Z}_{i1}^T \mathbf{g}(T_{i1}), \dots, \mathbf{Z}_{im_i}^T \mathbf{g}(T_{im_i}))$. We denote these projections by $\boldsymbol{\varphi}_{\Delta k}^* = \Pi_\Delta X_k$ and $\bar{\boldsymbol{\varphi}}_{\Delta k} = \Pi_{\Delta n} X_k$, and define another one by

$$\hat{\boldsymbol{\varphi}}_{\Delta k} = \hat{\Pi}_{\Delta n} X_k,$$

where

$$\hat{\Pi}_{\Delta n} X_k = \underset{\mathbf{g} \in \mathbf{G}_B}{\text{argmin}} \|X_k - \mathbf{Z}^T \mathbf{g}\|_n^\Delta.$$

The arguments in Section 5.2 also apply to this $\boldsymbol{\varphi}_{\Delta k}^*$.

Some matrices are necessary to present Proposition S.1 and we define them here. Let

$$\begin{aligned} \widetilde{\mathbf{H}} &= \begin{pmatrix} \sum_{i=1}^n \underline{\mathbf{X}}_i^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} \underline{\mathbf{X}}_i & \sum_{i=1}^n \underline{\mathbf{X}}_i^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} \underline{\mathbf{W}}_i \\ \sum_{i=1}^n \underline{\mathbf{W}}_i^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} \underline{\mathbf{X}}_i & \sum_{i=1}^n \underline{\mathbf{W}}_i^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} \underline{\mathbf{W}}_i \end{pmatrix} \\ &= \begin{pmatrix} \widetilde{\mathbf{H}}_{11} & \widetilde{\mathbf{H}}_{12} \\ \widetilde{\mathbf{H}}_{21} & \widetilde{\mathbf{H}}_{22} \end{pmatrix} \quad (\text{say}), \\ \widetilde{\mathbf{H}}_{11.2} &= \widetilde{\mathbf{H}}_{11} - \widetilde{\mathbf{H}}_{12} \widetilde{\mathbf{H}}_{22}^{-1} \widetilde{\mathbf{H}}_{21}, \quad \text{and} \quad \widetilde{\mathbf{H}}^{11} = (\widetilde{\mathbf{H}}_{11.2})^{-1}. \end{aligned}$$

Let $\widetilde{\Omega}_{\mathbf{V}n}$ be a $p \times p$ matrix whose (k, l) th element is

$$\frac{1}{n} \sum_{i=1}^n \mathbb{E} \left\{ (\underline{X}_{ik} - (\mathbf{Z}^T \boldsymbol{\varphi}_{\Delta k}^*)_i)^T \Delta_{0i} \mathbf{V}_i^{-1} \Delta_{0i} (\underline{X}_{il} - (\mathbf{Z}^T \boldsymbol{\varphi}_{\Delta l}^*)_i) \right\}.$$

Note that $n^{-1}\widetilde{\mathbf{H}}_{11.2}$ is an estimate of $\widetilde{\Omega}_{\mathbf{V}n}$. We assume that there exists a $p \times p$ positive definite matrix $\widetilde{\Omega}_{\mathbf{V}}$ such that

$$(S.51) \quad \lim_{n \rightarrow \infty} \widetilde{\Omega}_{\mathbf{V}n} = \widetilde{\Omega}_{\mathbf{V}}.$$

We present Propositions S.1-S.3 before stating the assumptions for these propositions. By using Lemma S.1 we can prove Proposition S.1 based on the same arguments as those in [4].

PROPOSITION S.1. (*Asymptotic normality of $\widehat{\beta}_{\mathbf{V}}$*) Under Assumption S in Section 2 for the norm here, (S.51), and Assumptions A1', A2', A3, A4', A5', and A6', we have

$$\widehat{\beta}_{\mathbf{V}} = \beta_0 + \widetilde{\mathbf{H}}^{11} \sum_{i=1}^n (\underline{\mathbf{X}}_i - \underline{\mathbf{W}}_i \widetilde{\mathbf{H}}_{22}^{-1} \widetilde{\mathbf{H}}_{21})^T \Delta_{0i} \mathbf{V}_i^{-1} \epsilon_i + o_p\left(\frac{1}{\sqrt{n}}\right).$$

We also have

$$\widetilde{\Gamma}_{\mathbf{V}}^{-1/2} (\widehat{\beta}_{\mathbf{V}} - \beta_0) \xrightarrow{d} \mathbf{N}(0, \mathbf{I}_p),$$

where $\widetilde{\Gamma}_{\mathbf{V}}$ is

$$\widetilde{\mathbf{H}}^{11} \sum_{i=1}^n \left\{ (\underline{\mathbf{X}}_i - \underline{\mathbf{W}}_i \widetilde{\mathbf{H}}_{22}^{-1} \widetilde{\mathbf{H}}_{21})^T \Delta_{0i} \mathbf{V}_i^{-1} \Sigma_i \mathbf{V}_i^{-1} \Delta_{0i} (\underline{\mathbf{X}}_i - \underline{\mathbf{W}}_i \widetilde{\mathbf{H}}_{22}^{-1} \widetilde{\mathbf{H}}_{21}) \right\} \widetilde{\mathbf{H}}^{11}.$$

We give in Proposition S.2 the semiparametric efficiency bound for estimation of β_0 . It can be proved in the same way as Lemma 1 of [4] and the proof is omitted. We denote the semiparametric efficient score function of β by

$$\tilde{\mathbf{l}}_{\beta}^* = (\tilde{l}_{\beta 1}^*, \dots, \tilde{l}_{\beta p}^*)^T.$$

Its expression is given in Proposition S.2. When $\mathbf{V}_i = \Sigma_i$, we denote $\varphi_{\Delta k}^*(t)$ by $\tilde{\varphi}_{eff,k}^*(t)$.

PROPOSITION S.2. (*Semiparametric efficiency bound*) Under the same assumptions as in Proposition S.1, we have

$$\tilde{l}_{\beta k}^* = \sum_{i=1}^n (\underline{\mathbf{X}}_{ik} - \underline{\mathbf{Z}}^T \tilde{\varphi}_{eff,k}^*)^T \Delta_{0i} \Sigma_i^{-1} \{ \underline{\mathbf{Y}}_i - \underline{\mu}(\underline{\mathbf{X}}_i \beta_0 + \underline{\mathbf{Z}}^T \mathbf{g}_0)_i \},$$

and the semiparametric efficient information matrix for β is given by

$$\lim_{n \rightarrow \infty} \frac{1}{n} \mathbf{E} \{ \tilde{\mathbf{l}}_{\beta}^* (\tilde{\mathbf{l}}_{\beta}^*)^T \} = \widetilde{\Omega}_{\Sigma} \text{ with } \mathbf{V}_i = \Sigma_i \text{ in (S.51).}$$

Proposition S.3 is parallel to Proposition 3. It can be proved in the same way as Corollary 1 of [4], and it also follows from Proposition S.1 and Lemma S.1 (vii). Thus the proof is omitted.

PROPOSITION S.3. (*Oracle efficient estimator*) *Under the same assumptions as in Proposition S.1, we have with $\mathbf{V}_i = \boldsymbol{\Sigma}_i$ in (2.2)*

$$\sqrt{n} \tilde{\Omega}_{\boldsymbol{\Sigma}}^{1/2} (\hat{\boldsymbol{\beta}}_{\boldsymbol{\Sigma}} - \boldsymbol{\beta}_0) \xrightarrow{d} \mathbf{N}(0, \mathbf{I}_p).$$

Now we describe assumptions for the above propositions. Here we need Assumption A6' since we need some results from the empirical process theory in dealing with general link functions.

Assumption A1'.

- (i) $\mu(x)$ is twice continuously differentiable and $\inf_{x \in R} \mu'(x) > 0$.
- (ii) For some positive constant C_{B9} , we have $\limsup_{|x| \rightarrow \infty} |\mu(x)|/|x|^{C_{B9}} < \infty$.

Assumption A2'. The joint density functions $f_{ij}(t)$ and $f_{ijj'}(s, t)$ are uniformly bounded and we have for some positive constants C_{B1} and C_{B2} ,

$$C_{B1} < \frac{1}{n} \sum_{i=1}^n \sum_{j=1}^{m_i} f_{ij}(t) < C_{B2} \text{ on } [0, 1]$$

and $C_{B1} < \frac{1}{n} \sum_{i=1}^n \sum_{j \neq j'} f_{ijj'}(s, t) < C_{B2} \text{ on } [0, 1]^2$.

Assumption A4'. For some positive constants C_{B5} and C_{B6} , we have uniformly in i ,

$$C_{B5} \leq \lambda_{\min}(\boldsymbol{\Sigma}_i) \leq \lambda_{\max}(\boldsymbol{\Sigma}_i) \leq C_{B6}.$$

Assumption A5'. For some positive constants C_{B7} and C_{B8} , we have uniformly in i ,

$$C_{B7} \leq \lambda_{\min}(\mathbf{V}_i) \leq \lambda_{\max}(\mathbf{V}_i) \leq C_{B8}.$$

Assumption A6'. For some positive constants C_{B10} and C_{B11} , we have uniformly in i ,

$$\max_{1 \leq i \leq n} C_{B10} \mathbf{E}\{\exp(|\epsilon_i|^2/C_{B10}) - 1 | \underline{\mathbf{X}}_i, \underline{\mathbf{Z}}_i, \underline{\mathbf{T}}_i\} \leq C_{B11}.$$

To prove Proposition S.1, we have only to proceed as in [3] by replacing their \mathbf{Z}_{ij} , \mathbf{Z}_i , and $\boldsymbol{\varphi}_k^*(t)$ with \mathbf{W}_{ij} , \mathbf{W}_i , and $\mathbf{Z}^T \boldsymbol{\varphi}_{\Delta k}^*(t)$, respectively. We just state the relevant changes and remarks in the following:

- (i) Lemmas S.2-S.4 of [3]: We reorganize these lemmas in Lemma S.1 given later. Its (i)-(iii), (iv) and (vi) correspond to Lemma S.2, the latter half of Lemma S.3 and Lemma S.4 of [3], respectively. The former half of Lemma S.3 of [3] seems to be used in their Corollary 1. However, it can be relaxed to (v) of Lemma S.1 here.
- (ii) Lemma S.8 of [3]: The regressors \mathbf{X}_{ij} and \mathbf{W}_{ij} still form a VC class and we can proceed completely in the same way as in [3].

We state Lemma S.1 in the following. It can be proved it in the same way as Lemma 1.

LEMMA S.1. *Assume that Assumptions A1', A2', A3, A4', A5' hold. Then we have the following results.*

- (i) *There are positive constants C_1 and C_2 such that*

$$C_1 \|\mathbf{g}\|_{G,2} \leq \|\mathbf{Z}^T \mathbf{g}\|^\Delta \leq C_2 \|\mathbf{g}\|_{G,2}$$

for any $\mathbf{g} \in \mathbf{G}$.

- (ii) *There are positive constants C_3 and C_4 such that*

$$\|\mathbf{g}\|_{G,\infty}^2 \leq C_3 K_n \|\mathbf{g}\|_{G,2}^2 \leq C_4 K_n (\|\mathbf{Z}^T \mathbf{g}\|^\Delta)^2$$

for any $\mathbf{g} \in \mathbf{G}_B$.

- (iii) *There is a positive constant C_5 such that for any $\boldsymbol{\beta} \in \mathbb{R}^p$ and $\mathbf{g} \in \mathbf{G}_B$,*

$$\|\mathbf{X}^T \boldsymbol{\beta} + \mathbf{Z}^T \mathbf{g}\|_\infty \leq C_5 K_n^{1/2} \|\mathbf{X}^T \boldsymbol{\beta} + \mathbf{Z}^T \mathbf{g}\|^\Delta,$$

where $\|v\|_\infty = \max_{i,j} |v_{ij}|$. Besides we have for some positive constant C_6 ,

$$\|v\|^\Delta \leq C_6 \|v\|_\infty.$$

- (iv)

$$\sup_{\mathbf{g}_1, \mathbf{g}_2 \in \mathbf{G}_B} \left| \frac{\langle \mathbf{Z}^T \mathbf{g}_1, \mathbf{Z}^T \mathbf{g}_2 \rangle_n^\Delta - \langle \mathbf{Z}^T \mathbf{g}_1, \mathbf{Z}^T \mathbf{g}_2 \rangle^\Delta}{\|\mathbf{Z}^T \mathbf{g}_1\|^\Delta \|\mathbf{Z}^T \mathbf{g}_2\|^\Delta} \right| = O_p(K_n \sqrt{\log n/n}).$$

- (v) *For any positive constant M , we have*

$$\langle X_j - \mathbf{Z}^T \mathbf{g}_j, X_k - \mathbf{Z}^T \mathbf{g}_k \rangle_n^\Delta - \langle X_j - \mathbf{Z}^T \mathbf{g}_j, X_k - \mathbf{Z}^T \mathbf{g}_k \rangle^\Delta = o_p(1)$$

uniformly in $\mathbf{g}_j \in \mathbf{G}_B$ and $\mathbf{g}_k \in \mathbf{G}_B$ satisfying $\|\mathbf{g}_j\|_{G,2} \leq M$ and $\|\mathbf{g}_k\|_{G,2} \leq M$, respectively.

(vi) For any stochastic process δ_n taking values at T_{ij} satisfying that $\|\delta_n\|_\infty$ is uniformly bounded in n and $\{\delta_{n,ij}\}_{j=1}^{m_i}$ are mutually independent in i , we have

$$\sup_{\mathbf{g} \in \widehat{\mathcal{G}}_B} \left| \frac{\langle \delta_n, \mathbf{Z}^T \mathbf{g} \rangle_n^\Delta - \langle \delta_n, \mathbf{Z}^T \mathbf{g} \rangle^\Delta}{\|\mathbf{Z}^T \mathbf{g}\|^\Delta} \right| = O_p(\sqrt{K_n/n}) \|\delta_n\|_\infty.$$

(vii) We also have Assumption S for the norm here. Then we have for $k = 1, \dots, p$, $\|\widehat{\varphi}_{\Delta k}\|_\infty = O_p(1)$,

$$\|\mathbf{Z}^T(\varphi_{\Delta k}^* - \widehat{\varphi}_{\Delta k})\|_n^\Delta = o_p(1), \quad \text{and} \quad \|\mathbf{Z}^T(\varphi_{\Delta k}^* - \widehat{\varphi}_{\Delta k})\|^\Delta = o_p(1).$$

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EFFICIENT ESTIMATION IN SEMIVARYING COEFFICIENT MODELS FOR LONGITUDINAL/CLUSTERED DATA

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In semivarying coefficient modeling of longitudinal/clustered data, of primary interest is usually the parametric component which involves unknown constant coefficients. First we study semiparametric efficiency bound for estimation of the constant coefficients in a general setup. It can be achieved by spline regression using the true within-subject covariance matrices, which are often unavailable in reality. Thus we propose an estimator when the covariance matrices are unknown and depend only on the index variable. To achieve this goal, we estimate the covariance matrices using residuals obtained from a preliminary estimation based on working independence and both spline and local linear regression. Then, using the covariance matrix estimates, we employ spline regression again to obtain our final estimator. It achieves the semiparametric efficiency bound under normality assumption and has the smallest asymptotic covariance matrix among a class of estimators even when normality is violated. Our theoretical results hold either when the number of within-subject observations diverges or when it is uniformly bounded. In addition, the local linear estimator of the nonparametric component is superior to the spline estimator in terms of numerical performance. The proposed method is compared with the working independence estimator and some existing method via simulations and application to a real data example.

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1. Introduction. Suppose we have a scalar response Y , and two p -dimensional and q -dimensional covariate vectors \mathbf{X} and \mathbf{Z} . Longitudinal data consist of $(Y_{ij}, \mathbf{X}_{ij}, \mathbf{Z}_{ij}, T_{ij}), i = 1, \dots, n, j = 1, \dots, m_i$, where Y_{ij} , $\mathbf{X}_{ij} = (X_{ij1}, \dots, X_{ijp})^T$ and $\mathbf{Z}_{ij} = (Z_{ij1}, \dots, Z_{ijq})^T$ are respectively the values of Y , \mathbf{X} and \mathbf{Z} of the i th subject at the j th observation time $T_{ij} \in [0, 1]$. Such kind of data are commonly acquired for various purposes, such as evidence based knowledge discovery and empirical study, in a wide range of subject areas. When the subjects are changed to clusters and the T_{ij} 's are observations on some index variable other than time, they are usually called clustered data. We assume that all the covariates are uniformly bounded for technical reasons. Besides, we let $Z_{ij1} \equiv 1$ and suppose \mathbf{X}_{ij} has no constant element for all i and j .

For $i = 1, \dots, n$, denote

$$\underline{\mathbf{X}}_i = (\mathbf{X}_{i1}, \dots, \mathbf{X}_{im_i})^T, \underline{\mathbf{Z}}_i = (\mathbf{Z}_{i1}, \dots, \mathbf{Z}_{im_i})^T, \text{ and } \underline{T}_i = (T_{i1}, \dots, T_{im_i})^T.$$

A popular model for longitudinal data analysis is the semivarying coefficient model, which is specified by

$$(1.1) \quad \begin{aligned} & \text{E}(Y_{ij} | \mathbf{X}_{ij}, \mathbf{Z}_{ij}, T_{ij}, \underline{\mathbf{X}}_i, \underline{\mathbf{Z}}_i, \underline{T}_i) \\ & = \text{E}(Y_{ij} | \mathbf{X}_{ij}, \mathbf{Z}_{ij}, T_{ij}) \equiv \mu(\mathbf{X}_{ij}^T \boldsymbol{\beta} + \mathbf{Z}_{ij}^T \mathbf{g}(T_{ij})) = \mu_{ij}, \end{aligned}$$

where \mathbf{A}^T stands for the transpose of a matrix \mathbf{A} . In model (1.1), $\mu(x)$ is a known strictly increasing smooth link function, $\boldsymbol{\beta}$ is an unknown regression coefficient vector, and $\mathbf{g}(t) = (g_1(t), \dots, g_q(t))^T$ is a vector of unknown smooth functions. Define

$$(1.2) \quad \boldsymbol{\epsilon}_i = (\epsilon_{i1}, \dots, \epsilon_{im_i})^T = \underline{Y}_i - \underline{\mu}_i, \text{ and } \boldsymbol{\Sigma}_i = \text{Var}(\boldsymbol{\epsilon}_i | \underline{\mathbf{X}}_i, \underline{\mathbf{Z}}_i, \underline{T}_i),$$

where $\underline{Y}_i = (Y_{i1}, \dots, Y_{im_i})^T$, $\underline{\mu}_i = (\mu_{i1}, \dots, \mu_{im_i})^T$, and $\boldsymbol{\Sigma}_i$ is an $m_i \times m_i$ positive definite matrix depending on $\underline{\mathbf{X}}_i$, $\underline{\mathbf{Z}}_i$, and \underline{T}_i , $i = 1, \dots, n$. This is a standard marginal model in longitudinal data analysis [24].

Model (1.1) consists of a parametric component, which provides information on the constant impacts of some important covariates, and a nonparametric component which captures the dynamic impacts of the other covariates. In this way the model is able to reflect unknown nonlinear structures in the data while retaining similar interpretability as the classical linear models at the same time. There is an extensive literature on the variable selection, structure identification, estimation, and inference issues [6, 8, 12, 22, 25]. In particular, often of primary interest is to have access to the parametric component while the nonparametric component is viewed as the nuisance

part. In this regard, it is well known that assuming independence or some mis-specified working covariance structure yields less efficient estimation of the constant coefficients. Therefore, a substantial portion of the existing literature aimed at improving the efficiency via modeling and estimating the within-subject covariance structure [6, 7, 10, 18, 26, 27, 28], which is itself a challenging task.

In this article, we focus on the identity link function and make contributions to the efficient estimation problem for model (1.1) in three directions. First, we allow some of the m_i 's to tend to infinity. As far as we know, this setup has not been treated before and the problem is nontrivial. Our results also hold when the m_i 's are uniformly bounded and ϵ_i satisfies the sub-Gaussian property. See the supplement [5] for the details. When all of the m_i 's are diverging, that is, if we have densely observed data, it becomes a kind of functional data problem and is out of the scope of this paper. Second, we study explicit expression of the semiparametric efficiency bound for estimation of β and asymptotic normality of the generalized estimating equations (GEE) spline estimator under general covariance structures and error distributions. Using the true covariance matrices in the GEE estimation leads to optimality among all GEE estimators of the parametric component. Furthermore, it achieves the semiparametric efficiency bound when the errors are conditionally normal. Our results are in parallel to that for partially linear and partially linear additive models given by [13] and [4] respectively. Those models are among a rich variety of semiparametric ways of modeling longitudinal data, and they differ from semivarying coefficient models in that their nonparametric components admit more direct additive expressions. Partially linear (additive) models were also considered by [14, 15, 16, 17, 23], among which [14, 15, 16, 23] used kernel method and [17] used spline estimation.

Our third contribution is to deal with adaptive efficient estimation when the within-subject covariance matrices are estimated nonparametrically using the data at hand. Notice that [4] ignored this practical issue and did not consider estimation of the covariances, and [13] suggested using some parametric specification which can be estimated \sqrt{n} -consistently. We consider the case where the nonparametric within-subject covariance matrices depend only on the observation times but not on the other covariates. Such assumptions are reasonable because we do not assume that the observation times are regular across different subjects or they are dense. Indeed, with irregular and/or sparse observation times, estimating the covariances in a completely nonparametric way, by letting them to be dependent on all of the T_{ij} , \mathbf{X}_{ij} and \mathbf{Z}_{ij} nonparametrically, is particularly problematic and even

unreliable as the curse-of-dimensionality problem arises. Our covariance estimator is constructed based on residuals yielded by an initial estimation. The final estimator of the true value of β is then given by plugging-in the covariance estimates to the GEE spline estimation. We show the asymptotic equivalence of our final estimator to the oracle efficient estimator which uses the true covariance matrices in the GEE spline estimation.

The above result is partly motivated by the study of [14] on efficient estimation in partially linear models under the same nonparametric covariance structure. However, the kernel profile method taken by [14] involves only local linear regression, thus, to achieve semiparametric efficiency it requires some complicated iterative backfitting calculation except for the identity link function [15, 16]. By comparison, our approach to estimating the parametric and nonparametric components in the mean function is different and much simpler. We ingeniously use both spline approximation and local linear estimation to avoid complicated calculation while allowing for the asymptotic equivalence property at the same time. To the best of our knowledge, there are no existing results for semivarying coefficient models, especially when some of the m_i 's tend to infinity or when the Σ_i s are estimated.

Our final estimator is some kind of feasible generalized least squares (FGLS) estimator since we replace the within-subject covariance matrices with their nonparametric estimates. Even if our assumption on the covariance matrices fails to hold, it still possesses the asymptotic normality under mild conditions and still makes use of some information of the covariance matrices. For example, if the covariances depend on some time-dependent covariates, to some extent such effects are still captured by our method. In this sense, compared with existing methods which use either parametrically estimated or some ad-hoc covariance matrices [7, 18, 21], our approach is more adaptive to the unknown covariance matrices. A promising cluster bootstrap inference method was proposed by [2]; it assumes some parametric within-cluster covariance structure, however. In the case where there is one observation for each subject/cluster, our assumption on the covariance matrices reduces to that of [20], which also suggested to improve the efficiency in a similar manner.

Our simulation study shows that numerically the proposed method outperforms the working independence approach and the quadratic inference functions (QIF) method by [18], and it behaves close to the oracle estimator which uses the true covariance matrices. Note that, while the QIF procedure is suitable when there is some kind of regularity and stationarity in the error process, our procedure adapts to both non-stationarity and irregularity. We also applied our method to the CD4 count dataset and identified some

interesting new effects not detected by the working independence approach.

After the semiparametric efficient estimation, we can estimate and make inference on the nonparametric component in the same way as in dealing with varying coefficient models, using the difference between the response and the estimated parametric part [25]. When p and q are both diverging and the model is sparse, [6] suggested a simultaneous variable selection and structure identification procedure and showed its consistency property. By combining the method with the proposed estimation procedure and by putting together the corresponding consistency and efficiency results, we have an efficient estimation procedure in this case.

The organization of this paper is as follows. In Section 2 we derive the semiparametric efficiency bound for the constant coefficient vector β and asymptotic normality of GEE spline estimators. In Section 3, we propose an efficient estimator of β when the errors have some general covariance structure and state its asymptotic equivalence to the oracle estimator which assumes the covariance matrices are known. Section 4 summarizes and discusses results of our simulation and empirical studies used to assess numerical performance of the proposed efficient estimator. Section 5 contains some technical assumptions and proof of the asymptotic equivalence. Placed in the supplementary material [5] are proofs of the other theoretical results, some lemmas, and results when the m_i 's are uniformly bounded.

2. Semiparametric efficient estimation of β . In this section, \mathbf{V}_i is a given inverse weight matrix depending only on $\underline{\mathbf{X}}_i$, $\underline{\mathbf{Z}}_i$, and \underline{T}_i , $i = 1, \dots, n$. We use a K_n -dimensional equispaced B-spline basis on $[0, 1]$, denoted by $\mathbf{B}(t)$, to approximate the function $\mathbf{g}(t)$. See [19] for the definition and properties of B-spline bases. We set

$$\mathbf{W}_{ij} = \mathbf{Z}_{ij} \otimes \mathbf{B}(T_{ij}) \text{ and } \underline{\mathbf{W}}_i = (\mathbf{W}_{i1}, \dots, \mathbf{W}_{im_i})^T,$$

where \otimes is the Kronecker product, and denote the true values of β and $\mathbf{g}(t)$ by β_0 and $\mathbf{g}_0(t) = (g_{01}(t), \dots, g_{0q}(t))^T$ respectively. Then we estimate β_0 and $\mathbf{g}_0(t)$ by minimizing with respect to β and γ simultaneously the following objective function:

$$(2.1) \quad \sum_{i=1}^n (\underline{Y}_i - \underline{\mu}(\underline{\mathbf{X}}_i\beta + \underline{\mathbf{W}}_i\gamma))^T \mathbf{V}_i^{-1} (\underline{Y}_i - \underline{\mu}(\underline{\mathbf{X}}_i\beta + \underline{\mathbf{W}}_i\gamma)),$$

where $\boldsymbol{\gamma} \in \mathbb{R}^{qK_n}$ and the j th element of $\underline{\mu}(\underline{\mathbf{X}}_i\boldsymbol{\beta} + \underline{\mathbf{W}}_i\boldsymbol{\gamma})$ is $\mu(\mathbf{X}_{ij}^T\boldsymbol{\beta} + \mathbf{W}_{ij}^T\boldsymbol{\gamma})$. Thus the generalized estimating equations are

$$(2.2) \quad \begin{aligned} & \sum_{i=1}^n \underline{\mathbf{X}}_i^T \Delta_i \mathbf{V}_i^{-1} (\underline{Y}_i - \underline{\mu}(\underline{\mathbf{X}}_i\boldsymbol{\beta} + \underline{\mathbf{W}}_i\boldsymbol{\gamma})) = 0, \\ \text{and} \quad & \sum_{i=1}^n \underline{\mathbf{W}}_i^T \Delta_i \mathbf{V}_i^{-1} (\underline{Y}_i - \underline{\mu}(\underline{\mathbf{X}}_i\boldsymbol{\beta} + \underline{\mathbf{W}}_i\boldsymbol{\gamma})) = 0, \end{aligned}$$

where Δ_i is an $m_i \times m_i$ diagonal matrix defined by

$$\Delta_i = \text{diag}(\mu'(\mathbf{X}_{i1}^T\boldsymbol{\beta} + \mathbf{W}_{i1}^T\boldsymbol{\gamma}), \dots, \mu'(\mathbf{X}_{im_i}^T\boldsymbol{\beta} + \mathbf{W}_{im_i}^T\boldsymbol{\gamma})).$$

Denote the solution to (2.2) by $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$ and $\widehat{\boldsymbol{\gamma}}_{\mathbf{V}} \equiv (\widehat{\gamma}_{1V}^T, \dots, \widehat{\gamma}_{qV}^T)^T$. Then the GEE spline estimator with weight matrices \mathbf{V}_i^{-1} , $i = 1, \dots, n$, for $\boldsymbol{\beta}_0$ is $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$ and that for $\mathbf{g}_0(t)$ is $(\widehat{\gamma}_{1V}^T \mathbf{B}(t), \dots, \widehat{\gamma}_{qV}^T \mathbf{B}(t))^T$.

Hereafter we focus on the identity link function and present the asymptotic normality of $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$ in Proposition 1 under general error distributions as specified in Assumption A6 given in Section 5. We allow some of the m_i 's to diverge in a way like

$$\sum_{i=1}^n m_i^5 = O(n) \quad \text{and} \quad \max_{1 \leq i \leq n} m_i = O(n^{1/8}).$$

See Assumptions A1 and A2 for the specific conditions on the m_i 's. We refer to the supplement [5] for the results for general link functions when the m_i 's are uniformly bounded and the $\underline{\epsilon}_i$'s satisfy the sub-Gaussian property.

First, we introduce some function spaces, inner products and projections. Let L_2 denote the space of square integrable functions on $[0, 1]$ and recall $\mathbf{B}(t)$ is the equispaced B-spline basis on $[0, 1]$. We define two function spaces:

$$\begin{aligned} \mathbf{G} &= \{(g_1, \dots, g_q)^T \mid g_j \in L_2, j = 1, \dots, q\}, \\ \text{and } \mathbf{G}_B &= \{(\mathbf{B}^T \boldsymbol{\gamma}_1, \dots, \mathbf{B}^T \boldsymbol{\gamma}_q)^T \mid \boldsymbol{\gamma} = (\boldsymbol{\gamma}_1^T, \dots, \boldsymbol{\gamma}_q^T)^T \in \mathbb{R}^{qK_n}\}. \end{aligned}$$

Note that $\mathbf{G}_B \subset \mathbf{G}$. Next, let v_1 and v_2 be two stochastic processes each taking scalar values at T_{ij} , $i = 1, \dots, n$, $j = 1, \dots, m_i$. Then we define two inner products of v_1 and v_2 by

$$\langle v_1, v_2 \rangle_n^V = \frac{1}{n} \sum_{i=1}^n \underline{v}_{1i}^T \mathbf{V}_i^{-1} \underline{v}_{2i} \quad \text{and} \quad \langle v_1, v_2 \rangle^V = \mathbb{E}\{\langle v_1, v_2 \rangle_n^V\},$$

where \underline{v}_{1i} and \underline{v}_{2i} are defined in the same way as \underline{T}_i , and we define the associated norms by $\|v\|_n^V = (\langle v, v \rangle_n^V)^{1/2}$ and $\|v\|^V = (\langle v, v \rangle^V)^{1/2}$. The projections, with respect to $\|\cdot\|^V$, of the k th element of \mathbf{X} onto $\mathbf{Z}^T \mathbf{G}$ and $\mathbf{Z}^T \mathbf{G}_B$ are given by

$$(2.3) \quad \Pi_{\mathbf{V}} X_k = \operatorname{argmin}_{\mathbf{g} \in \mathbf{G}} \|X_k - \mathbf{Z}^T \mathbf{g}\|^V \quad \text{and} \quad \Pi_{\mathbf{V}_n} X_k = \operatorname{argmin}_{\mathbf{g} \in \mathbf{G}_B} \|X_k - \mathbf{Z}^T \mathbf{g}\|^V,$$

where $\|X_k - \mathbf{Z}^T \mathbf{g}\|^V = \frac{1}{n} \mathbb{E} \left\{ \sum_{i=1}^n (\underline{X}_{ik} - \underline{(\mathbf{Z}^T \mathbf{g})}_i)^T \mathbf{V}_i^{-1} (\underline{X}_{ik} - \underline{(\mathbf{Z}^T \mathbf{g})}_i) \right\}$, with $\underline{X}_{ik} = (X_{i1k}, \dots, X_{im_i k})^T$ and $\underline{(\mathbf{Z}^T \mathbf{g})}_i = (\mathbf{Z}_{i1}^T \mathbf{g}(T_{i1}), \dots, \mathbf{Z}_{im_i}^T \mathbf{g}(T_{im_i}))$. Hereafter we write

$$\varphi_{\mathbf{V}_k}^* = \Pi_{\mathbf{V}} X_k \in \mathbf{G} \quad \text{and} \quad \bar{\varphi}_{\mathbf{V}_k} = \Pi_{\mathbf{V}_n} X_k \in \mathbf{G}_B.$$

Assumption S

- (i) The projections $\varphi_{\mathbf{V}_k}^*(t)$, $k = 1, \dots, p$, and the varying coefficient function \mathbf{g}_0 are twice continuously differentiable on $[0, 1]$, and they and their second order derivatives are uniformly bounded in n .
- (ii) We take $K_n = \lfloor c_K n^{1/5} \rfloor$ for some positive constant c_K , where $\lfloor x \rfloor$ is the largest integer no greater than x .

Assumption S(i) is a mild and standard assumption for semiparametric models. We consider the existence and smoothness properties of $\varphi_{\mathbf{V}_k}^*(t)$ in Section 5. Recall that all the covariates are assumed to be uniformly bounded. Since the relevant functions are assumed to be at least twice continuously differentiable, we recommend quadratic or cubic spline approximation. Then the order of K_n specified in Assumption S(ii) is optimal. If the smoothness of different functions varies, we refer to [1] for the convergence rate interfere phenomenon.

The following matrices are necessary in order to present asymptotic normality of $\hat{\beta}_{\mathbf{V}}$:

$$(2.4) \quad \mathbf{H} = \begin{pmatrix} \sum_{i=1}^n \underline{\mathbf{X}}_i^T \mathbf{V}_i^{-1} \underline{\mathbf{X}}_i & \sum_{i=1}^n \underline{\mathbf{X}}_i^T \mathbf{V}_i^{-1} \underline{\mathbf{W}}_i \\ \sum_{i=1}^n \underline{\mathbf{W}}_i^T \mathbf{V}_i^{-1} \underline{\mathbf{X}}_i & \sum_{i=1}^n \underline{\mathbf{W}}_i^T \mathbf{V}_i^{-1} \underline{\mathbf{W}}_i \end{pmatrix} \\ = \begin{pmatrix} \mathbf{H}_{11} & \mathbf{H}_{12} \\ \mathbf{H}_{21} & \mathbf{H}_{22} \end{pmatrix} \quad (\text{say}),$$

$$\mathbf{H}_{11 \cdot 2} = \mathbf{H}_{11} - \mathbf{H}_{12} \mathbf{H}_{22}^{-1} \mathbf{H}_{21}, \quad \text{and} \quad \mathbf{H}^{11} = (\mathbf{H}_{11 \cdot 2})^{-1}.$$

Let $\Omega_{\mathbf{V}_n}$ be a $p \times p$ matrix whose (k, l) th element is

$$\langle X_k - \mathbf{Z}^T \varphi_{\mathbf{V}_k}^*, X_l - \mathbf{Z}^T \varphi_{\mathbf{V}_l}^* \rangle^V \\ = \frac{1}{n} \sum_{i=1}^n \mathbb{E} \left\{ (\underline{X}_{ik} - \underline{(\mathbf{Z}^T \varphi_{\mathbf{V}_k}^*)}_i)^T \mathbf{V}_i^{-1} (\underline{X}_{il} - \underline{(\mathbf{Z}^T \varphi_{\mathbf{V}_l}^*)}_i) \right\}.$$

Note that $n^{-1}\mathbf{H}_{11.2}$ is an estimate of $\Omega_{\mathbf{V}n}$. We assume that there exists a $p \times p$ positive definite matrix $\Omega_{\mathbf{V}}$ such that

$$(2.5) \quad \lim_{n \rightarrow \infty} \Omega_{\mathbf{V}n} = \Omega_{\mathbf{V}}.$$

Now we are ready to state the asymptotic normality of $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$ under general error distributions as specified in Assumption A6 given in Section 5. Its proof is given in the supplement [5]. We denote the normal distribution with mean η and covariance Ω by $\mathbf{N}(\eta, \Omega)$, and by “ \xrightarrow{d} ” we mean convergence in distribution. Let \mathbf{I}_l be the l -dimensional identity matrix.

PROPOSITION 1. (*Asymptotic normality of $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$*) Under Assumption S, (2.5), and Assumptions A1-6 given in Section 5, we have

$$\widehat{\boldsymbol{\beta}}_{\mathbf{V}} = \boldsymbol{\beta}_0 + \mathbf{H}^{11} \sum_{i=1}^n (\mathbf{X}_i - \mathbf{W}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21})^T \mathbf{V}_i^{-1} \boldsymbol{\epsilon}_i + o_p\left(\frac{1}{\sqrt{n}}\right).$$

We also have

$$\Gamma_{\mathbf{V}}^{-1/2} (\widehat{\boldsymbol{\beta}}_{\mathbf{V}} - \boldsymbol{\beta}_0) \xrightarrow{d} \mathbf{N}(0, \mathbf{I}_p),$$

where $\Gamma_{\mathbf{V}}$ is given by

$$(2.6) \quad \mathbf{H}^{11} \sum_{i=1}^n \left\{ (\mathbf{X}_i - \mathbf{W}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21})^T \mathbf{V}_i^{-1} \boldsymbol{\Sigma}_i \mathbf{V}_i^{-1} (\mathbf{X}_i - \mathbf{W}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21}) \right\} \mathbf{H}^{11}.$$

Under (2.5), $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$ is \sqrt{n} -consistent for $\boldsymbol{\beta}_0$. We can estimate its asymptotic covariance $\Gamma_{\mathbf{V}}$ given in (2.6) by replacing the $\boldsymbol{\Sigma}_i$'s with some estimates based on $\widehat{\boldsymbol{\beta}}_{\mathbf{V}}$ and $\widehat{\boldsymbol{\gamma}}_{\mathbf{V}}$, for example, we can replace $\boldsymbol{\Sigma}_i$ with $\widetilde{\boldsymbol{\epsilon}}_i \widetilde{\boldsymbol{\epsilon}}_i^T$ where

$$\widetilde{\boldsymbol{\epsilon}}_i = \mathbf{Y}_i - \mathbf{X}_i^T \widehat{\boldsymbol{\beta}}_{\mathbf{V}} - \mathbf{W}_i^T \widehat{\boldsymbol{\gamma}}_{\mathbf{V}}.$$

However, this approach may be too crude and it does not make use of the common information on the covariance structure contained in different subjects. Alternatively, we can estimate the $\boldsymbol{\Sigma}_i$'s by applying smoothing techniques to some residuals based on some assumption on the covariance structure. We investigate this problem in Section 3.

Next, Proposition 2 gives the semiparametric efficiency bound for estimation of $\boldsymbol{\beta}_0$. It can be proved in almost the same way as in Section 4.4 of [13] and Lemma 1 of [4] and the proof is omitted. We denote the semiparametric efficient score function of $\boldsymbol{\beta}$ by

$$\mathbf{l}_{\boldsymbol{\beta}}^* = (l_{\beta_1}^*, \dots, l_{\beta_p}^*)^T.$$

Its expression is given in Proposition 2. Then we denote $\boldsymbol{\varphi}_{\boldsymbol{\Sigma}_k}^*(t)$ by $\boldsymbol{\varphi}_{eff,k}^*(t)$ when $\mathbf{V}_i = \boldsymbol{\Sigma}_i$ in (2.1).

PROPOSITION 2. (*Semiparametric efficiency bound*) Under the same assumptions as in Proposition 1, we have

$$l_{\beta k}^* = \sum_{i=1}^n (\underline{X}_{ik} - \underline{(Z^T \varphi_{eff,k}^*)}_i)^T \Sigma_i^{-1} \{ \underline{Y}_i - \underline{X}_i^T \beta_0 - \underline{(Z^T \mathbf{g}_0)}_i \},$$

and the semiparametric efficient information matrix for β is given by

$$\lim_{n \rightarrow \infty} \frac{1}{n} \mathbb{E} \{ \mathbf{l}_{\beta}^* (\mathbf{l}_{\beta}^*)^T \} = \Omega_{\Sigma} \text{ with } \mathbf{V}_i = \Sigma_i \text{ in (2.5).}$$

Proposition 3 gives the asymptotic normality of $\widehat{\beta}_{\Sigma}$, the so called oracle estimator, which uses the true covariance structure in the GEE spline regression. It also asserts that $\widehat{\beta}_{\Sigma}$ achieves the semiparametric efficiency bound derived from Proposition 2. The proof is given in the supplement [5].

PROPOSITION 3. (*Oracle efficient estimator*) If we take $\mathbf{V}_i = \Sigma_i$ in (2.2) then, under the same assumptions as in Proposition 1, we have

$$\sqrt{n} \Omega_{\Sigma}^{1/2} (\widehat{\beta}_{\Sigma} - \beta_0) \xrightarrow{d} \mathbf{N}(0, \mathbf{I}_p).$$

In practice, usually the Σ_i 's are unknown and we have no direct access to the semiparametric efficient score function or the oracle estimator. In the next section we study nonparametric estimation of the covariances so as to improve the efficiency.

3. Efficient estimation of β . The semiparametric efficiency bound of β given in Proposition 2 indicates that knowledge, or at least estimation, of the Σ_i 's is necessary in order to construct a semiparametric efficient estimator. On the other hand, as discussed in the Introduction, when the Σ_i 's are unknown it is almost impossible to estimate them in a fully nonparametric way. Fortunately, for longitudinal or clustered data sets, it is reasonable to make some assumptions such as

$$(3.1) \quad \Sigma_i = \Sigma(\underline{T}_i), \quad i = 1, \dots, n,$$

where the (j, j) th element of Σ_i is given by $\sigma^2(T_{ij})$ and the (j, j') th element is given by $\sigma(T_{ij}, T_{ij'})$ when $j \neq j'$, for some smooth functions $\sigma^2(t)$ and $\sigma(s, t)$. Based on (3.1), in Section 3.1 we construct nonparametric estimates of the covariances and then use them to derive an FGLS procedure to improve the efficiency, and we show in Section 3.2 its asymptotic equivalence to the oracle estimator $\widehat{\beta}_{\Sigma}$.

3.1. *Methodology.* A preliminary estimation of β_0 and g_0 is necessary before we can estimate the covariances. For simplicity and robustness, we utilize working independence in the GEE spline estimation. As noted following Proposition 1 we could then use the resultant residuals to estimate the covariance matrices directly. However it is intuitively better to further make use of the covariance structure (3.1) by applying some nonparametric smoothing techniques to the residuals. In addition, alternative to the spline estimator, we could apply smoothing techniques to the pseudo responses $\underline{Y}_i - \underline{X}_i^T \hat{\beta}_V$ to obtain another estimator of g_0 . We take this latter approach for technical and numerical reasons given in Remark 1. After the preliminary estimation, for each $i = 1, \dots, n$, we estimate Σ_i by applying local linear regression and denote the resultant estimate by $\hat{\Sigma}_i$. Our final estimator of β_0 , denoted by $\hat{\beta}_{\hat{\Sigma}}$, is then obtained by taking $V_i = \hat{\Sigma}_i$, $i = 1, \dots, n$, in the GEE spline estimation. Note that in the trivial case where m_i is fixed for all i and the T_{ij} 's are equi-spaced, we can estimate Σ_i without using any smoothing techniques.

Let K be a given kernel function. Our covariance estimation procedure is formally specified as follows:

Step 1. Estimate β_0 by the GEE spline method given in Section 2 with $V_i = I_{m_i}$, $i = 1, \dots, n$, and denote the resultant working independence estimate by $\hat{\beta}_I$.

Step 2. Estimate $g_0(t)$ by applying local linear regression to $\{Y_{ij} - \mathbf{X}_{ij}^T \hat{\beta}_I, i = 1, \dots, n, j = 1, \dots, m_i\}$, using bandwidth h_1 . We denote the resulting estimate by $\hat{g}(t)$, which is written as

$$(3.2) \quad \hat{g}(t) = D_q(A_{1n}(t))^{-1} \frac{1}{N_1 h_1} \sum_{i=1}^n \sum_{j=1}^{m_i} \mathbf{Z}_{ij} \otimes \begin{pmatrix} 1 \\ \frac{T_{ij}-t}{h_1} \end{pmatrix} K\left(\frac{T_{ij}-t}{h_1}\right) (Y_{ij} - \mathbf{X}_{ij}^T \hat{\beta}_I),$$

where $N_1 = \sum_{i=1}^n m_i$, $D_q = I_q \otimes (1 \ 0)$, and

$$A_{1n}(t) = \frac{1}{N_1 h_1} \sum_{i=1}^n \sum_{j=1}^{m_i} (\mathbf{Z}_{ij} \mathbf{Z}_{ij}^T) \otimes \begin{pmatrix} 1 & \frac{T_{ij}-t}{h_1} \\ \frac{T_{ij}-t}{h_1} & \left(\frac{T_{ij}-t}{h_1}\right)^2 \end{pmatrix} K\left(\frac{T_{ij}-t}{h_1}\right).$$

Step 3. Calculate the residuals, denoted as $\hat{\epsilon}_{ij}$, $i = 1, \dots, n$ and $j = 1, \dots, m_i$, by

$$\hat{\epsilon}_{ij} = Y_{ij} - \mathbf{X}_{ij}^T \hat{\beta}_I - \mathbf{Z}_{ij}^T \hat{g}(T_{ij}).$$

Step 4. Estimate the variance function $\sigma^2(t)$ by applying to the squared residuals local linear regression with bandwidth h_2 . Denote the resul-

tant estimate by $\widehat{\sigma}^2(t)$; it can be expressed as
(3.3)

$$\widehat{\sigma}^2(t) = (10)(A_{2n}(t))^{-1} \frac{1}{N_1 h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \left(\frac{1}{\frac{T_{ij}-t}{h_2}} \right) K\left(\frac{T_{ij}-t}{h_2}\right) (\widehat{\epsilon}_{ij})^2,$$

where

$$A_{2n}(t) = \frac{1}{N_1 h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \left(\frac{1}{\frac{T_{ij}-t}{h_2}} \quad \frac{\frac{T_{ij}-t}{h_2}}{\left(\frac{T_{ij}-t}{h_2}\right)^2} \right) K\left(\frac{T_{ij}-t}{h_2}\right).$$

Step 5. Estimate the covariance function $\sigma(s, t)$ by applying to $\{\widehat{\epsilon}_{ij}\widehat{\epsilon}_{ij'}, j \neq j', i = 1, \dots, n\}$ local linear regression with bandwidth h_3 . We denote the resultant estimate by $\widehat{\sigma}(s, t)$; it has the following expression:

(3.4)

$$\widehat{\sigma}(s, t) = (100)(A_{3n}(s, t))^{-1} \times \frac{1}{N_2 h_3^2} \sum_{i=1}^n \sum_{j \neq j'} \left(\frac{1}{\frac{T_{ij}-s}{h_3} \frac{T_{ij'}-t}{h_3}} \right) K\left(\frac{T_{ij}-s}{h_3}\right) K\left(\frac{T_{ij'}-t}{h_3}\right) \widehat{\epsilon}_{ij} \widehat{\epsilon}_{ij'},$$

where $N_2 = \sum_{i=1}^n m_i(m_i - 1)$ and

$$A_{3n}(s, t) = \frac{1}{N_2 h_3^2} \sum_i \sum_{j \neq j'} \left(\frac{1}{\frac{T_{ij}-s}{h_3} \frac{T_{ij'}-t}{h_3}} \right) \left(1 \quad \frac{T_{ij}-s}{h_3} \quad \frac{T_{ij'}-t}{h_3} \right) K\left(\frac{T_{ij}-s}{h_3}\right) K\left(\frac{T_{ij'}-t}{h_3}\right).$$

Step 6. Calculate $\widehat{\Sigma}_i$ by combining the results from steps 4 and 5 by letting

$$\widehat{\Sigma}_i(j, j') = \widehat{\sigma}(T_{ij}, T_{ij'}) I(j \neq j') + \widehat{\sigma}^2(T_{ij}) I(j = j'),$$

and then estimate β_0 with $\mathbf{V}_i = \widehat{\Sigma}_i$ in the GEE (2.2). Denote the resultant estimate of β_0 by $\widehat{\beta}_{\widehat{\Sigma}}$.

In general the covariance function estimate $\widehat{\sigma}(s, t)$ given by step 5 may not be positive semidefinite. We can modify it by truncating the eigenfunctions in its spectral decomposition that have eigenvalues not exceeding some nonnegative constant λ_L . Then we have positive definite covariance estimates if we replace $\widehat{\sigma}(s, t)$ with this modified version in step 6.

REMARK 1. When we calculate $\widehat{\beta}_I$ in step 1, we also have $\widehat{\gamma}_I$ and get the set of residuals $\{\widetilde{\epsilon}_{ij} = Y_{ij} - \mathbf{X}_{ij}^T \widehat{\beta}_I - \mathbf{W}_{ij}^T \widehat{\gamma}_I\}$. Then we could omit steps 2 and 3 of our procedure by exploiting this set of residuals when we estimate Σ_i in steps 4-6. However, our simulation results summarized in Section 4 indicate that this simplified approach is inferior to the proposed one. Intuitively speaking, to achieve the semiparametric efficiency in the GEE spline estimation of β_0 , to some extent the accompanying estimation of $\mathbf{g}_0(t)$ requires undersmoothing and thus it often exhibits spurious wiggling patterns. Besides, it is difficult to justify theoretically this simplified approach as the local property of spline estimators seems to be intractable.

3.2. *Asymptotic equivalence.* In this section we establish the asymptotic equivalence between the data-driven estimator $\widehat{\beta}_{\widehat{\Sigma}}$ and the oracle estimator $\widehat{\beta}_{\Sigma}$ by exploiting some desirable properties of $\widehat{\Sigma}_i$. First, we specify our assumptions on the smoothness of $\mathbf{g}_0(t)$, $\sigma^2(t)$ and $\sigma(s, t)$. We need Assumption B given below, which is more restrictive than usual, in order to evaluate the difference between $\widehat{\Sigma}_i^{-1}$ and Σ_i^{-1} .

Assumption B.

- (i) Assumption (3.1) holds.
- (ii) The true varying coefficient function $\mathbf{g}_0(t)$ is three times continuously differentiable on $[0, 1]$.
- (iii) The variance function $\sigma^2(t)$ is three times continuously differentiable on $[0, 1]$.
- (iv) The covariance function $\sigma(s, t)$ is three times continuously differentiable on $[0, 1]^2$.

In the following we collect our assumptions on the kernel function K and the three bandwidths used in the construction of the proposed estimator. Assumption H(i) on K is a standard one. When Assumption B holds, our assumptions on the bandwidths h_1 , h_2 and h_3 are not restrictive. For example, the optimal order of h_1 and h_2 is $n^{-1/5}$ which falls into the specified range. A larger order is recommended only for h_3 due to the two-dimensional smoothing in step 5. However, since the actual number of observations in local linear regression in step 5 of the above procedure is N_2 we anticipate that bandwidth choice will not seriously affect the performance of our final estimator.

Assumption H.

- (i) The kernel function K is some continuously differentiable symmetric density function with a compact support.

- (ii) The bandwidths h_1 , h_2 and h_3 satisfy $h_1 = c_1 n^{-a_h}$ for some $1/6 < a_h \leq 1/4$, $h_2 = c_2 n^{-b_h}$ for some $1/6 < b_h \leq 1/4$ and $h_3 = c_3 n^{-c_h}$ for some $1/6 < c_h < 1/4$, where c_1 , c_2 and c_3 are some positive constants.

The asymptotic expression of $\widehat{\Sigma}_i$ is given in Proposition 4, which is verified in the supplementary material [5]. Note that we need more elaborate representations than those used by [14] since we deal with a $(p+qK_n)$ -dimensional linear regression model. Note also that the functions B_j , $j = 1, \dots, 4$, that appear in Proposition 4 are implicitly defined in the proof of the proposition and only their boundedness property is needed in the proof of Theorem 1.

PROPOSITION 4. (*Representations of the covariance estimators*) Under the assumptions in Proposition 1 with $\mathbf{V}_i = \mathbf{I}_{m_i}$, and Assumptions B and H, we have the following representations of $\widehat{\sigma}^2(t)$ and $\widehat{\sigma}(s, t)$. Uniformly in t ,

$$\widehat{\sigma}^2(t) - \sigma^2(t) = B_1(t)h_2^2 + B_2(t)E_1(t) + O_p(h_1^3 + h_2^3) + O_p\left(\frac{\log n}{nh_1} + \frac{\log n}{nh_2}\right)$$

where

$$\begin{aligned} E_1(t) &= \frac{1}{N_1 h_2} \sum_{i=1}^n \sum_{j=1}^{m_i} \left(\frac{1}{\frac{T_{ij}-t}{h_2}} \right) K\left(\frac{T_{ij}-t}{h_2}\right) (\epsilon_{ij}^2 - \sigma^2(T_{ij})) \\ &= O_p\left(\sqrt{\frac{\log n}{nh_2}}\right) \quad \text{uniformly in } t, \end{aligned}$$

and $B_1(t)$ and $B_2(t)$ are bounded functions. Uniformly in s and t ($s \neq t$),

$$\begin{aligned} \widehat{\sigma}(s, t) - \sigma(s, t) &= B_3(s, t)h_2^2 + B_4(s, t)E_2(s, t) + O_p(h_1^3) + O_p\left(\frac{\log n}{nh_1}\right) \\ &\quad + O_p(h_3^3) + O_p\left(\frac{\log n}{nh_3^2}\right), \end{aligned}$$

where

$$\begin{aligned} E_2(s, t) &= \frac{1}{N_2 h_3^2} \sum_{i=1}^n \sum_{j \neq j'} \left(\frac{1}{\frac{\frac{T_{ij}-s}{h_3}}{\frac{T_{ij'}-t}{h_3}}} \right) K\left(\frac{T_{ij}-s}{h_3}\right) K\left(\frac{T_{ij'}-t}{h_3}\right) (\epsilon_{ij}\epsilon_{ij'} - \sigma(T_{ij}, T_{ij'})) \\ &= O_p\left(\sqrt{\frac{\log n}{nh_3^2}}\right) \quad \text{uniformly in } s \text{ and } t, \end{aligned}$$

and $B_3(s, t)$ and $B_4(s, t)$ are bounded functions.

We state in Theorem 1 the desirable equivalence property of $\widehat{\beta}_{\Sigma}$ to the oracle estimator. The proof uses Proposition 4; it is tedious and technical and thus is postponed to Section 5.4. We have not yet obtained a similar result for general link functions even when the m_i 's are uniformly bounded, and that is a future research topic.

THEOREM 1. *Under the assumptions in Proposition 4, we have*

$$\widehat{\beta}_{\Sigma} = \widehat{\beta}_{\Sigma} + o_p(n^{-1/2}).$$

Note that even if (3.1) fails to hold, we still have the asymptotic equivalence in Theorem 1 and the asymptotic normality in Proposition 1 with $\mathbf{V}_i = \text{Var}(\underline{\epsilon}_i | \underline{T}_i)$ when $\text{Var}(\underline{\epsilon}_i | \underline{T}_i)$ is represented by $\sigma^2(t)$ and $\sigma(s, t)$. We are still exploiting some information on Σ_i .

Besides, we can replace the three times continuously differentiability with the twice continuously differentiability and the Hölder continuity of the second derivatives of order α_1 , α_2 , and α_3 in assumptions B(ii), B(iii), and B(iv), respectively. In this case, the bandwidths in steps 2, 4, and 5 of our method have to satisfy the condition

$$\sqrt{n}(h_1^{2+\alpha_1} + h_2^{2+\alpha_2} + h_3^{2+\alpha_3}) \rightarrow 0.$$

Note that α_3 must be positive because step 5 of our procedure requires two-dimensional smoothing. Then we can prove similar results when $0 \leq \alpha_1 < 1$, $0 \leq \alpha_2 < 1$, and $0 < \alpha_3 < 1$. Specifically, the $O_p(h_j^3)$ terms in Proposition 4 will be replaced by $O_p(h_j^{2+\alpha_j})$, $j = 1, 2, 3$.

REMARK 2. *In Proposition 2, no assumptions on the structure of the Σ_i 's or the conditional normality of the $\underline{\epsilon}_i$'s is imposed. However, as mentioned before it is difficult to estimate the Σ_i 's in a fully nonparametric way and thus we impose assumption (3.1). On the other hand, when (3.1) holds, we should use this information in calculating the semiparametric efficient score function. Unfortunately, under general errors this task seems intractable and we have no results in this regard. Nevertheless, when (3.1) and some regularity conditions hold, we come up with some remedies to improve the efficiency, as compared to using some (arbitrary) working covariance structure. Indeed, $\widehat{\beta}_{\Sigma}$ has the smallest asymptotic variance among all $\widehat{\beta}_{\mathbf{V}}$ in this case, based on Propositions 1-3, Theorem 1, and the fact that it is an FGLS estimator. Furthermore, it is semiparametric efficient when $\underline{\epsilon}_i$ is normally distributed conditionally on $\underline{\mathbf{X}}_i$, $\underline{\mathbf{Z}}_i$ and \underline{T}_i , as discussed in A.1 of [23].*

4. Numerical studies.

4.1. *Simulation study.* In our simulation study summarized in this section, the data were generated from the following model:

$$Y_{ij} = \mathbf{X}_{ij}^T \boldsymbol{\beta}_0 + \mathbf{Z}_{ij}^T \mathbf{g}_0(T_{ij}) + \epsilon_i(T_{ij}), \quad j = 1, \dots, m_i, \quad i = 1, \dots, n,$$

with the first component of \mathbf{Z}_{ij} being taken as 1. The number of observation time points in the i th subject was set as $m_i = m_0 + \text{binomial}(m_r, 0.65)$. Then the observation time points T_{ij} were uniformly distributed over the interval $[(j-1)/(m_0+m_r), j/(m_0+m_r)]$, $j = 1, \dots, m_i$. We note that when $m_i = m_0 + m_r$, the subject is observed at all follow-up time points; when $m_i < m_0 + m_r$, the subject may be lost to follow up. This setup is intended to model real and more complicated scenarios that often happen in practice. We set $m_0 = 6$ and $m_r = 6$. We generated the other $(p+q-1)$ -dimensional covariates from a multivariate Gaussian distribution, and we considered the following coefficients settings:

$$\begin{aligned} p &= 4, \quad q = 4, \quad \boldsymbol{\beta}_0 = (5, 5, -5, -5)^T \text{ and} \\ \mathbf{g}_0(t) &= (3.5 \sin(2\pi t), 5(1-t)^2, 3.5(\exp(-(3t-1)^2) + \exp(-(4t-3)^2)) - \\ &\quad 1.5, 3.5t^{1/2})^T. \end{aligned}$$

The random error process $\epsilon_i(t)$ was simulated from an ARMA(1, 1) Gaussian process with mean zero and covariance function $\text{cov}(\epsilon_i(s), \epsilon_i(t)) = \omega \rho^{|s-t|}$. We set $\omega = 4.95$ and considered $\rho = 0.4$ or 0.8 .

We considered two types of working covariance structure: working independence covariances (under the column ‘‘Independent’’) and the proposed covariance estimates (under the column ‘‘Efficient’’). For the sake of comparison, we also considered the true covariances (under the column ‘‘Oracle’’). In addition, we considered using the covariance estimator with the crude raw residuals obtained from Step 1 and omitting Steps 2 and 3 (under the column ‘‘Crude’’). Finally, we note that we adjusted the covariance function $\hat{\sigma}(s, t)$ by setting all negative eigenvalues to be zero. We also considered a strictly positive threshold $\lambda_L = 0.05$ and set all eigenvalues lower than λ_L to be zero. The estimator using this covariance estimate is denoted by ‘‘Positive.’’

Throughout the numerical studies, following [9], we used cubic splines and took the spline dimension K_n as $K_n = \lfloor 2n^{1/5} \rfloor$. We report in Table 1 the average estimation bias and estimated standard error (SE) obtained from 200 repetitions. The empirical standard errors are very close to the estimated standard errors and thus are omitted. In general, the efficient estimator could yield smaller estimation bias and variance, compared to the naive estimator

assuming working independence. In particular, the standard error for the efficient estimator is only 20 ~ 50% of that of the working independence estimator, indicating a remarkable reduction. In addition, we note that the efficient estimator has very similar performance to that of the oracle estimator. Regarding the crude estimator, as it is based on a simplified residual construction it produces relatively less accurate covariance estimation. Thus, its estimation bias and standard error are respectively larger than that for the efficient estimator. The positive estimator includes an adjustment when estimating the covariance function by setting eigenvalues lower than a positive cut-off to be zero while the efficient estimator only adjusts the negative eigenvalues. Therefore, it is slightly more biased than the efficient estimator. In all the considered cases, the crude and positive estimators are still more efficient than the naive working independence estimator.

There are also other methods based on estimating equations in the literature. We specifically considered the one based on quadratic inference function (QIF) [18] in which, to incorporate the longitudinal dependence, the correlation matrix is approximated using a matrix expansion. We followed all the settings specified in [18] to implement this approach, and we set any negative eigenvalue to zero whenever it occurred. From the numerical results summarized in in Table 1, we notice that this approach is more efficient than the estimator assuming working independence but is less efficient than our proposed method. The QIF approach indirectly models the correlations using some matrix approximation while our method directly models the covariances. Therefore our method may incorporate a more accurate covariance structure in the estimation and thus achieving better efficiency.

In all the numerical analysis, h_1 and h_2 were selected via the commonly used leave-one-subject-out cross-validation. The bandwidth h_3 used in the estimation of the covariance structure were selected to be larger than the bandwidth used in estimating the regression coefficients. Under the column “Efficient” we used $h_3 = 2h_1$ in all simulations. To examine effects of the bandwidth choice, we considered various choices of h_3 in the numerical studies and obtained quite similar results. Under the column “Different h_3 ”, we report the results for another case where $h_3 = 1.5h_1$, which are similar to those obtained when $h_3 = 2h_1$.

Our procedure does not require any iteration. In practice it may be interesting to refine the estimation of coefficients and covariances using iterations and obtain a final estimation upon convergence. We report the numerical results under the “Iterative” column. The bias and SE are very close to those obtained without iteration (under the “efficient” column).

TABLE 1. Estimation results of 200 simulations. “Independent” corresponds to $V_i = I_{m_i}$; “Efficient” refers to using $V_i = \widehat{\Sigma}_i$; “Oracle” refers to using the true Σ_i as V_i ; “Crude” refers to using residuals directly from Step 1 to estimate the covariances; “Positive” means we set a positive threshold for the covariance eigenvalues; “Quadratic” refers to the QIF based method; “Different h_3 ” means using a different choice of h_3 in our efficient estimation; “Iterative” indicates an iterative estimation approach.

n	ρ	Independent		Efficient		Oracle		Crude		Positive		Quadratic		Different h_3		Iterative		
		bias	SE	bias	SE	bias	SE	bias	SE	bias	SE	bias	SE	bias	SE	bias	SE	
100	0.4	β_1	.0214	-.0726	.0128	-.0366	.0133	-.0245	.0165	-.0425	.0173	-.0411	.0154	-.0421	-.0152	.0375	-.0146	.0361
		β_2	-.0218	.0727	-.0186	.0362	-.0146	.0251	-.0165	.0442	.0176	.0423	.0102	.0425	-.0098	.0375	-.0095	.0352
		β_3	-.0309	.0718	-.0126	.0364	-.0147	.0245	-.0127	.0435	.0205	.0425	.0095	.0455	-.0122	.0369	-.0099	.0360
		β_4	.0199	-.0736	.0145	-.0369	.0132	-.0246	.0210	-.0438	-.0096	-.0425	-.0113	-.0398	.0098	.0373	-.0086	.0362
200	0.4	β_1	-.0072	-.0525	-.0082	-.0247	-.0028	-.0176	-.0122	-.0337	-.0113	-.0329	.0049	-.0302	.0056	.0274	.0045	.0228
		β_2	.0088	.0528	.0136	.0226	.0034	.0174	.0115	.0356	-.0164	.0334	.0089	.0345	-.0099	.0274	-.0066	.0219
		β_3	-.0071	.0526	.0075	.0256	.0112	.0174	-.0146	.0354	.0120	.0323	-.0076	.0312	.0072	.0273	.0034	.0259
		β_4	.0094	-.0525	.0124	-.0272	.0132	.0178	-.0204	.0355	-.0095	.0329	-.0075	.0305	-.0043	.0276	-.0035	.0274
100	0.8	β_1	.0257	.0723	.0245	.0334	-.0070	.0109	.0347	.0335	.0202	.0366	.0112	.0378	.0082	.0336	.0065	.0325
		β_2	-.0179	-.0731	-.0122	.0328	-.0112	.0106	.0436	.0332	.0163	.0378	-.0109	.0344	-.0075	.0335	-.0034	.0323
		β_3	.0388	-.0729	-.0257	-.0335	.0214	-.0107	.0279	-.0326	.0197	-.0372	-.0179	-.0394	.0166	.0337	.0121	.0328
		β_4	-.0193	.0735	.0447	.0334	-.0122	.0108	-.0345	.0326	-.0168	.0354	.0184	.0404	-.0182	.0338	.0157	.0325
200	0.8	β_1	.0173	-.0497	.0149	.0194	.0057	.0089	.0144	.0248	-.0044	.0214	.0089	.0250	-.0124	.0202	.0056	.0199
		β_2	.0169	.0512	-.0146	.0196	-.0010	.0092	-.0167	.0242	.0036	.0215	-.0064	.0248	.0138	.0200	-.0049	.0199
		β_3	-.0364	.0499	.0145	.0190	.0058	.0090	.0135	.0232	.0042	.0215	-.0053	.0212	.0165	.0204	.0052	.0178
		β_4	.0289	-.0496	-.0139	.0182	-.0035	.0089	-.0222	.0238	-.0038	.0214	.0083	.0196	-.0148	.0200	-.0050	.0179

We next considered the situation where m_i might diverge for some subjects i . We randomly selected $n_0 = Cn^{3/8}$ subjects such that their observation points are $Bn^{1/8}m_i$ equally spaced on $[0, 1]$ and we let the remaining $n - n_0$ subjects to have m_i observations, where m_i was generated in the same way as described above. All the other model settings are identical to that in the previous simulation studies. For different values of B and C , we obtained the results given in Table 2. We notice that all the considered estimators improve with relatively smaller biases and smaller standard errors as compared with the respective bounded m_i case. The efficient estimator still performs much better than the independent estimator in all cases. We did not experiment with the QIF method by [18] as it is not tailored for the case of diverging m_i and becomes relatively unstable in this case.

4.2. Real data example. We now present an application of our method to the CD4 count data from the AIDS Clinical Trial Group 193A Study [11]. The data came from a randomized, double-blind study of AIDS patients with CD4 counts of ≤ 50 cells/mm³. The patients were randomized to one of four treatments with roughly equal group sizes; each consisted of a daily regimen of 600 mg of zidovudine. Treatment 1 is zidovudine alternating monthly with 400 mg didanosine; Treatment 2 is zidovudine plus 225 mg of zalcitabine; Treatment 3 is zidovudine plus 400 mg of didanosine; Treatment 4 is a triple therapy consisting of zidovudine plus 400 mg of didanosine plus 400 mg of nevirapine. Measurements of CD4 counts were scheduled to be collected at baseline and at eight week intervals during the 40 weeks of follow-up. However, the real observation times were unbalanced due to mistimed measurements, skipped visits and dropouts. The number of measurements of CD4 counts during the 40 weeks of follow-up varied from 1 to 9, with a median of 4. The response variable was taken as the log-transformed CD4 counts, $Y = \log(\text{CD4 counts} + 1)$. There was also gender and baseline age information about each patient. A total of 1309 patients were enrolled in the study. We eliminated the 122 patients who dropped out immediately after the baseline measurement.

We considered the following available covariates: treatments 2, 3 and 4 (coded by three indicator variables for treatment groups 2, 3 and 4, respectively), age (years), sex (coded as 1 for male and 0 for female), and interaction effects between these covariates. Using the group SCAD structure identification procedure of Cheng et al. (2014), we found that the coefficients for treatment 3, treatment 4 and the interaction between treatment 2 and sex are varying, and the coefficients given in Table 3 are constants. The group SCAD procedure also suggested that we remove all the other interac-

TABLE 2. Estimation results of 200 simulations. “Independent” corresponds to $\mathbf{V}_i = \mathbf{I}_{m_i}$; “Efficient” refers to using $\mathbf{V}_i = \hat{\Sigma}_i$; “Oracle” refers to using the true Σ_i as \mathbf{V}_i . \mathbf{B} adjusts the diverging m_i and \mathbf{C} controls the proportion of cases with diverging m_i .

n	ρ	$\mathbf{B} = 1.5, \mathbf{C} = 4$				$\mathbf{B} = 2, \mathbf{C} = 3$								
		Independent bias	Independent SE	Efficient bias	Efficient SE	Oracle bias	Oracle SE	Independent bias	Independent SE	Efficient bias	Efficient SE	Oracle bias	Oracle SE	
100	0.4	β_1	.0182	.0707	.0087	.0361	-.0017	.0204	.0105	.0710	.0039	.0315	-.0026	.0174
		β_2	-.0186	.0717	-.0172	.0329	-.0055	.0205	-.0180	.0715	-.0095	.0313	-.0046	.0174
		β_3	-.0236	.0702	.0041	.0336	-.0056	.0205	-.0122	.0730	-.0104	.0323	.0010	.0176
		β_4	.0100	.0702	-.0034	.0346	.0008	.0205	.0141	.0707	.0105	.0317	.0034	.0174
200	0.4	β_1	-.0130	.0517	-.0157	.0228	-.0037	.0153	-.0085	.0510	-.0060	.0223	-.0036	.0134
		β_2	.0146	.0516	.0177	.0227	.0028	.0151	-.0066	.0513	-.0062	.0225	-.0018	.0135
		β_3	-.0151	.0512	.0041	.0224	.0011	.0152	.0094	.0510	-.0015	.0225	-.0016	.0136
		β_4	-.0076	.0517	.0065	.0229	.0038	.0153	.0062	.0514	.0001	.0224	.0006	.0137
100	0.8	β_1	.0181	.0683	-.0175	.0213	.0028	.0102	-.0154	.0703	.0042	.0212	-.0040	.0087
		β_2	-.0111	.0682	-.0147	.0203	.0028	.0102	-.0152	.0690	.0028	.0215	.0001	.0087
		β_3	-.0030	.0674	-.0105	.0199	-.0015	.0100	.0129	.0677	.0044	.0208	-.0002	.0092
		β_4	.0260	.0675	.0125	.0208	.0028	.0101	-.0076	.0699	-.0032	.0215	.0008	.0088
200	0.8	β_1	-.0017	.0499	-.0024	.0132	.0014	.0076	-.0141	.0489	.0111	.0157	-.0001	.0067
		β_2	-.0005	.0496	.0006	.0129	-.0001	.0076	-.0136	.0490	-.0145	.0147	-.0003	.0069
		β_3	.0045	.0499	.0041	.0133	.0004	.0076	.0058	.0491	.0016	.0142	-.0001	.0069
		β_4	-.0052	.0496	-.0059	.0130	-.0009	.0075	.0071	.0483	.0041	.0150	-.0001	.0072

tion effects. The estimated varying intercept (i.e. effect of treatment 1) and the varying coefficients are displayed in Figure 1 along with 95% confidence intervals. The constant coefficient estimates and their estimated standard errors are provided in Table 3. To facilitate a comparison, we reported the results using the estimators assuming working independence and the efficient estimator proposed in this paper. Let $\boldsymbol{\theta} = (\boldsymbol{\beta}^T, \boldsymbol{\gamma}^T)^T$ and $\underline{\mathbf{U}}_i = (\underline{\mathbf{X}}_i, \underline{\mathbf{W}}_i)$. In practice, the variances for the efficient parameter estimates were obtained from the first p diagonal elements of the following matrix:

$$\left(\sum_{i=1}^n \underline{\mathbf{U}}_i^T \widehat{\boldsymbol{\Sigma}}_i^{-1} \underline{\mathbf{U}}_i \right)^{-1},$$

and for the working independence parameter estimates the variances were obtained from the first p diagonal elements of the following matrix:

$$\left(\sum_{i=1}^n \underline{\mathbf{U}}_i^T \underline{\mathbf{U}}_i \right)^{-1} \sum_{i=1}^n \underline{\mathbf{U}}_i^T \widehat{\boldsymbol{\Sigma}}_i \underline{\mathbf{U}}_i \left(\sum_{i=1}^n \underline{\mathbf{U}}_i^T \underline{\mathbf{U}}_i \right)^{-1}.$$

TABLE 3

Estimation results for CD4 count data. “Independent” corresponds to using $\mathbf{V}_i = \mathbf{I}_{m_i}$; “Efficient” refers to using $\mathbf{V}_i = \widehat{\boldsymbol{\Sigma}}_i$; “Quadratic” refers to the QIF based method.

Covariates	Independent		Efficient		Quadratic	
	Coefficients	SE	Coefficients	SE	Coefficients	SE
treatment 2	.3614	.2257	.4038	.2027	.3532	.1318
age	.0946	.0274	.0818	.0245	.0882	.0171
sex	.1704	.1768	.2246	.1587	.1187	.1034
treatment 3:sex	-.2922	.2472	-.2908	.2209	-.2625	.2485
treatment 4:sex	-.5321	.2416	-.5653	.2146	-.5580	.1574

Eyeballing the estimation results in Table 3, we note that the estimated constant coefficients for treatment 2, age, and the interaction between treatment 4 and sex are all quite significant. The constant coefficient estimates for sex are not significant but are still kept in the model since we include the interactions between treatments and sex. The efficient estimates for all the constant and varying coefficients have smaller standard errors than the respective estimates assuming working independence. In fact, the Wald test statistic for the coefficient of treatment 2 is $.3614/.2257 = 1.60 < 1.96$ under the working independence, failing to declare a significant difference. On the other hand, the Wald test statistic for the same coefficient is $.4038/.2027 = 1.99 > 1.96$ from the efficient estimation, leading to a significant treatment difference. Other than these, because the sample size in this study was rather

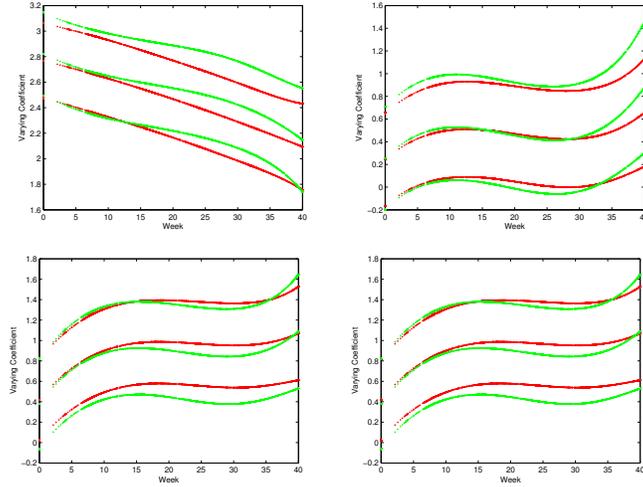


FIG 1. *Estimated varying-coefficients along with 95% confidence intervals for the intercept (upper left), treatment 3 (upper right), treatment 4 (lower left), and interaction between treatment 2 and sex (lower right). The red curves are efficient estimators while the green curves are estimators obtained under working independence.*

large, the two types of estimates for all the constant and varying coefficients appear to be very similar. For the sake of comparison, we also present the estimation results for these regression coefficients from the estimating equation methods based on the QIF method [18]. The conclusions on the estimation significance and effect direction remain the same as for the efficient estimation while the magnitude of the estimated coefficients slightly differs. For this particular dataset, sometimes the QIF estimator seems to have smaller standard error than the efficient estimator. An explanation is that it chooses a covariance structure like compound symmetry in the matrix basis, thus it will be more efficient than our estimator when this structure is plausible (which is possibly the case here). Otherwise, it is generally not as good when the covariance structure is mis-specified.

In general, the CD4 count tends to increase with age in the fitted model. Our estimation results suggest that there exist interaction effects between treatment and sex. Specifically, for the females ($\text{sex}=0$), subjects receiving treatments 2, 3 and 4 tend to have increasingly higher CD4 counts than those under treatment 1. The effect for treatment 2 (as compared with treatment 1) is estimated as a constant and is significant, while those for the other two treatment groups are varying (the upper right and the lower left panels in Figure 1) with even greater positive differences from treatment 1. For the

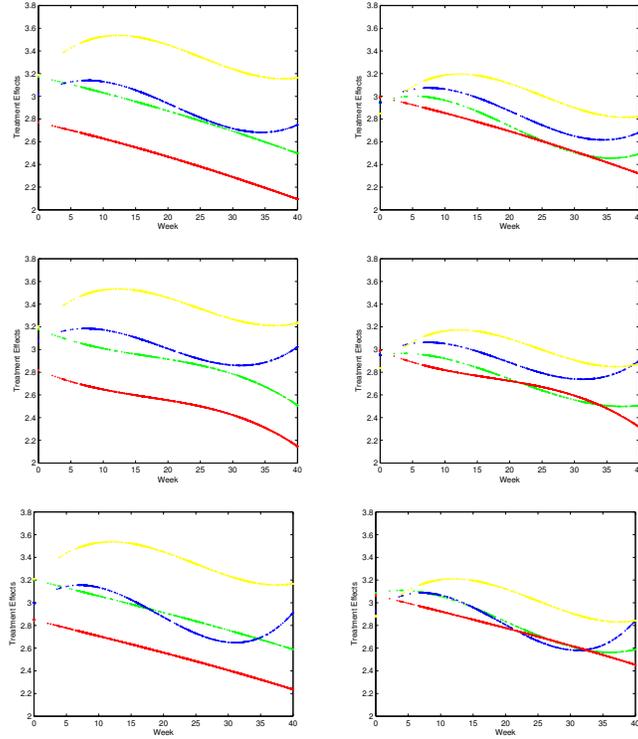


FIG 2. *Estimated treatment effects for the four treatment groups. The panels in the top, middle and bottom rows are respectively the proposed efficient estimates, the estimates assuming independence and the estimates based on the QIF method. The panels in the left and right columns are respectively for the females and the males. Red, green, blue and yellow curves are for treatment groups 1, 2, 3 and 4, respectively.*

males ($\text{sex}=1$), subjects receiving treatments 2, 3 and 4 also tend to have higher mean CD4 counts than those receiving treatment 1. The interaction between treatment 2 and sex is varying over time (the lower right panel in Figure 1) while those for treatments 3 and 4 are constant. The effects of treatments 3 and 4 are significantly different from that of treatment 1, judging from Table 3. Also, we notice that the differences between treatments seem to be greater between the females than between the males.

The estimated effects of the four treatment groups are plotted in Figure 2 for the efficient estimator, the working independence estimator and the QIF estimator. Note that treatment effects given by the efficient estimator rarely cross each other, giving nice interpretation and ordering of the different treatments, whereas this is not the case for those given by the QIF

or the working independence estimator. Previous authors identified a similar pattern on the order of magnitude of the time-varying treatment effects [14]. However, they ignored the interactions between the treatments and sex. Our findings suggest the treatment effect curves might be rather different between the males and the females.

5. Proofs of the main results.

5.1. *Additional assumptions and definitions.* In this paper, we denote the Euclidean norm of a vector a by $|a|$. Let $\lambda_{\min}(A)$ and $\lambda_{\max}(A)$ stand for the minimum and maximum eigenvalues of a symmetric matrix A , respectively. Besides, C, C_1, C_2, \dots are generic positive constants and the values may vary from line to line.

We denote the density function of T_{ij} , $i = 1, \dots, n$ and $j = 1, \dots, m_i$, by $f_{ij}(t)$ and the joint density function of T_{ij} and $T_{ij'}$ ($j \neq j'$) by $f_{ijj'}(s, t)$. In Assumptions A1 and A2, we consider sparse and irregular observation times. Note that we carry out two-dimensional smoothing in step 5 and there are three bandwidths involved in our method. Therefore we impose these restrictive assumptions to avoid complicated assumptions involving m_i, m_{\max} , and the bandwidths simultaneously. Roughly speaking, these assumptions imply we should have $\sum_{i=1}^n m_i^5 = O(n)$.

Assumption A1. For some positive constant C_{A1} , we have

$$m_{\max} \equiv \max_{1 \leq i \leq n} m_i = O(n^{1/8}) \quad \text{and} \quad \sum_{i=1}^n m_i < C_{A1}n.$$

Assumption A2. The joint density functions $f_{ij}(t)$ and $f_{ijj'}(s, t)$ are uniformly bounded and we have for some positive constant C_{A2} ,

$$\begin{aligned} \frac{1}{C_{A2}} &< \frac{1}{n} \sum_{i=1}^n \frac{1}{m_i} \sum_{j=1}^{m_i} f_{ij}(t) \leq \frac{1}{n} \sum_{i=1}^n m_i^4 \sum_{j=1}^{m_i} f_{ij}(t) < C_{A2} \text{ on } [0, 1], \quad \text{and} \\ \frac{1}{C_{A2}} &< \frac{1}{n} \sum_{i=1}^n \sum_{j \neq j'} f_{ijj'}(s, t) \leq \frac{1}{n} \sum_{i=1}^n m_i^3 \sum_{j \neq j'} f_{ijj'}(s, t) < C_{A2} \text{ on } [0, 1]^2. \end{aligned}$$

Assumption A3. For some positive constants C_{A3} and C_{A4} , we have uniformly in i and j ,

$$C_{A3} \mathbf{I}_{p+q} \leq \mathbb{E} \left\{ \begin{pmatrix} \mathbf{X}_{ij} \mathbf{X}_{ij}^T & \mathbf{X}_{ij} \mathbf{Z}_{ij}^T \\ \mathbf{Z}_{ij} \mathbf{X}_{ij}^T & \mathbf{Z}_{ij} \mathbf{Z}_{ij}^T \end{pmatrix} \middle| T_{ij} \right\} \leq C_{A4} \mathbf{I}_{p+q}.$$

Assumption A4. For some positive constants C_{A5} and C_{A6} , we have uniformly in i ,

$$C_{A5} \leq \lambda_{\min}(\boldsymbol{\Sigma}_i) \leq \lambda_{\max}(\boldsymbol{\Sigma}_i) \leq C_{A6}m_i.$$

Assumption A5. For some positive constants C_{A7} and C_{A8} , we have uniformly in i ,

$$C_{A7} \leq \lambda_{\min}(\mathbf{V}_i) \leq \lambda_{\max}(\mathbf{V}_i) \leq C_{A8}m_i.$$

Assumption A6. For some positive constants C_{A9} and C_{A10} , we have uniformly in i and j ,

$$\mathbb{E}\{\exp(C_{A9}|\epsilon_{ij}|) \mid \underline{\mathbf{X}}_i, \underline{\mathbf{Z}}_i, \underline{\mathbf{T}}_i\} < C_{A10}.$$

Assumption A3 is a standard one and is necessary for identification of the constant coefficients and the varying coefficient functions. When $\underline{\epsilon}_i$ consists of some stochastic process and i.i.d. errors, we have

$$\mathbb{E}\{\underline{\epsilon}_i \underline{\epsilon}_i^T \mid \underline{\mathbf{T}}_i\} = \Xi(\underline{\mathbf{T}}_i) + \eta^2 \mathbf{I}_{m_i},$$

where $\Xi(\underline{\mathbf{T}}_i)$ is positive definite. Hence we impose Assumptions A4 and A5 on \mathbf{V}_i and $\boldsymbol{\Sigma}_i$, respectively. In [4], it is assumed that $\underline{\epsilon}_i$ has the sub-Gaussian property in order to deal with general link functions. The sub-Gaussian assumption prevents m_i from tending to infinity. Assumption A6, which is less restrictive, is enough for the considered identity link function since we do not need to employ any results from the empirical process theory in this case.

For $\mathbf{g} = (g_1, \dots, g_q)^T \in \mathbf{G}$, we define the sup and L_2 norms by

$$\|\mathbf{g}\|_{G,\infty} = \sum_{j=1}^q \sup_{t \in [0,1]} |g_j(t)| \quad \text{and} \quad \|\mathbf{g}\|_{G,2}^2 = \sum_{j=1}^q \int_0^1 g_j^2(t) dt.$$

Assumptions A2 and A3 imply there are positive constants C_1 and C_2 such that

$$(5.1) \quad C_1 \|\mathbf{g}\|_{G,2} \leq \|\mathbf{Z}^T \mathbf{g}\|^V \leq C_2 \|\mathbf{g}\|_{G,2}$$

for any $\mathbf{g} \in \mathbf{G}$. The details are given in Lemma 1. In (2.3), we define two kinds of projections of X_k . We also define another one here by

$$(5.2) \quad \widehat{\varphi}_{\mathbf{V}k} = \widehat{\Pi}_{\mathbf{V}n} X_k,$$

where $\widehat{\Pi}_{\mathbf{V}n} X_k = \operatorname{argmin}_{\mathbf{g} \in \mathbf{G}_B} \|X_k - \mathbf{Z}^T \mathbf{g}\|_n^V$.

5.2. *Spline approximation and projections.* Now we consider the approximation error by spline functions. Recall that we assume all the relevant functions are at least twice continuously differentiable and that they and their second order derivatives are uniformly bounded. Hence the sup norm of approximation errors by spline functions is bounded from above by $C_{approx}K_n^{-2}$, where C_{approx} depends on the relevant functions. See Corollary 6.26 of [19].

In the following we establish the existence and properties of the projections $\varphi_{\mathbf{V}k}^*$, $k = 1, \dots, p$. Note that $\langle \cdot, \cdot \rangle^V$ and $\| \cdot \| ^V$ are defined on $\{v \mid \sum_{i,j} E(v_{ij}^2) < \infty\}$ and that $\{\mathbf{Z}^T \mathbf{g}\}$ is a closed linear subspace due to (5.1). Therefore the projections $\varphi_{\mathbf{V}k}^* = (\varphi_{\mathbf{V}k1}^*, \dots, \varphi_{\mathbf{V}kq}^*)^T$, $k = 1, \dots, p$, exist uniquely. Next, we set

$$(5.3) \quad \mathbf{V}_i^{-1} = (v_i^{j_1 j_2}).$$

Note that $\varphi_{\mathbf{V}k}^* = \Pi_{\mathbf{V}} X_k$ defined in (2.3) satisfies

$$\langle X_k - \mathbf{Z}^T \Pi_{\mathbf{V}} X_k, \mathbf{Z}^T \mathbf{g} \rangle^V = 0 \quad \forall \mathbf{g} \in \mathbf{G}.$$

By representing the above equality explicitly, we can derive the following integral equations for $\varphi_{\mathbf{V}k}^*(t)$. For $d_1 = 1, \dots, q$,

$$(5.4) \quad \sum_{d_2=1}^q a_{d_2}^{(d_1)}(t) \varphi_{\mathbf{V}k d_2}^*(t) = b^{(d_1)}(t) + \int_0^1 \sum_{d_2=1}^q c_{d_2}^{(d_1)}(s, t) \varphi_{\mathbf{V}k d_2}^*(s) ds,$$

where

$$\begin{aligned} a_{d_2}^{(d_1)}(t) &= \frac{1}{n} \sum_{i=1}^n \sum_{j=1}^{m_i} E\{Z_{ij d_2} v_i^{j j} Z_{ij d_1} \mid T_{ij} = t\} f_{ij}(t), \\ b^{(d_1)}(t) &= \frac{1}{n} \sum_{i=1}^n \sum_{1 \leq j_1, j_2 \leq m_i} E\{X_{ij_1 k} v_i^{j_1 j_2} Z_{ij_2 d_1} \mid T_{ij_2} = t\} f_{ij_2}(t), \\ c_{d_2}^{(d_1)}(s, t) &= -\frac{1}{n} \sum_{i=1}^n \sum_{j_1 \neq j_2} E\{Z_{ij_1 d_2} v_i^{j_1 j_2} Z_{ij_2 d_1} \mid T_{ij_1} = s, T_{ij_2} = t\} f_{ij_1 j_2}(s, t). \end{aligned}$$

Let $\mathbf{A}(t)$ be the $q \times q$ matrix whose (d_1, d_2) th element is $a_{d_2}^{(d_1)}(t)$. Assumptions A2 and A3 imply that $|\mathbf{A}(t)| \neq 0$ on $[0, 1]$ and we set

$$\psi_{\mathbf{V}k d_1}^*(t) = \sum_{d_2=1}^q a_{d_2}^{(d_1)}(t) \varphi_{\mathbf{V}k d_2}^*(t).$$

Then (5.4) reduces to (S.2) of [3] and the same argument there applies. Therefore $\varphi_{\mathbf{V}k}^*(t)$ has the required smoothness properties under similar regularity conditions.

5.3. *Remarks on the proofs of Propositions 1–3.* We can proceed as in [13] (and [3]) by replacing Z_{ij} , \underline{Z}_i , and $\varphi_k^*(t)$ in [13] (and \mathbf{Z}_{ij} , \mathbf{Z}_i , and $\varphi_k^*(\mathbf{t})$ in [3]) with \mathbf{W}_{ij} , $\underline{\mathbf{W}}_i$, and $\mathbf{Z}^T \varphi_{\mathbf{V}_k}^*(t)$, respectively. They used several lemmas to prove their results. We reorganize the corresponding lemmas in our setup into Lemma 1 given in the following. Its proof and outlines of the proofs of Propositions 1–3 are given in the supplement [5].

LEMMA 1. *Assume that Assumptions A1–5 hold.*

(i) *There are positive constants C_1 and C_2 such that*

$$C_1 \|\mathbf{g}\|_{G,2} \leq \|\mathbf{Z}^T \mathbf{g}\|^V \leq C_2 \|\mathbf{g}\|_{G,2}$$

for any $\mathbf{g} \in \mathbf{G}$.

(ii) *There are positive constants C_3 and C_4 such that*

$$\|\mathbf{g}\|_{G,\infty}^2 \leq C_3 K_n \|\mathbf{g}\|_{G,2}^2 \leq C_4 K_n (\|\mathbf{Z}^T \mathbf{g}\|^V)^2$$

for any $\mathbf{g} \in \mathbf{G}_B$.

(iii) *There is a positive constant C_5 such that for any $\boldsymbol{\beta} \in \mathbb{R}^p$ and $\mathbf{g} \in \mathbf{G}_B$,*

$$\|\mathbf{X}^T \boldsymbol{\beta} + \mathbf{Z}^T \mathbf{g}\|_\infty \leq C_5 K_n^{1/2} \|\mathbf{X}^T \boldsymbol{\beta} + \mathbf{Z}^T \mathbf{g}\|^V,$$

where $\|v\|_\infty = \max_{i,j} |v_{ij}|$. Besides, for some positive constant C_6 ,

$$\|v\|^V \leq C_6 \|v\|_\infty.$$

(iv)

$$\sup_{\mathbf{g}_1, \mathbf{g}_2 \in \mathbf{G}_B} \left| \frac{\langle \mathbf{Z}^T \mathbf{g}_1, \mathbf{Z}^T \mathbf{g}_2 \rangle_n^V - \langle \mathbf{Z}^T \mathbf{g}_1, \mathbf{Z}^T \mathbf{g}_2 \rangle^V}{\|\mathbf{Z}^T \mathbf{g}_1\|^V \|\mathbf{Z}^T \mathbf{g}_2\|^V} \right| = O_p(K_n \sqrt{\log n/n}).$$

(v) *For any positive constant M , we have*

$$\langle X_j - \mathbf{Z}^T \mathbf{g}_j, X_k - \mathbf{Z}^T \mathbf{g}_k \rangle_n^V - \langle X_j - \mathbf{Z}^T \mathbf{g}_j, X_k - \mathbf{Z}^T \mathbf{g}_k \rangle^V = o_p(1)$$

uniformly in $\mathbf{g}_j \in \mathbf{G}_B$ and $\mathbf{g}_k \in \mathbf{G}_B$ satisfying $\|\mathbf{g}_j\|_{G,2} \leq M$ and $\|\mathbf{g}_k\|_{G,2} \leq M$.

(vi) *For any process δ_n taking scalar values at T_{ij} satisfying that $\|\delta_n\|_\infty$ is uniformly bounded in n and $\{\delta_{n,ij}\}_{j=1}^{m_i}$ are mutually independent in i ,*

$$\sup_{\mathbf{g} \in \mathbf{G}_B} \left| \frac{\langle \delta_n, \mathbf{Z}^T \mathbf{g} \rangle_n^V - \langle \delta_n, \mathbf{Z}^T \mathbf{g} \rangle^V}{\|\mathbf{Z}^T \mathbf{g}\|^V} \right| = O_p(\sqrt{K_n/n}) \|\delta_n\|_\infty.$$

(vii) *We also suppose Assumption S holds. Then we have for $k = 1, \dots, p$,*
 $\|\widehat{\boldsymbol{\varphi}}_{\mathbf{V}_k}\|_\infty = O_p(1),$

$$\|\mathbf{Z}^T (\boldsymbol{\varphi}_{\mathbf{V}_k}^* - \widehat{\boldsymbol{\varphi}}_{\mathbf{V}_k})\|_n^V = o_p(1), \quad \text{and} \quad \|\mathbf{Z}^T (\boldsymbol{\varphi}_{\mathbf{V}_k}^* - \widehat{\boldsymbol{\varphi}}_{\mathbf{V}_k})\|^V = o_p(1).$$

5.4. *Proof of Theorem 1.* Since we consider the identity link function, we have explicit expressions of $\widehat{\boldsymbol{\beta}}_{\boldsymbol{\Sigma}} - \boldsymbol{\beta}_0$ and $\widehat{\boldsymbol{\beta}}_{\widehat{\boldsymbol{\Sigma}}} - \boldsymbol{\beta}_0$:

$$(5.5) \quad \begin{aligned} \widehat{\boldsymbol{\beta}}_{\boldsymbol{\Sigma}} - \boldsymbol{\beta}_0 &= \mathbf{H}^{11} \sum_{i=1}^n (\mathbf{X}_i - \mathbf{W}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21})^T \boldsymbol{\Sigma}_i^{-1} \boldsymbol{\varepsilon}_i \\ &\quad - \mathbf{H}^{11} \sum_{i=1}^n (\mathbf{X}_i - \mathbf{W}_i \mathbf{H}_{22}^{-1} \mathbf{H}_{21})^T \boldsymbol{\Sigma}_i^{-1} (\mathbf{W}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \\ &= I_1 - I_2 \quad (\text{say}) \end{aligned}$$

and

$$(5.6) \quad \begin{aligned} \widehat{\boldsymbol{\beta}}_{\widehat{\boldsymbol{\Sigma}}} - \boldsymbol{\beta}_0 &= \widehat{\mathbf{H}}^{11} \sum_{i=1}^n (\mathbf{X}_i - \mathbf{W}_i \widehat{\mathbf{H}}_{22}^{-1} \widehat{\mathbf{H}}_{21})^T \widehat{\boldsymbol{\Sigma}}_i^{-1} \boldsymbol{\varepsilon}_i \\ &\quad - \widehat{\mathbf{H}}^{11} \sum_{i=1}^n (\mathbf{X}_i - \mathbf{W}_i \widehat{\mathbf{H}}_{22}^{-1} \widehat{\mathbf{H}}_{21})^T \widehat{\boldsymbol{\Sigma}}_i^{-1} (\mathbf{W}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \\ &= \widehat{I}_1 - \widehat{I}_2 \quad (\text{say}), \end{aligned}$$

where $\widehat{\mathbf{H}}^{11}$, $\widehat{\mathbf{H}}_{22}$ and $\widehat{\mathbf{H}}_{21}$ are defined as in (2.4) with $\mathbf{V}_i = \widehat{\boldsymbol{\Sigma}}_i$, $i = 1, \dots, n$, and $\boldsymbol{\gamma}^* = (\boldsymbol{\gamma}_1^{*T}, \dots, \boldsymbol{\gamma}_q^{*T})^T$ satisfies $|\mathbf{B}^T(t) \boldsymbol{\gamma}_j^* - g_{0j}(t)| \leq C_g K_n^{-2}$, $j = 1, \dots, q$, for some positive constant C_g that depends on $\mathbf{g}_0(t)$. Proposition 4 and Assumption A4 imply that with probability tending to 1, we have

$$C_1 \mathbf{I}_{m_i} \leq \widehat{\boldsymbol{\Sigma}}_i \leq C_2 m_i \mathbf{I}_{m_i}$$

uniformly in i for some positive constants C_1 and C_2 . As for $\widehat{\boldsymbol{\Sigma}}_i^{-1}$, we have

$$\begin{aligned} \widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1} &= \widehat{\boldsymbol{\Sigma}}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} \\ &= \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} + \widehat{\boldsymbol{\Sigma}}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1}. \end{aligned}$$

It follows from Proposition 4, Assumption A4, and the above identity that

$$(5.7) \quad \widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1} = \boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1} + m_i^2 O_p \left(h_2^4 + h_3^4 + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2} \right).$$

The last term in the right-hand side of (5.7) is in the sense of eigenvalue evaluation. By using Assumption A4 and Proposition 4, we get an expression of each element of $\boldsymbol{\Sigma}_i^{-1} (\boldsymbol{\Sigma}_i - \widehat{\boldsymbol{\Sigma}}_i) \boldsymbol{\Sigma}_i^{-1}$. This expression, along with the assumptions for Theorem 1 and the local property of the B-spline basis, will be employed in the proofs of the following lemmas. These lemmas, assuming the same assumptions, are needed in order to evaluate $\widehat{I}_1 - I_1$ and their proofs are given in the supplementary material [5].

LEMMA 2. Let $h_{12,kl}$ and $\widehat{h}_{12,kl}$ be the (k, l) element of \mathbf{H}_{12} and $\widehat{\mathbf{H}}_{12}$, respectively. Then we have uniformly in k and l ,

$$\begin{aligned} \frac{1}{n}h_{12,kl} &= O_p(K_n^{-1}), \\ \frac{1}{n}(h_{12,kl} - \widehat{h}_{12,kl}) &= K_n^{-1}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right), \\ \left\{ \sum_{l=1}^{qK_n} (n^{-1}h_{12,kl})^2 \right\}^{1/2} &= O_p(K_n^{-1/2}), \\ \left[\sum_{l=1}^{qK_n} \{n^{-1}(h_{12,kl} - \widehat{h}_{12,kl})\}^2 \right]^{1/2} &= K_n^{-1/2}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right). \end{aligned}$$

LEMMA 3. With probability tending to 1, we have

$$C_1K_n^{-1} \leq \lambda_{\min}(n^{-1}\mathbf{H}_{22}) \leq \lambda_{\max}(n^{-1}\mathbf{H}_{22}) \leq C_2K_n^{-1}$$

for some positive constants C_1 and C_2 . We also have

$$\begin{aligned} &\max \{ |\lambda_{\min}(n^{-1}(\widehat{\mathbf{H}}_{22} - \mathbf{H}_{22}))|, |\lambda_{\max}(n^{-1}(\widehat{\mathbf{H}}_{22} - \mathbf{H}_{22}))| \} \\ &= K_n^{-1}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right). \end{aligned}$$

Then we have

$$\max \{ |\lambda_{\min}(n^{-1}\widehat{\mathbf{H}}_{22})|, |\lambda_{\max}(n^{-1}\widehat{\mathbf{H}}_{22})| \} = O_p(K_n^{-1})$$

and $\max \{ |\lambda_{\min}((n^{-1}\widehat{\mathbf{H}}_{22})^{-1} - (n^{-1}\mathbf{H}_{22})^{-1})|, |\lambda_{\max}((n^{-1}\widehat{\mathbf{H}}_{22})^{-1} - (n^{-1}\mathbf{H}_{22})^{-1})| \}$ is also bounded from above by $K_nO_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right)$.

LEMMA 4.

$$\begin{aligned} \frac{1}{n}\widehat{\mathbf{H}}_{11} &= \frac{1}{n}\mathbf{H}_{11} + o_p(1) \\ \frac{1}{n}\widehat{\mathbf{H}}_{12}\left(\frac{1}{n}\widehat{\mathbf{H}}_{22}\right)^{-1}\frac{1}{n}\widehat{\mathbf{H}}_{21} &= \frac{1}{n}\mathbf{H}_{12}\left(\frac{1}{n}\mathbf{H}_{22}\right)^{-1}\frac{1}{n}\mathbf{H}_{21} + o_p(1), \end{aligned}$$

where $o_p(1)$ means both componentwise and in the meaning of eigenvalue evaluation. Hence we have

$$n\widehat{\mathbf{H}}^{11} = n\mathbf{H}^{11} + o_p(1).$$

LEMMA 5. *We have for some positive constants C_1 and C_2 ,*

$$\frac{C_1}{K_n} \mathbf{I}_{qK_n} \leq \text{cov} \left(\frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T \boldsymbol{\Sigma}_i^{-1} \boldsymbol{\epsilon}_i \right) \leq \frac{C_2}{K_n} \mathbf{I}_{qK_n}.$$

In addition we have

$$\begin{aligned} & \left| \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{W}_i^T (\widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1}) \boldsymbol{\epsilon}_i \right| \\ &= \sqrt{\frac{n}{K_n}} O_p \left(\frac{\log n}{nh_1} + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2} \right) + \sqrt{\frac{n}{K_n}} O_p (h_1^3 + h_2^3 + h_3^3) \\ & \quad + O_p (h_2^2 + h_3^2) + O_p \left(\frac{1}{\sqrt{nh_2}} + \frac{1}{\sqrt{nh_3^2}} + \frac{1}{\sqrt{nK_n h_2}} + \frac{1}{\sqrt{nK_n h_3^2}} \right). \end{aligned}$$

LEMMA 6. *We have for some positive constants C_1 and C_2 ,*

$$C_1 \mathbf{I}_p \leq \text{cov} \left(\frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{X}_i^T \boldsymbol{\Sigma}_i^{-1} \boldsymbol{\epsilon}_i \right) \leq C_2 \mathbf{I}_p.$$

In addition we have

$$\begin{aligned} & \left| \frac{1}{\sqrt{n}} \sum_{i=1}^n \mathbf{X}_i^T (\widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1}) \boldsymbol{\epsilon}_i \right| \\ &= \sqrt{n} O_p \left(\frac{\log n}{nh_1} + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2} \right) + \sqrt{n} O_p (h_1^3 + h_2^3 + h_3^3) \\ & \quad + O_p (h_2^2 + h_3^2) + O_p \left(\frac{1}{\sqrt{nh_2}} + \frac{1}{\sqrt{nh_3^2}} \right). \end{aligned}$$

Now we prove that $\widehat{I}_1 - I_1 = o_p(n^{-1/2})$. Write

$$I_1 = \mathbf{H}^{11} \sum_{i=1}^n \mathbf{X}_i^T \boldsymbol{\Sigma}_i^{-1} \boldsymbol{\epsilon}_i - \mathbf{H}^{11} \mathbf{H}_{12} \mathbf{H}_{22}^{-1} \sum_{i=1}^n \mathbf{W}_i^T \boldsymbol{\Sigma}_i^{-1} \boldsymbol{\epsilon}_i = \mathbf{H}^{11} (I_{11} - I_{12}) \text{ (say)}.$$

We define \widehat{I}_{11} and \widehat{I}_{12} similarly. From Proposition 1 and Lemma 4, we have only to prove

$$(5.8) \quad \frac{1}{\sqrt{n}} (\widehat{I}_{11} - I_{11}) = o_p(1) \quad \text{and} \quad \frac{1}{\sqrt{n}} (\widehat{I}_{12} - I_{12}) = o_p(1).$$

The former result in (5.8) can be handled in the same way as the latter and we consider only the latter. Write

$$\begin{aligned}
\frac{1}{\sqrt{n}}(\widehat{I}_{12} - I_{12}) &= \frac{1}{n}\widehat{\mathbf{H}}_{12}\left(\frac{1}{n}\widehat{\mathbf{H}}_{22}\right)^{-1}\frac{1}{\sqrt{n}}\sum_{i=1}^n\mathbf{W}_i^T(\widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1})\boldsymbol{\epsilon}_i \\
&\quad + \frac{1}{n}\widehat{\mathbf{H}}_{12}\left\{\left(\frac{1}{n}\widehat{\mathbf{H}}_{22}\right)^{-1} - \left(\frac{1}{n}\mathbf{H}_{22}\right)^{-1}\right\}\frac{1}{\sqrt{n}}\sum_{i=1}^n\mathbf{W}_i^T\boldsymbol{\Sigma}_i^{-1}\boldsymbol{\epsilon}_i \\
&\quad + \left(\frac{1}{n}\widehat{\mathbf{H}}_{12} - \frac{1}{n}\mathbf{H}_{12}\right)\left(\frac{1}{n}\mathbf{H}_{22}\right)^{-1}\frac{1}{\sqrt{n}}\sum_{i=1}^n\mathbf{W}_i^T\boldsymbol{\Sigma}_i^{-1}\boldsymbol{\epsilon}_i \\
&= DI_{12}^{(1)} + DI_{12}^{(2)} + DI_{12}^{(3)} \quad (\text{say}).
\end{aligned}$$

Lemmas 2, 3, and 5 imply

$$\begin{aligned}
DI_{12}^{(1)} &= \sqrt{n}O_p\left(\frac{\log n}{nh_1} + \frac{\log n}{nh_2} + \frac{\log n}{nh_3^2}\right) + \sqrt{n}O_p(h_1^3 + h_2^3 + h_3^3) \\
&\quad + \sqrt{K_n}O_p\left(\frac{1}{\sqrt{nh_2}} + \frac{1}{\sqrt{nh_3^2}} + \frac{1}{\sqrt{nK_n}h_2} + \frac{1}{\sqrt{nK_n}h_3^2}\right) \\
&\quad + \sqrt{K_n}O_p(h_2^2 + h_3^2) = o_p(1), \\
DI_{12}^{(2)} &= \sqrt{K_n}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right) = o_p(1), \\
DI_{12}^{(3)} &= \sqrt{K_n}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right) = o_p(1).
\end{aligned}$$

Hence we have established

$$(5.9) \quad \widehat{I}_1 - I_1 = o_p(n^{-1/2}).$$

Next we deal with $\widehat{I}_2 - I_2$ and two more lemmas are necessary.

LEMMA 7. *We have*

$$\begin{aligned}
&\left|\frac{1}{\sqrt{n}}\sum_{i=1}^n\mathbf{W}_i^T\boldsymbol{\Sigma}_i^{-1}(\mathbf{W}_i\boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T\mathbf{g}_0)_i})\right| = O_p(\sqrt{n}K_n^{-5/2}) \quad \text{and} \\
&\left|\frac{1}{\sqrt{n}}\sum_{i=1}^n\mathbf{W}_i^T(\widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1})(\mathbf{W}_i\boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T\mathbf{g}_0)_i})\right| \\
&= \sqrt{n}K_n^{-5/2}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right).
\end{aligned}$$

LEMMA 8. *We have*

$$\begin{aligned} & \left| \frac{1}{\sqrt{n}} \sum_{i=1}^n \underline{\mathbf{X}}_i^T \underline{\boldsymbol{\Sigma}}_i^{-1} (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \right| = O_p(\sqrt{n} K_n^{-2}) \quad \text{and} \\ & \left| \frac{1}{\sqrt{n}} \sum_{i=1}^n \underline{\mathbf{X}}_i^T (\widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1}) (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \right| \\ & = \sqrt{n} K_n^{-2} O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right). \end{aligned}$$

Now we can show that $\widehat{I}_2 - I_2 = o_p(n^{-1/2})$. Write

$$\begin{aligned} I_2 &= \mathbf{H}^{11} \sum_{i=1}^n \underline{\mathbf{X}}_i^T \boldsymbol{\Sigma}_i^{-1} (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \\ &\quad - \mathbf{H}^{11} \mathbf{H}_{12} \mathbf{H}_{22}^{-1} \sum_{i=1}^n \underline{\mathbf{W}}_i^T \boldsymbol{\Sigma}_i^{-1} (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \\ &= \mathbf{H}^{11} (I_{21} - I_{22}) \quad (\text{say}). \end{aligned}$$

We define \widehat{I}_{21} and \widehat{I}_{22} similarly and write $\widehat{I}_2 = \widehat{\mathbf{H}}^{11} (\widehat{I}_{21} - \widehat{I}_{22})$. From Proposition 1 and Lemma 4, we have only to prove

$$\frac{1}{\sqrt{n}} (\widehat{I}_{21} - I_{21}) = o_p(1) \quad \text{and} \quad \frac{1}{\sqrt{n}} (\widehat{I}_{22} - I_{22}) = o_p(1).$$

The former result in the above can be handled in the same way as the latter and we consider only the latter. Write

$$\begin{aligned} & \frac{1}{\sqrt{n}} (\widehat{I}_{22} - I_{22}) \\ &= \frac{1}{n} \widehat{\mathbf{H}}_{12} \left(\frac{1}{n} \widehat{\mathbf{H}}_{22} \right)^{-1} \frac{1}{\sqrt{n}} \sum_{i=1}^n \underline{\mathbf{W}}_i^T (\widehat{\boldsymbol{\Sigma}}_i^{-1} - \boldsymbol{\Sigma}_i^{-1}) (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \\ &\quad + \frac{1}{n} \widehat{\mathbf{H}}_{12} \left\{ \left(\frac{1}{n} \widehat{\mathbf{H}}_{22} \right)^{-1} - \left(\frac{1}{n} \mathbf{H}_{22} \right)^{-1} \right\} \frac{1}{\sqrt{n}} \sum_{i=1}^n \underline{\mathbf{W}}_i^T \boldsymbol{\Sigma}_i^{-1} (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}) \\ &\quad + \left(\frac{1}{n} \widehat{\mathbf{H}}_{12} - \frac{1}{n} \mathbf{H}_{12} \right) \left(\frac{1}{n} \mathbf{H}_{22} \right)^{-1} \frac{1}{\sqrt{n}} \sum_{i=1}^n \underline{\mathbf{W}}_i^T \boldsymbol{\Sigma}_i^{-1} (\underline{\mathbf{W}}_i \boldsymbol{\gamma}^* - \underline{(\mathbf{Z}^T \mathbf{g}_0)_i}). \\ &= DI_{22}^{(1)} + DI_{22}^{(2)} + DI_{22}^{(3)} \quad (\text{say}) \end{aligned}$$

Lemmas 2, 3, and 7 imply

$$DI_{22}^{(j)} = \sqrt{n}K_n^{-2}O_p\left(h_2^2 + h_3^2 + \sqrt{\frac{\log n}{nh_2}} + \sqrt{\frac{\log n}{nh_3^2}}\right) = o_p(1), \quad j = 1, 2, 3.$$

Hence we have established

$$\widehat{I}_2 - I_2 = o_p(n^{-1/2}).$$

The desired result follows from (5.5), (5.6), (5.9) and the above result.

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SUPPLEMENTARY MATERIAL

Supplement A: Some technical material

(doi: xx.xxxx/xx-AOSxxxxSUPP). Proofs of the propositions and lemmas, and results for the case of uniformly bounded m_i and general link function.

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