





THE ANALYSIS OF A RANDOMIZED COMPLETE BLOCK DESIGN WHEN OBSERVATIONS ARE SUBJECT TO ARBITRARY RICHT CENSORSHIP

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Based on arbitrarily right censored observations, asymptotically distribution free tests are proposed for testing the equivalence of K treatments in the analysis of a randomized complete block design with random block effect. Multiple comparisons procedures which incorporate a pairwise ranking scheme are also proposed for determining which, if any, treatments differ from each other.



Key words and phrases: Asymptotically distribution free test; Multiple comparisons procedure; Friedman test; Ordered alternative; Gehan statistic. AIR FORCE OFFICE OF SCIENTIFIC RESEARCH (AFSC) NOTICE OF TRANCMUTTAL TO DDC This test for a start how been reviewed and is Distribution are the control of 1990 14% AFR 190-12 (7b). A. D. BLCSA Technical Information Officer

1. INTRODUCTION

Let $(x_{11}^0, \cdots, x_{K1}^0)', \cdots, (x_{1n}^0, \cdots, x_{Kn}^0)'$ be independent, identically distributed random vectors with a continuous joint distribution function G^0 and marginal distribution functions F_i^0 , $i = 1, \cdots, K$. The null hypothesis H_0 , which we wish to test, is that G^0 is symmetric in its K arguments, i.e. that

$$G^{0}(x_{i_{1}}^{0}, \cdots, x_{i_{K}}^{0}) = G^{0}(x_{1}^{0}, \cdots, x_{K}^{0})$$

for all permutations (i_1, \cdots, i_K) of $(1, \cdots, K)$. Note that H_0 implies that

$$F_1^0(x) = F_2^0(x) = \cdots = F_k^0(x)$$
, for all $x \in \mathbb{R}$.

Such a hypothesis testing problem arises when we test the equivalence of K treatments in the analysis of a randomized complete block design and assume that the blocks themselves are drawn at random from a population of blocks. There are several standard nonparametric tests for this case, for example, Friedman test and the aligned rank order test (Mehra & Sarangi (1967), and Sen (1968)). For an ordered alternative H₁:

$$F_1^0(x) \le F_2^0(x) \le \cdots \le F_K^0(x)$$
, for all $x \in R$,

where at least one of the inequalities is strict for some x, we have tests proposed by Doksum (1967) and Hollander (1967). If one is not only interested in a single global test of whether the K treatments are equivalent, then multiple comparisons procedures are more appropriate (cf Miller (1966, 1977)).

Now suppose that a clinical trial is conducted to compare K treatments, the parameter of interest is the length of survival. It is common that at the end of the trial, there may be incomplete survival information on certain individuals. More specifically, the response X_{ij}^{0} may be censored from right by an independent variable Z_{ij} so that the n K-tuples $(X_{ij}^{0}, \dots, X_{Kj}^{0})'$ cannot always be observed. Rather our observations consist of nK pairs $(X_{ij}, \Delta_{ij})'$, where $X_{ij} = \min(X_{ij}^{0}, Z_{ij})$ and $\Delta_{ij} = 1$, if X_{ij}^{0} is observed and zero otherwise. Furthermore, for mathematical convenience Z_{ij} is assumed to be governed by a continuous distribution function $J_i(\cdot)$, $i = 1, \dots, K$, $j = 1, \dots, n$.

In the parametric statistics, the procedure for testing H_0 based on observations $(X_{ij}, \Delta_{ij})'$ is complicated and no results have been obtained. Although a generalized Friedman test (Patel (1975)) is available for testing H_0 based on censored observations, it is rather inefficient when there are too many censored K-tuples in the data. As an extreme example, for the data $(12^+, 9^+, 13)', (9, 8^+, 5^+)', (4, 3^+, 2^+)', (2, 1^+, 1^+)',$ where "+" denotes censoring, the generalized Friedman test which uses information only within blocks leads to no conclusion about H_0 .

In this article, we propose and analyze test procedure: which allow interblock comparisons for testing H_0 based on observations $(X_{ij}, \Delta_{ij})'$. A multiple comparisons procedure which selects treatments, if any, that differ from one another in terms of enhanced survival is also presented.

The corresponding K sample problems have been investigated by Breslow (1970), Crowley & Thomas (1975), and Koziol & Reid (1977).

2. DEFINITIONS AND A BASIC THEOREM

Let \overline{F}_i^e and \overline{F}_i be the empirical and the theoretical survival functions of X_{ij} . Also, let \widetilde{F}_i^e and \widetilde{F}_i be the empirical and the theoretical subdistribution functions of uncensored X_{ij} , i.e.

$$\widetilde{F}_{i}(s) = P(X_{ij} \le s, \Delta_{ij} = 1) \text{ and}$$

$$\widetilde{F}_{i}^{e}(s) = n^{-1} \sum_{j=1}^{n} I(X_{ij} \le s, \Delta_{ij} = 1)$$

where I(A) is the indicator function of the event A , $i = 1, \dots K$. Furthermore, the joint subdistribution functions of $(X_{ij}, X_{i'j})'$, $(X_{ij}, X_{i'j}, X_{kj}, X_{k'j})'$ and $(X_{1j}, \dots, X_{Kj})'$ are defined by $\tilde{\nu}_{ii'}(s, t; \delta, \epsilon) = P(X_{ij} \le s, X_{i'j} \le t, \Delta_{ij} = \delta, \Delta_{i'j} = \epsilon)$, $\tilde{H}_{ii'kk'}(s, t, s', t'; \delta, \epsilon, \delta', \epsilon') = P(X_{ij} \le s, X_{i'j} \le t, X_{kj} \le s', X_{k'j} \le t', \Delta_{ij} = \delta, \Delta_{i'j} = \epsilon, \Delta_{kj} = \delta', \Delta_{k'j} = \epsilon')$, and

$$\widetilde{G}(s_1, \cdots, s_K; \delta_1, \cdots, \delta_K) = P(X_{1j} \le s_1, \cdots, X_{Kj} \le s_K, \Delta_{1j} = \delta_1, \cdots, \Delta_{Kj} = \delta_K),$$

respectively,

where i, i', k, and k' denote distinct indices. The corresponding empirical subdistribution functions are defined by

$$\begin{split} \widetilde{D}_{1i}^{e}, (s,t;\delta,\varepsilon) &= n^{-1} \sum_{j=1}^{n} I(X_{1j} \le s, X_{1'j} \le t, \Delta_{1j} = \delta, \Delta_{1'j} = \varepsilon) , \\ \widetilde{H}_{1i'kk'}^{e}(s,t,s',t';\delta,\varepsilon,\delta',\varepsilon') &= \\ n^{-1} \sum_{j=1}^{n} I(X_{1j} \le s, X_{1'j} \le t, X_{kj} \le s', X_{k'j} \le t', \Delta_{1j} = \delta, \Delta_{1'j} = \varepsilon, \Delta_{kj} = \delta', \Delta_{k'j} = \varepsilon') \end{split}$$

$$\widetilde{G}^{e}(s_{1}, \cdots, s_{K}; \delta_{1}, \cdots, \delta_{K}) = n^{-1} \sum_{j=1}^{n} I(X_{1j} \leq s_{1}, \cdots, X_{Kj} \leq s_{K}, \Delta_{1j} = \delta_{1}, \cdots, \Delta_{Kj} = \delta_{K}).$$

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All the procedures proposed in this article are based on the Gehan scoring function ψ , where, for any two pairs of observations $(X_{ij}, \Delta_{ij})'$ and $(X_{i'j'}, \Delta_{i'j'})'$,

$$\psi(X_{ij}, \Delta_{ij}, X_{i'j}, \Delta_{i'j}) = \begin{cases} +1, & X_{ij} > X_{i'j}, & \Delta_{i'j} = 1 \\ -1, & X_{ij} < X_{i'j}, & \Delta_{ij} = 1 \\ 0, & \text{otherwise.} \end{cases}$$

Now, let $p_{ii'} = E\psi(X_{ik}, \Delta_{ik}, X_{i'k'}, \Delta_{i'k'})$, where $i \neq i'$ and $k \neq k'$. Under H_0 , $p_{ii'} = 0$ which is independent of censoring distributions J_i and J_i , (cf Efron (1967) and Mantel (1967)). Consider Gehan's statistic (1965) $V_{ii'in}$ for populations i and i':

$$v_{ii',n} = n^{-\frac{3}{2}} \sum_{j=1}^{n} \sum_{j'=1}^{n} \psi(x_{ij}, \Delta_{ij}, x_{i'j'}, \Delta_{i'j})$$

The following Theorem whose proof is in the Appendix provides the asymptotic distribution of random vectors $\langle V_{ii,n}^{\star} \rangle$, where $V_{ii,n}^{\star} = \frac{n^2 \Sigma}{n^2 \Sigma} \sum_{\substack{\Sigma \\ j=1}}^{n} (\psi(X_{ij}, \Delta_{ij}, X_{i'j'}, \Delta_{i'j'}) - p_{ii'})$, $i, i' = 1, \cdots, K$ and i < i'.

<u>Theorem 1</u>. As $n \neq \infty$, the random vector $\langle V_{ii',n}^* \rangle$ converges in distribution to a multivariate normal random vector with mean 0 and covariance matrix $\ddagger (\sigma_{ii',kk'})$, i < i', k < k'. Under H₀,

$$\sigma_{ii',kk'} = \sigma_{ii',kk'}^{0} =$$

and

$$\begin{split} & E\left(\widetilde{F}_{\mathbf{i}},(X_{\mathbf{i}\mathbf{j}})-\Delta_{\mathbf{i}\mathbf{j}}\widetilde{F}_{\mathbf{i}},(X_{\mathbf{i}\mathbf{j}})+\Delta_{\mathbf{i}},_{\mathbf{j}}\widetilde{F}_{\mathbf{i}}(X_{\mathbf{i}'\mathbf{j}})-\widetilde{F}_{\mathbf{i}}(X_{\mathbf{i}'\mathbf{j}})\right)\\ & \left(\widetilde{F}_{\mathbf{k}},(X_{\mathbf{k}\mathbf{j}})-\Delta_{\mathbf{k}\mathbf{j}}\widetilde{F}_{\mathbf{k}},(X_{\mathbf{k}\mathbf{j}})+\Delta_{\mathbf{k}'\mathbf{j}}\widetilde{F}_{\mathbf{k}}(X_{\mathbf{k}'\mathbf{j}})-\widetilde{F}_{\mathbf{k}}(X_{\mathbf{k}'\mathbf{j}})\right) \;. \end{split}$$

If the censoring variables Z_{1j}, \dots, Z_{Kj} are interchangeable (hereafter referred to as Condition A), then $J_1 = J_2 = \dots = J_K$ and, under H_0 , the random pairs $(X_{1j}, \Delta_{1j})', \dots, (X_{Kj}, \Delta_{Kj})'$ are also interchangeable, $j = 1, \dots, n$. For future references, let $\tilde{F} = \tilde{F}_1 = \dots = \tilde{F}_K$ and $\bar{F} = \bar{F}_1 = \dots = \bar{F}_K$ and also let

$$\sigma^{2} = E\left(\widetilde{F}(X_{ij}) - \Delta_{ij}\widetilde{F}(X_{ij})\right)^{2} \text{ and}$$
$$= E\left(\widetilde{F}(X_{ij}) - \Delta_{ij}\widetilde{F}(X_{ij})\right)\left(\widetilde{F}(X_{i'j}) - \Delta_{i'j}\widetilde{F}(X_{i'j})\right).$$

τ

3. MULTIPLE COMPARISONS UNDER H

When it is less important to test the overall hypothesis H_0 than to compare certain populations on an individual basis, a multiple comparisons procedure is more desirable than a single global test. The decision of which, if any, populations differ from one another can be made by examining the individual comparison $V_{ii',n}$. We would conclude that populations i and i' differ if $|V_{ii',n}|$ is sufficiently large. A conservative multiple comparisons procedure at level α can be obtained through an inequality due to Šidák (1967), i.e. if $U = (U_1, \dots, U_r)'$ is normally distributed with mean Q and correlation matrix R, then

$$P_{r}(\max_{1 \le i \le r} |U_{i}| \le u | \bigcup_{r} N_{r}(\bigcup_{r}, R)) \ge$$

$$P_{r}(\max_{1 \le i \le r} |U_{i}| \le u | \bigcup_{r} N_{r}(\bigcup_{r}, I_{r})).$$

It follows from Theorem 1 that, for large $\,n$, one would judge that populations i and i' as different at level α if

$$|v_{ii',n}|/(\hat{\sigma}_{ii',ii'}^{0})^{\frac{1}{2}} > \xi_{\beta/2}$$
,

where $\xi_{\beta/2}$ is the $100(1 - \beta/2)$ percentage point of the N(0,1) distribution, $(1-\beta)^{K(K-1)/2} = 1 - \alpha$, and $\hat{\sigma}_{ii',ii'}^{0}$ is a (strongly) consistent estimator of $\sigma_{ii',ii'}^{0}$:

$$\hat{\sigma}_{ii',ii'}^{0} = \sum_{\delta=0}^{1} \sum_{\epsilon=0}^{1} \int \left[\widetilde{F}_{i'}^{e}(s) - \delta \overline{F}_{i}^{e}(s) + \epsilon \overline{F}_{i}^{e}(t) - \widetilde{F}_{i}^{e}(t) \right]^{2} d\widetilde{D}_{ii'}^{e}(s,t;\delta,\epsilon) .$$

Another multiple comparisons procedure can be obtained through the Bonferroni inequality. But as indicated by Koziol and Reid (1977, p. 1154), this procedure is less powerful than the one based on Šidák inequality.

Some improvement of the above results can be made under Condition A (the interchangeability of Z_{1j}, \cdots, Z_{Kj}). It can be shown that, under H_0 and Condition A, the asymptotic covariance structure of $\langle \frac{V_{11',n}}{(\sigma^2-\tau)^{\frac{1}{2}}} \rangle$ is identical to that of the vector having K(K-1)/2 components $Y_1 - Y_{1'}$, $1 \le i < i' \le K$, where $Y = (Y_1, \cdots, Y_K)' \sim N_K(0, I_K)$, and I_K is the identity matrix. Therefore, one would conclude that populations i and i' differ at level α if

$$\frac{|v_{ii',n}|}{(\hat{\sigma}_{n}^{2}-\hat{\tau}_{n})^{\frac{1}{2}}} > q_{K}^{\alpha} ,$$

where q_{K}^{α} is the 100(1- α) percentage point of the distribution of the range of K independent unit normal random variables (cf. Pearson and Hartley (1966), Tables 22 and 23) and $\hat{\sigma}_{n}^{2}$ and $\hat{\tau}_{n}$ are (strongly) consistent estimators of σ^{2} and τ :

$$\hat{\upsilon}_{n}^{2} = \int (\tilde{F}^{e}(s) - \overline{F}^{e}(s))^{2} d\tilde{F}^{e}(s) - \int (\tilde{F}^{e}(s))^{2} d(\overline{F}^{e}(s) + \tilde{F}^{e}(s)) ,$$

$$\binom{K}{2} \hat{\tau}_{n} = \sum_{\delta,\epsilon=0}^{1} \sum_{i=1}^{K-1} \sum_{i'=i+1}^{K} \int (\tilde{F}^{e}(s) - \delta \overline{F}^{t}(s)) (\tilde{F}^{e}(t) - \epsilon \overline{F}^{e}(t)) d\tilde{D}_{ii'}^{e}(s,t;\delta,\epsilon) ,$$

$$\tilde{F}^{e}(s) = K^{-1} \sum_{i=1}^{K} \tilde{F}_{i}^{e}(s) \text{ and } \overline{F}^{e}(s) = K^{-1} \sum_{i=1}^{K} \overline{F}_{i}^{e}(s) .$$

4. TESTING H₀ AGAINST ORDERED ALTERNATIVE H₁

In this section, we present a test statistic S_n which is a generalization of the Jonckheere K-sample test (Jonckheere (1954), Patel & Hoel (1973)) for testing H_0 against H_1 based on observations $(X_{ij}, \Delta_{ij})'$, where

$$S_n = \sum_{i=1}^{K-1} \sum_{i'=i+1}^{K} V_{ii',n}$$

Large values of S_n suggest rejection of the null hypothesis H_0 . It follows from Theorem 1 that, under H_0 , S_n converges in distribution to a normal random variable with mean 0 and variance

$$\sum_{i=1}^{K-1} \sum_{i'=i+1}^{K} \sum_{k=1}^{K-1} \sum_{k'=k+1}^{K} \sigma_{ii',kk'}^{0}$$

Note that $\sigma_{11',kk'}^{0}$, where i, i', k and k' are distinct integers, can be estimated consistently by

$$\hat{\sigma}_{ii',kk'}^{0} = \sum_{\delta,\varepsilon,\delta',\varepsilon'=0}^{1} \int \left(\widetilde{F}_{i'}^{e}(s) - \delta \overline{F}_{i'}^{e}(s) + \varepsilon \overline{F}_{i}^{e}(t) - \widetilde{F}_{i}^{e}(t) \right)$$

$$\left(\widetilde{F}_{k'}^{e}(s') - \delta' \overline{F}_{k'}^{e}(s') + \varepsilon' \overline{F}_{k}^{e}(t') - \widetilde{F}_{k}^{e}(t') \right) d \widetilde{H}_{ii'kk'}^{e}(s,t,s',t';\delta,\varepsilon,\delta',\varepsilon') .$$

5. A GLOBAL TEST FOR HO

If we are interested in testing H_0 against a general alternative hypothesis that C^0 is not symmetric in its K arguments, then a global test is more appropriate. Unfortunately, it is not feasible to get such a test under unequal patterns of censorship operative on K populations. In this Section, we assume that the censoring variables Z_{1j}, \cdots, Z_{Kj} are interchangeable (Condition A) and present a generalized Breslow test (1970) for testing H_0 based on observations $(X_{ij}, \Delta_{ij})'$.

Define a vector score statistic $W_n = (W_{1n}, \cdots, W_{Kn})'$, where W_n is the total score comparing the ith sample with the remaining (K-1) samples, i.e.

$$W_{in} = \sum_{\substack{i'=1\\i'\neq i}}^{K} V_{ii',n} .$$

It follows from Theorem 1 that, under H_0 , W_n converges in distribution to a normal random vector with mean 0 and covariance matrix

$$\Gamma = \begin{pmatrix} \gamma^{2} & \eta & \cdots & \eta \\ \eta & \gamma^{2} & \cdots & \eta \\ \vdots & \ddots & \ddots & \vdots \\ \eta & \eta & \cdots & \gamma^{2} \end{pmatrix}_{K \times K},$$

where $\gamma^2 = E\phi^2$, $\eta = E\phi\phi'$,

$$\phi = (K-1)(\widetilde{F}(X_{1j}) - \Delta_{1j}\overline{F}(X_{1j})) + \sum_{m=2}^{K} \Delta_{mj}\overline{F}(X_{mj}) \quad \text{and}$$

$$\phi' = (K-1)(\widetilde{F}(X_{Kj}) - \Delta_{Kj}\overline{F}(X_{Kj})) + \sum_{\ell=1}^{K-1} \Delta_{\ell j}\overline{F}(X_{\ell j}) \quad .$$

Again, γ^2 and η can be estimated consistently, for example, by $\hat{\gamma}_n^2$ and $\hat{\eta}_n$, where

$$\hat{\gamma}_{n}^{2} = \sum_{\delta_{1}, \dots, \delta_{K}=0} \int \left[(K-1) \left(\widetilde{F}^{e}(s_{1}) - \delta_{1} \overline{F}^{e}(s_{1}) \right) + \sum_{m=2}^{K} \delta_{m} \overline{F}^{e}(s_{m}) \right]^{2} d\widetilde{G}^{e}(s_{1}, \dots, s_{K}; \delta_{1}, \dots, \delta_{K}),$$

and

$$\widehat{f}_{n} = \sum_{\delta_{1}, \cdots, \delta_{K} \neq 0} \int \left[(K-1) \left(\widetilde{F}^{e}(s_{1}) - \delta_{1} \widetilde{F}^{e}(s_{1}) \right) + \sum_{m=2}^{K} \delta_{m} \widetilde{F}^{e}(s_{m}) \right]$$

$$\left[(K-1) \left(\widetilde{F}^{e}(s_{K}) - \delta_{K} \widetilde{F}^{e}(s_{K}) + \sum_{\ell=1}^{K-1} \delta_{\ell} \widetilde{F}^{e}(s_{\ell}) \right] d\widetilde{G}^{e}(s_{1}, \cdots, s_{K}; \delta_{1}, \cdots, \delta_{K}) .$$

The latent roots of Γ are $(\gamma^2 + (K-1)\eta)$, which is zero, with the latent vector $\underline{q}_K = (1, \cdots, 1)'/K^{\frac{1}{2}}$ and $(\gamma^2 - \eta)$ of multiplicity (K-1) with (K-1) latent (any set of) vectors orthogonal to $(1, \cdots, 1)', \underline{q}_1, \cdots, \underline{q}_{K-1}$, say (cf Rao (1973), p. 67). For example, when K = 3, $\underline{q}_1 = (\frac{3}{2})^{\frac{1}{2}}(-\frac{1}{2}, 1, -\frac{1}{2})'$, $\underline{q}_2 = (\frac{1}{2})^{\frac{1}{2}}(\frac{1}{2}, -\frac{1}{2}, 0)'$, $\underline{q}_3 = (\frac{1}{3})^{\frac{1}{2}}(1, 1, 1)'$. In general, the \underline{q}_1 are perhaps most easily found by means of the Gram-Schmidt orthogonalization process. Since Γ is symmetric, therefore, $Q'\Gamma Q = \Lambda_{K \times K}$, where $Q = (\underline{q}_1, \cdots, \underline{q}_K)$ which is an orthogonal matrix, $\Lambda_{K \times K} = \text{diag}(\lambda, \cdots, \lambda, 0)$ and $\lambda = \gamma^2 - \eta$. It follows that, under H_0 ,

$$T_{n} = \hat{\lambda}_{n}^{-1} \sum_{i=1}^{K-1} (q'_{i} \tilde{w}_{n})^{2}$$

is asymptotically distributed in a chi-squared distribution with K-1 degrees

of freedom, where $\hat{\lambda}_n = \hat{\gamma}_n^2 - \hat{\eta}_n$. Large values of T_n suggest a rejection decision of H_0 .

For K = 2 and unequal patterns of censorship, an asymptotically distribution free test was studied by Wei (1979) for testing H_0 based on observations $(X_{ij}, \Delta_{ij})'$, i = 1, 2; $j = 1, \cdots, n$. This test is reduced to the above generalized Breslow test when the two censoring distributions J_1 and J_2 are equal.

6. REMARKS

In practice, all the consistent estimators in this article can be obtained through simple summation processes. Therefore, it is feasible to evaluate the test procedures by hand calculations and extremely easy if a small programmable calculator is available.

Although there are several multivariate parametric models available for life testing in reliability (cf Freund (1961), Marshall & Olkin (1967), and Block & Basu (1974)), none is satisfactory for survivability theory, especially for our current settings. For example, there is no <u>continuous</u> multivariate distribution function which has <u>exponential</u> marginals and possesses a physical interpretation in survival analysis. This probably makes nonparametric procedures more appealing in multivariate survival studies.

Also, for lack of appropriate parametric models, the efficiency study of our new test procedures seems unfeasible. However, since the new procedures allow interblock comparisons, we expect that they are more powerful than the procedures based on Friedman statistic.

7. APPENDIX

Proof of Theorem 1.

Let

$$\psi_{\mathbf{i}\mathbf{i}}^{0}(\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}) = E[\psi(\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}, \mathbf{X}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}, \boldsymbol{\Delta}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}) | \mathbf{X}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}, \boldsymbol{\Delta}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}, \mathbf{A}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}] - P_{\mathbf{i}\mathbf{i}^{\prime}} \text{ and}$$

$$\psi_{\mathbf{i}\mathbf{i}^{\prime}}^{1}(\mathbf{X}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}, \boldsymbol{\Delta}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}) = E[\psi(\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}, \mathbf{X}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}, \boldsymbol{\Delta}_{\mathbf{i}^{\prime}\mathbf{j}^{\prime}}, | \mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}] - P_{\mathbf{i}\mathbf{i}^{\prime}}, \text{ where } \mathbf{j} \neq \mathbf{j}^{\prime}.$$

Also, let

$$\mathbb{V}_{\mathtt{i}\mathtt{i}',\mathtt{n}}^{\star\star} = \mathfrak{n}^{-\frac{1}{2}} \Big(\sum_{\mathtt{j}=1}^{\mathtt{n}} (\psi_{\mathtt{i}\mathtt{i}}^{0}, (\mathtt{X}_{\mathtt{i}\mathtt{j}}, \mathtt{\Delta}_{\mathtt{i}\mathtt{j}}) + \psi_{\mathtt{i}\mathtt{i}}^{1}, (\mathtt{X}_{\mathtt{i}'\mathtt{j}}, \mathtt{\Delta}_{\mathtt{i}'\mathtt{j}})) \Big)$$

and

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$$g(\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}, \mathbf{X}_{\mathbf{i}'\mathbf{j}'}, \boldsymbol{\Delta}_{\mathbf{i}'\mathbf{j}'}) = \psi(\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}, \mathbf{X}_{\mathbf{i}'\mathbf{j}'}, \boldsymbol{\Delta}_{\mathbf{i}'\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}'} - \psi_{\mathbf{i}\mathbf{i}}^{0}, (\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}) - \psi_{\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}'\mathbf{j}'}, \boldsymbol{\Delta}_{\mathbf{i}'\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}'} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{0}, (\mathbf{X}_{\mathbf{i}\mathbf{j}}, \boldsymbol{\Delta}_{\mathbf{i}\mathbf{j}}) - \psi_{\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}'\mathbf{j}'}, \boldsymbol{\Delta}_{\mathbf{i}'\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}'} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{0}, (\mathbf{X}_{\mathbf{i}\mathbf{j}}, \mathbf{A}_{\mathbf{i}\mathbf{j}}) - \psi_{\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}'\mathbf{j}'}, \mathbf{A}_{\mathbf{i}'\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}'} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{0}, (\mathbf{X}_{\mathbf{i}\mathbf{j}}, \mathbf{A}_{\mathbf{i}\mathbf{j}}) - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}'\mathbf{j}'}, \mathbf{A}_{\mathbf{i}'\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{0}, (\mathbf{X}_{\mathbf{i}\mathbf{j}}, \mathbf{A}_{\mathbf{i}\mathbf{j}'}) - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}\mathbf{j}\mathbf{j}'}, \mathbf{A}_{\mathbf{i}'\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}\mathbf{i}\mathbf{j}'}, \mathbf{A}_{\mathbf{i}\mathbf{i}\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1}, (\mathbf{X}_{\mathbf{i}\mathbf{i}\mathbf{j}'}, \mathbf{A}_{\mathbf{i}\mathbf{i}\mathbf{j}'}) - \mathbf{P}_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'}^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}\mathbf{i}'^{1} - \psi_{\mathbf{i}\mathbf{i}\mathbf{i}'^{1} - \psi_{\mathbf{i}\mathbf{i}'}^{1} -$$

Then,

$$E(V_{ii',n}^{\star} - V_{ii',n}^{\star\star})^{2} = n^{-3}E\left[\sum_{j=1}^{n} \sum_{j'=1}^{n} g(X_{ij}, \Delta_{ij}, X_{i'j'}, \Delta_{i'j'})\right]^{2}$$
$$= n^{-3} \sum_{j=1}^{n} \sum_{j'=1}^{n} \sum_{\ell=1}^{n} \sum_{\ell=1}^{n} h(j, j', \ell, \ell'), \qquad (A.1)$$

where
$$h(j,j',\ell,\ell') = E[g(X_{ij}, \Delta_{ij}, X_{i'j'}, \Delta_{i'j'})g(X_{i\ell}, \Delta_{i\ell}, X_{i'\ell'}, \Delta_{i'\ell'})]$$
.
Because g is bounded, we can ignore any u terms of the sum in (A.1) if u
is of order $Q(n^3)$. Consider the following cases for which the number of
terms is with order larger than or equal to $O(n^3)$ (where j,j, l and l'
represent four distinct indices):

It follows that $E(V_{ii',n}^* - V_{ii',n}^{**})^2 \rightarrow 0$, as $n \rightarrow \infty$. By Corollary 6 of Lehmann (1975), p. 289) and the fact that the vector $\langle V_{ii',n}^{**} \rangle$ has a multivariate normal limiting distribution $N(Q, \ddagger)$, the vector $\langle V_{ii',n}^* \rangle$ has the same multivariate normal limiting distribution $N(Q, \ddagger)$. Under H_0 , $P_{ii'} = 0$, it follows that $V_{ii',n} = V_{ii',n}^*$,

$$\psi_{ii}^{0}, (X_{ij}, \Delta_{ij}) = \widetilde{F}_{i}, (X_{ij}) - \Delta_{ij}\overline{F}_{i}, (X_{ij}) \text{ and}$$

$$\psi_{ii}^{1}, (X_{i'j'}, \Delta_{i'j'}) = \Delta_{i'j'}, \overline{F}_{i}(X_{i'j'}) - \widetilde{F}_{i}(X_{i'j'}) .$$
Q.E.D.

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