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Testing the Equality of Mean Vectors for Paired Doubly Multivariate Observations in Blocked Compound Symmetric Covariance Matrix Setup

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Abstract

In this article we develop a 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 test is implemented with two real data sets.

Keywords Blocked compound symmetry; Block T^2 ; Paired doubly multivariate data; Hotelling's T^2 statistic.

Mathematics Subject Classification 62H15; 62H12.

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 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 Block T^2 (BT^2) 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. 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 measurements ($q = 2$) 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 $N_{uq}(\boldsymbol{\mu}_y, \mathbf{I}_u \otimes (\mathbf{\Sigma}_{y0} - \mathbf{\Sigma}_{y1}) + \mathbf{J}_u \otimes \mathbf{\Sigma}_{y1})$, where $\boldsymbol{\mu}_y \in \mathbb{R}^{uq}$ and $\mathbf{I}_u \otimes (\mathbf{\Sigma}_{y0} - \mathbf{\Sigma}_{y1}) + \mathbf{J}_u \otimes \mathbf{\Sigma}_{y1}$ 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 $\mathbf{\Omega}$. 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 observations on each individual. Thus, $\mathbf{y}_{r,s}, \dots, \mathbf{y}_{r,s}$ are paired with $\mathbf{x}_{r,s}, \dots, \mathbf{x}_{r,s}$ respectively. 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 the following Table 1.

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

2 The Hypothesis

We want to test the equality of the mean vectors by considering the data as doubly multivariate and has BCS structure. 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

$$\begin{pmatrix} \boldsymbol{\Sigma}_{yy} & \boldsymbol{\Sigma}_{yx} \\ \boldsymbol{\Sigma}_{xy} & \boldsymbol{\Sigma}_{xx} \end{pmatrix} = \begin{bmatrix} \mathbf{I}_u \otimes (\boldsymbol{\Sigma}_y^0 - \boldsymbol{\Sigma}_y^1) + \mathbf{J}_u \otimes \boldsymbol{\Sigma}_y^1 & \mathbf{J}_u \otimes \mathbf{W} \\ \mathbf{J}_u \otimes \mathbf{W} & \mathbf{I}_u \otimes (\boldsymbol{\Sigma}_x^0 - \boldsymbol{\Sigma}_x^1) + \mathbf{J}_u \otimes \boldsymbol{\Sigma}_x^1 \end{bmatrix},$$

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 $\boldsymbol{\mu}_d = E(\mathbf{y} - \mathbf{x}) = \boldsymbol{\mu}_y - \boldsymbol{\mu}_x$. Now to estimate $\text{Cov}(\mathbf{y} - \mathbf{x}) = \boldsymbol{\Sigma}_{yy} - \boldsymbol{\Sigma}_{yx} - \boldsymbol{\Sigma}_{xy} + \boldsymbol{\Sigma}_{xx}$, we need the estimates of $q \times q$ matrices $\boldsymbol{\Sigma}_y^1, \boldsymbol{\Sigma}_y^0, \boldsymbol{\Sigma}_x^1, \boldsymbol{\Sigma}_x^0$ 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 $\boldsymbol{\delta} = \boldsymbol{\mu}_d = E(\mathbf{y} - \mathbf{x}) = \boldsymbol{\mu}_y - \boldsymbol{\mu}_x$, and

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

where

$$\boldsymbol{\Gamma}_0 = \boldsymbol{\Sigma}_y^0 + \boldsymbol{\Sigma}_x^0 - 2\mathbf{W}, \quad (2.4)$$

and

$$\boldsymbol{\Gamma}_1 = \boldsymbol{\Sigma}_y^1 + \boldsymbol{\Sigma}_x^1 - 2\mathbf{W}. \quad (2.5)$$

Thus, instead of deriving the estimates of $\boldsymbol{\Sigma}_y^1, \boldsymbol{\Sigma}_y^0, \boldsymbol{\Sigma}_x^1, \boldsymbol{\Sigma}_x^0$ 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 Orthogonalization

Let $\mathbf{Z} = \underset{u \times u}{\mathbf{H}'} \otimes \mathbf{I}_q$ with \mathbf{H} an orthogonal Helmert matrix whose first column is proportional to a vector of 1's. Let $\mathbf{b} = \mathbf{Z}\mathbf{d}$. Therefore, $E(\mathbf{b}) = \mathbf{Z}\boldsymbol{\delta}$ and

$\text{Cov}(\mathbf{b}) = \mathbf{Z}\mathbf{\Gamma}\mathbf{Z}'$. Then, the transformed samples $\mathbf{Z}\mathbf{d}_1, \mathbf{Z}\mathbf{d}_2, \dots, \mathbf{Z}\mathbf{d}_n$ are i.i.d $N_{uq}(\mathbf{Z}\boldsymbol{\delta}; \mathbf{Z}\mathbf{\Gamma}\mathbf{Z}')$. We should note that \mathbf{Z} is not a function of either $\mathbf{\Gamma}_0$, nor $\mathbf{\Gamma}_1$.

In Lemma 3.1 in Roy and Fonseca (2012), it is shown that we may write

$$\mathbf{Z}\mathbf{\Gamma}\mathbf{Z}' = \begin{bmatrix} \mathbf{\Delta}_2 & \mathbf{0} \\ \mathbf{0} & \mathbf{I}_{u-1} \otimes \mathbf{\Delta}_1 \end{bmatrix},$$

where

$$\begin{aligned} \mathbf{\Delta}_1 &= \mathbf{\Gamma}_0 - \mathbf{\Gamma}_1, \\ \text{and } \mathbf{\Delta}_2 &= \mathbf{\Gamma}_0 + (u-1)\mathbf{\Gamma}_1. \end{aligned}$$

We consider the vectors \mathbf{b} and $\boldsymbol{\delta}$ be partitioned in u subvectors as $\mathbf{b} = (\mathbf{b}'_1, \dots, \mathbf{b}'_u)'$ and $\boldsymbol{\delta} = (\boldsymbol{\delta}'_1, \dots, \boldsymbol{\delta}'_u)'$. Then $\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_u$ are independently normally distributed such that

$$\begin{aligned} \mathbf{b}_1 &\sim N_q(\mathbf{Z}\boldsymbol{\delta}_1; \mathbf{\Delta}_2) \\ \text{and } \mathbf{b}_s &\sim N_q(\mathbf{Z}\boldsymbol{\delta}_s; \mathbf{\Delta}_1) \quad \text{for fixed } s = 2, \dots, u. \end{aligned}$$

Now, for each fixed r , we consider the vectors \mathbf{d}_r and \mathbf{b}_r be partitioned in u subvectors as $\mathbf{d}_r = (\mathbf{d}'_{r,1}, \dots, \mathbf{d}'_{r,u})'$ and $\mathbf{b}_r = (\mathbf{b}'_{r,1}, \dots, \mathbf{b}'_{r,u})'$, similarly, $\bar{\mathbf{d}} = (\bar{\mathbf{d}}'_{\bullet 1}, \dots, \bar{\mathbf{d}}'_{\bullet u})'$ with $\bar{\mathbf{d}}_{\bullet s} = \frac{1}{n} \sum_{r=1}^n \mathbf{d}_{r,s}$ for $s = 1, \dots, u$; and $\bar{\mathbf{b}} = (\bar{\mathbf{b}}'_{\bullet 1}, \dots, \bar{\mathbf{b}}'_{\bullet u})'$ with $\bar{\mathbf{b}}_{\bullet s} = \frac{1}{n} \sum_{r=1}^n \mathbf{b}_{r,s}$ for $s = 1, \dots, u$.

It is reasonable to base the test statistic of H_o on these vectors. In the following section we will find unbiased estimates of $\mathbf{\Delta}_1$ and $\mathbf{\Delta}_2$.

3 Unbiased Estimates of $\mathbf{\Delta}_1$ and $\mathbf{\Delta}_2$

To find the unbiased estimates $\mathbf{\Delta}_1$ and $\mathbf{\Delta}_2$ we first need to find unbiased estimates of $\mathbf{\Gamma}_0$ and $\mathbf{\Gamma}_1$. Clearly, $\bar{\mathbf{d}} = (\bar{\mathbf{d}}'_{\bullet 1}, \dots, \bar{\mathbf{d}}'_{\bullet u})' \sim N_{uq}(\boldsymbol{\delta}; \frac{1}{n}\mathbf{\Gamma})$ with $\mathbf{\Gamma} = \text{Cov}(\mathbf{d}) = \mathbf{I}_u \otimes (\mathbf{\Gamma}_0 - \mathbf{\Gamma}_1) + \mathbf{J}_u \otimes \mathbf{\Gamma}_1$. The equicorrelated hypothesis of $\mathbf{\Gamma}$ assures that

$$\mathbb{E} [(\mathbf{d}_{r,s} - \boldsymbol{\delta}_s)(\mathbf{d}_{r,s^*} - \boldsymbol{\delta}_{s^*})'] = \begin{cases} \mathbf{\Gamma}_0 & \text{if } s = s^* \\ \mathbf{\Gamma}_1 & \text{if } s \neq s^*, \end{cases}$$

and

$$\mathbb{E} \left[(\bar{\mathbf{d}}_{\bullet s} - \boldsymbol{\delta}_s) (\bar{\mathbf{d}}_{\bullet s^*} - \boldsymbol{\delta}_{s^*})' \right] = \text{Cov}(\bar{\mathbf{d}}_{\bullet s}, \bar{\mathbf{d}}_{\bullet s^*}) = \begin{cases} \frac{1}{n} \boldsymbol{\Gamma}_0 & \text{if } s = s^* \\ \frac{1}{n} \boldsymbol{\Gamma}_1 & \text{if } s \neq s^*, \end{cases}$$

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

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

then

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

Therefore,

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

Similarly, we have

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

then

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

Therefore,

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

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

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

and

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

respectively. Thus, unbiased estimates $\tilde{\mathbf{\Delta}}_0$ and $\tilde{\mathbf{\Delta}}_1$ of $\mathbf{\Delta}_0$ and $\mathbf{\Delta}_1$, respectively, are

$$\begin{aligned} \tilde{\mathbf{\Delta}}_1 &= \tilde{\mathbf{\Gamma}}_0 - \tilde{\mathbf{\Gamma}}_1, \\ \text{and } \tilde{\mathbf{\Delta}}_2 &= \tilde{\mathbf{\Gamma}}_0 + (u-1)\tilde{\mathbf{\Gamma}}_1. \end{aligned}$$

Furthermore, an unbiased estimate $\tilde{\mathbf{\Gamma}}$ of $\mathbf{\Gamma}$ is

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

But, $\tilde{\mathbf{\Gamma}}$ does not follow a Wishart distribution. Therefore, we cannot use the Hotelling's T^2 distribution to test the hypothesis (2.3). However, we will derive a similar statistic by deriving the distributions of $\tilde{\mathbf{\Delta}}_1$ and $\tilde{\mathbf{\Delta}}_2$.

4 Distributions of $\tilde{\mathbf{\Delta}}_1$ and $\tilde{\mathbf{\Delta}}_2$

For derivations of the distributions of $\tilde{\mathbf{\Delta}}_1$ and $\tilde{\mathbf{\Delta}}_2$ in this section we need the following definition.

Definition 1. *Let*

$$\mathbf{A} = \begin{bmatrix} \mathbf{A}_{11} & \mathbf{A}_{12} & \cdots & \mathbf{A}_{1u} \\ \vdots & \ddots & & \vdots \\ \vdots & & \ddots & \vdots \\ \mathbf{A}_{u1} & \mathbf{A}_{u2} & \cdots & \mathbf{A}_{uu} \end{bmatrix}$$

be a block matrix with square blocks. Then we define block-trace and block-sum operators as follows:

$$\text{blktr}(\mathbf{A}) = \sum_{i=1}^u \mathbf{A}_{ii} \quad \text{and} \quad \text{blksum}(\mathbf{A}) = \sum_{i=1}^u \sum_{j=1}^u \mathbf{A}_{ij}.$$

Let us denote $\mathbf{P}_m = \frac{1}{m} \mathbf{J}_m$ and $\mathbf{Q}_m = \mathbf{I}_m - \mathbf{P}_m$ mutually orthogonal projector matrices of (any) order m . Let \mathbf{D} be the matrix $\mathbf{D} = (\mathbf{d}_1, \dots, \mathbf{d}_n)' = (\mathbf{D}_1, \dots, \mathbf{D}_u)$, that is, \mathbf{D} is a data matrix from $N_{uq}(\boldsymbol{\delta}; \boldsymbol{\Gamma}) = N_{uq}(\boldsymbol{\mu}_y - \boldsymbol{\mu}_x; \mathbf{I}_u \otimes (\boldsymbol{\Gamma}_0 - \boldsymbol{\Gamma}_1) + \mathbf{J}_u \otimes \boldsymbol{\Gamma}_1)$ (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 $\bar{\mathbf{d}} = \frac{1}{n} \mathbf{D}' \mathbf{1}_n$ is independent of $\mathbf{S} = \frac{1}{n} \mathbf{D}' \mathbf{Q}_n \mathbf{D}$.

However, since $\bar{\mathbf{d}} = \frac{1}{n} \mathbf{D}' \mathbf{1}_n$ is independent of

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

it is also independent of

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

and of

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

Therefore $\bar{\mathbf{d}}$ is independent of $\tilde{\mathbf{\Gamma}} = \mathbf{I}_u \otimes (\tilde{\mathbf{\Gamma}}_0 - \tilde{\mathbf{\Gamma}}_1) + \mathbf{J}_u \otimes \tilde{\mathbf{\Gamma}}_1$.

Let us look at the estimators of two positive definite matrices in the model. Simple calculations yields

$$\tilde{\mathbf{\Gamma}}_0 - \tilde{\mathbf{\Gamma}}_1 = \frac{n}{(n-1)(u-1)} \left(\text{blktr}(\mathbf{S}) - \frac{1}{u} \text{blksum}(\mathbf{S}) \right),$$

and

$$\tilde{\mathbf{\Gamma}}_0 + (u-1)\tilde{\mathbf{\Gamma}}_1 = \frac{n}{(n-1)u} \text{blksum}(\mathbf{S}).$$

Lemma 1. *It holds*

$$\tilde{\mathbf{\Gamma}}_0 - \tilde{\mathbf{\Gamma}}_1 = \frac{n}{(n-1)(u-1)} \text{blktr}((\mathbf{Q}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{Q}_u \otimes \mathbf{I}_q)),$$

and

$$\tilde{\mathbf{\Gamma}}_0 + (u-1)\tilde{\mathbf{\Gamma}}_1 = \frac{n}{(n-1)} \text{blktr}((\mathbf{P}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{P}_u \otimes \mathbf{I}_q)).$$

Proof. One can easily find that every block of $(\mathbf{P}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{P}_u \otimes \mathbf{I}_q)$ is equal to $\frac{1}{u^2} \text{blksum}(\mathbf{S})$. That is why $\text{blktr}((\mathbf{P}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{P}_u \otimes \mathbf{I}_q)) = \frac{1}{u} \text{blksum}(\mathbf{S})$. It follows that

$$\begin{aligned} \text{blktr}((\mathbf{Q}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{Q}_u \otimes \mathbf{I}_q)) &= \text{blktr}(((\mathbf{I}_u - \mathbf{P}_u) \otimes \mathbf{I}_q) \mathbf{S} ((\mathbf{I}_u - \mathbf{P}_u) \otimes \mathbf{I}_q)) \\ &= \text{blktr}(\mathbf{S}) - \frac{1}{u} \text{blksum}(\mathbf{S}). \end{aligned}$$

Then the results for $\tilde{\mathbf{\Gamma}}_0 - \tilde{\mathbf{\Gamma}}_1$ and $\tilde{\mathbf{\Gamma}}_0 + (u-1)\tilde{\mathbf{\Gamma}}_1$ follow. \square

It is easy to see that for any $uq \times 1$ vector \mathbf{t} it holds $\mathbf{D}\mathbf{t} \sim N_n(\boldsymbol{\delta}'\mathbf{t} \cdot \mathbf{1}_n; \mathbf{t}'\mathbf{\Gamma}\mathbf{t} \cdot \mathbf{I}_n)$. Since \mathbf{Q}_n is idempotent, $\mathbf{1}'_n \mathbf{Q}_n \mathbf{1}_n = 0$ and $\text{tr}(\mathbf{Q}_n) = n-1$, according to Theorem 1.4.2 in Muirhead (2005) it holds

$$\frac{1}{\mathbf{t}'\mathbf{\Gamma}\mathbf{t}} \mathbf{t}' \mathbf{D}' \mathbf{Q}_n \mathbf{D} \mathbf{t} \sim \chi^2(n-1).$$

Now, using 8b.2(ii) in Rao (1973), we get

$$\mathbf{S} = \frac{1}{n} \mathbf{D}' \mathbf{Q}_n \mathbf{D} \sim \text{Wishart}_{uq} \left(\frac{1}{n} \mathbf{\Gamma}, n-1 \right).$$

Theorem 1. *Distributions of $(n-1)(u-1) \left(\tilde{\Gamma}_0 - \tilde{\Gamma}_1 \right)$ and $(n-1) \left(\tilde{\Gamma}_0 + (u-1)\tilde{\Gamma}_1 \right)$ are independent, and*

$$(n-1)(u-1) \left(\tilde{\Gamma}_0 - \tilde{\Gamma}_1 \right) \sim \text{Wishart}_q \left((\Gamma_0 - \Gamma_1), (n-1)(u-1) \right),$$

$$(n-1) \left(\tilde{\Gamma}_0 + (u-1)\tilde{\Gamma}_1 \right) \sim \text{Wishart}_q \left((\Gamma_0 + (u-1)\Gamma_1), n-1 \right),$$

Proof. Let $e_{i,u}$ be the i -th column of \mathbf{I}_u . Then for any $q \times 1$ vector t we have

$$\begin{aligned} n t' \text{blktr} \left((\mathbf{Q}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{Q}_u \otimes \mathbf{I}_q) \right) t &= n \sum_{i=1}^u t' (e'_{i,u} \mathbf{Q}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{Q}_u e_{i,u} \otimes \mathbf{I}_q) t \\ &= n \sum_{i=1}^u (e'_{i,u} \mathbf{Q}_u \otimes t') \mathbf{S} (\mathbf{Q}_u e_{i,u} \otimes t) = n \text{tr} \left((\mathbf{Q}_u \otimes t') \mathbf{S} (\mathbf{Q}_u \otimes t) \right). \end{aligned}$$

Since $(\mathbf{Q}_u \otimes t') \Gamma (\mathbf{Q}_u \otimes t) = t' (\Gamma_0 - \Gamma_1) t \cdot \mathbf{Q}_u$ is a multiple of idempotent matrix, its only positive eigenvalue is $t' (\Gamma_0 - \Gamma_1) t$ with multiplicity $r(\mathbf{Q}_u) = u-1$.

Now Lemma 2 in Klein and Žežula (2010) implies that

$$n \text{tr} \left((\mathbf{Q}_u \otimes t') \mathbf{S} (\mathbf{Q}_u \otimes t) \right) \sim t' (\Gamma_0 - \Gamma_1) t \cdot \chi^2((n-1)(u-1)).$$

Then it follows that

$$n \text{blktr} \left((\mathbf{Q}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{Q}_u \otimes \mathbf{I}_q) \right) \sim \text{Wishart}_q \left((\Gamma_0 - \Gamma_1), (n-1)(u-1) \right).$$

Similarly, for any $q \times 1$ vector t we have

$$\begin{aligned} n t' \text{blktr} \left((\mathbf{P}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{P}_u \otimes \mathbf{I}_q) \right) t &= n \sum_{i=1}^u t' (e'_{i,u} \mathbf{P}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{P}_u e_{i,u} \otimes \mathbf{I}_q) t \\ &= n \sum_{i=1}^u (e'_{i,u} \mathbf{P}_u \otimes t') \mathbf{S} (\mathbf{P}_u e_{i,u} \otimes t) = n \text{tr} \left((\mathbf{P}_u \otimes t') \mathbf{S} (\mathbf{P}_u \otimes t) \right). \end{aligned}$$

Since $(\mathbf{P}_u \otimes t') \Gamma (\mathbf{P}_u \otimes t) = t' (\Gamma_0 + (u-1)\Gamma_1) t \cdot \mathbf{P}_u$ is a multiple of idempotent matrix, its only positive eigenvalue is $t' (\Gamma_0 + (u-1)\Gamma_1) t$ with multiplicity $r(\mathbf{P}_u) = 1$. Again, Lemma 2 in Klein and Žežula (2010) implies that $n \text{tr} \left((\mathbf{P}_u \otimes t') \mathbf{S} (\mathbf{P}_u \otimes t) \right) \sim t' (\Gamma_0 + (u-1)\Gamma_1) t \cdot \chi^2(n-1)$. That is why

$$n \text{blktr} \left((\mathbf{P}_u \otimes \mathbf{I}_q) \mathbf{S} (\mathbf{P}_u \otimes \mathbf{I}_q) \right) \sim \text{Wishart}_q \left((\Gamma_0 + (u-1)\Gamma_1), (n-1) \right).$$

The desired result follows from Lemma 1. The independence of the two statistics is a consequence of the fact that $\mathbf{P}_u \mathbf{Q}_u = 0$. \square

5 Proposed Test Statistic in BCS Covariance Structure Setup

Because $\tilde{\Gamma}_1 = \frac{1}{u} (\tilde{\Delta}_2 - \tilde{\Delta}_1)$ does not have a Wishart distribution, we cannot use the Hotelling's T^2 distribution to test the hypothesis (2.3) directly. However, since $\bar{\mathbf{b}}_{\bullet 1} \sim N_q \left(\mathbf{Z}\boldsymbol{\delta}_1; \frac{1}{n} \mathbf{\Delta}_2 \right)$ and $\bar{\mathbf{b}}_{\bullet i} \sim N_q \left(\mathbf{Z}\boldsymbol{\delta}_i; \frac{1}{n} \mathbf{\Delta}_1 \right)$ for $i = 2, \dots, u$, and all these random variables are independent, we have under H_o

$$\sqrt{n} \bar{\mathbf{b}}_{\bullet 1} \sim N_q(0; \mathbf{\Delta}_2) \quad \text{and} \quad \sqrt{\frac{n}{u-1}} \sum_{i=2}^u \bar{\mathbf{b}}_{\bullet i} \sim N_q(0; \mathbf{\Delta}_1).$$

These averages are independent of both $\tilde{\Delta}_2$ and $\tilde{\Delta}_1$. Using Theorem 1, we can now form two independent Hotelling's T^2 statistics, namely

$$n \bar{\mathbf{b}}_{\bullet 1}' \tilde{\Delta}_2^{-1} \bar{\mathbf{b}}_{\bullet 1} \sim T_{q, n-1}^2 \quad \text{and} \quad \frac{n}{u-1} \sum_{i=2}^u \sum_{j=2}^u \bar{\mathbf{b}}_{\bullet i}' \tilde{\Delta}_1^{-1} \bar{\mathbf{b}}_{\bullet j} \sim T_{q, (n-1)(u-1)}^2.$$

Thus, a natural statistic for the test of H_o is

$$\begin{aligned} BT^2 &= n \bar{\mathbf{b}}_{\bullet 1}' \tilde{\Delta}_2^{-1} \bar{\mathbf{b}}_{\bullet 1} + \frac{n}{u-1} \sum_{i=2}^u \sum_{j=2}^u \bar{\mathbf{b}}_{\bullet i}' \tilde{\Delta}_1^{-1} \bar{\mathbf{b}}_{\bullet j} = n \bar{\mathbf{b}}' \begin{pmatrix} \tilde{\Delta}_2^{-1} & 0 \\ 0 & \mathbf{P}_{u-1} \otimes \tilde{\Delta}_1^{-1} \end{pmatrix} \bar{\mathbf{b}} \\ &= n \bar{\mathbf{d}}' \mathbf{Z}' \begin{pmatrix} (\tilde{\Gamma}_0 + (u-1)\tilde{\Gamma}_1)^{-1} & 0 \\ 0 & \mathbf{P}_{u-1} \otimes (\tilde{\Gamma}_0 - \tilde{\Gamma}_1)^{-1} \end{pmatrix} \mathbf{Z} \bar{\mathbf{d}} \\ &\stackrel{H_o}{\sim} T_{q, n-1}^2 + T_{q, (n-1)(u-1)}^2. \end{aligned}$$

We will call it Block T^2 . The resulting distribution is the convolution of two T^2 's. If $X \sim T_{q, n}^2$ then we can equivalently write $X \sim GF\left(\frac{q}{2}, \frac{n+1}{2}, \frac{1}{n}\right)$, where $GF(p, m, \alpha)$ denotes the generalized F-distribution with pdf

$$f(x) = \frac{\alpha^p}{B(p, m-p)} \frac{x^{p-1}}{(1+\alpha x)^m},$$

and $B(\cdot, \cdot)$ is the beta function. Dyer (1982) determined the distribution of the convolution of generalized F-distributed random variables. Therefore, it is not a hard task to compute the p-value of the test statistic (or critical values of the test) with a suitable software.

Alternatively, we can also use Block F (BF) as

$$BF = n\bar{\mathbf{b}}' \begin{pmatrix} \frac{n-q}{(n-1)q} \tilde{\Delta}_2^{-1} & 0 \\ 0 & \frac{(n-1)(u-1)-q+1}{(n-1)(u-1)q} \mathbf{P}_{u-1} \otimes \tilde{\Delta}_1^{-1} \end{pmatrix} \bar{\mathbf{b}} \stackrel{H_0}{\sim} F_{q, n-q} + F_{q, (n-1)(u-1)-q+1}.$$

It is to be noted that the expression of the type $c \cdot \mathbf{x}' \mathbf{A}^{-1} \mathbf{x}$ can also be computed without matrix inversion using the formula

$$c \cdot \mathbf{x}' \mathbf{A}^{-1} \mathbf{x} = \frac{|\mathbf{A} + c \cdot \mathbf{x} \mathbf{x}'|}{|\mathbf{A}|} - 1,$$

see Rencher (1998), p. 409.

6 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 Ω with five decimal places is

$$\hat{\Omega} = \begin{bmatrix} \begin{bmatrix} 0.00068 & 0.00030 \\ 0.00030 & 0.00077 \end{bmatrix} & \begin{bmatrix} 0.00030 & 0.00021 \\ 0.00064 & 0.00082 \end{bmatrix} \\ \begin{bmatrix} 0.00030 & 0.00064 \\ 0.00021 & 0.00082 \end{bmatrix} & \begin{bmatrix} 0.00141 & 0.00119 \\ 0.00119 & 0.00184 \end{bmatrix} \end{bmatrix}.$$

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). The test statistic is with 4 and 11 degrees of freedom. Using BCS covariance structure we get Block T^2 statistic as **8.91911** and Block F statistic as **4.05414** with common p -value = **0.166586**. 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 Block T^2 and Block F statistics. Thus, the patients are not at risk of 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 data sets for two time points are given in Tables 2 and 3 respectively.

Table 2 Mineral Content in Bones

Subject Number	Dominant radius	Radius	Dominant humerus	Humerus	Dominant ulna	Ulna
1	1.103	1.052	2.139	2.238	0.873	0.872
2	0.842	0.859	1.873	1.741	0.590	0.744
3	0.925	0.873	1.887	1.809	0.767	0.713
4	0.857	0.744	1.739	1.547	0.706	0.674
5	0.795	0.809	1.734	1.715	0.549	0.654
6	0.787	0.779	1.509	1.474	0.782	0.571
7	0.933	0.880	1.695	1.656	0.737	0.803
8	0.799	0.851	1.740	1.777	0.618	0.682
9	0.945	0.876	1.811	1.759	0.853	0.777
10	0.921	0.906	1.954	2.009	0.823	0.765
11	0.792	0.825	1.624	1.657	0.686	0.668
12	0.815	0.751	2.204	1.846	0.678	0.546
13	0.755	0.724	1.508	1.458	0.662	0.595
14	0.880	0.866	1.786	1.811	0.810	0.819
15	0.900	0.838	1.902	1.606	0.723	0.677
16	0.764	0.757	1.743	1.794	0.586	0.541
17	0.733	0.748	1.863	1.869	0.672	0.752
18	0.932	0.898	2.028	2.032	0.836	0.805
19	0.856	0.786	1.390	1.324	0.578	0.610
20	0.890	0.950	2.187	2.087	0.758	0.718
21	0.688	0.532	1.650	1.378	0.533	0.482
22	0.940	0.850	2.334	2.225	0.757	0.731
23	0.493	0.616	1.037	1.268	0.546	0.615
24	0.835	0.752	1.509	1.422	0.618	0.664

Table 3 Mineral Content in Bones (After 1 year)

Subject Number	Dominant radius	Radius	Dominant humerus	Humerus	Dominant ulna	Ulna
1	1.027	1.051	2.268	2.246	0.869	0.964
2	0.857	0.817	1.718	1.710	0.602	0.689
3	0.875	0.880	1.953	1.756	0.765	0.738
4	0.873	0.698	1.668	1.443	0.761	0.698
5	0.811	0.813	1.643	1.661	0.551	0.619
6	0.640	0.734	1.396	1.378	0.753	0.515
7	0.947	0.865	1.851	1.686	0.708	0.787
8	0.886	0.806	1.742	1.815	0.687	0.715
9	0.991	0.923	1.931	1.776	0.844	0.656
10	0.977	0.925	1.933	2.106	0.869	0.789
11	0.825	0.826	1.609	1.651	0.654	0.726
12	0.851	0.765	2.352	1.980	0.692	0.526
13	0.770	0.730	1.470	1.420	0.670	0.580
14	0.912	0.875	1.846	1.809	0.823	0.773
15	0.905	0.826	1.842	1.579	0.746	0.729
16	0.756	0.727	1.747	1.860	0.656	0.506
17	0.765	0.764	1.923	1.941	0.693	0.740
18	0.932	0.914	2.190	1.997	0.883	0.785
19	0.843	0.782	1.242	1.228	0.577	0.627
20	0.879	0.906	2.164	1.999	0.802	0.769
21	0.673	0.537	1.573	1.330	0.540	0.498
22	0.949	0.900	2.130	2.159	0.804	0.779
23	0.463	0.637	1.041	1.265	0.570	0.634
24	0.776	0.743	1.442	1.411	0.585	0.640

We also compare our findings with the conventional Hotelling's T^2 statistic.

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

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

The unbiased estimate of $\mathbf{\Gamma}_0$ and $\mathbf{\Gamma}_1$ are

$$\widehat{\mathbf{\Gamma}}_0 = \begin{bmatrix} 0.00154 & 0.00063 & 0.00026 \\ 0.00063 & 0.00726 & -0.00031 \\ 0.00026 & -0.00031 & 0.00157 \end{bmatrix}.$$

and

$$\widehat{\mathbf{\Gamma}}_1 = \begin{bmatrix} 0.00029 & 0.00103 & -0.00011 \\ 0.00103 & 0.00365 & -0.00017 \\ -0.00011 & -0.00017 & 0.00031 \end{bmatrix}.$$

respectively. Using the above the unbiased estimates the estimate of the BCS covariance matrix $\mathbf{\Gamma}$ is

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

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). The test statistic is with 6 and 23 degrees of freedom. Using BCS covariance structure we get Block T^2 statistic as **4.07386** and Block F statistic as **1.23987** with p -value = **0.72936**. 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 block statistics we get p -value = 0.72936, 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.

7 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.

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Appendix

Estimator of unstructured Σ

$$\widehat{\Sigma} = \begin{bmatrix} 1278 & 2180 & 0861 & 1001 & 1967 & 0742 & 1271 & 2461 & 0840 & 1019 & 1937 & 0820 \\ 2180 & 7898 & 1556 & 1762 & 6574 & 1150 & 2469 & 8474 & 1837 & 1868 & 6899 & 1424 \\ 0861 & 1556 & 1039 & 0769 & 1678 & 0683 & 0820 & 2036 & 1026 & 0834 & 1713 & 0698 \\ \hline 1001 & 1762 & 0769 & 1082 & 2041 & 0802 & 1025 & 2081 & 0777 & 1068 & 2072 & 0889 \\ 1967 & 6574 & 1678 & 2041 & 6870 & 1578 & 2212 & 7380 & 1974 & 2184 & 7289 & 1869 \\ 0742 & 1150 & 0683 & 0802 & 1578 & 0928 & 0823 & 1540 & 0678 & 0853 & 1630 & 0960 \\ \hline 1271 & 2469 & 0820 & 1025 & 2212 & 0823 & 1487 & 2827 & 0860 & 1070 & 2315 & 0890 \\ 2461 & 8474 & 2036 & 2081 & 7380 & 1540 & 2827 & 10068 & 2296 & 2251 & 8056 & 1756 \\ 0840 & 1837 & 1026 & 0777 & 1974 & 0678 & 0860 & 2296 & 1103 & 0832 & 2033 & 0723 \\ \hline 1019 & 1868 & 0834 & 1068 & 2184 & 0853 & 1070 & 2251 & 0832 & 1127 & 2259 & 0928 \\ 1937 & 6899 & 1713 & 2072 & 7289 & 1630 & 2315 & 8056 & 2033 & 2259 & 8083 & 1884 \\ 0820 & 1424 & 0698 & 0888 & 1869 & 0960 & 0890 & 1756 & 0723 & 0928 & 1884 & 1202 \end{bmatrix}.$$

Table 1. Upper Percentage Points of Hotelling T²-Distribution (Empirical)

99th percentiles of the null distribution of $n\bar{\mathbf{d}}'(\mathbf{S})^{-1}\bar{\mathbf{d}}$ for $n = 10$

		Number of Variables, p									
Number of Simulations ↓		1	2	3	4	5	6	7	8	9	10
10,000				31.816	56.556						
50,000				31.673	55.393						
60,000				31.987	56.193						
75,000				31.978	56.213						
100,000				32.025	56.396						
150,000				32.231							
200,000											
Tabulated T ²		10.561	19.460	32.598	54.890						

Table 2. Upper Percentage Points of Hotelling T²-Distribution (Empirical)

95th percentiles of the null distribution of $n\bar{\mathbf{d}}'(\mathbf{S})^{-1}\bar{\mathbf{d}}$ for $n = 10$

		Number of Variables, p									
Number of Simulations ↓		1	2	3	4	5	6	7	8	9	10
10,000				16.692	28.892						
50,000				16.893	27.375						
60,000				16.940	27.436						
75,000				16.968	27.471						
100,000				16.976	27.436						
150,000				16.888							
200,000											
Tabulated T ²		5.117	10.033	16.766	27.202						

Table 3. Upper Percentage Points of Hotelling T²-Distribution (Empirical)

99th percentiles of the null distribution of $n\bar{\mathbf{d}}'(\mathbf{S})^{-1}\bar{\mathbf{d}}$ for $n = 6$

Number of Simulations ↓	Number of Variables, p									
	1	2	3	4	5	6	7	8	9	10
10,000			152.751	970.247						
50,000			147.980	1071.151						
60,000			146.073	1078.554						
75,000			142.673	1034.931						
100,000			142.007	1032.025						
150,000			144.952	1030.806						
200,000			144.430	1028.524						
Tabulated T ²	16.258	45.000	147.283	992.494						

Table 4. Upper Percentage Points of Hotelling T²-Distribution (Empirical)

95th percentiles of the null distribution of $n\bar{\mathbf{d}}'(\mathbf{S})^{-1}\bar{\mathbf{d}}$ for $n = 6$

Number of Simulations ↓	Number of Variables, p									
	1	2	3	4	5	6	7	8	9	10
10,000			46.448	186.954						
50,000			45.767	197.804						
60,000			45.767	197.599						
75,000			45.502	192.608						
100,000			45.771	193.740						
150,000			45.907	193.877						
200,000			46.120	192.608						
Tabulated T ²	6.608	17.361	46.383	192.468						

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