

## Recent developments of multivariate multiple comparisons among mean vectors

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**Abstract.** We discuss multivariate multiple comparison procedure among mean vectors. In general, it is difficult to find the exact critical value that is used for this problem. So, some approximation procedures have been discussed by many authors. In this paper, we review some results concerning the following approximation procedures: (i) multivariate Tukey-Kramer type procedure and (ii) approximation procedure based on Bonferroni's inequality.

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### §1. Introduction

The study of the subjects of multiple comparisons under univariate and multivariate analysis has been done by many authors (for example, see Hochberg and Tamhane [13] and Hsu [14]). This paper is concerned with multivariate multiple comparisons among mean vectors and we will review some results of this topic.

We first consider the simultaneous confidence intervals for multiple comparisons among mean vectors from the multivariate normal populations. When we discuss multivariate multiple comparisons among mean vectors, we usually deal with the simultaneous confidence intervals. So, it is important to construct the simultaneous confidence intervals among mean vectors. Let  $\mu_i$  be the mean vector from  $i$ -th population. Let  $M = [\mu_1, \dots, \mu_k]$  be the unknown  $p \times k$  matrix of  $k$  mean vectors corresponding to the  $k$  treatments and let  $\widehat{M} = [\widehat{\mu}_1, \dots, \widehat{\mu}_k]$  be the unbiased estimator of  $M$  such that  $\text{vec}(X)$  is distributed as  $N_{kp}(\mathbf{0}, V \otimes \Sigma)$ , where  $X = \widehat{M} - M$ ,  $V = [v_{ij}]$  is a known

$k \times k$  positive definite matrix and  $\Sigma$  is an unknown  $p \times p$  positive definite matrix, and  $\text{vec}(\cdot)$  denotes the column vector formed by stacking the columns of the matrix under each other. Also, let  $\mathbf{S}$  be an unbiased estimator of  $\Sigma$  such that  $\nu\mathbf{S}$  is independent of  $\widehat{\mathbf{M}}$  and is distributed as a Wishart distribution  $W_p(\Sigma, \nu)$ . Then, in general, the simultaneous confidence intervals for pairwise comparisons among mean vectors or comparisons with a control can be written as the form:

$$(1.1) \quad \mathbf{a}'\mathbf{M}\mathbf{b} \in \left[ \mathbf{a}'\widehat{\mathbf{M}}\mathbf{b} \pm t(\mathbf{b}'\mathbf{V}\mathbf{b})^{1/2}(\mathbf{a}'\mathbf{S}\mathbf{a})^{1/2} \right], \quad \forall \mathbf{a} \in \mathbb{R}^p, \forall \mathbf{b} \in \mathbb{B},$$

where  $\mathbb{R}^p$  is the set of any nonzero real  $p$ -dimensional vectors and  $\mathbb{B}$  is a subset in the  $k$ -dimensional space. We note that the value  $t^2$  in (1.1) is the upper  $100\alpha$  percentile of the  $T_{\max}^2$ -type statistic,

$$(1.2) \quad T_{\max}^2 = \max_{\mathbf{b} \in \mathbb{B}} \left\{ \frac{(\mathbf{X}\mathbf{b})'\mathbf{S}^{-1}\mathbf{X}\mathbf{b}}{\mathbf{b}'\mathbf{V}\mathbf{b}} \right\},$$

where  $0 < \alpha < 1$  and the coverage probability for (1.1) is  $1 - \alpha$ . In order to construct actually simultaneous confidence intervals (1.1) with the confidence level  $1 - \alpha$ , it is necessary to find the value  $t$ . However, in general, it is difficult to find the exact value  $t$  even the cases of pairwise comparisons and comparisons with a control. Then large sample approximations based on asymptotic expansion for the upper percentiles of  $T_{\max}^2$ -type statistic have been discussed by Siotani [33], [34], [35], Krishnaiah [19], Siotani, Hayakawa and Fujikoshi [36], Seo and Siotani [31], Seo [26] and so on. In particular, Siotani [33], Seo and Siotani [31] and Seo [26] discussed the first order and the modified second order Bonferroni approximation that are approximation procedures based on Bonferroni's inequality.

In the case of pairwise comparisons, a subset  $\mathbb{B}$  is given by

$$\mathbb{B} = \mathbb{C} \equiv \{\mathbf{c} \in \mathbb{R}^k : \mathbf{c} = \mathbf{e}_i - \mathbf{e}_j, 1 \leq i < j \leq k\},$$

where  $\mathbf{e}_i$  is a unit vector of the  $k$ -dimensional space having 1 at  $i$ -th component and 0 at others. Therefore, we can also express (1.1) as

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[ \mathbf{a}'(\widehat{\boldsymbol{\mu}}_i - \widehat{\boldsymbol{\mu}}_j) \pm t_{p,V} (d_{ij}\mathbf{a}'\mathbf{S}\mathbf{a})^{1/2} \right], \forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i < j \leq k,$$

where  $t_{p,V}^2$  is the upper  $100\alpha$  percentile of  $T_{\max \cdot p}^2$  statistic,

$$T_{\max \cdot p}^2 = \max_{1 \leq i < j \leq k} \{(\mathbf{x}_i - \mathbf{x}_j)'(d_{ij}\mathbf{S})^{-1}(\mathbf{x}_i - \mathbf{x}_j)\},$$

and  $d_{ij} = v_{ii} - 2v_{ij} + v_{jj}$ .

In the case of pairwise comparisons with  $\mathbf{V} = \mathbf{I}$ ,  $T_{\max \cdot p}^2$  statistic is reduced as the same as half of the multivariate Studentized range statistic  $R_{\max}^2$

(see, e.g., Seo and Siotani [31]). Seo, Mano and Fujikoshi [29] proposed the multivariate Tukey-Kramer procedure (MTK procedure) which is a simple procedure by replacing with the upper percentile of the  $R_{\max}^2$  statistic as an approximation to the one of  $T_{\max}^2$ -type statistic for any positive definite matrix  $\mathbf{V}$ . This procedure is an extension of Tukey-Kramer procedure (TK procedure) (Tukey [42], Kramer [17], [18]). For the TK procedure, the generalized Tukey conjecture is known as the statement that the TK procedure yields the conservative simultaneous confidence intervals for all pairwise comparisons among means (see, e.g., Benjamini and Braun [2]). For the theoretical discussion to prove the generalized Tukey conjecture, see, Hayter [10], [11], Brown [3], Uusipaikka [43] and Spurrier and Isham [38]. For the MTK procedure, the multivariate version of the generalized Tukey conjecture has been affirmatively proved in the case of three correlated mean vectors by Seo, Mano and Fujikoshi [29], and Nishiyama and Seo [23] gives the affirmative proof of the conjecture in the case of four mean vectors. Further, relating to the conjecture, Seo [27] and Nishiyama and Seo [23] gave the upper bound for conservativeness of the MTK procedure. The related discussion for the univariate case is referred to Somerville [37].

In the case of comparisons with a control, we have

$$\mathbb{B} = \mathbb{D} \equiv \{\mathbf{d} \in \mathbb{R}^k : \mathbf{d} = \mathbf{e}_i - \mathbf{e}_k, 1 \leq i \leq k-1\},$$

where  $k$ -th population is the control. Then we can write (1.1) as

$$\begin{aligned} \mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) \in [\mathbf{a}'(\hat{\boldsymbol{\mu}}_i - \hat{\boldsymbol{\mu}}_k) \pm t_{c.V} (d_{ik}\mathbf{a}'\mathbf{S}\mathbf{a})^{1/2}], \\ \forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i \leq k-1, \end{aligned}$$

where  $t_{c.V}^2$  is the upper  $100\alpha$  percentile of  $T_{\max.c}^2$  statistic,

$$T_{\max.c}^2 = \max_{1 \leq i \leq k-1} \{(\mathbf{x}_i - \mathbf{x}_k)'(d_{ik}\mathbf{S})^{-1}(\mathbf{x}_i - \mathbf{x}_k)\},$$

and  $d_{ik} = v_{ii} - 2v_{ik} + v_{kk}$ .

For comparisons with a control, concerning to the MTK procedure, Seo [26] proposed a conservative approximate simultaneous confidence procedure. Its conservativeness has been affirmatively proved by Seo [26] and Nishiyama [21] in the case of three and four correlated mean vectors, respectively. In addition Seo and Nishiyama [30] and Nishiyama [21] gave the upper bound for the conservativeness of this procedure. For the univariate case of the comparisons with a control, approximate procedures for unbalanced designs are discussed by Dutt et al. [7], Dunnett [6] and so on.

Also, approximation procedures based on Bonferroni's inequality for the upper percentiles of  $T_{\max}^2$ -type statistic have been proposed under class of elliptical distributions by Seo [28], Okamoto and Seo [25] and Okamoto [24], and

they evaluated the effect of nonnormality. Besides, under general distributions, Kakizawa [16] discussed these approximation procedures.

On the other hand, recently, in many practical applications of modern multivariate statistics (e.g. DNA microarray data) the number of feature  $p$  exceeds  $N$ , so that a straightforward use of  $T^2$ -type statistics is impossible due to singularity of the sample covariance matrix. Thus, to cope with this high dimensional situation, it would be desirable to develop new tests for  $N \leq p$ , and investigate their asymptotic properties when both  $N$  and  $p$  are going to infinity; this asymptotic framework is also known as  $(N, p)$ -*asymptotics* (see, e.g., Dempster [4], [5], Bai and Saradanasa [1], Fujikoshi, Himeno and Wakaki [9] and Himeno [12]). For this problem, under multivariate normality, Takahashi et al. [41] and Hyodo, Takahashi and Nishiyama [15] proposed a test procedure for multiple comparisons among mean vectors based on Dempster trace criterion by Dempster [4], [5].

The rest of the paper is organized as follows. Section 2 provides description of the multivariate Tukey-Kramer procedure and similar conservative approximate simultaneous confidence procedure for comparisons with a control. In Section 3, we consider the approximation procedures based on Bonferroni's inequality. We describe some large sample approximations based on asymptotic expansion for the upper percentiles of  $T_{\max}^2$ -type statistic under normality and class of elliptical distributions. Also, we introduce some asymptotic results in high dimensional settings under normality. At last, we provide some concluding remarks.

## §2. Conservative approximate simultaneous confidence procedure

In this section, we describe the multivariate Tukey-Kramer procedure and similar conservative approximate simultaneous confidence procedure for comparisons with a control. In addition we discuss their conservativeness.

### 2.1. The multivariate Tukey-Kramer procedure

In this subsection, we discuss the multivariate Tukey-Kramer procedure (MTK procedure) and its properties.

The simultaneous confidence intervals for all pairwise comparisons by the MTK procedure are given by

$$(2.1) \quad \mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[ \mathbf{a}'(\hat{\boldsymbol{\mu}}_i - \hat{\boldsymbol{\mu}}_j) \pm t_{p, I} \sqrt{d_{ij} \mathbf{a}' \mathbf{S} \mathbf{a}} \right], \\ \forall \mathbf{a} \in \mathbb{R}^p, \quad 1 \leq i < j \leq k,$$

where  $t_{p,I}^2$  is the upper  $100\alpha$  percentile of  $T_{\max, p}^2$  statistic with  $\mathbf{V} = \mathbf{I}$ , that is,  $t_{p,I}^2 = q^2/2$  and  $q^2 \equiv q_{p,k,\nu}^2(\alpha)$  is the upper  $100\alpha$  percentile of the  $p$ -variate Studentized range statistic with parameters  $k$  and  $\nu$ . By a reduction of relating to the coverage probability of (2.1), Seo, Mano and Fujikoshi [29] proved that the coverage probability in the case  $k = 3$  is equal or greater than  $1 - \alpha$  for any positive definite matrix  $\mathbf{V}$ . Using the same reduction, Seo [27] discussed the bound of conservative simultaneous confidence levels.

Consider the probability

$$(2.2) \quad Q(t, \mathbf{V}, \mathbb{B}) = \Pr\{(\mathbf{X}\mathbf{b})'(\nu\mathbf{S})^{-1}(\mathbf{X}\mathbf{b}) \leq t(\mathbf{b}'\mathbf{V}\mathbf{b}), \forall \mathbf{b} \in \mathbb{B}\},$$

where  $t$  is any fixed constant. Without loss of generality, we may assume  $\Sigma = \mathbf{I}_p$  when we consider the probability (2.2).

When  $t = t_p^* (\equiv t_{p,I}^2/\nu)$  and  $\mathbb{B} = \mathbb{C}$ , the coverage probability (2.2) is the same as the coverage probability of (2.1). The conservativeness of the simultaneous confidence intervals (2.1) means that  $Q(t_p^*, \mathbf{V}, \mathbb{C}) \geq Q(t_p^*, \mathbf{I}, \mathbb{C}) = 1 - \alpha$ . The inequality is known as the multivariate generalized Tukey conjecture. Then Seo and Nishiyama [30] gave the following theorem for the upper bound of coverage probability by using same line of the proof of Theorem 3.2 in Seo, Mano and Fujikoshi [29].

**Theorem 2.1. (Seo and Nishiyama [30])** *Let  $Q(t, \mathbf{V}, \mathbb{B})$  be the coverage probability (2.2) with a known matrix  $\mathbf{V}$  for the case  $k = 3$ . Then, for any positive definite matrix  $\mathbf{V}$ , it holds that*

$$1 - \alpha = Q(t_p^*, \mathbf{I}, \mathbb{C}) \leq Q(t_p^*, \mathbf{V}, \mathbb{C}) < Q(t_p^*, \mathbf{V}_0, \mathbb{C}),$$

where  $t_p^* = t_{p,I}^2/\nu$ ,  $\mathbb{C} = \{\mathbf{c} \in \mathbb{R}^k : \mathbf{c} = \mathbf{e}_i - \mathbf{e}_j, 1 \leq i < j \leq k\}$  and  $\mathbf{V}_0$  has the condition such that  $\sqrt{d_{12}} = \sqrt{d_{13}} + \sqrt{d_{23}}$  or  $\sqrt{d_{13}} = \sqrt{d_{12}} + \sqrt{d_{23}}$  or  $\sqrt{d_{23}} = \sqrt{d_{12}} + \sqrt{d_{13}}$ .

Also, in the case  $k = 4$ , Nishiyama and Seo [23] gave the following theorem for conservativeness of the simultaneous confidence intervals and upper bound of coverage probability.

**Theorem 2.2. (Nishiyama and Seo [23])** *Let  $Q(t, \mathbf{V}, \mathbb{B})$  be the coverage probability (2.2) with a known matrix  $\mathbf{V}$  for the case  $k = 4$ . Then in the case of  $k = 4$ ,*

$$1 - \alpha = Q(t_p^*, \mathbf{I}, \mathbb{C}) \leq Q(t_p^*, \mathbf{V}, \mathbb{C}) < Q(t_p^*, \mathbf{V}_1, \mathbb{C}),$$

holds for any positive definite matrix  $\mathbf{V}$  where  $t_p^* = t_{p,I}^2/\nu$ ,  $\mathbf{V}_1$  satisfies with two equations in six patterns; " $\sqrt{d_{ij}} = \sqrt{d_{i\ell}} + \sqrt{d_{j\ell}}$  and  $\sqrt{d_{ij}} = \sqrt{d_{im}} + \sqrt{d_{jm}}$ " and  $i, j, \ell, m$  take another value each other.

We note that the condition of  $\mathbf{V}_0$  in Theorem 2.1 is an extension of the result in Seo [27] and the condition of  $\mathbf{V}_1$  in Theorem 2.2 is a matrix with one of the following six patterns:

- (i)  $\sqrt{d_{12}} = \sqrt{d_{13}} + \sqrt{d_{23}}$  and  $\sqrt{d_{12}} = \sqrt{d_{14}} + \sqrt{d_{24}}$
- (ii)  $\sqrt{d_{13}} = \sqrt{d_{12}} + \sqrt{d_{23}}$  and  $\sqrt{d_{13}} = \sqrt{d_{14}} + \sqrt{d_{34}}$
- (iii)  $\sqrt{d_{14}} = \sqrt{d_{12}} + \sqrt{d_{24}}$  and  $\sqrt{d_{14}} = \sqrt{d_{13}} + \sqrt{d_{34}}$
- (iv)  $\sqrt{d_{23}} = \sqrt{d_{12}} + \sqrt{d_{13}}$  and  $\sqrt{d_{23}} = \sqrt{d_{24}} + \sqrt{d_{34}}$
- (v)  $\sqrt{d_{24}} = \sqrt{d_{12}} + \sqrt{d_{14}}$  and  $\sqrt{d_{24}} = \sqrt{d_{23}} + \sqrt{d_{34}}$
- (vi)  $\sqrt{d_{34}} = \sqrt{d_{13}} + \sqrt{d_{14}}$  and  $\sqrt{d_{34}} = \sqrt{d_{23}} + \sqrt{d_{24}}$ .

Also we note that there does not exist  $\mathbf{V}_0$  and  $\mathbf{V}_1$  as a positive definite matrix. However, we can find  $\mathbf{V}_0$  and  $\mathbf{V}_1$  as a positive semi-definite matrix. For example one of such matrices are given by

$$\mathbf{V}_0 = \begin{bmatrix} 4 & 0 & 2 \\ 0 & 4 & 2 \\ 2 & 2 & 2 \end{bmatrix}, \quad \mathbf{V}_1 = \begin{bmatrix} 3 & 0 & 1 & 2 \\ 0 & 6 & 4 & 2 \\ 1 & 4 & 3 & 2 \\ 2 & 2 & 2 & 2 \end{bmatrix}.$$

In connection with above Theorems, we have the following conjecture for the case  $k \geq 5$ .

**Conjecture 2.3. (Nishiyama and Seo [23])** *Let  $Q(t, \mathbf{V}, \mathbb{B})$  be the coverage probability for (2.2) with a known matrix  $\mathbf{V}$ . Then*

$$1 - \alpha = Q(t_p^*, \mathbf{I}, \mathbb{C}) \leq Q(t_p^*, \mathbf{V}, \mathbb{C}) < Q(t_p^*, \mathbf{V}_p, \mathbb{C})$$

*holds for any positive definite matrix  $\mathbf{V}$ , where  $t_p^* = t_{p, I}^2 / \nu$  and  $\mathbf{V}_p$  satisfies with  $(k - 2)$  equations in  $k(k - 1)/2$  patterns: “ $\sqrt{d_{ij}} = \sqrt{d_{i\ell_1}} + \sqrt{d_{j\ell_1}}$  and  $\sqrt{d_{ij}} = \sqrt{d_{i\ell_2}} + \sqrt{d_{j\ell_2}}$  and ... and  $\sqrt{d_{ij}} = \sqrt{d_{i\ell_{k-2}}} + \sqrt{d_{j\ell_{k-2}}}$ ”,  $i, j, \ell_1, \ell_2, \dots, \ell_{k-3}$  and  $\ell_{k-2}$  take another value each other.*

## 2.2. A conservative approximate procedure for comparisons with a control

In this subsection, concerning to the MTK procedure, we discuss a conservative approximate simultaneous confidence procedure for comparisons with a control and its conservativeness.

Seo [26] proposed following conservative approximate simultaneous confidence procedure:

$$(2.3) \quad \mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) \in \left[ \mathbf{a}'(\hat{\boldsymbol{\mu}}_i - \hat{\boldsymbol{\mu}}_k) \pm t_{c \cdot V_{c1}} \sqrt{d_{ik} \mathbf{a}' \mathbf{S} \mathbf{a}} \right],$$

$$\forall \mathbf{a} \in \mathbb{R}^p, \quad 1 \leq i \leq k-1,$$

where  $t_{c \cdot V_{c1}}$  is the upper  $100\alpha$  percentile of  $T_{\max \cdot c}^2$  statistic with  $\mathbf{V} = \mathbf{V}_{c1}$ , and  $\mathbf{V}_{c1}$  satisfies with  $d_{ij} = d_{ik} + d_{jk}$ ,  $1 \leq i < j \leq k-1$ . Further, Seo [26] gave the conjecture that the simultaneous confidence intervals for this procedure (2.3) are always conservative. For this conjecture, its proof for the case of  $k = 3$  is given by Seo [26].

Since the coverage probability (2.2) with  $t = t_{c \cdot V}^2/\nu$  and  $\mathbb{B} = \mathbb{D}$  is the same as the coverage probability of (2.3), we obtain the following theorems for the upper bound of coverage probability by the similar derivation of Theorem 2.1 and Theorem 2.2.

**Theorem 2.4. (Seo and Nishiyama [30])** *Let  $Q(t, \mathbf{V}, \mathbb{B})$  be the coverage probability (2.2) with a known matrix  $\mathbf{V}$  for the case  $k = 3$ . Then, for any positive definite matrix  $\mathbf{V}$ , it holds that*

$$1 - \alpha = Q(t_c^*, \mathbf{V}_2, \mathbb{D}) \leq Q(t_c^*, \mathbf{V}, \mathbb{D}) < Q(t_c^*, \mathbf{V}_3, \mathbb{D}),$$

where  $t_c^* = t_{c \cdot V_2}^2/\nu$ ,  $\mathbb{D} = \{\mathbf{d} \in \mathbb{R}^k : \mathbf{d} = \mathbf{e}_i - \mathbf{e}_k, \quad 1 \leq i \leq k-1\}$  and  $\mathbf{V}_2$  satisfies with  $d_{12} = d_{13} + d_{23}$  and  $\mathbf{V}_3$  satisfies with  $\sqrt{d_{12}} = |\sqrt{d_{13}} - \sqrt{d_{23}}|$ .

**Theorem 2.5. (Nishiyama [21])** *Let  $Q(q, \mathbf{V}, \mathbb{B})$  be the coverage probability for (2.2) with a known matrix  $\mathbf{V}$  for the case  $k = 4$ . Then*

$$1 - \alpha = Q(t_c^*, \mathbf{V}_4, \mathbb{D}) \leq Q(t_c^*, \mathbf{V}, \mathbb{D}) < Q(t_c^*, \mathbf{V}_5, \mathbb{D})$$

holds for any positive definite matrix  $\mathbf{V}$ , where  $t_c^* = t_{c \cdot V_4}^2/\nu$ ,  $\mathbf{V}_4$  satisfies with  $d_{12} = d_{14} + d_{24}$ ,  $d_{13} = d_{14} + d_{34}$  and  $d_{23} = d_{24} + d_{34}$ , and  $\mathbf{V}_5$  satisfies with  $\sqrt{d_{12}} = |\sqrt{d_{14}} - \sqrt{d_{24}}|$ ,  $\sqrt{d_{13}} = |\sqrt{d_{14}} - \sqrt{d_{34}}|$  and  $\sqrt{d_{23}} = |\sqrt{d_{24}} - \sqrt{d_{34}}|$ .

We note that there does not exist  $\mathbf{V}_3$  in Theorem 2.4 and  $\mathbf{V}_5$  in Theorem 2.5 as a positive definite matrix. However, we can find  $\mathbf{V}_3$  and  $\mathbf{V}_5$  as a positive semi-definite matrix. For example one of such matrices are given by

$$\mathbf{V}_3 = \begin{bmatrix} 4 & 2 & 0 \\ 2 & 2 & 2 \\ 0 & 2 & 4 \end{bmatrix}, \quad \mathbf{V}_5 = \begin{bmatrix} 4 & 2 & 2 & 0 \\ 2 & 2 & 2 & 2 \\ 2 & 2 & 2 & 2 \\ 0 & 2 & 2 & 4 \end{bmatrix}.$$

Also, we can find one of  $\mathbf{V}_2$  in Theorem 2.4 and  $\mathbf{V}_4$  in Theorem 2.5 as follows:

$$\mathbf{V}_2 = \begin{bmatrix} 1 & 0 & 0.5 \\ 0 & 1 & 0.5 \\ 0.5 & 0.5 & 1 \end{bmatrix}, \quad \mathbf{V}_4 = \begin{bmatrix} 1 & 0 & 0 & 0.5 \\ 0 & 1 & 0 & 0.5 \\ 0 & 0 & 1 & 0.5 \\ 0.5 & 0.5 & 0.5 & 1 \end{bmatrix}.$$

In connection with above theorems, we have the following conjecture for the case  $k \geq 5$ .

**Conjecture 2.6. (Nishiyama [21])** *Let  $Q(t, \mathbf{V}, \mathbb{B})$  be the coverage probability for (2.2) with a known matrix  $\mathbf{V}$ . Then*

$$1 - \alpha = Q(t_c^*, \mathbf{V}_{c1}, \mathbb{D}) \leq Q(t_c^*, \mathbf{V}, \mathbb{D}) < Q(t_c^*, \mathbf{V}_{c2}, \mathbb{D})$$

*holds for any positive definite matrix  $\mathbf{V}$ , where  $t_c^* = t_{c, \mathbf{V}_{c1}}^2 / \nu$  and  $\mathbf{V}_{c1}$  satisfies with  $d_{ij} = d_{ik} + d_{jk}$  for all  $i, j$  ( $1 \leq i < j \leq k-1$ ) and  $\mathbf{V}_{c2}$  satisfies with  $\sqrt{d_{ij}} = |\sqrt{d_{ik}} - \sqrt{d_{jk}}|$  for all  $i, j$  ( $1 \leq i < j \leq k-1$ ).*

### §3. Approximation procedures based on Bonferroni's inequality

In this section, we discuss approximation procedures based on Bonferroni's inequality, that is, the first order Bonferroni approximation and the modified second order Bonferroni approximation (see, e.g., Siotani [33], Seo and Siotani [31], [32] and Seo [26]). At first, we describe the first and modified second order Bonferroni approximations, and introduce a result of asymptotic expansion under multivariate normal distribution. Also, we review some asymptotic results in high dimensional settings. At last, some results of asymptotic expansions under elliptical distributions are described.

#### 3.1. Asymptotic expansion under normality

In this subsection, we describe the first order Bonferroni approximation and the modified second order Bonferroni approximation. Also, we introduce a result of asymptotic expansion under normality.

Put  $\mathbf{z}_i = (\mathbf{b}_i' \mathbf{V} \mathbf{b}_i)^{-1/2} \mathbf{X} \mathbf{b}_i$ ,  $i = 1, \dots, r$ , where  $\mathbf{b}_i$ 's are given vectors. Let  $\mathbb{B}^k = \{\mathbf{b}_1, \dots, \mathbf{b}_r\}$ , and let  $t^2$  be the exact upper  $100\alpha$  percentile of generalized  $T_{\max}^2$ -type statistic (1.2). Then  $\mathbf{z}_i$  has the  $p$ -dimensional normal distribution with mean vector  $\mathbf{0}$  and covariance matrix  $\mathbf{\Sigma}$ .

By the first order Bonferroni's inequality for  $\Pr\{T_{\max}^2 > t^2\}$ ;

$$\sum_{i=1}^r \Pr\{\mathbf{z}_i' \mathbf{S}^{-1} \mathbf{z}_i > t^2\} - \beta(t^2) < \Pr\{T_{\max}^2 > t^2\} < \sum_{i=1}^r \Pr\{\mathbf{z}_i' \mathbf{S}^{-1} \mathbf{z}_i > t^2\},$$



where

$$\beta(t^2) = \sum_{i=1}^{k-1} \sum_{j=i+1}^k \Pr \{ \mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t^2, \mathbf{z}'_j \mathbf{S}^{-1} \mathbf{z}_j > t^2 \}.$$

Then the first order approximation  $t_1^2$  is given as a critical value that satisfies the equality

$$\sum_{i=1}^r \Pr \{ \mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t_1^2 \} = \alpha.$$

We note that  $t_1^2$  is overestimated, and the statistic  $\mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i$  is reduced to the Hotelling's  $T^2$  statistic with  $\nu$  degrees of freedom (d.f.); that is,

$$t_1^2 = \frac{\nu p}{\nu - p + 1} F_{p, \nu - p + 1} \left( \frac{\alpha}{r} \right),$$

where  $F_{p, \nu - p + 1}(\alpha/r)$  is the upper  $\alpha/r$  percentile of  $F$ -distribution with  $p$  and  $\nu - p + 1$  d.f.'s. Also, the modified second order approximation  $t_M^2$  by the modified second order Bonferroni procedure is defined as a critical value that satisfies the equality

$$\sum_{i=1}^r \Pr \{ \mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t_M^2 \} - \sum_{i=1}^{k-1} \sum_{j=i+1}^k \Pr \{ \mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t_1^2, \mathbf{z}'_j \mathbf{S}^{-1} \mathbf{z}_j > t_1^2 \} = \alpha.$$

We note that  $t_2^2 < t_M^2 < t_1^2$  (see, Figure 1), where  $t_2^2$  is a second order approximation defined as a critical value that satisfies the equality

$$\sum_{i=1}^r \Pr \{ \mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t_2^2 \} - \sum_{i=1}^{k-1} \sum_{j=i+1}^k \Pr \{ \mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t_2^2, \mathbf{z}'_j \mathbf{S}^{-1} \mathbf{z}_j > t_2^2 \} = \alpha.$$

Hence the modified second order approximation  $t_M^2$  can be written as

$$t_M^2 = \frac{\nu p}{\nu - p + 1} F_{p, \nu - p + 1} \left( \frac{\alpha + \beta(t_1^2)}{r} \right).$$

Though we have to evaluate  $\beta(t_1^2)$  in order to obtain the modified second order approximation  $t_M^2$ , it is difficult to obtain the exact evaluation. As the large sample approximations, however when  $\mathbf{V} = \mathbf{I}$ , an asymptotic expansion formula was given by Siotani [33] and its simplified and practical formula was obtained in Seo and Siotani [31]. Also, for any positive definite matrix  $\mathbf{V}$ , asymptotic expansion formula up to the term of order  $\nu^{-2}$  was derived by Seo [26].

**Theorem 3.1.** (Seo [26]) *With the notations*

$$\begin{aligned}\eta_{ij} &= \frac{\chi^2}{2(1 - \rho_{ij}^2)}, \\ g_a(\eta_{ij}) &= \frac{1}{\Gamma(a)} \eta_{ij}^{a-1} e^{-\eta_{ij}} \quad (a > 0), \quad G_a(\eta_{ij}) = \int_{\eta_{ij}}^{\infty} g_a(t) dt \\ g_{p/2-1}(\eta_{ij}) &\equiv -\frac{1}{2\sqrt{\pi}} \eta_{ij}^{-3/2} e^{-\eta_{ij}} \text{ for } p = 1; \quad \equiv 0 \text{ for } p = 2, \\ \left(\frac{1}{2}p\right)_m &= \frac{p}{2} \cdot \left(\frac{p}{2} + 1\right) \cdots \left(\frac{p}{2} + m - 1\right),\end{aligned}$$

it holds that

$$\begin{aligned}\Pr\{\mathbf{z}'_i \mathbf{S}^{-1} \mathbf{z}_i > t_1^2, \mathbf{z}'_j \mathbf{S}^{-1} \mathbf{z}_j > t_1^2\} \\ = A_0(\rho_{ij}) + \nu^{-1} A_1(\rho_{ij}) + \nu^{-2} A_2(\rho_{ij}) + O(\nu^{-3}),\end{aligned}$$

where  $\chi \equiv \chi_p(\alpha/r)$  is the upper  $\alpha/r$  percentile of the  $\chi^2$  distribution with  $p$  d.f. and

$$\begin{aligned}\rho_{ij} &= \frac{\mathbf{b}'_i \mathbf{V} \mathbf{b}_j}{(\mathbf{b}'_i \mathbf{V} \mathbf{b}_i)^{1/2} (\mathbf{b}'_j \mathbf{V} \mathbf{b}_j)^{1/2}}, \\ A_0(\rho_{ij}) &= (1 - \rho_{ij})^{p/2} \sum_{m=0}^{\infty} \frac{(\frac{1}{2}p)_m}{m!} \rho_{ij}^{2m} G_{p/2+m}^2(\eta_{ij}), \\ A_1(\rho_{ij}) &= \frac{1}{2} (1 - \rho_{ij}^2)^{p/2-2} \chi^2 \sum_{m=0}^{\infty} \frac{(\frac{1}{2}p)_m}{m!} \rho_{ij}^{2m} g_{p/2+m}(\eta_{ij}) \\ &\quad \times \left[ \{\rho_{ij}^2 (\chi^2 + 2m) - 2m\} G_{p/2+m}(\eta_{ij}) + \frac{2m+1}{p+2m} \chi^2 g_{p/2+m}(\eta_{ij}) \right], \\ A_2(\rho_{ij}) &= \frac{1}{48} (1 - \rho_{ij}^2)^{p/2-4} \chi^2 \sum_{m=0}^{\infty} \frac{(\frac{1}{2}p)_m}{m!} \rho_{ij}^{2m} \left[ a_1(\rho_{ij}) g_{p/2-1+m}(\eta_{ij}) G_{p/2+m}(\eta_{ij}) \right. \\ &\quad \left. + a_2(\rho_{ij}) g_{p/2+m}(\eta_{ij}) G_{p/2+m}(\eta_{ij}) + a_3(\rho_{ij}) g_{p/2+m}^2(\eta_{ij}) \right].\end{aligned}$$

For details of coefficients  $a_1(\rho_{ij})$ ,  $a_2(\rho_{ij})$  and  $a_3(\rho_{ij})$ , see Seo [26].

From Theorem 3.1, the modified second order Bonferroni approximation to the generalized  $T_{\max}^2$  statistic is given by

$$(3.1) \quad t_M^2 = \frac{\nu p}{\nu - p + 1} F_{p, \nu-p+1} \left( \frac{\alpha + \beta(t_1^2)}{r} \right),$$

where

$$\beta(t_1^2) = \sum_{i=1}^{k-1} \sum_{j=i+1}^k \{A_0(\rho_{ij}) + \nu^{-1} A_1(\rho_{ij}) + \nu^{-2} A_2(\rho_{ij})\} + O(\nu^{-3}).$$

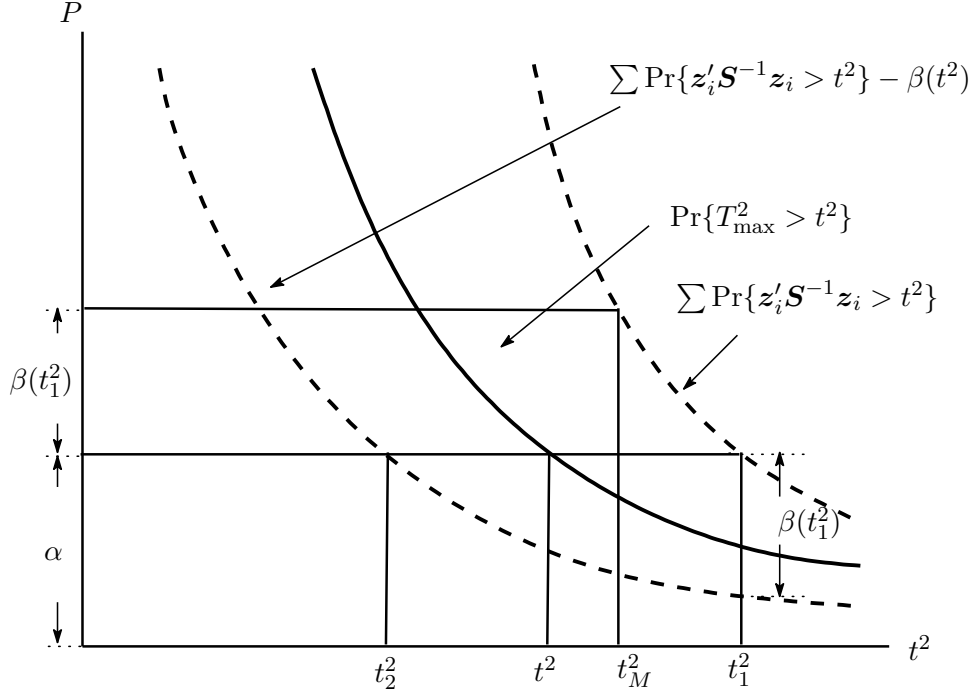


Figure 1: Illustration of the modified second order approximation

In the case of pairwise comparisons, we note that

$$\mathbb{B} = \mathbb{C} \equiv \{\mathbf{c} \in \mathbb{R}^k : \mathbf{c} = \mathbf{e}_i - \mathbf{e}_j, \ 1 \leq i < j \leq k\},$$

and  $r = k(k-1)/2$ .

**Theorem 3.2. (Seo [26])** *The modified second order approximation  $t_{M,p}^2$  for pairwise comparisons among the correlated mean vectors is given by (3.1) with  $r = k(k-1)/2$  and*

$$\rho_{ij} = \frac{\mathbf{c}_i' \mathbf{V} \mathbf{c}_j}{(\mathbf{c}_i' \mathbf{V} \mathbf{c}_i)^{1/2} (\mathbf{c}_j' \mathbf{V} \mathbf{c}_j)^{1/2}},$$

and then the approximate simultaneous confidence intervals are given by

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in [\mathbf{a}'(\hat{\boldsymbol{\mu}}_i - \hat{\boldsymbol{\mu}}_j) \pm t_{M,p} (d_{ij} \mathbf{a}' \mathbf{S} \mathbf{a})^{1/2}], \forall \mathbf{a} \in \mathbb{R}^p, \ 1 \leq i < j \leq k,$$

where  $d_{ij} = v_{ii} - 2v_{ij} + v_{jj}$ .

When  $\mathbf{V} = \mathbf{I}$ , the result in Theorem 3.2 can be reduced to the one in Seo and Siotani [31].

Next, in the case of comparisons with a control, we note that

$$\mathbb{B} = \mathbb{D} \equiv \{\mathbf{d} \in \mathbb{R}^k : \mathbf{d} = \mathbf{e}_i - \mathbf{e}_k, 1 \leq i \leq k-1\},$$

and  $r = k-1$ .

**Theorem 3.3. (Seo [26])** *The modified second order approximation  $t_{M.c}^2$  for comparisons among the correlated mean vectors with a control is given by (3.1) with  $r = k-1$  and*

$$\rho_{ij} = \frac{\mathbf{d}_i' \mathbf{V} \mathbf{d}_j}{(\mathbf{d}_i' \mathbf{V} \mathbf{d}_i)^{1/2} (\mathbf{d}_j' \mathbf{V} \mathbf{d}_j)^{1/2}},$$

and then the approximate simultaneous confidence intervals are given by

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) \in [\mathbf{a}'(\hat{\boldsymbol{\mu}}_i - \hat{\boldsymbol{\mu}}_k) \pm t_{M.c} (d_{ik} \mathbf{a}' \mathbf{S} \mathbf{a})^{1/2}], \forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i \leq k-1,$$

where  $d_{ik} = v_{ii} - 2v_{ik} + v_{kk}$ .

When  $\mathbf{V} = \mathbf{I}$ , the result in Theorem 3.3 can be reduced to the one in Seo and Siotani [32].

### 3.2. Multiple comparisons for high dimensional data

In this subsection, we will present the results for pairwise comparisons and comparisons with a control in high dimensional settings under  $k$  independent multivariate normal populations. It is well known that when the dimension is larger than the total sample size, the sample covariance matrix becomes singular, and hence it will be impossible to define Hotelling's  $T^2$ -type statistic. To tackle this problem efficiently, the Dempster trace criterion (D-criterion) for one and two samples can be used. The technique considered in the current study develops results derived in Dempster [4], [5]. A similar approach for multivariate linear hypotheses has been also discussed by Fujikoshi, Himeno and Wakaki [9], Himeno [12], Nishiyama et al. [22] and many other authors.

Let  $\mathbf{x}_j^{(i)}$  ( $j = 1, 2, \dots, N_i$ ,  $i = 1, 2, \dots, k$ ) be independently distributed as the  $p$ -dimensional normal distribution with mean vector  $\boldsymbol{\mu}_i$  and common covariance matrix  $\boldsymbol{\Sigma}$ . Let the  $i$ -th sample mean vector and the pooled sample covariance matrix be

$$\bar{\mathbf{x}}^{(i)} = \frac{1}{N_i} \sum_{j=1}^{N_i} \mathbf{x}_j^{(i)}, \quad \mathbf{S} = \frac{1}{n} \sum_{i=1}^k \sum_{j=1}^{N_i} (\mathbf{x}_j^{(i)} - \bar{\mathbf{x}}^{(i)})(\mathbf{x}_j^{(i)} - \bar{\mathbf{x}}^{(i)})',$$

respectively, where  $n = \sum_{i=1}^k N_i - k$ . To adjust the high-dimensional setting to the unbalanced case, we consider the following asymptotic frameworks:

$$(A1) \quad N_1, \dots, N_k, p \rightarrow \infty, \quad N_i \asymp p \quad (i = 1, \dots, k),$$

$$(A2) \quad \text{tr } \Sigma^i \asymp p \quad (i = 1, 2, \dots, 8),$$

where the notation “ $a \asymp b$ ” means that  $a = O(b)$  and  $b = O(a)$ . Now consider an example of  $\Sigma$  which satisfies the assumption (A2). The eigenvalues  $\lambda_1 \geq \dots \geq \lambda_p$  of covariance matrix  $\Sigma$  are assumed to obey the following model:

$$(M1) \quad \lambda_j = \alpha_j p^{\delta_j} \quad (j = 1, \dots, m) \text{ and } \lambda_\ell = c_\ell \quad (\ell = m + 1, \dots, p).$$

Here,  $\alpha_j (> 0)$ ,  $\delta_j$  ( $1/8 \geq \delta_1 \geq \dots \geq \delta_k > 0$ ) and  $c_\ell (> 0)$  are unknown constants preserving the ordering that  $\lambda_1 \geq \dots \geq \lambda_p$ , and  $m$  is an unknown positive integer.

In high dimensional case, for pairwise comparisons, the following  $D_{\max}$ -type test statistic based on D-criterion was proposed by Hyodo, Takahashi and Nishiyama [15]:

$$D_{\max \cdot p} = \max_{1 \leq i < j \leq k} \{D_{ij}\},$$

where

$$(3.2) \quad D_{ij} = \frac{p}{\hat{\sigma}} \left\{ \frac{(\mathbf{y}^{(i)} - \mathbf{y}^{(j)})'(\mathbf{y}^{(i)} - \mathbf{y}^{(j)})}{d_{ij} \text{tr } \mathbf{S}} - 1 \right\}.$$

Here,  $d_{ij} = 1/N_i + 1/N_j$ ,  $\mathbf{y}^{(\ell)} = \bar{\mathbf{x}}^{(\ell)} - \boldsymbol{\mu}_\ell$  ( $\ell = 1, 2, \dots, k$ ),  $\hat{\sigma} = \sqrt{2p\hat{a}_2/\hat{a}_1^2}$  and  $\hat{a}_i$ 's are the consistent estimators of  $a_i = \text{tr } \Sigma^i/p$ . Further, for comparisons with a control, the following statistic

$$D_{\max \cdot c} = \max_{1 \leq i \leq k-1} \{D_{ik}\},$$

where

$$(3.3) \quad D_{ik} = \frac{p}{\hat{\sigma}} \left\{ \frac{(\mathbf{y}^{(i)} - \mathbf{y}^{(k)})'(\mathbf{y}^{(i)} - \mathbf{y}^{(k)})}{d_{ik} \text{tr } \mathbf{S}} - 1 \right\}$$

was considered.

In Hyodo, Takahashi and Nishiyama [15], they derived the approximations for the upper percentiles of these statistics using the first order Bonferroni approximation procedure. After that Takahashi, et al. [41] gave an extension of the results by Hyodo, Takahashi and Nishiyama [15] to the unbalanced case. They also investigate the robustness of the extended multiple comparison procedures under non-normality. Their simulation results indicate that

the extended procedures appear to perform well for a number of non-normal distributions with high dimensional settings. We can thereby recommend the use of  $D_{\max}$ -type statistics for both pairwise comparisons and comparisons with a control for the unbalanced case with very small sample sizes and very high-dimensionality.

Consider the following simultaneous confidence intervals for mean vectors:

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[ \mathbf{a}'(\bar{\mathbf{x}}^{(i)} - \bar{\mathbf{x}}^{(j)}) \pm d_p \sqrt{d_{ij}(\text{tr } \mathbf{S})\mathbf{a}'\mathbf{a}} \right],$$

$$\forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i < j \leq k,$$

where  $d_p^2 = 1 + (\hat{\sigma}/p)z_p$  and  $z_p \equiv z_p(\alpha)$  is the upper  $100\alpha$  percentile of the  $D_{\max \cdot p}$  statistic. However, it is difficult to give the exact value of  $z_p$ . By applying Bonferroni's inequality to  $\Pr\{D_{\max \cdot p} > z_p\}$ , we get

$$\Pr\{D_{\max \cdot p} > z_p\} < \sum_{i=1}^{k-1} \sum_{j=i+1}^k \Pr\{D_{ij} > z_p\}.$$

We then define the first order Bonferroni approximation for  $z_p$  as such  $z_{1 \cdot p}$  which satisfies

$$\sum_{i=1}^{k-1} \sum_{j=i+1}^k \Pr\{D_{ij} > z_{1 \cdot p}\} = \alpha$$

for a given  $\alpha$ . The approximation of  $z_{1 \cdot p}$  is established based on the following results.

**Theorem 3.4. (Hyodo, Takahashi and Nishiyama [15])** *We assume (A1) and (A2). Then Cornish-Fisher expansion of the upper  $100\alpha$  percentile of  $D_{ij}$  is derived as*

$$\begin{aligned} z(\alpha, a_1, a_2, a_3, a_4) = & z_\alpha + \frac{1}{\sqrt{p}} \frac{\sqrt{2}a_3}{3\sqrt{a_2^3}}(z_\alpha^2 - 1) + \frac{1}{p} \left\{ \frac{a_4}{2a_2^2} z_\alpha(z_\alpha^2 - 3) \right. \\ & \left. - \frac{2a_3^2}{9a_2^3} z_\alpha(2z_\alpha^2 - 5) \right\} + \frac{1}{2n} z_\alpha + o(p^{-1}), \end{aligned}$$

where  $z_\alpha$  is the upper  $100\alpha$  percentile of the standard normal distribution.

In practice,  $a_i$ 's are unknown. Hence, to use the result of in Theorem 3.4, we need their estimators that are expected to be good in high-dimension setting. As sample counterparts of  $a_i$ 's, we use their consistent estimators derived in

Srivastava [39], Srivastava and Yanagihara [40] and Hyodo, Takahashi and Nishiyama [15] as

$$\begin{aligned}\hat{a}_1 &= \frac{\text{tr } \mathbf{S}}{p}, \quad \hat{a}_2 = \frac{n^2}{(n+2)(n-1)p} \left\{ \text{tr } \mathbf{S}^2 - \frac{(\text{tr } \mathbf{S})^2}{n} \right\}, \\ \hat{a}_3 &= \frac{n^4}{(n+4)(n+2)(n-1)(n-2)p} \left\{ \text{tr } \mathbf{S}^3 - \frac{3}{n} \text{tr } \mathbf{S}^2 \text{tr } \mathbf{S} + \frac{2}{n^2} (\text{tr } \mathbf{S})^3 \right\}, \\ \hat{a}_4 &= \frac{n^3}{(n+6)(n+4)(n+2)(n+1)(n-1)(n-2)(n-3)p} \\ &\quad \times \left[ b_1 \text{tr } \mathbf{S}^4 + b_2 \text{tr } \mathbf{S}^3 \text{tr } \mathbf{S} + b_3 (\text{tr } \mathbf{S}^2)^2 + b_4 \text{tr } \mathbf{S}^2 (\text{tr } \mathbf{S})^2 + b_5 (\text{tr } \mathbf{S})^4 \right]\end{aligned}$$

where

$$\begin{aligned}b_1 &= n^2(n^2 + n + 2), \quad b_2 = -4n(n^2 + n + 2), \quad b_3 = -n(2n^2 + 3n - 6), \\ b_4 &= 2n(5n + 6), \quad b_5 = -(5n + 6).\end{aligned}$$

The consistency of these estimators is guaranteed by the following theorem.

**Theorem 3.5.** *We assume (A1) and (A2). Then it holds that  $\hat{a}_i \xrightarrow{P} a_i$  ( $i = 1, 2, 3, 4$ ).*

By using Theorem 3.4 and consistent estimator of  $a_i$ 's, we can obtain the approximation of  $z_{1\cdot p}$  as  $\hat{z}_{1\cdot p} = z(\alpha_p, \hat{a}_1, \hat{a}_2, \hat{a}_3, \hat{a}_4)$ ,  $\alpha_p = \alpha/K$  and  $K = k(k-1)/2$ .

Also the simultaneous confidence intervals for comparisons with a control are given by

$$\begin{aligned}\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) &\in \left[ \mathbf{a}'(\bar{\mathbf{x}}^{(i)} - \bar{\mathbf{x}}^{(k)}) \pm d_c \sqrt{d_{ik}(\text{tr } \mathbf{S}) \mathbf{a}' \mathbf{a}} \right], \\ &\quad \forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i \leq k-1,\end{aligned}$$

where  $d_c^2 = 1 + (\hat{\sigma}/p)z_c$  and  $z_c \equiv z_c(\alpha)$  is the upper  $100\alpha$  percentile of the  $D_{\max \cdot c}$  statistic. Using Theorem 3.4 again, the estimator of  $z_c$  can be obtained as  $\hat{z}_{1\cdot c} = z(\alpha_c, \hat{a}_1, \hat{a}_2, \hat{a}_3, \hat{a}_4)$ , where  $\alpha_c = \alpha/(k-1)$ .

### 3.3. Multiple comparisons in elliptical populations

In this subsection, we will present the results for pairwise multiple comparisons and comparisons with a control among mean vectors under  $k$  independent

elliptical populations. For this case, in order to obtain conservative approximate simultaneous confidence intervals, Bonferroni's inequality is applied to  $T_{\max}^2$ -type statistic. In previous studies (Seo [28], Okamoto and Seo [25] and Okamoto [24]), two approximations based on Bonferroni's inequality have been proposed. The first order Bonferroni approximation becomes conservative too much when the number of populations or the kurtosis parameter is large. In such cases, we recommend to use the modified second order Bonferroni approximation instead of the first order Bonferroni approximation. Under elliptical populations with equal sample size, the first and the modified second order Bonferroni approximations are discussed by Seo [28]. For unequal sample sizes, the first order Bonferroni approximation is discussed by Okamoto and Seo [25]. In addition, Okamoto [24] proposed the modified second order Bonferroni approximation.

Let  $\mathbf{x}_1^{(j)}, \dots, \mathbf{x}_{N_j}^{(j)}$  ( $j = 1, \dots, k$ ) be  $N_j$  independent observations on  $\mathbf{x}^{(j)}$  that has an elliptical distribution with parameters  $\boldsymbol{\mu}_j (p \times 1)$  and  $\boldsymbol{\Lambda}^{(j)} (p \times p)$ , i.e.,  $E_p(\boldsymbol{\mu}_j, \boldsymbol{\Lambda}^{(j)})$  (see, e.g., Muirhead [20] and Fang, Kotz and Ng [8]). Here, its density function and characteristic function are

$$f(\mathbf{x}^{(j)}) = c_p^{(j)} |\boldsymbol{\Lambda}^{(j)}|^{-\frac{1}{2}} g_j((\mathbf{x}^{(j)} - \boldsymbol{\mu}_j)' \boldsymbol{\Lambda}^{(j)-1} (\mathbf{x}^{(j)} - \boldsymbol{\mu}_j))$$

for some non-negative function  $g_j$ , where  $c_p^{(j)}$  is a normalizing constant and  $\boldsymbol{\Lambda}^{(j)}$  is a positive definite matrix, and

$$\phi(\mathbf{t}) = \exp(i\mathbf{t}'\boldsymbol{\mu}_j) \psi(\mathbf{t}'\boldsymbol{\Lambda}^{(j)}\mathbf{t})$$

for some function  $\psi$ , where  $i = \sqrt{-1}$ , respectively. Note that  $E[\mathbf{x}^{(j)}] = \boldsymbol{\mu}_j$  and  $\text{Cov}[\mathbf{x}^{(j)}] = \boldsymbol{\Sigma}^{(j)} = -2\psi'(0)\boldsymbol{\Lambda}^{(j)}$ . We also define the kurtosis parameter by  $\kappa = \{\psi''(0)/(\psi'(0))^2\} - 1$ . Elliptical distributions include the multivariate normal, the multivariate  $t$ , the contaminated normal distributions and so on.

We assume that the following conditions:

$$\begin{aligned} \text{(C1)} \quad & \boldsymbol{\Sigma} = \boldsymbol{\Sigma}^{(1)} = \dots = \boldsymbol{\Sigma}^{(k)}, \\ \text{(C2)} \quad & E[\|\mathbf{x}^{(j)}\|^8] < \infty \quad (j = 1, \dots, k), \\ \text{(C3)} \quad & \lim_{\|\mathbf{t}\| \rightarrow \infty} \sup |E[\exp(i\mathbf{t}'\mathbf{d}^{(j)})]| < 1 \quad (j = 1, \dots, k), \end{aligned}$$

where  $\mathbf{d}^{(j)} = (x_1^{(j)}, \dots, x_p^{(j)}, x_1^{(j)2}, \dots, x_p^{(j)2})$  ( $j = 1, \dots, k$ ). Now consider simultaneous confidence intervals for pairwise multiple comparisons among mean vectors with the confidence level  $1 - \alpha$ :

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_j) \in \left[ \mathbf{a}'(\bar{\mathbf{x}}^{(i)} - \bar{\mathbf{x}}^{(j)}) \pm t_p \sqrt{d_{ij} \mathbf{a}' S \mathbf{a}} \right], \forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i < j \leq k,$$



where  $d_{ij} = 1/N_i + 1/N_j$  and  $t_p^2 \equiv t_p^2(\alpha)$  is the upper  $100\alpha$  percentile of  $T_{\max \cdot p}^2$  statistic defined by

$$T_{\max \cdot p}^2 = \max_{1 \leq i < j \leq k} \{T_{ij}^2\},$$

where

$$T_{ij}^2 = d_{ij}^{-1}(\mathbf{y}^{(i)} - \mathbf{y}^{(j)})' S^{-1}(\mathbf{y}^{(i)} - \mathbf{y}^{(j)}),$$

and  $\mathbf{y}^{(\ell)} = \bar{\mathbf{x}}^{(\ell)} - \boldsymbol{\mu}_\ell$  ( $\ell = 1, \dots, k$ ). In order to construct simultaneous confidence intervals, it is required to obtain the upper percentiles of  $T_{\max}^2$ -type statistic, i.e.  $t_p$ . At first we will introduce the first order Bonferroni approximation. We note that the statistic  $T_{ij}^2$  is reduced to the Hotelling's  $T^2$ -type statistic ( $F$  statistic) under normality. However, under the class of the elliptical distributions,  $T_{ij}^2$  is no longer an  $F$  statistic, and hence the first order approximation cannot be exactly expressed as the upper percentiles of  $F$  distribution. Therefore Okamoto and Seo [25] derived an asymptotic expansion for the first order Bonferroni approximations of  $t_p$ :

$$\begin{aligned} t_{1, \chi^2}^2(\alpha) &= \chi_p^2\left(\frac{\alpha}{K}\right) - \frac{1}{2NK} \chi_p^2\left(\frac{\alpha}{K}\right) \\ &\quad \times \sum_{\ell=1}^{k-1} \sum_{m=\ell+1}^k \left\{ \frac{1}{p} c_{\ell m}^{(0)} - \frac{1}{p(p+2)} c_{\ell m}^{(2)} \chi_p^2\left(\frac{\alpha}{K}\right) \right\}, \\ t_{1, F}^2(\alpha) &= \frac{np}{n-p+1} F_{p, n-p+1}\left(\frac{\alpha}{K}\right) - \frac{1}{2NK} \chi_p^2\left(\frac{\alpha}{K}\right) \\ &\quad \times \sum_{\ell=1}^{k-1} \sum_{m=\ell+1}^k \left\{ \left( \frac{1}{p} c_{\ell m}^{(0)} + sp \right) - \left( \frac{1}{p(p+2)} c_{\ell m}^{(2)} - s \right) \chi_p^2\left(\frac{\alpha}{K}\right) \right\}, \end{aligned}$$

where  $N = \max\{N_1, \dots, N_k\}$ ,  $K = k(k-1)/2$ ,  $s = 1/(\sum_{\ell=1}^k r_\ell)$  and  $r_\ell = N_\ell/N$ . Also,  $\chi_p(\alpha)$  denotes upper  $100\alpha$  percentile of chi-square distribution with  $p$  d.f. and  $F_{p, n-p+1}(\alpha)$  denotes upper  $100\alpha$  percentile of  $F$  distribution with  $p$  and  $n-p+1$  d.f.'s. For details of coefficients  $c_{\ell m}^{(0)}$  and  $c_{\ell m}^{(2)}$ , see Okamoto and Seo [25].

Next, we will introduce the modified second order Bonferroni approximation. Letting  $\mathbf{z}^{(\ell)} = \sqrt{N_\ell}(\bar{\mathbf{x}}^{(\ell)} - \boldsymbol{\mu}_\ell)$  for  $\ell = 1, \dots, k$  and  $w_{ij} = \sqrt{r_j/(r_i + r_j)}$ . And let  $\mathbf{y}_1 = w_{12}\mathbf{z}^{(1)} - w_{21}\mathbf{z}^{(2)}$ ,  $\mathbf{y}_2 = w_{13}\mathbf{z}^{(1)} - w_{31}\mathbf{z}^{(3)}$ ,  $\dots$ ,  $\mathbf{y}_K = w_{k-1, k}\mathbf{z}^{(k-1)} - w_{k, k-1}\mathbf{z}^{(k)}$ . Then the modified second order Bonferroni approximation  $t_M^2$  is defined as a critical value that satisfies the equality

$$\sum_{i=1}^K \Pr(\mathbf{y}_i' S^{-1} \mathbf{y}_i > t_M^2) = \alpha + \beta(t_1^2).$$

In order to derive the modified second order Bonferroni approximation, two cases of joint probabilities:

$$\begin{aligned}\beta_{1 \cdot ij\ell m}(t_1^2) &= \Pr(T_{ij}^2 > t_1^2, T_{\ell m}^2 > t_1^2), \\ \beta_{2 \cdot ij\ell}(t_1^2) &= \Pr(T_{i\ell}^2 > t_1^2, T_{j\ell}^2 > t_1^2)\end{aligned}$$

are needed to evaluate under the elliptical populations. Here, index  $i, j, \ell, m$  are all distinct. In general, it is difficult to obtain the exact value of these probabilities. Okamoto [24] derived asymptotic expansions for these probabilities.

**Theorem 3.6. (Okamoto [24])** *Assume that (C1)-(C3). Then it holds that*

$$\begin{aligned}\beta_{1 \cdot ij\ell m}(t_1^2) &= G_{\frac{p}{2}}^2(\eta_1) + \frac{1}{N} \left( c_1 g_{\frac{p}{2}}(\eta_1) G_{\frac{p}{2}}(\eta_1) + c_2 g_{\frac{p}{2}}^2(\eta_1) \right) + o(N^{-1}), \\ \beta_{2 \cdot ij\ell}(t_1^2) &= (1 - v_0)^{\frac{p}{2}} \sum_{m=0}^{\infty} \frac{(\frac{1}{2}p)_m}{m!} v_0^m \\ &\quad \times \left\{ G_{\frac{p}{2}+m}(\eta_2) + \frac{1}{N} \left( d_1 g_{\frac{p}{2}+m}(\eta_2) G_{\frac{p}{2}+m}(\eta_2) + d_2 g_{\frac{p}{2}+m}^2(\eta_2) \right) \right\} + o(N^{-1}),\end{aligned}$$

where

$$\begin{aligned}\eta_1 &= \frac{1}{2}t_1^2, \quad \eta_2 = \frac{1}{2(1-v_0)}t_1^2, \\ G_{\frac{p}{2}}(\eta_1) &= \int_{\eta_1}^{\infty} g_{\frac{p}{2}}(t)dt, \quad G_{\frac{p}{2}+m}(\eta_2) = \int_{\eta_2}^{\infty} g_{\frac{p}{2}+m}(t)dt, \\ g_{\frac{p}{2}}(t) &= \frac{1}{\Gamma(\frac{p}{2})}t^{\frac{p}{2}-1}e^{-t}, \quad g_{\frac{p}{2}+m}(t) = \frac{1}{\Gamma(\frac{p}{2}+m)}t^{\frac{p}{2}+m-1}e^{-t}.\end{aligned}$$

For details of coefficients  $c_1, c_2, d_1, d_2$  and  $v_0$ , see Okamoto [24]. We note that, when sample sizes are all same, the result in Theorem 3.6 can be reduced to the one in Seo [28].

By using Theorem 3.6, Okamoto [24] proposed the modified second order Bonferroni approximations which are obtained as following form:

$$\begin{aligned}t_{M \cdot \chi^2}^2(\alpha) &= \chi_p^2(\gamma) - \frac{1}{2NK} \chi_p^2(\gamma) \\ &\quad \times \sum_{\ell=1}^{k-1} \sum_{m=\ell+1}^k \left( \frac{1}{p} c_{\ell m}^{(0)} - \frac{1}{p(p+2)} c_{\ell m}^{(2)} \chi_p^2(\gamma) \right), \\ t_{M \cdot F}^2(\alpha) &= \frac{np}{n-p+1} F_{p, n-p+1}(\gamma) - \frac{1}{2NK} \chi_p^2(\gamma) \\ &\quad \times \sum_{\ell=1}^{k-1} \sum_{m=\ell+1}^k \left\{ \left( \frac{1}{p} c_{\ell m}^{(0)} + sp \right) - \left( \frac{1}{p(p+2)} c_{\ell m}^{(2)} - s \right) \chi_p^2(\gamma) \right\},\end{aligned}$$

where

$$\gamma = \frac{1}{K} \left( \alpha + \sum_{\substack{i \neq j \neq \ell \neq m, \\ i \neq \ell, i \neq m, j \neq m}}^k \beta_{1 \cdot ij\ell m}(t_1^2) + \sum_{i \neq j \neq \ell, i \neq \ell}^k \beta_{2 \cdot ij\ell}(t_1^2) \right).$$

In the case of comparisons with a control, letting the  $k$ -th population be a control, the simultaneous confidence intervals are given by

$$\mathbf{a}'(\boldsymbol{\mu}_i - \boldsymbol{\mu}_k) \in \left[ \mathbf{a}'(\bar{\mathbf{x}}^{(i)} - \bar{\mathbf{x}}^{(k)}) \pm t_c \sqrt{d_{ik} \mathbf{a}' S \mathbf{a}} \right], \forall \mathbf{a} \in \mathbb{R}^p, 1 \leq i \leq k-1,$$

and the value  $t_c^2 \equiv t_c^2(\alpha)$  is chosen to satisfy

$$\Pr \{T_{\max \cdot c}^2 > t_c^2\} = \alpha,$$

where

$$\begin{aligned} T_{\max \cdot c}^2 &= \max_{1 \leq i \leq k-1} \{T_{ik}^2\}, \\ T_{ik}^2 &= d_{ik}^{-1}(\mathbf{y}^{(i)} - \mathbf{y}^{(k)})' S^{-1}(\mathbf{y}^{(i)} - \mathbf{y}^{(k)}). \end{aligned}$$

The approximate simultaneous confidence intervals for comparisons with a control are also given based on the same principle. Okamoto and Seo [25] derived the first order Bonferroni approximation of  $t_c$ :

$$\begin{aligned} t_{1, \chi^2 \cdot c}^2(\alpha) &= \chi_p^2 \left( \frac{\alpha}{k-1} \right) - \frac{1}{2N(k-1)} \chi_p^2 \left( \frac{\alpha}{k-1} \right) \\ &\quad \times \sum_{\ell=1}^{k-1} \left\{ \frac{1}{p} c_{\ell k}^{(0)} - \frac{1}{p(p+2)} c_{\ell k}^{(2)} \chi_p^2 \left( \frac{\alpha}{k-1} \right) \right\}, \\ t_{1, F \cdot c}^2(\alpha) &= \frac{np}{n-p+1} F_{p, n-p+1} \left( \frac{\alpha}{k-1} \right) - \frac{1}{2N(k-1)} \chi_p^2 \left( \frac{\alpha}{k-1} \right) \\ &\quad \times \sum_{\ell=1}^{k-1} \left\{ \left( \frac{1}{p} c_{\ell k}^{(0)} + sp \right) - \left( \frac{1}{p(p+2)} c_{\ell k}^{(2)} - s \right) \chi_p^2 \left( \frac{\alpha}{k-1} \right) \right\}. \end{aligned}$$

In addition, Okamoto [24] proposed the modified second order Bonferroni ap-

proximation of  $t_c$ :

$$\begin{aligned} t_{M \cdot \chi^2 \cdot c}^2(\alpha) &= \chi_p^2(\gamma_c) - \frac{1}{2N(k-1)} \chi_p^2(\gamma_c) \\ &\quad \times \sum_{\ell=1}^{k-1} \left( \frac{1}{p} c_{\ell k}^{(0)} - \frac{1}{p(p+2)} c_{\ell k}^{(2)} \chi_p^2(\gamma_c) \right), \\ t_{M \cdot F \cdot c}^2(\alpha) &= \frac{np}{n-p+1} F_{p, n-p+1}(\gamma_c) - \frac{1}{2N(k-1)} \chi_p^2(\gamma_c) \\ &\quad \times \sum_{\ell=1}^{k-1} \left\{ \left( \frac{1}{p} c_{\ell k}^{(0)} + sp \right) - \left( \frac{1}{p(p+2)} c_{\ell k}^{(2)} - s \right) \chi_p^2(\gamma_c) \right\}, \end{aligned}$$

$$\text{where } \gamma_c = \left( \alpha + \sum_{i \neq j \neq \ell, i \neq \ell}^k \beta_{2 \cdot ij\ell}(t_1^2) \right) / (k-1).$$

#### §4. Concluding remarks

In this paper, we concerned with multivariate multiple comparisons among mean vectors and introduced some results of this topic.

It is well known that, in general, finding the exact value of the upper  $100\alpha$  percentile of  $T_{\max}^2$ -type statistic is difficult even the cases of pairwise comparisons and comparisons with a control. Then Siotani [33], Seo and Siotani [31], [32] and Seo [26] proposed approximation procedures based on Bonferroni's inequality and they gave large sample approximations based on asymptotic expansion for the upper percentiles of  $T_{\max}^2$ -type statistic under normality. Also, these approximation procedures have been discussed under class of elliptical distributions by Seo [28], Okamoto and Seo [25] and Okamoto [24], and under general distributions discussed by Kakizawa [16]. Recently, for high-dimensional data, Takahashi et al. [41] and Hyodo, Takahashi and Nishiyama [15] proposed a test procedure for multiple comparisons among mean vectors under multivariate normality.

On the other hand, Seo, Mano and Fujikoshi [29] proposed the multivariate Tukey-Kramer procedure (MTK procedure) which is a simple procedure by replacing with the upper percentile of the  $R_{\max}^2$  statistic as an approximation to the one of  $T_{\max}^2$  type statistic for any positive definite matrix  $\mathbf{V}$ . For the MTK procedure, the multivariate version of the generalized Tukey conjecture has been affirmatively proved in the case of three and four correlated mean vectors by Seo, Mano and Fujikoshi [29] and Nishiyama and Seo [23], respectively. Further, relating to the conjecture, Seo [27], Seo and Nishiyama [30] and Nishiyama and Seo [23] gave the upper bound for conservativeness

of the MTK procedure. In the case of comparisons with a control, concerning to the MTK procedure, similar conservative approximate simultaneous confidence procedure has been proposed and discussed its properties (see, Seo [26], Seo and Nishiyama [30] and Nishiyama [21]). It is important to prove these conjectures. However, it is difficult to prove completely. So, we left as a future problem.

For details of proofs of theorems and numerical results for the procedures which introduced in this paper, see each article.

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