

Working Paper SERIES

Date April 3, 2013

WP # 0017MSS-253-2013

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Abstract

In this article we develop a new test statistic for testing the equality of mean vectors for paired doubly multivariate observations for q response variables and u sites in blocked compound symmetric covariance matrix setting. The new testing is implemented with two real data sets.

Keywords Blocked compound symmetry; Paired doubly multivariate data; a natural extension of the Hotelling's T^2 statistic.

JEL Classification: C12

1 Introduction

In this article we develop a statistical method for testing the equality of mean vectors for paired doubly multivariate or paired two-level multivariate observations, where more than one response variable (q) is measured on each experimental unit on more than one site (u) in two separate time points. It is very common in clinical trial study to collect measurements on more than one response variable at different body positions at two different time points on the same group of people to test the effectiveness of a medicine or any dietary supplement. Hotelling's T^2 statistic is the conventional method to test the equality of mean vectors. However, Hotelling's T^2 statistic

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is based on the unbiased estimate of the unstructured variance-covariance matrix. Nevertheless, when the data is doubly multivariate, variance-covariance matrix may have some structure, and one should use an unbiased estimate of that structure to test the equality of mean vectors. In this article we obtain a natural extension of the Hotelling's T^2 statistic, the RL statistic, which uses an unbiased estimate of the structured variance-covariance matrix that is present in a data set.

Osteoporosis or porous bone is an age-related disorder involving in a progressive decrease in bone mass due to the loss of minerals - mainly calcium. As a result, bones become weakened and more susceptible to fractures. In a person with severe osteoporosis, fractures can occur from lifting even light objects, or from falls that would not even bruise or injure the average person. Currently it is estimated that one of every four post-menopausal women has osteoporosis. Although it is more common in white or Asian women older than 50 years, osteoporosis can occur in almost any person at any age: osteoporosis is not just an 'old womans disease'. In fact, more than 2 million American men have osteoporosis. The estimated national cost for osteoporosis and related injuries is \$14 billion each year in the United States. Fortunately, we can do several things to ensure that bones are not at risk for these men and women. Numerous studies have shown a positive relationship between exercise or dietary supplement, and building stronger bones- at every stage of a man's and woman's life. Some specific exercise or dietary supplement tend to increase bone mineral content and mass (Starnes et al., 2012). Suppose an investigator measures the mineral content of three bones, radius, humerus and ulna ($q = 3$) by photon absorptiometry to examine whether a particular dietary supplement would slow the bone loss in older women. All three measurements are recorded on the dominant and non-dominant sides ($u = 2$) for each woman. These doubly multivariate measurements are taken on 24 women. The bone mineral contents for all these 24 women are also measured after one year of their participation in the experimental program to test whether this particular dietary supplement reverse the bone loss in these women in one year.

In another example of a bone densitometry study where bone mineral density (BMD) are obtained from 12 patients. On each femoral (right and left femoral, $u = 2$) two BMD measure-

ments ($q = 2$) are taken, one at the femoral neck and the other one at the trochanter region. These four measurements are also observed on each of these 12 patients after two years to test whether the BMD is lower in these patients in two years to diagnose if the patients are at risk for osteopenia.

In this article we assume the doubly multivariate observations have a blocked compound symmetry (BCS) covariance structure (Rao, 1945, 1953). Different sites may have different measurement variations for the variables, and we must take these variations into account while analyzing doubly multivariate data. Roy and Leiva (2011) have observed advantages of using this BCS structure over the usual unstructured variance-covariance matrix while analyzing doubly multivariate data. The main advantage of using BCS structure over unstructured variance-covariance matrix is that the number of unknown parameters declines substantially; thus helps in analyzing the data in small sample set-up in expensive clinical trials. However, testing the validity of this BCS covariance structure (Roy and Leiva, 2011) is crucial before using it for any statistical analysis. A BCS structure can be written as

$$\begin{aligned} \mathbf{\Gamma} &= \begin{bmatrix} \mathbf{\Sigma}_0 & \mathbf{\Sigma}_1 & \dots & \mathbf{\Sigma}_1 \\ \vdots & \ddots & & \vdots \\ \vdots & & \ddots & \vdots \\ \mathbf{\Sigma}_1 & \mathbf{\Sigma}_1 & \dots & \mathbf{\Sigma}_0 \end{bmatrix} \\ &= \mathbf{I}_u \otimes (\mathbf{\Sigma}_0 - \mathbf{\Sigma}_1) + \mathbf{J}_u \otimes \mathbf{\Sigma}_1, \end{aligned} \tag{1.1}$$

where \mathbf{I}_u is the $u \times u$ identity matrix, $\mathbf{1}_u$ is a $u \times 1$ vector of ones, $\mathbf{J}_u = \mathbf{1}_u \mathbf{1}'_u$ and \otimes represents the Kronecker product. We assume $\mathbf{\Sigma}_0$ is a positive definite symmetric $q \times q$ matrix, $\mathbf{\Sigma}_1$ is a symmetric $q \times q$ matrix, and the constraints $-\frac{1}{u-1}\mathbf{\Sigma}_0 < \mathbf{\Sigma}_1$ and $\mathbf{\Sigma}_1 < \mathbf{\Sigma}_0$, which mean that $\mathbf{\Sigma}_0 - \mathbf{\Sigma}_1$ and $\mathbf{\Sigma}_0 + (u-1)\mathbf{\Sigma}_1$ are positive definite matrices, so that the $qu \times qu$ matrix $\mathbf{\Gamma}$ is positive definite (for a proof, see Lemma 2.1 in Roy and Leiva (2011)). The $q \times q$ block diagonals $\mathbf{\Sigma}_0$ in $\mathbf{\Gamma}$ represent the variance-covariance matrix of the q response variables at any given site, whereas the $q \times q$ block off diagonals $\mathbf{\Sigma}_1$ in $\mathbf{\Gamma}$ represent the covariance matrix of the q response variables between any two sites. We also assume that $\mathbf{\Sigma}_0$ is constant for all sites and $\mathbf{\Sigma}_1$ is constant for all site pairs. The matrix $\mathbf{\Gamma}$ is also known as equicorrelated partitioned matrix with equicorrelation matrices $\mathbf{\Sigma}_0$ and $\mathbf{\Sigma}_1$ (Leiva, 2007; Roy and Leiva, 2008).

Let $\mathbf{y}_{r,s}$ be a q -variate vector of measurements on the r^{th} individual at the s^{th} site; $r = 1, \dots, n$, $s = 1, \dots, u$. The n individuals are all independent. Let $\mathbf{y}_r = (\mathbf{y}'_{r,1}, \dots, \mathbf{y}'_{r,u})'$ be the uq -variate vector of all measurements corresponding to the r^{th} individual. Finally, let $\mathbf{y}_1, \mathbf{y}_2, \dots, \mathbf{y}_n$ be a random sample of size n drawn from the population $N_{uq}(\boldsymbol{\mu}_y, \mathbf{I}_u \otimes (\boldsymbol{\Sigma}_{y0} - \boldsymbol{\Sigma}_{y1}) + \mathbf{J}_u \otimes \boldsymbol{\Sigma}_{y1})$, where $\boldsymbol{\mu}_y \in \mathbb{R}^{uq}$ and $\mathbf{I}_u \otimes (\boldsymbol{\Sigma}_{y0} - \boldsymbol{\Sigma}_{y1}) + \mathbf{J}_u \otimes \boldsymbol{\Sigma}_{y1}$ is assumed to be a $uq \times uq$ positive definite matrix. Thus, the number of unknown parameters to be estimated is only $q(q+1)$ in comparison to the number of unknown parameters $uq(uq+1)/2$ in an unstructured variance-covariance matrix $\boldsymbol{\Omega}$. Suppose $\mathbf{x}_{r,s}$ be the corresponding q -variate vector of measurements on the r^{th} individual at the s^{th} site; $r = 1, \dots, n$, $s = 1, \dots, u$ after a time gap or after a treatment of the same n independent individuals. We stack all the q responses by sites as before and assume $\mathbf{x} \sim N_{uq}(\boldsymbol{\mu}_x, \mathbf{I}_u \otimes (\boldsymbol{\Sigma}_{x0} - \boldsymbol{\Sigma}_{x1}) + \mathbf{J}_u \otimes \boldsymbol{\Sigma}_{x1})$. Therefore, we see that \mathbf{x} and \mathbf{y} are correlated. Let $\mathbf{d} = \mathbf{y} - \mathbf{x}$. Here we assume the natural pairing of the doubly multivariate

Table 1 Data Structure

Pair number	Before treatment	After treatment	Difference $\mathbf{d}_r = \mathbf{y}_r - \mathbf{x}_r$
1	\mathbf{y}_1	\mathbf{x}_1	\mathbf{d}_1
2	\mathbf{y}_2	\mathbf{x}_2	\mathbf{d}_2
\vdots	\vdots	\vdots	\vdots
n	\mathbf{y}_n	\mathbf{x}_n	\mathbf{d}_n

observations on each individual. Thus, $\mathbf{y}_{r,s}$ is paired with $\mathbf{x}_{r,s}$ for all $s = 1, \dots, u$. That is, \mathbf{y}_r from the first set of samples is paired with \mathbf{x}_r from the second set of samples, $r = 1, 2, \dots, n$. The situation is described in Table 1.

2 The Hypothesis

We want to test the equality of the mean vectors by considering the data as doubly multivariate and has BCS structure (1.1). That is, we want to test the following hypothesis

$$H_0 : \boldsymbol{\mu}_y = \boldsymbol{\mu}_x, \quad \text{vs.} \quad H_1 : \boldsymbol{\mu}_y \neq \boldsymbol{\mu}_x. \quad (2.2)$$

We assume that $n > uq$. As \mathbf{y} and \mathbf{x} are correlated and have a multivariate normal distribution:

$$\begin{pmatrix} \mathbf{y} \\ \mathbf{x} \end{pmatrix} \sim N_{2uq} \left[\begin{pmatrix} \boldsymbol{\mu}_y \\ \boldsymbol{\mu}_x \end{pmatrix}, \begin{pmatrix} \boldsymbol{\Sigma}_{yy} & \boldsymbol{\Sigma}_{yx} \\ \boldsymbol{\Sigma}_{xy} & \boldsymbol{\Sigma}_{xx} \end{pmatrix} \right],$$

where

$$\begin{pmatrix} \Sigma_{yy} & \Sigma_{yx} \\ \Sigma_{xy} & \Sigma_{xx} \end{pmatrix} = \begin{bmatrix} \mathbf{I}_u \otimes (\Sigma_{\mathbf{y}}^0 - \Sigma_{\mathbf{y}}^1) + \mathbf{J}_u \otimes \Sigma_{\mathbf{y}}^1 & \mathbf{J}_u \otimes \mathbf{W} \\ \mathbf{J}_u \otimes \mathbf{W} & \mathbf{I}_u \otimes (\Sigma_{\mathbf{x}}^0 - \Sigma_{\mathbf{x}}^1) + \mathbf{J}_u \otimes \Sigma_{\mathbf{x}}^1 \end{bmatrix},$$

where \mathbf{W} is a $q \times q$ symmetric matrix. It represents the covariance among q responses before and after a treatment for each site, and we assume this covariance is constant for all site pairs. Straightway the above hypothesis (2.2) is equivalent to test

$$H_o : \boldsymbol{\mu}_d = \mathbf{0}, \quad \text{vs.} \quad H_1 : \boldsymbol{\mu}_d \neq \mathbf{0}, \quad (2.3)$$

where $\boldsymbol{\mu}_d = \text{E}(\mathbf{y} - \mathbf{x}) = \boldsymbol{\mu}_y - \boldsymbol{\mu}_x$. Now to estimate $\text{Cov}(\mathbf{y} - \mathbf{x}) = \Sigma_{yy} - \Sigma_{yx} - \Sigma_{xy} + \Sigma_{xx}$, we need the estimates of $q \times q$ matrices $\Sigma_{\mathbf{y}}^1, \Sigma_{\mathbf{y}}^0, \Sigma_{\mathbf{x}}^1, \Sigma_{\mathbf{x}}^0$ and \mathbf{W} . However, by reparameterization we can resolve this problem of estimating so many matrices as shown in the following section.

2.1 An Alternative Formulation of the Problem

The above hypothesis testing problem can be formulated in an alternative way by reparametrizing the variance-covariance matrix $\text{Cov}(\mathbf{y} - \mathbf{x})$. Now $\mathbf{d}_1, \mathbf{d}_2, \dots, \mathbf{d}_n$ are independent and identically distributed (i.i.d.) $N_{uq}(\boldsymbol{\delta}; \boldsymbol{\Gamma})$ where $\boldsymbol{\delta} = \boldsymbol{\mu}_d = \text{E}(\mathbf{y} - \mathbf{x}) = \boldsymbol{\mu}_y - \boldsymbol{\mu}_x$, and

$$\begin{aligned} \boldsymbol{\Gamma} = \text{Cov}(\mathbf{d}) &= \text{Cov}(\mathbf{y} - \mathbf{x}) \\ &= \Sigma_{yy} - \Sigma_{yx} - \Sigma_{xy} + \Sigma_{xx} \\ &= \mathbf{I}_u \otimes (\boldsymbol{\Gamma}_0 - \boldsymbol{\Gamma}_1) + \mathbf{J}_u \otimes \boldsymbol{\Gamma}_1, \end{aligned}$$

where

$$\boldsymbol{\Gamma}_0 = \Sigma_{\mathbf{y}}^0 + \Sigma_{\mathbf{x}}^0 - 2\mathbf{W}, \quad (2.4)$$

and

$$\boldsymbol{\Gamma}_1 = \Sigma_{\mathbf{y}}^1 + \Sigma_{\mathbf{x}}^1 - 2\mathbf{W}. \quad (2.5)$$

Thus, instead of deriving the estimates of $\Sigma_{\mathbf{y}}^1, \Sigma_{\mathbf{y}}^0, \Sigma_{\mathbf{x}}^1, \Sigma_{\mathbf{x}}^0$ and \mathbf{W} , it is sufficient to derive the estimates of $\boldsymbol{\Gamma}_0$ and $\boldsymbol{\Gamma}_1$ from the random samples $\mathbf{d}_1, \mathbf{d}_2, \dots, \mathbf{d}_n$.

2.2 Matrix Result

If $\Gamma_0 - \Gamma_1 = (\Sigma_y^0 - \Sigma_y^1) + (\Sigma_x^0 - \Sigma_x^1)$ and $\Gamma_0 + (u-1)\Gamma_1 = (\Sigma_y^0 + (u-1)\Sigma_y^1) + (\Sigma_x^0 + (u-1)\Sigma_x^1) - 2u\mathbf{W}$ are invertible matrices, then Γ^{-1} exists and is given by

$$\Gamma^{-1} = \mathbf{I}_u \otimes \mathbf{A} + \mathbf{J}_u \otimes \mathbf{B},$$

where

$$\mathbf{A} = (\Gamma_0 - \Gamma_1)^{-1}$$

and

$$\mathbf{B} = \frac{1}{u} \left[(\Gamma_0 + (u-1)\Gamma_1)^{-1} - (\Gamma_0 - \Gamma_1)^{-1} \right].$$

This result generalizes the one given by Bertlett (1951) for the case $q = 1$.

3 An Unbiased Estimate of Γ

To find an unbiased estimate of the BCS structure Γ we first need to find unbiased estimates of Γ_0 and Γ_1 . Now, the $uq \times 1$ vectors $\mathbf{d}_1, \mathbf{d}_2, \dots, \mathbf{d}_n$ are i.i.d. $N_{uq}(\boldsymbol{\delta}; \Gamma)$ where $\boldsymbol{\delta} = \boldsymbol{\mu}_d = \boldsymbol{\mu}_y - \boldsymbol{\mu}_x$, and $\Gamma = \text{Cov}(\mathbf{d}) = \mathbf{I}_u \otimes (\Gamma_0 - \Gamma_1) + \mathbf{J}_u \otimes \Gamma_1$ with Γ_0 and Γ_1 are defined in (2.4) and (2.5) respectively. For each fixed r , we consider the vectors \mathbf{d}_r and $\boldsymbol{\delta}$ be partitioned in u subvectors as $\mathbf{d}_r = (\mathbf{d}'_{r,1}, \dots, \mathbf{d}'_{r,u})'$ and $\boldsymbol{\delta} = (\boldsymbol{\delta}'_1, \dots, \boldsymbol{\delta}'_u)'$. Similarly, $\bar{\mathbf{d}} = (\bar{\mathbf{d}}'_1, \dots, \bar{\mathbf{d}}'_u)'$ with $\bar{\mathbf{d}}_s = \frac{1}{n} \sum_{r=1}^n \mathbf{d}_{r,s}$ for $s = 1, \dots, u$. The equicorrelated hypothesis of Γ assures that

$$\text{E} [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s)(\mathbf{d}_{r,s^*} - \boldsymbol{\delta}_{s^*})'] = \begin{cases} \Gamma_0 & \text{if } s = s^* \\ \Gamma_1 & \text{if } s \neq s^*, \end{cases}$$

and

$$\begin{aligned} \text{E} [(\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s)(\bar{\mathbf{d}}_{s^*} - \boldsymbol{\delta}_{s^*})'] &= \text{E} \left[\left[\left(\frac{1}{n} \sum_{r=1}^n \mathbf{d}_{r,s} \right) - \boldsymbol{\delta}_s \right] \left[\left(\frac{1}{n} \sum_{r^*=1}^n \mathbf{d}_{r^*,s^*} \right) - \boldsymbol{\delta}_{s^*} \right]' \right] \\ &= \frac{1}{n^2} \sum_{r=1}^n \text{E} [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s)(\mathbf{d}_{r,s^*} - \boldsymbol{\delta}_{s^*})'] \\ &= \begin{cases} \frac{1}{n} \Gamma_0 & \text{if } s = s^* \\ \frac{1}{n} \Gamma_1 & \text{if } s \neq s^*, \end{cases} \end{aligned}$$

because $\mathbf{d}_{r,s}$ and \mathbf{d}_{r^*,s^*} are independent if $r \neq r^*$. Now,

$$\begin{aligned} \mathbf{C}_0 &= \sum_{s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s) (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s)' \\ &= \sum_{s=1}^u \sum_{r=1}^n [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) - (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s)] [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) - (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s)]' \\ &= \sum_{s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) (\mathbf{d}_{r,s} - \boldsymbol{\delta}_s)' - \sum_{s=1}^u n (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s) (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s)', \end{aligned}$$

then

$$\begin{aligned} \mathbb{E}[\mathbf{C}_0] &= \sum_{s=1}^u \sum_{r=1}^n \mathbb{E} [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) (\mathbf{d}_{r,s} - \boldsymbol{\delta}_s)'] - \sum_{s=1}^u n \mathbb{E} [(\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s) (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s)'] \\ &= \sum_{s=1}^u (n\boldsymbol{\Gamma}_0 - \boldsymbol{\Gamma}_0) = u(n-1)\boldsymbol{\Gamma}_0. \end{aligned}$$

Therefore,

$$\mathbb{E} \left[\frac{1}{(n-1)u} \mathbf{C}_0 \right] = \boldsymbol{\Gamma}_0.$$

Similarly, we have

$$\begin{aligned} \mathbf{C}_1 &= \sum_{s=1}^u \sum_{s^* \neq s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s) (\mathbf{d}_{r,s^*} - \bar{\mathbf{d}}_{s^*})' \\ &= \sum_{s=1}^u \sum_{s^* \neq s=1}^u \sum_{r=1}^n [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) - (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s)] [(\mathbf{d}_{r,s^*} - \boldsymbol{\delta}_{s^*}) - (\bar{\mathbf{d}}_{s^*} - \boldsymbol{\delta}_{s^*})]' \\ &= \sum_{s=1}^u \sum_{s^* \neq s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) (\mathbf{d}_{r,s^*} - \boldsymbol{\delta}_{s^*})' - \sum_{s=1}^u \sum_{s^* \neq s=1}^u n (\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s) (\bar{\mathbf{d}}_{s^*} - \boldsymbol{\delta}_{s^*})', \end{aligned}$$

then

$$\begin{aligned} \mathbb{E}[\mathbf{C}_1] &= \sum_{s=1}^u \sum_{s^* \neq s=1}^u \sum_{r=1}^n \mathbb{E} [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s) (\mathbf{d}_{r,s^*} - \boldsymbol{\delta}_{s^*})'] - \sum_{s=1}^u \sum_{s^* \neq s=1}^u n \mathbb{E} [(\bar{\mathbf{d}}_s - \boldsymbol{\delta}_s) (\bar{\mathbf{d}}_{s^*} - \boldsymbol{\delta}_{s^*})'] \\ &= u(u-1)n\boldsymbol{\Gamma}_1 - u(u-1)\boldsymbol{\Gamma}_1 = u(u-1)(n-1)\boldsymbol{\Gamma}_1. \end{aligned}$$

Therefore,

$$\mathbb{E} \left[\frac{1}{(n-1)u(u-1)} \mathbf{C}_1 \right] = \boldsymbol{\Gamma}_1.$$

Consequently, unbiased estimators of $\boldsymbol{\Gamma}_0$ and $\boldsymbol{\Gamma}_1$ are

$$\tilde{\boldsymbol{\Gamma}}_0 = \frac{1}{(n-1)u} \mathbf{C}_0,$$

and

$$\tilde{\Gamma}_1 = \frac{1}{(n-1)u(u-1)} \mathbf{C}_1,$$

respectively. Therefore, an unbiased estimate $\tilde{\Gamma}$ of Γ is

$$\tilde{\Gamma} = \mathbf{I}_u \otimes (\tilde{\Gamma}_0 - \tilde{\Gamma}_1) + \mathbf{J}_u \otimes \tilde{\Gamma}_1.$$

In the next section we will show that the mean vector $\bar{\mathbf{d}}$ is independent of the unbiased estimate of the variance-covariance matrix $\tilde{\Gamma}$. But, $\tilde{\Gamma}$ does not follow a Wishart distribution. Therefore, we cannot use the Hotelling's T^2 distribution to test the hypothesis (2.3). Thus, we will define a natural analogue of Hotelling's T^2 statistic, a RL statistic, in the BCS covariance matrix setting in the next section.

4 A Natural Extension of the Hotelling's T^2 Statistic in BCS Covariance Structure Setup

Let \mathbf{D} be the matrix $\mathbf{D} = (\mathbf{d}_1, \dots, \mathbf{d}_n)'$, that is, \mathbf{D} is a data matrix from $N_{uq}(\boldsymbol{\delta}; \Gamma) = N_{uq}(\boldsymbol{\mu}_y - \boldsymbol{\mu}_x; \mathbf{I}_u \otimes (\Gamma_0 - \Gamma_1) + \mathbf{J}_u \otimes \Gamma_1)$ (see Mardia et al. (1979) Section 3.3, p. 64). Then, using Corollary 3.3.3.2 of Theorem 3.3.3 from Mardia et al. (1979) Section 3.3, p. 66, we conclude that $\bar{\mathbf{d}} = \frac{1}{n} \mathbf{D}' \mathbf{1}_n = (\bar{d}'_1, \dots, \bar{d}'_u)'$, with $\bar{d}_s = \frac{1}{n} \sum_{r=1}^n d_{r,s}$ for $s = 1, \dots, u$, is independent of $\mathbf{S} = \frac{1}{n} \mathbf{D}' (\mathbf{I}_n - \frac{1}{n} \mathbf{1}_n \mathbf{1}'_n) \mathbf{D} := \frac{1}{n} \mathbf{D}' (\mathbf{I}_n - \frac{1}{n} \mathbf{J}_n) \mathbf{D} := \frac{1}{n} \mathbf{D}' \mathbf{H}_n \mathbf{D}$.

Using similar arguments, for each fixed $s = 1, \dots, u$, the $q \times 1$ vectors $\mathbf{d}_{1,s}, \mathbf{d}_{2,s}, \dots, \mathbf{d}_{n,s}$ are i.i.d $N_q(\boldsymbol{\delta}_s; \Gamma_0)$, and let \mathbf{D}_s denote the data matrix $\mathbf{D}_s = (\mathbf{d}_{1,s}, \dots, \mathbf{d}_{n,s})'$, from $N_q(\boldsymbol{\delta}_s; \Gamma_0)$. Note that $\mathbf{D} = (\mathbf{D}_1, \mathbf{D}_2, \dots, \mathbf{D}_u)$. Then, using the Corollary 3.3.3.2 of Theorem 3.3.3 from Mardia et al. (1979) Section 3.3, p. 66 again, we conclude that $\bar{\mathbf{d}}_s = \frac{1}{n} \mathbf{D}'_s \mathbf{1}_n = \frac{1}{n} \sum_{r=1}^n d_{r,s}$ is independent of

$$\begin{aligned} \mathbf{S}_s &= \frac{1}{n} \mathbf{D}'_s \left(\mathbf{I}_n - \frac{1}{n} \mathbf{1}_n \mathbf{1}'_n \right) \mathbf{D}_s := \frac{1}{n} \mathbf{D}'_s \left(\mathbf{I}_n - \frac{1}{n} \mathbf{J}_n \right) \mathbf{D}_s \\ &:= \frac{1}{n} \mathbf{D}'_s \mathbf{H}_n \mathbf{D}_s = \frac{1}{n} \sum_{r=1}^n (d_{r,s} - \bar{d}_s) (d_{r,s} - \bar{d}_s)'. \end{aligned}$$

Furthermore, from Exercise 3.4.5 in p. 89 of Mardia et al. (1979) we have

$$\mathbf{S}_s \sim \text{Wishart}_q \left(\frac{1}{n} \Gamma_0, n-1 \right).$$

Therefore,

$$\begin{aligned}\frac{1}{n}\mathbf{C}_0 &= \frac{1}{n} \sum_{s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s) (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s)' \\ &= \sum_{s=1}^u \mathbf{S}_s,\end{aligned}$$

is a sum of non independent Wishart $_q(\frac{1}{n}\mathbf{\Gamma}_0, n-1)$. However, since $\bar{\mathbf{d}} = \frac{1}{n}\mathbf{D}'\mathbf{1}_n = (\bar{\mathbf{d}}'_1, \dots, \bar{\mathbf{d}}'_u)'$

is independent of

$$\begin{aligned}\mathbf{S} &= \frac{1}{n}\mathbf{D}' \left(\mathbf{I}_n - \frac{1}{n}\mathbf{1}_n\mathbf{1}'_n \right) \mathbf{D} \\ &= \frac{1}{n} (\mathbf{D}_1, \dots, \mathbf{D}_u)' \left(\mathbf{I}_n - \frac{1}{n}\mathbf{1}_n\mathbf{1}'_n \right) (\mathbf{D}_1, \dots, \mathbf{D}_u) \\ &:= \frac{1}{n} (\mathbf{D}_1, \dots, \mathbf{D}_u)' \mathbf{H}_n (\mathbf{D}_1, \dots, \mathbf{D}_u) \\ &= \frac{1}{n} \begin{pmatrix} \mathbf{D}'_1 \mathbf{H}_n \mathbf{D}_1 & \mathbf{D}'_1 \mathbf{H}_n \mathbf{D}_2 & \cdots & \mathbf{D}'_1 \mathbf{H}_n \mathbf{D}_u \\ \mathbf{D}'_2 \mathbf{H}_n \mathbf{D}_1 & \mathbf{D}'_2 \mathbf{H}_n \mathbf{D}_2 & \cdots & \mathbf{D}'_2 \mathbf{H}_n \mathbf{D}_u \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{D}'_u \mathbf{H}_n \mathbf{D}_1 & \mathbf{D}'_u \mathbf{H}_n \mathbf{D}_2 & \cdots & \mathbf{D}'_u \mathbf{H}_n \mathbf{D}_u \end{pmatrix},\end{aligned}$$

$\bar{\mathbf{d}} = (\bar{\mathbf{d}}'_1, \dots, \bar{\mathbf{d}}'_u)'$ is independent of

$$\begin{aligned}\tilde{\mathbf{\Gamma}}_0 &= \frac{1}{(n-1)u} \mathbf{C}_0 = \frac{n}{(n-1)u} \left(\frac{1}{n} \right) \sum_{s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s) (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s)' \\ &= \frac{n}{(n-1)u} \left(\frac{1}{n} \right) \sum_{s=1}^u \mathbf{D}'_s \mathbf{H}_n \mathbf{D}_s \\ &= \frac{n}{(n-1)u} \sum_{s=1}^u \mathbf{S}_s,\end{aligned}$$

and $\bar{\mathbf{d}} = (\bar{\mathbf{d}}'_1, \dots, \bar{\mathbf{d}}'_u)'$ is independent of

$$\begin{aligned}\tilde{\mathbf{\Gamma}}_1 &= \frac{1}{(n-1)u(u-1)} \mathbf{C}_1 = \frac{n}{(n-1)u(u-1)} \left(\frac{1}{n} \right) \sum_{s=1}^u \sum_{s^* \neq s=1}^u \sum_{r=1}^n (\mathbf{d}_{r,s} - \bar{\mathbf{d}}_s) (\mathbf{d}_{r,s^*} - \bar{\mathbf{d}}_{s^*})' \\ &= \frac{n}{(n-1)u(u-1)} \sum_{s=1}^u \sum_{s^* \neq s=1}^u \mathbf{D}'_s \mathbf{H}_n \mathbf{D}_{s^*}.\end{aligned}$$

Therefore $\bar{\mathbf{d}}$ is independent of $\tilde{\mathbf{\Gamma}} = \mathbf{I}_u \otimes (\tilde{\mathbf{\Gamma}}_0 - \tilde{\mathbf{\Gamma}}_1) + \mathbf{J}_u \otimes \tilde{\mathbf{\Gamma}}_1$. But, $\tilde{\mathbf{\Gamma}}$ does not follow a Wishart distribution. Notice that $\tilde{\mathbf{\Gamma}}_0$ is however a sum of non independent Wishart distribution. As

a result, we cannot use the Hotelling's T^2 distribution to test the hypothesis (2.3). A natural analogue of Hotelling's T^2 statistic, a RL statistic, in this BCS framework under the null case can be defined as

$$RL = n\bar{\mathbf{d}}'(\tilde{\mathbf{\Gamma}})^{-1}\bar{\mathbf{d}},$$

with uq and $n - 1$ degrees of freedom. Now, to avoid inverting $\tilde{\mathbf{\Gamma}}$, an alternative formula for computing the test statistic RL can be written as

$$RL = \frac{|\tilde{\mathbf{\Gamma}} + n\bar{\mathbf{d}}\bar{\mathbf{d}}'|}{|\tilde{\mathbf{\Gamma}}|} - 1.$$

See Rencher (1998), p. 409.

5 Two Real Data Examples

In this section we demonstrate our new hypotheses testing (2.3) with two real data sets. The first data set is smaller in size than the second one.

Example 1. (Osteopenia Data): This data was given by Fernando Saraví, MD, PhD, at the Nuclear Medicine School, Mendoza, Argentina. Twelve patients ($n = 12$) were chosen for a bone densitometry study. Bone mineral density (BMD) were obtained from 12 subjects by a technique known as dual X-ray absorptiometry (DXA) using a GE Lunar Prodigy machine. The measurements are obtained from the hip region. In each femoral (right and left femoral, $u = 2$) two BMD measurements ($q = 2$) were taken, one at the femoral neck and the other at the trochanter region. These two measurements can be considered as taken from two different random variables because femoral neck is primarily a cortical bone whereas trochanter is essentially cancellous or trabecular bone. These four measurements were observed over a period of two years. We test whether the bone mineral density is lower in these patients in two years considering the data is doubly multivariate and has BCS structure.

The unbiased estimate of the unstructured $\mathbf{\Omega}$ with five decimal places is

$$\hat{\mathbf{\Omega}} = \frac{1}{(n-1)}\mathbf{S} = \begin{bmatrix} \begin{bmatrix} 0.00068 & 0.00030 \\ 0.00030 & 0.00077 \end{bmatrix} & \begin{bmatrix} 0.00030 & 0.00021 \\ 0.00064 & 0.00082 \end{bmatrix} \\ \begin{bmatrix} 0.00030 & 0.00064 \\ 0.00021 & 0.00082 \end{bmatrix} & \begin{bmatrix} 0.00141 & 0.00119 \\ 0.00119 & 0.00184 \end{bmatrix} \end{bmatrix}.$$

The unbiased estimates of the BCS covariance matrix $\mathbf{\Gamma}$ is

$$\mathbf{I}_u \otimes (\mathbf{\Gamma}_0 - \widehat{\mathbf{\Gamma}}_1) + \mathbf{J}_u \otimes \mathbf{\Gamma}_1 = \begin{bmatrix} \begin{bmatrix} 0.00105 & 0.00075 \\ 0.00075 & 0.00131 \end{bmatrix} & \begin{bmatrix} 0.00030 & 0.00043 \\ 0.00043 & 0.00082 \end{bmatrix} \\ \begin{bmatrix} 0.00030 & 0.00043 \\ 0.00043 & 0.00082 \end{bmatrix} & \begin{bmatrix} 0.00105 & 0.00075 \\ 0.00075 & 0.00131 \end{bmatrix} \end{bmatrix}.$$

From this estimate it appears that BCS is a good fit to the unstructured $\widehat{\mathbf{\Omega}}$ for the difference of observations \mathbf{d} . Using Roy and Leiva (2011) we see that the p -value = 0.2266 for the BCS fit when we use the asymptotic χ^2_ν approximation for $-2 \log \Lambda = 5.6532$ with $\nu = \frac{qu(qu+1)}{2} - q(q+1) = 4$ degrees of freedom.

The calculated Hotelling's T^2 statistic is 7.4832 with p -value = 0.3286 for hypotheses testing (2.3). Using BCS covariance structure we get RL statistic as 8.9184 with p -value = 0.2596. The test statistic is with 4 and 11 degrees of freedom. Thus, we conclude that the bone mineral density is not lower in two years in these patients using Hotelling's T^2 statistic as well as with RL statistic. Thus, the patients are not at risk for osteopenia.

Example 2. (Mineral Data): This data set is taken from Johnson and Wichern (2007, p. 43). An investigator measured the mineral content of bones (radius, humerus and ulna) by photon absorptiometry to examine whether dietary supplements would slow bone loss in 25 older women. Measurements were recorded for three bones on the dominant and nondominant sides. Thus, the data is doubly multivariate and clearly $u = 2$ and $q = 3$.

The bone mineral contents for the first 24 women one year after their participation in an experimental program is given in Johnson and Wichern (2007, p. 353). Thus, for our analysis we take only first 24 women in the first data set. We test whether there has been a bone loss considering the data as doubly multivariate and has BCS structure. We rearrange the variables in the data set by grouping together the mineral content of the dominant sides of radius, humerus and ulna as the first three variables, that is, the variables in the first location ($u = 1$) and then the mineral contents for the non-dominant side of the same bones ($u = 2$).

The unbiased estimate of the unstructured $\mathbf{\Omega}$ with five decimal places is

$$\widehat{\mathbf{\Omega}} = \frac{1}{(n-1)} \mathbf{S} = \begin{bmatrix} \begin{bmatrix} 0.00232 & 0.00080 & 0.00064 \\ 0.00080 & 0.01062 & -0.00022 \\ 0.00064 & -0.00022 & 0.00095 \end{bmatrix} & \begin{bmatrix} 0.00029 & 0.00138 & -0.00012 \\ 0.00067 & 0.00365 & -0.00060 \\ -0.00011 & 0.00026 & 0.00031 \end{bmatrix} \\ \begin{bmatrix} 0.00029 & 0.00067 & -0.00011 \\ 0.00138 & 0.00365 & 0.00026 \\ -0.00012 & -0.00060 & 0.00031 \end{bmatrix} & \begin{bmatrix} 0.00076 & 0.00046 & -0.00012 \\ 0.00046 & 0.00391 & -0.00040 \\ -0.00012 & -0.00040 & 0.00220 \end{bmatrix} \end{bmatrix}.$$

The unbiased estimate of the BCS covariance matrix $\mathbf{\Gamma}$ is

$$\mathbf{I}_u \otimes (\widehat{\mathbf{\Gamma}}_0 - \widehat{\mathbf{\Gamma}}_1) + \mathbf{J}_u \otimes \mathbf{\Gamma}_1 = \begin{bmatrix} \begin{bmatrix} 0.00154 & 0.00063 & 0.00026 \\ 0.00063 & 0.00726 & -0.00031 \\ 0.00026 & -0.00031 & 0.00157 \end{bmatrix} & \begin{bmatrix} 0.00029 & 0.00103 & -0.00011 \\ 0.00103 & 0.00365 & -0.00017 \\ -0.00011 & -0.00017 & 0.00031 \end{bmatrix} \\ \begin{bmatrix} 0.00029 & 0.00103 & -0.00011 \\ 0.00103 & 0.00365 & -0.00017 \\ -0.00011 & -0.00017 & 0.00031 \end{bmatrix} & \begin{bmatrix} 0.00154 & 0.00063 & 0.00026 \\ 0.00063 & 0.00726 & -0.00031 \\ 0.00026 & -0.00031 & 0.00157 \end{bmatrix} \end{bmatrix}.$$

From this estimate it appears that BCS is not a good fit to the unstructured $\widehat{\mathbf{\Omega}}$ for the difference of observations \mathbf{d} . Using Roy and Leiva (2011) we see that the p -value = 0.0010 for the BCS when we use the asymptotic χ^2_ν approximation for $-2 \log \Lambda = 27.8902$ with $\nu = \frac{qu(qu+1)}{2} - q(q+1) = 9$ degrees of freedom.

The calculated Hotelling's T^2 statistic is 9.0218 with p -value = 0.3616 for hypotheses testing (2.3). Using BCS covariance structure we get RL statistic as 4.0739 with p -value = 0.7774. The test statistic is with 6 and 23 degrees of freedom. Thus, we conclude that there has not been a bone loss using Hotelling's T^2 statistic with p -value = 0.3616. However, using the RL statistic we get p -value = 0.7774, which is the same conclusion obtained using Hotelling's T^2 statistic. That is, the dietary supplements is indeed slow the bone loss in 24 older women.

6 Concluding Remarks

In this article, we study the hypothesis testing of equality of mean vectors for paired two-level multivariate data with BCS covariance structure. The proposed methodology can readily be generalized to more than two levels. We are currently computing the empirical percentiles points of the null distribution of RL statistic for the hypothesis (2.3) through simulation studies. The results will be published soon.

ACKNOWLEDGEMENTS

The first author would like to thank the College of Business at the University of Texas at San Antonio for their continued support with this publication.

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