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MULTIPLE TESTING OF TWO-SIDED ALTERNATIVES WITH DEPENDENT DATA

Arthur Cohen and Harold B. Sackrowitz

Rutgers University

Abstract: Multiple testing procedures have become an integral element of analysis in many practical problems. The development of sound procedures has become an important statistical issue. Many procedures have been suggested and many criteria of goodness have been used. Most recent procedures are stepwise in nature. Perhaps the most fundamental (and typically overlooked) issue is the behavior of the multiple testing procedure as it relates to each individual testing problem.

In this paper we study two of the most popular stepwise procedures. We demonstrate that the individual tests they induce are inadmissible in some important two-sided testing models when correlation is present. That is, for each individual hypothesis testing problem, a test exists whose size is less than or equal that of the stepwise procedure test and whose power is greater than or equal that of the stepwise procedure test with some strict inequality. This means that the overall multiple testing procedure is inadmissible whenever a loss based on the number of Type I and Type II errors is used.

Key words and phrases: Closure principle, general linear model, inadmissibility, stepwise procedures, treatments vs control, vector risk.

1. Introduction

Triggered by new applications involving large numbers of hypothesis tests, there has been renewed interest in multiple testing procedures (MTP). Although new procedures have been proposed, the ability to evaluate procedures has lagged behind. Many recent procedures are stepwise in nature; eleven of eighteen procedures studied by Dudoit, Shaffer and Boldrick (2003)(DSB) are step-up or step-down, for example. At each stage we are told which, if any, hypotheses should be accepted or rejected and whether or not we should continue. This process does induce a test, based on all the data, for each individual hypothesis testing problem. However, the stepwise construction often makes it difficult to examine the individual tests. Yet perhaps the most fundamental (and typically overlooked) issue is the behavior of the MTP as it relates to individual testing problems.

In particular, suppose an individual test induced by a MTP is inadmissible for the standard hypothesis testing loss. That is, for that individual hypothesis testing problem, a test exists whose size is less than or equal that of the stepwise procedure test, and whose power is greater than or equal that of the stepwise procedure test, with some strict inequality. It would then follow that the overall procedure is inadmissible whenever the risk function is a monotone function of the expected number of Type I errors and the expected number of Type II errors. This is the main thought of this paragraph, and is what the reader needs to carry away as the main idea.

Now let $\boldsymbol{Z}$ be $k \times 1$ multivariate normal, with mean $\boldsymbol{\mu}$ and known covariance $\Sigma = (\sigma_{ij})$. Test k hypotheses $H_i : \mu_i = 0$ vs $K_i : \mu_i \neq 0$, $i = 1, \ldots, k$. Popular MTPs for this problem are the step-up and step-down procedures based on p-values determined by test statistics $W_i = |Z_i|/\sigma_{ii}^{1/2}$. The FDR controlling stepwise procedure of Benjamini and Hochberg (1995) and its offsprings (see for example Benjamini and Yekutieli (2001), Sarkar (2002), and several others listed in DSB (2003)) are covered by the results in Sections 3-5 of this paper. We emphasize that in this paper we focus only on the case where the alternative hypothesis is two-sided, i.e., $K_i : \mu_i \neq 0$, and where Σ is not diagonal.

Previous decision theory results were obtained, for a variety of models and loss functions, for one-sided alternatives or two-sided alternatives when Σ is diagonal. Such results, including some on inadmissibility, appear in Cohen and Sackrowitz (2005a,b, 2007), Cohen, Kolassa and Sackrowitz (2007), and in Muller, Parmigiani, Robert and Rousseau (2004).

Returning to the model of this paper in which we consider two-sided alternatives only, we assume at least *one* off-diagonal element of Σ is non-zero. We show that step-up and step-down procedures are inadmissible for a k-dimensional vector loss where each component of the vector loss is a 0-1 loss function for each individual hypothesis testing problem. The interpretation of the result is thus the following: if $\psi_i^{SD}(\boldsymbol{z})$ is the ith test for hypothesis H_i, for step-down, then there exists a test $\psi_i^*(\boldsymbol{z})$ whose size is less than or equal to the size of $\psi_i^{SD}(\boldsymbol{z})$ and whose power is greater than or equal to the power of $\psi_i^{SD}(\boldsymbol{z})$, with some strict inequality. Such a finding is somewhat surprising for it is not true if Σ is diagonal. The k-dimensional vector loss is the most liberal in the sense that the class of admissible MTPs is largest for this loss when compared to the 2-dimensional vector of CS (2005b) and when compared to the typical linear combination loss functions used by Lehmann (1957), Ishwaran and Rao (2003) and Genovese and Wasserman (2002).

Next consider the general linear model

$$\boldsymbol{y} = X\boldsymbol{\beta} + \boldsymbol{\epsilon}, \tag{1.1}$$

where $\boldsymbol{\epsilon}$ is $n \times 1$ multivariate normal, with mean $\boldsymbol{0}$ and covariance $\sigma^2 I$, σ^2 unknown, $\boldsymbol{\beta}$ is a $k \times 1$ vector of unknown parameters, and X is an $n \times k$ fixed matrix of rank $k < n$. Then $\hat{\boldsymbol{\beta}} \sim N(\boldsymbol{\beta}, \sigma^2 S^{-1})$, $S = X'X$, where $\hat{\boldsymbol{\beta}} = S^{-1}X'\boldsymbol{y}$. Test $H_i : \beta_i = 0$ vs $K_i : \beta_i \neq 0$, $i = 1, \ldots, k$. A condition, often satisfied, is found under which the usual step-wise procedures are inadmissible. This result is relevant for the selection of variables problem in multiple regression.

Another model for which a similar result holds is that for testing $(k-1)$ treatments against a control. That is, assume X_{ij}, $i = 1, \ldots, k$, $j = 1, \ldots, n$ are independent normal variables with means μ_i and unknown variance σ^2. Test $H_i : \nu_i = \mu_i - \mu_k = 0$ vs $K_i : \nu_i \neq 0$, $i = 1, \ldots, k-1$.

In Section 2 we give preliminaries and describe the stepwise procedures. Inadmissibility for the normal dependent model is given in Section 3. Results for the general linear model are presented in Section 4. Results for the problem of testing treatments against a control are given in Section 5.

2. Preliminaries and Stepwise Procedures

Assume $\boldsymbol{Z}$ is $k \times 1$ multivariate normal, with unknown mean $\boldsymbol{\mu}$ and known covariance Σ. Assume also that $\Sigma = (\sigma_{ij})$ has at least one non-zero off diagonal element. Without loss of generality we take $\sigma_{21} \neq 0$. We consider k testing problems, namely

$$H_i : \mu_i = 0 \text{ vs } K_i : \mu_i \neq 0, \quad i = 1, \ldots, k. \tag{2.1}$$

The alternatives in (2.1) are two-sided.

We regard the problem of testing the k hypotheses as a 2^k finite action problem, see Lehmann (1957). An action is designated by $\boldsymbol{a} = (a_1, \ldots, a_k)'$, where $a_i = 0$ or 1 for $i = 1, \ldots, k$. An action $a_i = 1$ means H_i is rejected, whereas if $a_i = 0$, H_i is accepted. Let $v_i(\mu_i) = 1$ if $\mu_i \neq 0$, and $v_i(\mu_i) = 0$ if $\mu_i = 0$.

Test functions for the ith testing problem are denoted by $\psi_i(\boldsymbol{z})$, where $\psi_i(\boldsymbol{z})$ is the probability of rejecting H_i given $\boldsymbol{z}$ is observed. Let $\boldsymbol{\psi}(\boldsymbol{z}) = \big(\psi_1(\boldsymbol{z}), \ldots, \psi_k(\boldsymbol{z})\big)$. A loss function is a function of $(\boldsymbol{a}, \boldsymbol{\mu})$. For an individual testing problem a 0-1 loss function is

$$a_i\big(1 - v_i(\mu_i)\big) + (1 - a_i)v_i(\mu_i) \tag{2.2}$$

or simply

$$a_i(1 - v_i) + (1 - a_i)v_i. \tag{2.3}$$

The corresponding risk function for a procedure $\boldsymbol{\psi}(\boldsymbol{z})$ for the ith problem is

$$R_i\big(\psi_i(\boldsymbol{z}), \boldsymbol{\mu}\big) = (1 - v_i)E_{\boldsymbol{\mu}}\psi_i(\boldsymbol{z}) + v_i E_{\boldsymbol{\mu}}\big(1 - \psi_i(\boldsymbol{z})\big). \tag{2.4}$$

A vector risk function for the multiple testing problem, called VRI, is

$$R(\boldsymbol{\psi}, \boldsymbol{\mu}) = \big(R_1(\psi_1, \boldsymbol{\mu}), \ldots, R_k(\psi_k, \boldsymbol{\mu})\big). \tag{2.5}$$

We conclude this section with a description of the step-up and step-down procedures for testing the two-sided alternatives in (2.1), see Hochberg and Tamhane (1987). Write $W_i = |Z_i|/\sigma_{ii}^{1/2}$.

For step-up, let $0 < C_1 < \cdots < C_k$ be a sequence of increasing critical values, and let $W_{(1)} \leq W_{(2)} \leq \cdots \leq W_{(k)}$ be the order statistics of $W_1, \ldots, W_k$.

(i) If $W_{(1)} \leq C_1$, accept $H_{(1)}$ where $H_{(1)}$ is the hypothesis corresponding to $W_{(1)}$. Otherwise reject all $H_{(i)}$. (2.6)

(ii) If $H_{(1)}$ is accepted, accept $H_{(2)}$ if $W_{(2)} \leq C_2$. Otherwise reject $H_{(2)}, \ldots, H_{(k)}$.

(iii) In general, at stage j, if $W_{(j)} \leq C_j$ accept $H_{(j)}$. Otherwise reject $H_{(j)}, \ldots, H_{(k)}$.

For step-down procedures, we use the same notation.

(i) If $W_{(k)} > C_k$, reject $H_{(k)}$. Otherwise accept all $H_{(i)}$. (2.7)

(ii) If $H_{(k)}$ is rejected, reject $H_{(k-1)}$ if $W_{(k-1)} > C_{k-1}$. Otherwise accept $H_{(1)}, \ldots, H_{(k-1)}$.

(iii) In general, at stage j, if $W_{(k-j+1)} > C_{k-j+1}$, reject $H_{(k-j+1)}$. Otherwise accept $H_{(1)}, \ldots, H_{(k-j+1)}$.

3. Normal Dependent Model

Let $\boldsymbol{Z} \sim N(\boldsymbol{\mu}, \Sigma)$, $\Sigma = (\sigma_{ij})$, $\sigma_{ij} \neq 0$ for some $i \neq j$. Test $H_i : \mu_i = 0$ vs $K_i : \mu_i \neq 0$. The risk function is VRI given in (2.6). It will be helpful to let $D = \begin{pmatrix} \sigma_{11} & & 0 \\ & \ddots & \\ 0 & & \sigma_{kk} \end{pmatrix}$, and let $\boldsymbol{U} = D^{-1/2}\boldsymbol{Z}$ so that $\boldsymbol{U} \sim N(\boldsymbol{\nu} = D^{-1/2}\boldsymbol{\mu},\ G = D^{-1/2}\Sigma D^{-1/2})$. Write $G = (g_{ij})$ so that $g_{ii} = 1$ and let $W_i = |U_i|$ for $i = 1, \ldots, k$. The density of $\boldsymbol{U}$ is

$$f_{\boldsymbol{U}}(\boldsymbol{u}; \boldsymbol{\nu}) = \Big(\frac{1}{(2\pi)^{\frac{k}{2}}|G|^{\frac{k}{2}}}\Big) \exp -\frac{1}{2}\big\{\boldsymbol{u}'G^{-1}\boldsymbol{u} + \boldsymbol{\nu}'G^{-1}\boldsymbol{\nu} - 2\boldsymbol{\nu}'G^{-1}\boldsymbol{u}\big\}. \qquad (3.1)$$

Equivalent hypotheses to those based on μ_i are $H_i : \nu_i = 0$ vs $K_i : \nu_i \neq 0$, for $i = 1, \ldots, k$. Let $\boldsymbol{\psi}^{SD}(\boldsymbol{u})$ be the step-down procedure described in Section 2.

Theorem 3.1. *Consider the normal model of this section and the testing problem* (2.1). *For the risk function* (2.5), *the step-down procedure* $\boldsymbol{\psi}^{SD}(\boldsymbol{u})$ *given at* (2.7) *is inadmissible.*

Proof. We show that the test $\psi_i^{SD}(\boldsymbol{u})$ is inadmissible for the equivalent testing problem $H_i : \nu_i = 0$ vs $K_i : \nu_i \neq 0$, $i = 1, \ldots, k$. Without loss of generality we take $\sigma_{12} = \sigma_{21} \neq 0$ and focus on H_1 vs K_1, with $\psi_1^{SD}(\boldsymbol{u}) = \psi_1^{SD}(G\boldsymbol{y}) = \phi_1^{SD}(\boldsymbol{y})$. We first make the transformation $\boldsymbol{Y} = G^{-1}\boldsymbol{U}$ so (3.1) yields the density of $\boldsymbol{Y}$ as

$$f_{\boldsymbol{Y}}(\boldsymbol{y};\boldsymbol{\nu}) = \alpha(\boldsymbol{\nu})h(\boldsymbol{y})\exp\{\boldsymbol{\nu}'\boldsymbol{y}\} = \alpha(\boldsymbol{\nu})h(\boldsymbol{y})\exp\{y_1\nu_1 + \boldsymbol{\nu}^{(2)'}\boldsymbol{y}^{(2)}\}, \qquad (3.2)$$

where $\boldsymbol{y}^{(2)} = (y_2,\ldots,y_k)'$, $\boldsymbol{\nu}^{(2)} = (\nu_2,\ldots,\nu_k)'$, α is a function of $\boldsymbol{\nu}$, and h is a function of $\boldsymbol{y}$. A result of Matthes and Truax (1967) is that a necessary condition for $\phi_1^{SD}(\boldsymbol{y})$ to be admissible is, conditional on $\boldsymbol{y}^{(2)}$, that the acceptance region in y_1 be an interval for almost all $\boldsymbol{y}^{(2)}$. To show $\phi_1^{SD}(\boldsymbol{y})$ is inadmissible we find three points $\boldsymbol{y}^*, \boldsymbol{y}^{**}, \boldsymbol{y}^{***}$ with $y_1^* > y_1^{**} > y_1^{***}$ for fixed $\boldsymbol{y}^{(2)}$, such that $\phi_1^{SD}(\boldsymbol{y}^*) = 0$, $\phi_1^{SD}(\boldsymbol{y}^{**}) = 1$ and $\phi_1^{SD}(\boldsymbol{y}^{***}) = 0$. This same pattern will hold for points in the neighborhoods of $\boldsymbol{y}^*, \boldsymbol{y}^{**}, \boldsymbol{y}^{***}$, and this will prove the theorem.

For now, let $\sigma_{21} > 0$ so that $g_{21} > 0$. Note that $|g_{i1}| < 1$ for $i = 2,\ldots,k$. To identify $\boldsymbol{y}^*, \boldsymbol{y}^{**}, \boldsymbol{y}^{***}$, recall $\boldsymbol{Y} = G^{-1}\boldsymbol{U}$. Now let $0 < \epsilon < (C_2 - C_1)/4$ and let

$$\begin{aligned} A = \Big\{\boldsymbol{u} : \frac{C_1 + C_2}{2} - \epsilon < u_1 < \frac{(C_1 + C_2)}{2} + \epsilon,& \\ -C_2 \le u_2 < -C_2 + \frac{\epsilon g_{21}}{2}, C_k + \epsilon < u_i < C_k + 2\epsilon,\ i = 3,\ldots,k\Big\}.& \qquad (3.3) \end{aligned}$$

Let

$$\boldsymbol{u}^* = \Big(\frac{C_2 + C_1}{2}, -C_2, C_k + 1.5\epsilon, \ldots, C_k + 1.5\epsilon\Big)'. \qquad (3.4)$$

Note that $\boldsymbol{u}^* \in A$ and, from (2.7), $\psi_2^{SD}(\boldsymbol{u}^*) = 0$ and $\psi_1^{SD}(\boldsymbol{u}^*) = 0$. Furthermore $\psi_1^{SD}(\boldsymbol{u}) = 0$ for all $\boldsymbol{u} \in A$. Now let

$$\boldsymbol{u}^{**} = \boldsymbol{u}^* - \epsilon(1, g_{21}, \ldots, g_{k1})' = \boldsymbol{u}^* - \epsilon\boldsymbol{g}. \qquad (3.5)$$

Note again from (2.7) that $\psi_1^{SD}(\boldsymbol{u}^{**}) = 1$. If $\boldsymbol{u} \in A$ is transformed the same way, $\boldsymbol{u} \to \boldsymbol{u} - \epsilon\boldsymbol{g}$, then $\psi_1^{SD}(\boldsymbol{u} - \epsilon\boldsymbol{g}) = 1$. Next let

$$\boldsymbol{u}^{***} = \boldsymbol{u}^* - u_1^*\boldsymbol{g} \qquad (3.6)$$

so that from (2.7), $\psi_1^{SD}(\boldsymbol{u}^{***}) = 0$. Finally note that $\boldsymbol{y}^* = G^{-1}\boldsymbol{u}^*$, $\boldsymbol{y}^{**} = \boldsymbol{y}^* - (\epsilon, 0, \ldots, 0)'$, $\boldsymbol{y}^{***} = \boldsymbol{y}^* - \big((C_2 + C_1)/2\big)(1, 0, \ldots, 0)'$, so that $y_1^* > y_1^{**} > y_1^{***}$ and $\boldsymbol{y}^{(2)*} = \boldsymbol{y}^{(2)**} = \boldsymbol{y}^{(2)***}$ with $\phi_1^{SD}(\boldsymbol{y}^*) = 0$, $\phi_1^{SD}(\boldsymbol{y}^{**}) = 1$, $\phi_1^{SD}(\boldsymbol{y}^{***}) = 0$. This completes the proof of the theorem for $\sigma_{21} > 0$.

For $\sigma_{21} < 0$, choose

$$\boldsymbol{u}^* = \Big(-\frac{C_2 + C_1}{2}, -C_2, C_k + 1.5\epsilon, \ldots, C_k + 1.5\epsilon\Big)', \qquad (3.7)$$

$$\boldsymbol{u}^{**} = \boldsymbol{u}^* + \epsilon(1, g_{21}, \ldots, g_{k1})', \qquad (3.8)$$

$$\boldsymbol{u}^{***} = \boldsymbol{u}^* + \Big(\frac{C_2 + C_1}{2}\Big)\boldsymbol{g}. \qquad (3.9)$$

Argue as in the case of $\sigma_{21} > 0$.

Theorem 3.2. *Under the assumptions of Theorem* 3.1*, the step-up procedure* $\boldsymbol{\psi}^{SU}(\boldsymbol{u})$ *given at* (2.6) *is inadmissible.*

Proof. The proof is similar to the proof of Theorem 3.1.

4. General Linear Model

The general linear model we study is given at (1.1). Our starting point here is $\hat{\boldsymbol{\beta}} \sim N(\boldsymbol{\beta}, \sigma^2 S^{-1})$, where at least one off diagonal element of $S^{-1} = A = (a_{ij})$ is non-zero. Without loss of generality we take $a_{21} \neq 0$. Let $V = \boldsymbol{y}'\boldsymbol{y} - \hat{\boldsymbol{\beta}}' S \hat{\boldsymbol{\beta}}$, let $T = \boldsymbol{y}'\boldsymbol{y}$, and note that $V/(n-k)$ is an unbiased estimator of σ^2 such that V/σ^2 is chi-square with $(n-k)$ degrees of freedom. The joint density of $(\hat{\boldsymbol{\beta}}, T)$, in exponential family form, is

$$\alpha(\boldsymbol{\beta}, \sigma^2) h(\hat{\boldsymbol{\beta}}, T) \exp\{\beta_1 \boldsymbol{S}_{(1)} \frac{\hat{\boldsymbol{\beta}}}{\sigma^2} + \boldsymbol{\beta}^{(2)} S^{(2)} \frac{\hat{\boldsymbol{\beta}}}{\sigma^2} - (\frac{1}{2}\sigma^2)T\}, \tag{4.1}$$

where $\hat{\boldsymbol{\beta}}' S \hat{\boldsymbol{\beta}} \leq T$, $\boldsymbol{S}_{(1)}$ is the first row of S and $S^{(2)}$ is the $(k-1) \times k$ matrix determined by the last $(k-1)$ rows of S, and $\hat{\boldsymbol{\beta}}^{(2)}$ is the $(k-1) \times 1$ subvector of $\hat{\boldsymbol{\beta}}$ that excludes $\hat{\beta}_1$.

To test $H_i : \beta_i = 0$ vs $K_i : \beta_i \neq 0$, stepwise procedures use the statistics

$$W_i = \frac{\hat{\beta}_i^2 (n-k)}{a_{ii}(T - \hat{\boldsymbol{\beta}}' S \hat{\boldsymbol{\beta}})}. \tag{4.2}$$

The W_i have $F_{1,n-k}$ distributions under H_i. We seek a sufficient condition under which $\psi_1^{SD}(\hat{\boldsymbol{\beta}}, T)$ is an inadmissible test for $H_1 : \beta_1 = 0$ vs $K_1 : \beta_1 \neq 0$ for the 0-1 loss function.

If we let $\boldsymbol{U} = S\hat{\boldsymbol{\beta}}$ then, in light of (4.1), we seek a sufficient condition such that the step-down test for H_1 has acceptance sections in u_1, for fixed $u_2, \ldots, u_k, T$ that are not intervals. That is, if $\phi_1^{SD}(\boldsymbol{u}, T) \equiv \psi_1^{SD}(\hat{\boldsymbol{\beta}}, T)$, we seek three values of u_1, say $u_1^*, u_1^{**}, u_1^{***}$, $u_1^* < u_1^{**} < u_1^{***}$ or $u_1^* > u_1^{**} > u_1^{***}$, such that $\phi_1^{SD}(u_1^*, \boldsymbol{u}^{(2)}) = 0$, $\phi_1^{SD}(u_1^{**}, \boldsymbol{u}^{(2)}) = 1$, and $\phi_1^{SD}(u_1^{***}, \boldsymbol{u}^{(2)}) = 0$, for some $\boldsymbol{u}^{(2)}$ fixed. Note that we can show $u_1 = \hat{\beta}_1 s_{11.2} + (s_{12}, \ldots, s_{1k}) S_{22}^{-1} \boldsymbol{u}^{(2)}$, where $s_{11.2} = s_{11} - (s_{12}, \ldots, s_{1k}) S_{22}^{-1} (s_{12}, \ldots, s_{1k})'$. This means we can look for $\hat{\beta}_1^*, \hat{\beta}_1^{**}, \hat{\beta}_1^{***}$ so that $\psi_1^{SD}(\hat{\boldsymbol{\beta}}, T)$ has the same behavior as $\phi_1^{SD}(\boldsymbol{u}, T)$ for fixed $\boldsymbol{U}^{(2)}, T$.

Recall that the test statistics are given in (4.2). Choose $\hat{\boldsymbol{\beta}}^*$ so that

$$\frac{(n-k)\hat{\beta}_i^{*2}}{a_{ii}(T - \hat{\boldsymbol{\beta}}^{*'} S \hat{\boldsymbol{\beta}}^*)} = \begin{cases} C_k + \Delta_1, & i = 3, \ldots, k \\ C_1 + \Delta_2, & i = 1 \\ C_2, & i = 2, \end{cases} \tag{4.3}$$

where $\Delta_1 > 0$, $0 < \Delta_2 < C_2 - C_1$. Thus $\psi_1(\hat{\boldsymbol{\beta}}^*, T) = \psi_2(\hat{\boldsymbol{\beta}}^*, T) = 0$ and $\psi_i(\hat{\boldsymbol{\beta}}^*, T) = 1$ for $i = 3, \ldots, k$. Let $\boldsymbol{g}' = (a_{11}, \ldots, a_{2k})$ be the first column of $A = S^{-1}$. Now consider

$$\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g}, \quad \epsilon > 0. \tag{4.4}$$

Note that

$$S(\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g}) = S\hat{\boldsymbol{\beta}}^* - \epsilon(1, 0, \ldots, 0)'. \tag{4.5}$$

Thus for the points $\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g}$ we have that $\boldsymbol{u}^{(2)} = (u_2, \ldots, u_k)'$ is fixed and u_1 is monotone in ϵ.

For ϵ sufficiently small we have, by continuity,

$$\frac{(n-k)(\hat{\beta}_i^* - \epsilon g_i^*)^2}{a_{ii}\big(T - (\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g})' S (\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g})\big)} > \begin{cases} C_k, & i = 3, \ldots, k \\ C_1, & i = 1 \end{cases}. \tag{4.6}$$

We want to show that, in addition,

$$\frac{(n-k)(\hat{\beta}_2^* - \epsilon g_2)^2}{a_{22}\big(T - (\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g})' S (\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g})\big)} > C_2 \tag{4.7}$$

for ϵ sufficiently small. To do this we look at the derivative with respect to ϵ of the left-hand side of (4.7) at $\epsilon = 0$. First note that by (4.5),

$$(\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g})' S (\hat{\boldsymbol{\beta}}^* - \epsilon \boldsymbol{g}) = \hat{\boldsymbol{\beta}}^{*'} S \hat{\boldsymbol{\beta}}^* - 2\epsilon \hat{\beta}_1^* + \epsilon^2 g_{11}.$$

Thus the derivative at $\epsilon = 0$ will be positive if and only if

$$-g_2 \hat{\beta}_2^* (T - \hat{\boldsymbol{\beta}}^{*'} S \hat{\boldsymbol{\beta}}^*) - \hat{\beta}_2^{*2} \hat{\beta}_1^* > 0. \tag{4.8}$$

Dividing through (4.8) by $(T - \hat{\boldsymbol{\beta}}^{*'} S \hat{\boldsymbol{\beta}}^*)$, recalling $g_2 = a_{21}$, and using (4.3), we rewrite (4.8) as

$$\hat{\beta}_2^* a_{21} + \sqrt{\frac{a_{11}(C_1 + \Delta_2) a_{22} C_2}{(n-k)^2}}\, |\hat{\beta}_2^*| < 0. \tag{4.9}$$

Since we may choose $\hat{\beta}_2^*$ to be positive or negative we choose it to have the sign opposite to a_{21}. Thus, we can find an ϵ^* say, so that $\hat{\boldsymbol{\beta}}^{**} = \boldsymbol{\beta}^* - \epsilon^* \boldsymbol{g}$ is such that $\psi_1(\hat{\boldsymbol{\beta}}^{**}, T) = 1$ provided

$$\frac{|a_{21}|}{\sqrt{a_{11} a_{22}}} > \frac{\sqrt{(C_1 + \Delta_2) C_2}}{n - k}. \tag{4.10}$$

Since Δ_2 can be arbitrarily small and positive we can replace (4.10) with

$$\frac{|a_{21}|}{\sqrt{a_{11} a_{22}}} > \frac{\sqrt{C_1 C_2}}{n - k}. \tag{4.11}$$

Finally choose $\hat{\boldsymbol{\beta}}^{***} = \hat{\boldsymbol{\beta}}^{*} - (\hat{\beta}_1^*/a_{11})\boldsymbol{g}$ so that, from (4.2), $\psi_1(\hat{\boldsymbol{\beta}}^{***}, T) = 0$ provided $\hat{\boldsymbol{\beta}}^{***}$ lies in the sample space. However, note that this is true since

$$\begin{aligned} T - \big(\hat{\boldsymbol{\beta}}^{*} - (\frac{\hat{\beta}_1^*}{a_{11}})\boldsymbol{g}\big)' S \big(\hat{\boldsymbol{\beta}}^{*} - (\frac{\hat{\beta}_1^*}{a_{11}})\boldsymbol{g}\big) &= T - \hat{\boldsymbol{\beta}}^{*'} S \hat{\boldsymbol{\beta}}^{*} + \frac{2\hat{\beta}_1^{*2}}{a_{11}} - \frac{\hat{\beta}_1^2}{a_{11}} \\ &\geq T - \hat{\boldsymbol{\beta}}^{*'} S \hat{\boldsymbol{\beta}}^{*} > 0. \end{aligned}$$

We summarize the discussion in the following theorem.

Theorem 4.1. *Consider the general linear model of full rank* $y = X\boldsymbol{\beta} + \boldsymbol{\epsilon}$, *where* $\boldsymbol{y}$ *is* $n \times 1$, X *is* $n \times k$, $n > k$, $\boldsymbol{\beta}$ *is* $k \times 1$, $\boldsymbol{\epsilon} \sim N(\mathbf{0}, \sigma^2 I)$. *Test* $H_i : \beta_i = 0$ *vs* $K_i : \beta_i \neq 0$, $i = 1, \ldots, k$. *Suppose* $S = X'X$ *and* $S^{-1} = A$ *where* A *has some non-zero off diagonal element. Then* $\boldsymbol{\psi}^{SD}$ *is inadmissible for the risk function VRI provided* (4.11) *holds.*

Remark 4.2. A similar result holds for $\boldsymbol{\psi}^{SU}$.

Remark 4.3. Condition (4.11) will likely hold for cases when n is somewhat larger than k.

Remark 4.4. As a numerical example we offer the data set used in Stapleton (1995), page 127. A multiple regression model in which $n = 31$, $k = 7$ is displayed. From the table in Stapleton (1995) of estimates of correlations, we record the left-hand side of (4.11) for the variables age and max pulse as 0.2629. For $\alpha = 0.05$ the right-hand side of (4.11) is $\sqrt{2.05(2.4)/24} = 0.0924$ so that (4.11) is satisfied.

5. Testing Treatments Against Control

Let X_{ij} be independent normal variables with unknown means μ_i, $i = 1, \ldots, k$, $j = 1, \ldots, n$, and unknown variance σ^2. Test $H_i : \nu_i = \mu_i - \mu_k = 0$ vs $K_i : \nu_i \neq 0$, $i = 1, \ldots, k-1$. Two-sided squared t-statistics are

$$W_i = \frac{(n-1)k\big(\sqrt{n}(\bar{X}_i - \bar{X}_k)\big)^2}{2(V - n\bar{\boldsymbol{X}}'\bar{\boldsymbol{X}})}, \tag{5.1}$$

where $\bar{X}_i = \sum_{j=1}^n X_{ij}/n$, $\bar{\boldsymbol{X}} = (\bar{X}_1, \ldots, \bar{X}_k)'$, $V = \sum_{i=1}^k \sum_{j=1}^n X_{ij}^2$. The density of $\bar{\boldsymbol{X}}, V$ is

$$f_{\bar{\boldsymbol{X}},V}(\bar{\boldsymbol{x}}, V) = \alpha(\mu, \sigma^2) h(\bar{\boldsymbol{x}}, V) \exp -V/2\sigma^2 \exp n\bar{\boldsymbol{x}}'\boldsymbol{\mu}/\sigma^2, \;\; n\bar{\boldsymbol{x}}'\bar{\boldsymbol{x}} \leq V. \tag{5.2}$$

Let

$$A = \begin{pmatrix} 1 & 0 & \cdots & 0 & -1 \\ 0 & 1 & \cdots & 0 & -1 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & 1 & -1 \\ 1 & 1 & \cdots & 1 & 1 \end{pmatrix},$$

so that

$$A^{-1} = (\frac{1}{k}) \begin{pmatrix} (k-1) & -1 & \cdots & -1 & 1 \\ -1 & (k-1) & \cdots & -1 & 1 \\ \vdots & \vdots & \ddots & \vdots & \\ -1 & -1 & \cdots & (k-1) & 1 \\ -1 & -1 & \cdots & -1 & 1 \end{pmatrix}.$$

Note if we let $\boldsymbol{\nu} = A\boldsymbol{\mu}$ and $\boldsymbol{u} = (A^{-1})'\bar{\boldsymbol{x}}$, then $\exp n\bar{\boldsymbol{x}}'\boldsymbol{\mu} = \exp n\boldsymbol{u}'\boldsymbol{\nu}$. Thus we seek a condition under which the step-down procedure for H_1 has acceptance sections in u_1 for fixed $u_2, \ldots, u_k$, that are not intervals. As done in the previous section we identify three points $\bar{\boldsymbol{x}}^*$, $\bar{\boldsymbol{x}}^{**} = \bar{\boldsymbol{x}}^* - \epsilon\boldsymbol{g}$, $\bar{\boldsymbol{x}}^{***} = \bar{\boldsymbol{x}}^* - [(\bar{x}_1^* - \bar{x}_k^*)/2]\boldsymbol{g}$, with $\boldsymbol{g} = (1, 0, \ldots, 0, -1)'$, the first column of A', such that $\psi_1^{SD}(\bar{\boldsymbol{x}}^*) = 0$, $\psi_1^{SD}(\bar{\boldsymbol{x}}^{**}) = 1$, $\psi_1^{SD}(\bar{\boldsymbol{x}}^{***}) = 0$. Again, as done in the previous sections, choose $\bar{\boldsymbol{x}}^*$ so that $W_i = C_k + \Delta_1$, $i = 3, \ldots, k$, $W_1 = C_1 + \Delta_2$, $W_2 = C_2$. Such a choice of $\bar{\boldsymbol{x}}^*$, with $\bar{x}_2^* - \bar{x}_k^* < 0$, ensures that $\bar{\boldsymbol{x}}^*, \bar{\boldsymbol{x}}^{**}, \bar{\boldsymbol{x}}^{***}$ is in the sample space. Furthermore, arguing as in the previous section, this choice along with the condition

$$n(n-1)k > [C_1 C_2]^{\frac{1}{2}} \tag{5.3}$$

suffices to demonstrate that $\boldsymbol{\psi}^{SD}$ is inadmissible.

Remark 5.1. Condition (5.3) is easily satisfied in most cases.

Remark 5.2. A similar result holds for step-up.

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Department of Statistics, Rutgers University, Hill Center, Busch Campus, 110 Frelinghuysen Road, Piscataway NJ 08854-8019, U.S.A.

E-mail: artcohen@rci.rutgers.edu

Department of Statistics, Rutgers University, Hill Center, Busch Campus, 110 Frelinghuysen Road, Piscataway NJ 08854-8019, U.S.A.

E-mail: sackrowi@rci.rutgers.edu

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