

SIMULTANEOUS CONFIDENCE INTERVALS AMONG k MEAN VECTORS IN REPEATED MEASURES WITH MISSING DATA

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SYNOPTIC ABSTRACT

In this article, we consider a test for the equality among k mean vectors in the intraclass correlation model with monotone missing data. We derive simultaneous confidence intervals for all pairwise comparisons and for comparisons with a control by using the idea in Koizumi and Seo (2008). To find sampling distributions of T_{\max}^2 type statistic exactly is extremely difficult even if the observations are obtained complete. Therefore we consider the approximation to the upper percentage point of T_{\max}^2 type statistic by using Bonferroni's inequality. Finally, the accuracy and conservativeness for procedures proposed by in this paper are evaluated by the Monte Carlo simulation.

Key Words and Phrases: Intraclass correlation model; Monotone missing data; Simultaneous confidence intervals; Pairwise comparisons; Comparisons with a control; Hotelling's T^2 -statistic; Bonferroni inequality.

1. INTRODUCTION

Hotelling's T^2 -statistic is well known as a test statistic for the equality of two mean vectors (see, Hotelling (1931)). Simultaneous confidence intervals for multivariate multiple comparisons among k mean vectors has been considered by many authors (e.g., Roy and Bose (1953), Siotani, Hayakawa and Fujikoshi (1985)). Siotani (1959) has discussed in the approximation to the upper percentage point of T_{\max}^2 type statistic by using Bonferroni's inequality under the normal population. The first order Bonferroni approximation yields conservative simultaneous confidence intervals. But when the number of populations is large, this simultaneous confidence intervals become too conservative. So, Siotani (1959) derived the modified second order Bonferroni approximation by asymptotic expansion for the joint probability of Hotelling's T^2 statistics. This procedure doesn't always give the conservative simultaneous confidence intervals. But this procedure give a good approximation. Under the elliptical population, the modified second order Bonferroni approximation has been considered Seo (2002), Okamoto (2005) and so on. Recently, Kakizawa (2006) considered this problem under the general distribution. On the other hand, Seo, Mano and Fujikoshi (1994) has discussed in the multivariate Tukey-Kramer procedure for the case of pairwise comparisons among k mean vectors. The multivariate Tukey-Kramer procedure is an attractive and simple procedure. The multivariate generalized Tukey conjecture is known as the statement that the multivariate Tukey-Kramer procedure yields the conservative simultaneous confidence intervals for all pairwise comparisons. In the case of comparisons with a control, concerning to the multivariate Tukey-Kramer procedure, Seo (1995) proposed a conservative simultaneous confidence procedure.

When the missing observations are occur, we often use the approximate procedures. The well known procedure is EM algorithm proposed by Dempster, Laird and Rubin (1977). By the way, Srivastava (1985) proposed iterative numerical method to obtain maximum likelihood estimates by using Newton-Raphson method. On the other hand, Seo and Srivastava (2000) has derived an exact test statistic for the equality of mean components and the simultaneous confidence intervals for all contrasts and for linear contrasts with monotone

missing data. Recently, the exact test statistic for the equality of two mean vectors and Scheffé type of simultaneous confidence intervals have been given by Koizumi and Seo (2008). This is an extension of the procedure proposed by Seo and Srivastava (2000).

In this article, we discuss in simultaneous confidence intervals for multivariate multiple comparisons among k mean vectors in the intraclass correlation model with monotone missing data. In particular, we focus on the case of pairwise comparisons and the case of comparisons with a control for multivariate multiple comparison procedure. First, in Section 2, we introduce the notation in this paper and derive an unbiased estimator of unknown parameter. In Section 3, for the case $k = 2$, we describe the exact test statistic and the simultaneous confidence intervals which are the results in Koizumi and Seo (2008). In Section 4, we derive simultaneous confidence intervals among k mean vectors for all pairwise comparisons and for comparisons with a control by using Bonferroni's inequality. Finally, in Section 5, we investigate the accuracy and the conservativeness for the approximation to the upper percentage points of $T_{\max-p}^2$ and $T_{\max-c}^2$ statistics by 1,000,000 Monte Carlo simulation.

2. UNBIASED ESTIMATOR OF PARAMETER

Let $\mathbf{x}_1^{(i)}, \mathbf{x}_2^{(i)}, \dots, \mathbf{x}_{n^{(i)}}^{(i)}$ be the sample vectors from the i -th population ($i = 1, 2, \dots, k$). Also, we assume that

$$\mathbf{x}_1^{(i)}, \mathbf{x}_2^{(i)}, \dots, \mathbf{x}_{n^{(i)}}^{(i)} \stackrel{i.i.d.}{\sim} N_p(\boldsymbol{\mu}_i, \boldsymbol{\Sigma}),$$

where $\boldsymbol{\mu}_i = (\mu_1^{(i)}, \mu_2^{(i)}, \dots, \mu_p^{(i)})'$. And we assume that all covariance matrices are the same and $\boldsymbol{\Sigma} = \sigma^2[(1 - \rho)\mathbf{I}_p + \rho\mathbf{1}_p\mathbf{1}_p']$, where \mathbf{I}_p is a $p \times p$ identity matrix, $\mathbf{1}_p = (1, 1, \dots, 1)'$ is a p -vector and $\sigma^2, \rho \in [-1/(p-1), 1]$ are unknown parameters.

We consider the case when the missing observations are of the monotone-type. Our observations $\{x_{\ell j}^{(i)}\}$ can be written, without loss of generality, in the following form:

$$\begin{bmatrix} x_{11}^{(i)} & x_{12}^{(i)} & \cdots & \cdots & x_{1n_1^{(i)}}^{(i)} \\ \vdots & \vdots & \cdots & x_{2n_2^{(i)}}^{(i)} & * \\ \vdots & \vdots & \cdots & * & * \\ x_{p1}^{(i)} & \cdots & x_{pn_p^{(i)}}^{(i)} & * & * \end{bmatrix},$$

where $n_1^{(i)} \geq n_2^{(i)} \geq \dots \geq n_p^{(i)}$ and “*” means missing component. We shall consider the case $n_1^{(i)} = n_2^{(i)}$ ($\equiv n^{(i)}$). To provide a test or simultaneous confidence intervals, we rewrite the observations in the following form:

$$\begin{bmatrix} x_{11}^{(i)} & x_{12}^{(i)} & \cdots & x_{1n^{(i)}}^{(i)} \\ \vdots & \vdots & \cdots & \vdots \\ \vdots & \vdots & \cdots & x_{p_n^{(i)} n^{(i)}}^{(i)} \\ \vdots & x_{p_2^{(i)} 2}^{(i)} & * & * \\ x_{p_1^{(i)} 1}^{(i)} & * & * & * \end{bmatrix},$$

where $p \equiv p_1^{(i)} \geq p_2^{(i)} \geq \dots \geq p_n^{(i)}$. Since $n_1^{(i)} = n_2^{(i)}$, we note that $p_n^{(i)} \geq 2$.

Writing $\mathbf{x}_j^{(i)} = (x_{1j}^{(i)}, x_{2j}^{(i)}, \dots, x_{p_j^{(i)} j}^{(i)})'$, we have

$$\mathbf{x}_j^{(i)} \sim N_{p_j^{(i)}}(\boldsymbol{\mu}_j^{(i)}, \boldsymbol{\Sigma}_j^{(i)}), \quad j = 1, 2, \dots, n^{(i)},$$

where $\boldsymbol{\mu}_j^{(i)} = (\mu_{1j}^{(i)}, \mu_{2j}^{(i)}, \dots, \mu_{p_j^{(i)} j}^{(i)})'$ and $\boldsymbol{\Sigma}_j^{(i)} = \sigma^2[(1 - \rho)\mathbf{I}_{p_j^{(i)}} + \rho\mathbf{1}_{p_j^{(i)}}\mathbf{1}_{p_j^{(i)}}']$. Let $\mathbf{C}_j^{(i)}: (p_j^{(i)} - 1) \times p_j^{(i)}$ be a transformation matrix. $\mathbf{C}_j^{(i)}$ satisfies with $\mathbf{C}_j^{(i)}\mathbf{C}_j^{(i)'} = \mathbf{I}_{p_j^{(i)} - 1}$ and $\mathbf{C}_j^{(i)}\mathbf{1}_{p_j^{(i)}} = \mathbf{0}$. Clearly, then

$$\mathbf{y}_j^{(i)} = \mathbf{C}_j^{(i)}\mathbf{x}_j^{(i)} \sim N_{p_j^{(i)} - 1}(\mathbf{C}_j^{(i)}\boldsymbol{\mu}_j^{(i)}, \gamma^2\mathbf{I}_{p_j^{(i)} - 1}),$$

where $\gamma^2 \equiv \sigma^2(1 - \rho)$ and $\mathbf{y}_j^{(i)} = (y_{1j}^{(i)}, y_{2j}^{(i)}, \dots, y_{p_j^{(i)} - 1, j}^{(i)})'$. We shall write $\mathbf{C} : (p - 1) \times p$ for $\mathbf{C}_1^{(i)}$, since $p_1^{(i)} \equiv p$. When the missing patterns are same, we put $n_{\ell+1} \equiv n_{\ell+1}^{(1)} = n_{\ell+1}^{(2)} = \dots = n_{\ell+1}^{(k)}$, $\ell = 1, 2, \dots, p - 1$. Otherwise we put $n_{\ell+1} = \min_{i=1, 2, \dots, k} \{n_{\ell+1}^{(i)}\}$, $\ell = 1, 2, \dots, p - 1$. Hence we can calculate the estimators of parameters, that is, sample means of transformation data are given by

$$\bar{y}_{\ell.}^{(i)} = \frac{1}{n_{\ell+1}} \sum_{j=1}^{n_{\ell+1}} y_{\ell j}^{(i)}.$$

Further, we can obtain an unbiased estimator of γ^2 which is given by

$$f\hat{\gamma}^2 = \sum_{i=1}^k \sum_{\ell=1}^{p-1} \sum_{j=1}^{n_{\ell+1}} \left(y_{\ell j}^{(i)} - \bar{y}_{\ell.}^{(i)} \right)^2, \quad f = k \left(\sum_{\ell=1}^{p-1} n_{\ell+1} - p + 1 \right).$$

3. TWO SAMPLE PROBLEM

In this Section, we consider the case $k = 2$. Let sample mean vectors for the i -th population be $\bar{\mathbf{y}}^{(i)} = (\bar{y}_1^{(i)}, \bar{y}_2^{(i)}, \dots, \bar{y}_{p-1}^{(i)})'$, then we can obtain the following equations, as follows;

$$\begin{aligned} \mathbb{E}(\bar{\mathbf{y}}^{(1)} - \bar{\mathbf{y}}^{(2)}) &= \mathbf{C}(\boldsymbol{\mu}_1 - \boldsymbol{\mu}_2) \\ \text{Cov}(\bar{\mathbf{y}}^{(1)} - \bar{\mathbf{y}}^{(2)}) &= 2\gamma^2 \begin{bmatrix} n_2^{-1} & & \mathbf{0} \\ & \ddots & \\ \mathbf{0} & & n_p^{-1} \end{bmatrix} \equiv 2\gamma^2 \mathbf{V}. \end{aligned}$$

Hence, the exact test statistic T_{12}^2 is given by

$$T_{12}^2 \equiv \frac{(\bar{\mathbf{y}}^{(1)} - \bar{\mathbf{y}}^{(2)})' \mathbf{V}^{-1} (\bar{\mathbf{y}}^{(1)} - \bar{\mathbf{y}}^{(2)})}{2\hat{\gamma}^2}. \quad (1)$$

$T_{12}^2/(p-1)$ is distributed as F distribution with $p-1$ and f degrees of freedom under the null hypothesis.

We consider the simultaneous confidence intervals of $\mathbf{a}'(\boldsymbol{\mu}_1 - \boldsymbol{\mu}_2)$ for $\mathbf{a} \in \mathbb{R}_p^* \equiv \mathbb{R}^p - \{\mathbf{0}\}$, $\mathbf{a}'\mathbf{1}_p = 0$. Since $\mathbf{a}'\mathbf{1}_p = 0$, we can write it as $\mathbf{a}' = \tilde{\mathbf{a}}'\mathbf{C}$ for some $\tilde{\mathbf{a}} \in \mathbb{R}_{p-1}^*$, $\mathbf{C}\mathbf{1}_p = \mathbf{0}$. Therefore, we can obtain the simultaneous confidence intervals of $\mathbf{a}'(\boldsymbol{\mu}_1 - \boldsymbol{\mu}_2)$ with simultaneous confidence level $1 - \alpha$

$$\mathbf{a}'(\boldsymbol{\mu}_1 - \boldsymbol{\mu}_2) \in \left[\tilde{\mathbf{a}}'(\bar{\mathbf{y}}^{(1)} - \bar{\mathbf{y}}^{(2)}) \pm \sqrt{L_1} \right], \quad \forall \mathbf{a} \in \mathbb{R}_p^*, \quad (2)$$

where $L_1 = 2t_\alpha^2 \hat{\gamma}^2 \tilde{\mathbf{a}}'\mathbf{V}\tilde{\mathbf{a}}$ and t_α^2 is the upper 100α percentage point of T_{12}^2 statistic in (1).

4. k SAMPLE PROBLEM

Next, we consider the simultaneous confidence intervals for multivariate multiple comparisons among k mean vectors, that is, the simultaneous confidence intervals of $\mathbf{a}'\mathbf{M}\mathbf{b}$ for $\forall \mathbf{a} \in \mathbb{R}_p^*$, $\forall \mathbf{b} \in \mathbb{R}_{p-1}^*$, $\mathbf{a}'\mathbf{1}_p = 0$, $\mathbf{b}'\mathbf{1}_{p-1} = 0$, where $\mathbf{M} = [\boldsymbol{\mu}_1, \boldsymbol{\mu}_2, \dots, \boldsymbol{\mu}_k]$.

In the case of pairwise comparisons, \mathbf{b} is given by

$$\mathbf{b} = \mathbf{e}_i - \mathbf{e}_j, \quad 1 \leq i < j \leq k,$$

where \mathbf{e}_i is a unit k -dimensional vector having 1 at the i -th component and 0 at others. Hence, we consider the simultaneous confidence intervals of $\mathbf{a}'\mathbf{M}\mathbf{b} = \mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j)$.

We wish to find the percentage point t_p such that

$$\Pr(T_{ij}^2 \leq t_p^2, i < j, i, j = 1, 2, \dots, k) = 1 - \alpha, \quad (3)$$

where

$$T_{ij}^2 \equiv \frac{(\bar{\mathbf{y}}^{(i)} - \bar{\mathbf{y}}^{(j)})' \mathbf{V}^{-1} (\bar{\mathbf{y}}^{(i)} - \bar{\mathbf{y}}^{(j)})}{2\hat{\gamma}^2}.$$

We note that the above equation in (3) is equivalent to

$$\Pr(T_{\max\text{-}p}^2 > t_p^2) = \alpha,$$

where $T_{\max\text{-}p}^2 \equiv \max_{i < j} \{T_{ij}^2\}$.

So, we can obtain the simultaneous confidence intervals of $\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j)$ following form:

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[\tilde{\mathbf{a}}'(\bar{\mathbf{y}}^{(i)} - \bar{\mathbf{y}}^{(j)}) \pm \sqrt{L} \right], \quad \forall \mathbf{a} \in \mathbb{R}_p^*, \quad \mathbf{a}'\mathbf{1}_p = 0$$

where $\mathbf{a}' = \tilde{\mathbf{a}}'\mathbf{C}$, $L = 2t_p^2\hat{\gamma}^2\tilde{\mathbf{a}}'\mathbf{V}\tilde{\mathbf{a}}$ and t_p^2 is the upper 100α percentage points of $T_{\max\text{-}p}^2$ statistic. In order to construct the simultaneous confidence intervals with the given confidence level $1 - \alpha$, it is necessary to find the value of t_p . But the exact value of t_p is extremely difficult even if the observations are obtained complete. The approximate procedure based on Bonferroni's inequality is adopted in order to obtain conservative simultaneous confidence intervals estimation.

The probability P of the realization of at least one among the N -events E_1, E_2, \dots, E_N in the case of pairwise comparisons is given by

$$P = N\Pr\{E_1\} - \frac{1}{2}N(N-1)\Pr\{E_1, E_2\} + \dots \pm \Pr\{E_1, E_2, \dots, E_N\}.$$

Hence, we can obtain the following inequality:

$$P \leq N\Pr\{E_1\}. \quad (4)$$

We wish to find the percentage point t such that

$$\Pr(T_{\max\text{-}p}^2 > t_p^2) = \alpha,$$

where α is the significance level. The exact value of t_p is extremely difficult to find. We adopt the above inequality in (4). Hence, we can obtain the following result.

$$\Pr(T_{\max\text{-}p}^2 > t_p^2) \leq \sum_{i < j} \Pr(T_{ij}^2 > t_{1-p}^2) = \alpha$$

This approximate procedure is called the first order Bonferroni approximation. This procedure yields the conservative simultaneous confidence intervals. $t_{1,p}^2$ is essentially the upper percentage point of F distribution with $p - 1$ and f degrees of freedom. Therefore we construct the conservative simultaneous confidence intervals for pairwise comparisons among mean vectors as follows:

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[\tilde{\mathbf{a}}'(\bar{\mathbf{y}}^{(i)} - \bar{\mathbf{y}}^{(j)}) \pm \sqrt{L_2} \right], \quad \forall \mathbf{a} \in \mathbb{R}_p^*, \quad \mathbf{a}'\mathbf{1}_p = 0,$$

where $\mathbf{a}' = \tilde{\mathbf{a}}'\mathbf{C}$, $L_2 = 2t_{1,p}^2 \hat{\gamma}^2 \tilde{\mathbf{a}}'\mathbf{V}\tilde{\mathbf{a}}$, $t_{1,p}^2$ is the upper $100\alpha^*$ percentage points of T_{ij}^2 statistic and $\alpha^* \equiv 2\alpha/[k(k-1)]$.

In the case of comparisons with a control, \mathbf{b} is given by

$$\mathbf{b} = \mathbf{e}_i - \mathbf{e}_k, \quad i = 1, 2, \dots, k-1.$$

Here, we assume that the k -th treatment is a control treatment. Hence, we consider the simultaneous confidence intervals of $\mathbf{a}'\mathbf{M}\mathbf{b} = \mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k)$.

Similarly the case of pairwise comparisons, we construct the conservative simultaneous confidence intervals for comparisons with a control among mean vectors as follows:

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) \in \left[\tilde{\mathbf{a}}'(\bar{\mathbf{y}}^{(i)} - \bar{\mathbf{y}}^{(k)}) \pm \sqrt{L_3} \right], \quad \forall \mathbf{a} \in \mathbb{R}_p^*, \quad \mathbf{a}'\mathbf{1}_p = 0,$$

where $\mathbf{a}' = \tilde{\mathbf{a}}'\mathbf{C}$, $L_3 = 2t_{1,c}^2 \hat{\gamma}^2 \tilde{\mathbf{a}}'\mathbf{V}\tilde{\mathbf{a}}$, $t_{1,c}^2$ is the upper $100\alpha^{**}$ percentage points of T_{ik}^2 statistic and $\alpha^{**} \equiv \alpha/(k-1)$.

5. SIMULATION STUDIES

The accuracy and conservativeness for the first order Bonferroni approximate the upper percentage points of $T_{\max-p}^2$ and $T_{\max-c}^2$ statistics are evaluated by 1,000,000 Monte Carlo simulation, where $T_{\max-c}^2 \equiv \max_{i=1,2,\dots,k-1} \{T_{ik}^2\}$. Simulation parameters are as follows:

$$p = 4, 6,$$

$$n_1 = n_2 = 40, \quad n_3 = 30, \quad n_4 = 20, \quad (p = 4)$$

$$n_1 = n_2 = n_3 = 40, \quad n_4 = n_5 = 30, \quad n_6 = 20, \quad (p = 6)$$

$$k = 3, 5, 7, 9$$

$$\sigma^2 = 1, 4, 9, \quad \rho = 0.5$$

$$\tilde{\alpha}^* = \Pr(T_{\max-p}^2 > t_{1,p}^2)$$

$$\tilde{\alpha}^{**} = \Pr(T_{\max-c}^2 > t_{1,c}^2)$$

t^2 : simulated value of the upper percentage point

We note that the upper percentage points of T_{\max}^2 type statistic don't depend on unknown parameters. Hence, we delete σ^2 and ρ in our tables. This is a result for the case of pairwise comparisons and $p = 4$ in Table 1.

p	k	$1 - \alpha$	t^2	$t_{1,p}^2$	$1 - \tilde{\alpha}^*$	
4	3	0.90	8.48	8.84	0.914	
		0.95	10.16	10.42	0.955	
		0.99	13.95	14.05	0.990	
	5	4	0.90	10.87	11.48	0.921
			0.95	12.57	13.01	0.959
			0.99	16.34	16.55	0.991
		7	0.90	12.36	13.07	0.925
			0.95	14.08	14.58	0.960
			0.99	17.83	18.08	0.991
9	9	0.90	13.45	14.21	0.926	
		0.95	15.15	15.72	0.960	
		0.99	18.90	19.19	0.991	

Table 1. pairwise comparisons

From Table 1, the conservativeness for the first order Bonferroni approximation is large, when the number of population is large.

This is a result for the case of pairwise comparisons and $p = 6$ in Table 2.

p	k	$1 - \alpha$	t^2	$t_{1,p}^2$	$1 - \tilde{\alpha}^*$	
6	3	0.90	11.81	12.23	0.913	
		0.95	13.63	14.00	0.955	
		0.99	17.97	17.99	0.991	
	5	4	0.90	14.58	15.20	0.920
			0.95	16.48	16.90	0.958
			0.99	20.54	20.75	0.991
		7	0.90	16.28	16.97	0.922
			0.95	18.15	18.63	0.958
			0.99	22.14	22.41	0.991
	9	9	0.90	17.50	18.24	0.924
			0.95	19.35	19.87	0.959
			0.99	23.36	23.61	0.991

Table 2. pairwise comparisons

This is a result for the case of comparisons with a control and $p = 4$ in Table 3.

p	k	$1 - \alpha$	t^2	$t_{1,c}^2$	$1 - \tilde{\alpha}^{**}$
3		0.90	7.70	7.92	0.909
		0.95	9.34	9.50	0.953
		0.99	13.08	13.13	0.990
4		0.90	9.03	9.44	0.915
		0.95	10.70	10.99	0.956
		0.99	14.40	14.54	0.991
5		0.90	9.79	10.31	0.920
		0.95	11.46	11.84	0.958
		0.99	15.20	15.36	0.991
6		0.90	10.32	10.93	0.922
		0.95	11.99	12.45	0.959
		0.99	15.71	15.94	0.991

Table 3. comparisons with a control

This is a result for the case of comparisons with a control and $p = 6$ in Table 4.

p	k	$1 - \alpha$	t^2	$t_{1,p}^2$	$1 - \tilde{\alpha}^*$
3		0.90	10.94	11.17	0.908
		0.95	12.82	12.97	0.953
		0.99	16.91	17.00	0.990
4		0.90	12.47	12.91	0.915
		0.95	14.35	14.65	0.956
		0.99	18.39	18.57	0.991
5		0.90	13.35	13.91	0.918
		0.95	15.22	15.62	0.957
		0.99	19.28	19.48	0.991
6		0.90	13.98	14.60	0.920
		0.95	15.85	16.29	0.958
		0.99	19.89	20.12	0.991

Table 4. comparisons with a control

It may be noticed from Tables that our procedure gives a good approximation to the upper percentage point of T_{\max}^2 type statistic even if the case the number of population is not small.

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