The Annals of Statistics
2002, Vol. 30, No. 1, 239–257

SOME RESULTS ON FALSE DISCOVERY RATE IN STEPWISE MULTIPLE TESTING PROCEDURES[1]

BY SANAT K. SARKAR

Temple University

The concept of false discovery rate (FDR) has been receiving increasing attention by researchers in multiple hypotheses testing. This paper produces some theoretical results on the FDR in the context of stepwise multiple testing procedures with dependent test statistics. It was recently shown by Benjamini and Yekutieli that the Benjamini–Hochberg step-up procedure controls the FDR when the test statistics are positively dependent in a certain sense. This paper strengthens their work by showing that the critical values of that procedure can be used in a much more general stepwise procedure under similar positive dependency. It is also shown that the FDR-controlling Benjamini–Liu step-down procedure originally developed for independent test statistics works even when the test statistics are positively dependent in some sense. An explicit expression for the FDR of a generalized stepwise procedure and an upper bound to the FDR of a step-down procedure are obtained in terms of probability distributions of ordered components of dependent random variables before establishing the main results.

1. Introduction. The main purpose of this paper is to present some formulas and inequalities providing theoretical insight into when and what stepwise procedures control the false discovery rate (FDR) at a prespecified level in multiple hypotheses testing. The FDR, first introduced in multiple testing by Benjamini and Hochberg (1995), is the expected proportion of erroneously rejected null hypotheses. With V and R representing, respectively, the number of true null hypotheses rejected and the total number of null hypotheses rejected in a multiple testing procedure, let $Q = V/R$ if $R > 0$ and $= 0$ if $R = 0$. Then $E(Q)$ is the FDR of that procedure. As they have argued, it is an appropriate error rate to control in many practical situations, particularly where a large number of null hypotheses are involved. They also put forward an FDR-controlling step-up procedure that is more powerful than comparable procedures controlling the traditional familywise error (FWE) rate when the underlying test statistics are independent. Benjamini and Liu (1999) recently introduced a step-down procedure with the same property.

The concept of FDR is now being used in a wide variety of applications [Abramovich and Benjamini (1996), Basford and Tukey (1997), Drigalenko

Received August 2000; revised September 2001.

[1]Supported in part by NSA Grant MDA-904-01-10082.

AMS 2000 subject classifications. Primary 62H15, 62H99.

Key words and phrases. Generalized step-up–step-down procedure, Benjamini–Liu step-down procedure, positive regression dependency on subset, multivariate totally positive of order 2.

and Elston (1997) and Williams, Jones and Tukey (1999)]. It plays a key role in the development of asymptotically minimax model selection procedures by Abramovich, Benjamini, Donoho and Johnstone (2000). While the FDR has been receiving increasing attention by researchers in different fields of statistics, theoretical progress has not been made at a similar pace.

The FDR-related theoretical results available so far in the literature [Benjamini and Hochberg (1995) and Benjamini and Liu (1999)] assume that the underlying test statistics are independent, even though they are actually dependent in commonly encountered multiple testing situations. Therefore, one particular area in which the theory on FDR needs to be further developed is when the test statistics are dependent. In a recent paper, Benjamini and Yekutieli (2001) took an important first step toward that goal by showing that the Benjamini–Hochberg step-up procedure indeed controls the FDR in a more general situation where the test statistics exhibit some form of positive dependence, as in the case of the multivariate normal distribution with positive correlations and some other commonly encountered multivariate distributions. Some further theoretical advancement is made in this article. We establish two additional results, one extending the work of Benjamini and Yekutieli (2001) to a more general stepwise procedure and the other answering an open question concerning the Benjamini–Liu step-down procedure. More specifically, it is proved that, instead of the Benjamini–Hochberg step-up procedure, if one applies a generalized step-up–step-down procedure [Tamhane, Liu and Dunnett (1998)] with the same set of critical values, the FDR can still be controlled not only in the independence case but also in a more general situation where the test statistics are positively dependent in the sense of exhibiting positive regression dependency on the subset of statistics corresponding to true null hypotheses, a property, called the PRDS property, defined by Benjamini and Yekutieli (2001). Distributions satisfying this property include multivariate normal distributions that arise in many-to-one comparisons of means with one-sided alternatives and known variances, absolute values of studentized independent normals that arise in simultaneous testing of independent group means against two-sided alternatives and multivariate F that arise in many-to-one comparisons of variances with one-sided alternatives. The studentized multivariate normal distributions with positive correlations that arise in many-to-one comparisons of means with one-sided alternatives and unknown common variance are PRDS conditional on positive values, providing an example where the FDR is controlled at a level less than 0.5. In the other result, it is shown that the Benjamini–Liu step-down procedure controls the FDR when the statistics, under any alternatives, are positively dependent in the sense of being multivariate totally positive of order 2 (MTP_2) [Karlin and Rinott (1980)] and, under null hypotheses, are exchangeable. The equicorrelated standard multivariate normal with a nonnegative common correlation arising in many-to-one comparisons with one-sided alternatives in a balanced one-way layout is an example of such a distribution.

It is worthwhile to point out that although the consideration of a generalized step-up–step-down procedure in this paper is mainly motivated by our goal to extend the scope of a previous result, it is often more appropriate than simply a step-up or step-down procedure. For instance, in assessing the superiority of a test drug over placebo and known active controls, it might be necessary to make some preliminary comparisons to see if the clinical trial is sensitive in the sense of being able to detect significant differences between at least a specified number of the known actives and the placebo. A generalized step-up–step-down procedure, as argued by Tamhane, Liu and Dunnett (1998), is appropriate in this case.

An important result obtained in this article toward strengthening the work of Benjamini and Yekutieli (2001) is an expression for the FDR of a generalized step-up–step-down procedure of order r with any set of critical values written explicitly in terms of the probability distribution of the ordered components of the underlying test statistics. Once we have this expression, it becomes clear how to choose the critical values and what sort of dependence structure of the test statistics is required in a generalized step-up–step-down procedure to have control of the FDR. This result, evolving from the previous work of Sarkar and Chang (1997) and Sarkar (1998) where a similar issue concerning the Simes (1986) test has been resolved, is different from that of Benjamini and Yekutieli (2001) and covers a larger class of stepwise procedures, including both step-up and step-down procedures. An upper bound to the FDR of a step-down procedure has also been derived using additional results on ordered random variables before answering the open question related to the Benjamini–Liu procedure. The MTP_2 property provides some key inequalities, thereby playing a vital role in the development of the main results.

The setup of the paper is as follows. Section 2 recalls the generalized step-up–step-down procedure of order r in terms of p-values and the definition of the PRDS property with examples. Some useful formulas related to the FDR of a generalized step-up–step-down procedure and an inequality related to the FDR of a step-down procedure are reported in Section 3. The main results are proved in Section 4. Proofs of most of the technical results and formulas are deferred to the Appendix.

2. Preliminaries. We will recall two things in this section, Tamhane–Liu–Dunnett's generalized step-up–step-down procedure and Benjamini–Yekutieli's PRDS property.

2.1. *Generalized step-up–step-down procedure of order r.* Suppose there are n null hypotheses $H_1, \dots, H_n$ that are to be simultaneously tested using the corresponding observed p-values $p_1, \dots, p_n$. Let the p-values be ordered as $p_{1:n} \le \cdots \le p_{n:n}$ with the corresponding null hypotheses $H_{1:n}, \dots, H_{n:n}$, respectively. Then given the critical values $0 \le \alpha_{1:n} \le \cdots \le \alpha_{n:n} \le 1$, a generalized step-up–step-down test procedure of order r starts with $p_{n-r+1:n}$. If $p_{n-r+1:n} >$

$\alpha_{n-r+1:n}$, the test accepts $H_{n-r+1:n}, \ldots, H_{n:n}$ and goes to general step (a); otherwise, it rejects $H_{1:n}, \ldots, H_{n-r+1:n}$ and goes to general step (b).

GENERAL STEP (a). Starting with $i = n - r + 1$, the test starts with $p_{i-1:n}$. If $p_{i-1:n} \leq \alpha_{i-1:n}$, testing stops by rejecting $H_{1:n}, \ldots, H_{i-1:n}$; otherwise, it accepts $H_{i-1:n}$ and setting $i = i - 1$ returns to the beginning of this step. For $i = 1$, the test stops.

GENERAL STEP (b). Starting with $i = n - r + 1$, the test starts with $p_{i+1:n}$. If $p_{i+1:n} \geq \alpha_{i+1:n}$, testing stops by accepting $H_{i+1:n}, \ldots, H_{n:n}$; otherwise, it rejects $H_{i+1:n}$ and setting $i = i + 1$ returns to the beginning of this step. For $i = n$, the test stops.

When $r = 1$ (or n), a generalized step-up–step-down procedure of order r is an ordinary step-up (or step-down) procedure. Readers are referred to Finner (1999), Finner and Roters (1998, 1999) and Liu (1996) for some interesting theoretical results related to step-up and step-down tests.

2.2. *The PRDS property.* An n-dimensional random vector $\mathbf{X} = (X_1, \ldots, X_n)$ or the corresponding multivariate distribution is said to be positive regression dependent on a subset $\{X_i,\ i \in M\}$, or simply on M (PRDS on M), where $M \subseteq \{1, \ldots, n\}$, if

(2.1) $P\{\mathbf{X} \in \mathbf{C} | X_i\}$ is nondecreasing (nonincreasing) in X_i for each $i \in M$,

for any increasing (decreasing) set $\mathbf{C}$. A set $\mathbf{C}$ is increasing (decreasing) if and only if $\mathbf{x} = (x_1, \ldots, x_n) \in \mathbf{C}$ implies that $\mathbf{x}' = (x_1', \ldots, x_n') \in \mathbf{C}$ for any $x_i \leq x_i'$ $(x_i \geq x_i')$, $i = 1, \ldots, n$. For our main result on the FDR-controlling property of a generalized step-up–step-down procedure, we require the test statistics to have a multivariate distribution that is PRDS on $I_0 = \{1, \ldots, n_0\}$, that is, on the subset of statistics $(X_1, \ldots, X_{n_0})$ corresponding to the true null hypotheses. Before we give examples of such distributions, it is useful to observe that a more restrictive property, that is,

(2.2) $E\{\phi(\mathbf{X}) | X_i\}$ is nondecreasing (nonincreasing) in X_i for all $i = 1, \ldots, n$,

for any coordinatewise nondecreasing (nonincreasing) function $\phi(\mathbf{X})$ of $\mathbf{X}$, is actually implied by the multivariate totally positive of order 2 (MTP_2) property [Karlin and Rinott (1980)]. If the probability density $f(x_1, \ldots, x_n)$ of $\mathbf{X}$ satisfies the inequality

$$f\big(\min(x_1, y_1), \ldots, \min(x_n, y_n)\big) f\big(\max(x_1, y_1), \ldots, \max(x_n, y_n)\big) \geq f(x_1, \ldots, x_n) f(y_1, \ldots, y_n)$$

for any two points $(x_1, \ldots, x_n)$ and $(y_1, \ldots, y_n)$, then $\mathbf{X}$ or its distribution is said to be MTP_2. The multivariate distribution of independent test statistics is the most trivial example of an MTP_2 distribution. As discussed in Karlin and Rinott (1980), Sarkar and Chang (1997) and Sarkar (1998), the multivariate normal distribution with zero means and nonnegative correlations is MTP_2. Notice that if $\mathbf{X}$ is MTP_2, then so is $\mathbf{X}+\mu$. Therefore, the multivariate normal distribution with any means and nonnegative correlations is MTP_2. Next, let $X_i = (\nu_0/\nu_i)(V_i/V_0)$, $i = 1, \dots, n$, where $V_i \sim \sigma_i^2 \chi_{\nu_i}^2$, $i = 0, 1, \dots, n$, and are independent. Then the joint density of $\mathbf{X} = (X_1, \dots, X_n)$, which is that of multivariate F, is of the form

$$\int_0^\infty \prod_{i=1}^n f_i(x_i, y) g(y)\, dy,$$

where

$$f_i(x, y) = \left[(2\theta_i y)^{\nu_i/2} \Gamma\left(\frac{\nu_i}{2}\right)\right]^{-1} \exp\left(-\frac{x_i}{2\theta_i y}\right) x_i^{\nu_i/2-1}, \qquad \theta_i = \frac{\nu_0 \sigma_i^2}{\nu_i \sigma_0^2},$$

for $i = 1, \dots, n$, and $g(y)$ is the density of $1/\chi_{\nu_0}^2$. Since $f_i(x, y)$ is TP_2 in (x, y) for each i, this integral is MTP_2 [see, e.g., Sarkar and Chang (1997)]. Thus, the multivariate distribution of independent test statistics, multivariate normal with nonnegative correlations, and multivariate F are all PRDS on any subset.

The MTP_2 properties of the studentized multivariate normal distribution with nonnegative correlations and absolute values of studentized independent normals are not obvious. Nevertheless, the property (2.1) with I_0 corresponding to the true null hypotheses can be verified, conditional on positive values for the studentized multivariate normal distribution and without any such condition for absolute-valued studentized independent normals. Below we describe briefly how these can be verified, although similar results were independently derived by Benjamini and Yekutieli (2001) using different arguments.

Let $X_i = \sqrt{\nu} Y_i / S$, $i = 1, \dots, n$, where $\mathbf{Y} = (Y_1, \dots, Y_n)$ is multivariate normal with unit variances and nonnegative correlations and $S^2 \sim \chi_\nu^2$ independently of $\mathbf{Y}$. Then, with $\psi(Y_i, S) = P[\mathbf{Y} \in \mathbf{D}(S) | Y_i, S]$, where $\mathbf{D}(S) = \{\mathbf{Y} : (\sqrt{\nu} Y_1/S, \dots, \sqrt{\nu} Y_n/S) \in \mathbf{C}\}$,

$$\begin{aligned} P\{\mathbf{X} \in \mathbf{C} | X_i\} &= E_S[\psi(Y_i, S) | X_i, S], \\ &= E_{S^*}[\psi(S^* U_i, S^*(1 - U_i^2)^{1/2}) | U_i, S^*], \end{aligned} \tag{2.3}$$

where $U_i = Y_i / S^*$, $S^{*2} = S^2 + Y_i^2$. Now note that, for each $i \in I_0$, U_i and S^{*2} are independent. Furthermore, if $\mathbf{C}$ is increasing and satisfies $a'\mathbf{C} \subset a\mathbf{C}$ for any $0 < a < a'$ (e.g., if $\mathbf{C}$ is of the form $\prod_{i=1}^n [a_i, \infty)$ with positive a_i's), then $\psi(Y_i, S)$ is increasing in Y_i for fixed S, because of the MTP_2 property of $\mathbf{Y}$, and decreasing in S for fixed Y_i, because $\mathbf{D}(S)$ is decreasing in S. Therefore, the probability in (2.3) is increasing in U_i, and hence in X_i, as long as $X_i > 0$.

The distribution of $|\mathbf{Y}| = (|Y_1|, \dots, |Y_n|)$ is not MTP_2 unless the Y_i's are uncorrelated. Making the same kind of arguments as above for $|\mathbf{X}| = (|X_1|, \dots, |X_n|)$

when the underlying correlations are 0, we see that this is PRDS on I_0; that is, the absolute values of studentized independent normals are PRDS on I_0.

3. Some useful formulas and inequalities. We present some lemmas in this section, with proofs given in the Appendix, providing the formulas and inequalities required to prove our main results in the next section. Suppose that the null hypotheses $H_1, \dots, H_n$ are tested using some continuous test statistics $X_1, \dots, X_n$, respectively, that are identically, not necessarily independently, distributed under the null hypotheses. For any $J \subseteq \{1, \dots, n\}$, we will use the notation $X_{1:J} \le \cdots \le X_{|J|:J}$ for the ordered components of the subset $\{X_i,\ i \in J\}$; sometimes, however, we will call them $X_{1:n} \le \cdots \le X_{n:n}$ when $J = \{1, \dots, n\}$. Since a left-tailed test based on X_i can be converted to a right-tailed test based on some suitable transformation of X_i, without any loss of generality only right-tailed tests are being considered. Let $H_{1:n}, \dots, H_{n:n}$ be the hypotheses corresponding to $X_{1:n}, \dots, X_{n:n}$, respectively. Then the step-up–setp-down procedure of order r in terms of the $X_{i:n}$'s and the critical values $c_{1:n} \le \cdots \le c_{n:n}$, where $\Pr(X_1 \ge c_{i:n}) = \alpha_{n-i+1:n}$, for $i = 1, \dots, n$, starts with $X_{r:n}$. If $X_{r:n} < c_{r:n}$, it accepts $H_{1:n}, \dots, H_{r:n}$ and continues to test $H_{r+1:n}, \dots, H_{n:n}$ in a step-up manner using $(X_{r+1:n}, \dots, X_{n:n})$ and $(c_{r+1:n}, \dots, c_{n:n})$. Otherwise, it rejects $H_{r:n}, \dots, H_{n:n}$ and continues to test $H_{1:n}, \dots, H_{r-1:n}$ in a step-down manner using $(X_{1:n}, \dots, X_{r-1:n})$ and $(c_{1:n}, \dots, c_{r-1:n})$.

Let us suppose, without any loss of generality, that out of the total n null hypotheses, the first n_0 hypotheses $H_1, \dots, H_{n_0}$ are the true null hypotheses and the rest are false. Partitioning the space of $(X_1, \dots, X_n)$ in terms of the disjoint subsets

$$\begin{aligned} A^r_{j,n} &= \{X_{j:n} < c_{j:n}, X_{j+1:n} \ge c_{j+1:n}, \dots, X_{r:n} \ge c_{r:n}\} \qquad \text{for } j = 0, 1, \dots, r-1 \\ &= \{X_{r:n} < c_{r:n}, \dots, X_{j:n} < c_{j:n}, X_{j+1:n} \ge c_{j+1:n}\} \qquad \text{for } j = r, \dots, n, \end{aligned}$$

where $A^r_{0,n} = \{X_{1:n} \ge c_{1:n}, \dots, X_{r:n} \ge c_{r:n}\}$ and $A^r_{n,n} = \{X_{r:n} < c_{r:n}, \dots, X_{n:n} < c_{n:n}\}$, and observing that

$$A^r_{j,n} \equiv \{R = n - j\}, \qquad j = 0, 1, \dots, n,$$

we have

$$\begin{aligned} \text{FDR} &= E\{V I(R > 0)/R\} \\ &= \sum_{j=0}^{n-1} \frac{1}{n-j} E\{V I(R = n-j)\} \\ &= \sum_{j=0}^{n-1} \frac{1}{n-j} \sum_{i=1}^{n_0} E\{I(H_i \text{ is rejected},\ R = n-j)\}. \end{aligned} \tag{3.1}$$

Once the event $\{R = n - j\}$ occurs, resulting in acceptance of $H_{1:n}, \dots, H_{j:n}$ and rejection of $H_{j+1:n}, \dots, H_{n:n}$, the hypotheses H_i, $i = 1, \dots, n_0$, will be rejected if and only if $X_i \geq c_{j+1:n}$. Thus, we have

$$\text{FDR} = \sum_{i=1}^{n_0} \sum_{j=0}^{n-1} \frac{1}{n-j} P\{X_i \geq c_{j+1:n},\ R = n - j\}. \tag{3.2}$$

Before we proceed further to obtain a more explicit expression for (3.2), it is important to note that the following lemma, in addition to being useful for a later proof, provides a step in checking why (3.2) reduces to $P\{R > 0\}$ once all the hypotheses are assumed to be true.

LEMMA 3.1.

$$\sum_{i=1}^{n} P\{X_i \geq c_{j+1:n},\ R = n - j\} = (n - j) P\{R = n - j\}. \tag{3.3}$$

The following lemma gives an explicit expression for the FDR of a generalized step-up–step-down procedure of order r with any set of critical values in terms of the probability distribution of the ordered components of the underlying test statistics.

LEMMA 3.2. *The FDR of a generalized step-up–step-down procedure of order r for testing n null hypotheses $H_1, \dots, H_n$ in terms of right-tailed tests based on $X_1, \dots, X_n$ and critical values $c_{1:n} \leq \cdots \leq c_{n:n}$ is*

$$\begin{aligned} FDR = {} & \frac{1}{n-r+1} \sum_{i=1}^{n_0} P\{X_i \geq c_{r:n}\} \\ & + \sum_{i=1}^{n_0} \sum_{j=1}^{r-1} E\biggl[P\{X_{j:n} \geq c_{j:n}, \dots, X_{r:n} \geq c_{r:n} | X_i\} \\ & \qquad \times \biggl\{ \frac{I(X_i \geq c_{j:n})}{n-j+1} - \frac{I(X_i \geq c_{j+1:n})}{n-j} \biggr\} \biggr] \\ & + \sum_{i=1}^{n_0} \sum_{j=r}^{n-1} E\biggl[P\{X_{r:n} < c_r, \dots, X_{j:n} < c_{j:n} | X_i\} \\ & \qquad \times \biggl\{ \frac{I(X_i \geq c_{j+1:n})}{n-j} - \frac{I(X_i \geq c_{j:n})}{n-j+1} \biggr\} \biggr], \end{aligned} \tag{3.4}$$

where the probabilities are determined assuming that $H_1, \dots, H_{n_0}$ are the true hypotheses and the rest are false.

Next, we will present a lemma that provides an upper bound to the FDR of a step-down procedure (i.e., when $r = n$). Let $X_{n_0+1}, \dots, X_n$ be the statistics corresponding to the false hypotheses. Then, with $I_1 = \{n_{0+1}, \dots, n\}$, define $B_{j:I_1} = \{X_{j:I_1} < c_{n_0+j:n}, X_{j+1:I_1} \geq c_{n_0+j+1:n}, \dots, X_{n_1:I_1} \geq c_{n:n}\}$, which is the event that the step-down procedure based on $(X_{n_0+1}, \dots, X_n)$ and the critical values $(c_{n_0+1:n}, \dots, c_{n:n})$ will accept j and reject $n_1 - j$ of the false hypotheses for $j = 0, \dots, n_1$.

LEMMA 3.3. *For a step-down procedure for testing n null hypotheses $H_1, \dots, H_n$ in terms of right-tailed tests based on $X_1, \dots, X_n$ and critical values $c_{1:n} \leq \cdots \leq c_{n:n}$, we have*

$$FDR \leq \sum_{j=0}^{n_1} \frac{n_0 + j}{n} P\{X_{n_0:I_0} \geq c_{n_0+j:n}, B_{j,I_1}\}. \tag{3.5}$$

The next lemma presents a result on MTP_2 distributions that will be used later to determine critical values of an FDR-controlling step-down procedure.

LEMMA 3.4. *Let $X_{n_0:I_0} = \max(X_i,\ i \in I_0)$. If $(X_1, \dots, X_n)$ is MTP_2, then, for any fixed $1 \leq k \leq n_0$, the conditional distribution of $(X_{n_0:I_0}, X_{n_0+1}, \dots, X_n)$ given $X_{n_0:I_0} = X_k$ is MTP_2.*

4. Main results. The two main results of this paper are presented with proofs in this section.

THEOREM 4.1. *Suppose that we have a generalized step-up–step-down procedure of order r involving right-tailed tests based on continuous test statistics $(X_1, \dots, X_n)$ that are identically distributed with the common cdf $F(x)$ under the true null hypotheses. If the joint distribution of $(X_1, \dots, X_n)$ is PRDS on the subset of test statistics corresponding to the true null hypotheses, conditional on $\{X_i > a, i = 1, \dots, n\}$ for some fixed a, then the FDR of this procedure is less than or equal to $n_0\alpha/n$, where $0 < \alpha < 1 - F(a)$, if the critical values $c_{1:n} \leq \cdots \leq c_{n:n}$ satisfy $F(c_{j:n}) = 1 - (n - j + 1)\alpha/n$ for $j = 1, \dots, n$.*

PROOF. Our proof relies on Lemma 3.2. First, note that

$$\frac{I(X_i \geq c_{j:n})}{n - j + 1} - \frac{I(X_i \geq c_{j+1:n})}{n - j} \geq \text{ or } \leq 0 \tag{4.1}$$

according as $X_i \leq$ or $\geq c_{j+1:n}$. Also, since $c_{j:n} > a$ for all $j = 1, \dots, n$ and $\{X_{j:n} \geq c_{j:n}, \dots, X_{r:n} \geq c_{r:n}\}$ is an increasing set, the conditional probability

$P\{X_{j:n} \geq c_{j:n}, \dots, X_{r:n} \geq c_{r:n} | X_i\}$ is increasing in $X_i > a$ for all $i = 1, \dots, n_0$, $j = 1, \dots, r-1$ under the assumed PRDS condition. Therefore,

$$
\begin{aligned}
&E\biggl[P\{X_{j:n} \geq c_{j:n}, \dots, X_{r:n} \geq c_{r:n} | X_i\} \\
&\qquad \times \biggl\{\frac{I(X_i \geq c_{j:n})}{n-j+1} - \frac{I(X_i \geq c_{j+1:n})}{n-j}\biggr\}\biggr] \\
&\quad \leq P\{X_{j:n} \geq c_{j:n}, \dots, X_{r:n} \geq c_{r:n} | X_i = c_{j+1:n}\} \\
&\qquad \times \biggl\{\frac{P(X_i \geq c_{j:n})}{n-j+1} - \frac{P(X_i \geq c_{j+1:n})}{n-j}\biggr\}
\end{aligned}
\tag{4.2}
$$

for all $i = 1, \dots, n_0$, $j = 1, \dots, r-1$. Similar arguments can be made to obtain

$$
\begin{aligned}
&E\biggl[P\{X_{r:n} < c_{r:n}, \dots, X_{j:n} < c_{j:n} | X_i\} \\
&\qquad \times \biggl\{\frac{I(X_i \geq c_{j+1:n})}{n-j} - \frac{I(X_i \geq c_{j:n})}{n-j+1}\biggr\}\biggr] \\
&\quad \leq P\{X_{r:n} < c_{r:n}, \dots, X_{j:n} < c_{j:n} | X_i = c_{j+1:n}\} \\
&\qquad \times \biggl\{\frac{P(X_i \geq c_{j+1:n})}{n-j} - \frac{P(X_i \geq c_{j:n})}{n-j+1}\biggr\}
\end{aligned}
\tag{4.3}
$$

for all $i = 1, \dots, n_0$, $j = r, \dots, n-1$. The theorem then follows by applying (4.2) and (4.3) to Lemma 3.2. □

REMARK 4.1. The above theorem strengthens the work of Benjamini and Yekutieli (2001) by extending it to a more general scenario covering both step-up and step-down procedures. We establish that the FDR of a generalized step-up–step-down procedure can be controlled at any $0 < \alpha < 1$ if the test statistics are independent, or have a joint distribution that is multivariate normal with positive correlations, absolute-valued multivariate t corresponding to independent normals or multivariate F. For absolute-valued multivariate t corresponding to dependent normals with nonnegative correlations, the FDR can be controlled at a value less than 0.5. For example, in many-to-one comparisons of means in a one-way layout with one-sided alternatives, a generalized step-up–step-down procedure can control the FDR. Other specific situations where this theorem is applicable involve simultaneous testing of the means of several independent populations with a common but unknown variance against one- or two-sided alternatives and many-to-one comparisons of variances in a balanced one-way layout with one-sided alternatives. The necessary formulas developed in this article are, however, different, providing new results in the area of ordered random variables.

In the case of $r = 1$, that is, for a step-up procedure, a slightly stronger result than what is stated above actually follows when the statistics are independent. Notice that

$$\{X_{r:n} < c_{r:n}, \ldots, X_{j:n} < c_{j:n},\ X_i \geq c_{k:n}\}$$
$$= \{X_{r:J_i} < c_{r:n}, \ldots, X_{j:J_i} < c_{j:n},\ X_i \geq c_{k:n}\}$$

for all $k \geq j$, $1 \leq r \leq j \leq n-1$, where $J_i = \{1, \ldots, n\} - \{i\}$ and $X_{1:J_i} \leq \cdots \leq X_{n-1:J_i}$ are the ordered components of $\{X_j,\ j \in J_i\}$. Hence, when the X_i's are independent, we have equality in (4.3), implying that, for a step-up test involving independent test statistics,

$$\text{FDR} = \frac{n_0}{n}[1 - F(c_{1:n})] + \sum_{i=1}^{n_0}\sum_{j=1}^{n-1} P\{X_{r:J_i} < c_{r:n} \ldots, X_{j:J_i} < c_{j:n}\} \times \left\{\frac{[1 - F(c_{j+1:n})]}{n-j} - \frac{[1 - F(c_{j:n})]}{n-j+1}\right\}. \tag{4.4}$$

This becomes exactly equal to $n_0\alpha/n$ when the critical values satisfy the condition stated in Theorem 4.2 with $r = 1$. This is what Benjamini and Yekutieli (2001) have proved using different arguments.

We have a new result here on the FDR in a step-down procedure. In situations where the Benjamini–Hochberg step-up procedure controls the FDR, a step-down procedure with the same set of critical values also controls the FDR. It may not be a surprising result in the context of the FWE rate, because one can see that the event $\{R_r \geq k\}$, where R_r is the number of rejections in a generalized step-up–step-down procedure of order r, which is

$$\begin{aligned}\bigcup_{j=0}^{n-k} A_{j,n}^r &= \{X_{r:n} < c_{r:n}, \ldots, X_{n-k+1:n} < c_{n-k+1:n}\}^c \\ &\qquad \text{for } k = 0, 1, \ldots, n-r \\ &= \{X_{n-k+1:n} \geq c_{n-k+1:n}, \ldots, X_{r:n} \geq c_{r:n}\} \\ &\qquad \text{for } k = n-r+1, \ldots, n,\end{aligned} \tag{4.5}$$

is decreasing in r, implying that both V_r, the number of false rejections, and R_r are stochastically decreasing in r. Therefore, controlling the FWE of a step-up procedure will ensure the same property for the other step-up–step-down procedures, including the step-down procedure, with the same set of critical values. This is not so obvious in the context of the FDR. In other words, whether or not the probability distribution of V_r/R_r, conditional on $\{R_r > 0\}$, is stochastically decreasing in r is not clear. Still, why is it an important result that both step-down and step-up procedures corresponding to the same set of critical values control the FDR even if the step-up procedure is more powerful in the sense of ensuring an increased number of rejections? An answer lies in Abramovich, Benjamini, Donoho and Johnstone (2000). In the model selection problem they considered, the optimal penalized version is between the step-down (backward elimination) and step-up (forward selection) procedures with the same set of critical values that are known to control the FDR of the step-up procedure. They have shown that asymptotically, with the number of parameters increasing, the stopping points of the two procedures are close to each other, and therefore both control the FDR. The present work proves that both forward selection and backward elimination versions control the FDR in finite problems.

The above FDR-controlling step-down procedure is different from the Benjamini–Liu (1999) step-down procedure where the critical values $c_{j:n}$'s are such that

$$F(c_{j:n}) = \left[1 - \min\left(1, \frac{n}{j}\alpha\right)\right]^{1/j}, \qquad j = 1, \dots, n. \tag{4.6}$$

They have proved that this step-down procedure controls the FDR at α when the statistics are independent. What happens to the FDR of this procedure when the statistics are dependent? This is what we are going to answer next.

THEOREM 4.2. *The FDR of the Benjamini–Liu step-down procedure is controlled at α if the underlying test statistics are MTP_2 under any alternatives and exchangeable when the hypotheses are true.*

PROOF. Our proof relies on Lemma 3.3. Write B_{j,I_1}, for $j = 0, 1, \dots, n_1$, as $B_{j,I_1} = C_{j+1,I_1} - C_{j,I_1}$, where $C_{j,I_1} = \{X_{j:I_1} \ge c_{n_0+j:n}, \dots, X_{n_1:I_1} \ge c_{n:n}\}$, with C_{0,I_1} and $C_{n_1+1:I_1}$ being the null and sure events, respectively. The right-hand side of (3.5) can then be expressed as follows:

$$\begin{aligned}
&\frac{1}{n}\sum_{j=0}^{n_1}(n_0 + j)P\{X_{n_0:I_0} \ge c_{n_0+j:n}, C_{j+1,I_1} - C_{j,I_1}\} \\
&\quad = P\{X_{n_0:I_0} \ge c_{n:n}\} + \frac{1}{n}\sum_{j=1}^{n_1}\big[(n_0 + j - 1)P\{C_{j:I_1}, X_{n_0:I_0} \ge c_{n_0+j-1:n}\} \\
&\qquad\qquad - (n_0 + j)P\{C_{j:I_1}, X_{n_0:I_0} \ge c_{n_0+j:n}\}\big] \\
&\quad = P\{X_{n_0:I_0} \ge c_{n:n}\} \\
&\qquad + \frac{1}{n}\sum_{j=1}^{n_1} E\big[P\{C_{j:I_1} | X_{n_0:I_0}\}\big\{(n_0 + j - 1)I(X_{n_0:I_0} \ge c_{n_0+j-1:n}) \\
&\qquad\qquad - (n_0 + j)I(X_{n_0:I_0} \ge c_{n_0+j:n})\big\}\big].
\end{aligned} \tag{4.7}$$

Now suppose that the following condition holds:

$$E\{\phi(X_{n_0+1},\dots,X_n)|X_{n_0:I_0}\} \text{ is nondecreasing in } X_{n_0:I_0} \tag{4.8}$$

for any coordinatewise nondecreasing function ϕ of $(X_{n_0+1},\dots,X_n)$. Since C_{j,I_1} is nondecreasing in $(X_{n_0+1},\dots,X_n)$, we get, using the kind of arguments made in (4.2), that

$$\begin{aligned} &E\big[P\{C_{j,I_1}|X_{n_0:I_0}\}\{(n_0+j-1)I(X_{n_0:I_0}\ge c_{n_0+j-1:n}) \\ &\qquad\qquad - (n_0+j)I(X_{n_0:I_0}\ge c_{n_0+j:n})\}\big] \\ &\quad\le P\{C_{j:I_1}|X_{n_0:I_0}=c_{n_0+j:n}\}\{(n_0+j-1)P(X_{n_0:I_0}\ge c_{n_0+j-1:n}) \\ &\qquad\qquad - (n_0+j)P(X_{n_0:I_0}\ge c_{n_0+j:n})\}. \end{aligned} \tag{4.9}$$

Using this in the last line of (4.7) and going back to the first line, we finally have

$$\begin{aligned} \text{FDR} &\le \frac{1}{n}\sum_{j=0}^{n_1}(n_0+j)P\{X_{I_0:n_0}\ge c_{n_0+j:n}\} \\ &\quad\times\big[P\{C_{j+1,I_1}|X_{n_0:I_0}=c_{n_0+j+1:n}\} - P\{C_{j,I_1}|X_{n_0:I_0}=c_{n_0+j:n}\}\big]. \\ &\le \frac{1}{n}\max_{0\le j\le n_1}\big[(n_0+j)P\{X_{n_0:I_0}\ge c_{n_0+j:n}\}\big] \\ &\quad\times\sum_{j=0}^{n_1}\big[P\{C_{j+1,I_1}|X_{n_0:I_0}=c_{n_0+j+1:n}\} - P\{C_{j,I_1}|X_{n_0:I_0}=c_{n_0+j:n}\}\big] \\ &= \frac{1}{n}\max_{0\le j\le n_1}\big[(n_0+j)P\{X_{n_0:I_0}\ge c_{n_0+j:n}\}\big]. \end{aligned} \tag{4.10}$$

The second inequality in (4.10) uses the fact that the difference $P\{C_{j+1,I_1}|X_{n_0:I_0}=c_{n_0+j+1:n}\} - P\{C_{j,I_1}|X_{n_0:I_0}=c_{n_0+j:n}\}$, because of condition (4.8), is greater than or equal to $P\{B_{j,I_1}|X_{n_0:I_0}=c_{n_0+j:n}\}$ and hence is nonnegative for all $j=0,1,\dots,n_1$. Since $X_{n_0:I_0}<X_{|J|:J}$ for every $J\supseteq I_0$, the FDR in (4.10) is less than or equal to α for any n_0 if the $c_{j:n}$'s satisfy

$$\frac{j}{n}P\{\max(X_1,\dots,X_j)\ge c_{j:n}\}\le\alpha \qquad \text{for all } j=1,\dots,n, \tag{4.11}$$

assuming that all the hypotheses are true. When the X_j's are independent, the $c_{j:n}$'s satisfying (4.11) are those in (4.6) given by Benjamini and Liu (1999). The same $c_{j:n}$'s will satisfy (4.11) with dependent X_j's if the following property holds, at least when the underlying hypotheses are true:

$$P\{X_j\le c_{j:n}, j=1,\dots,n\}\ge\prod_{j=1}^{n}P\{X_j\le c_{j:n}\} \qquad \text{for all } (c_{1:n},\dots,c_{n:n}). \tag{4.12}$$

To see that conditions (4.8) and (4.12) hold for the multivariate distributions considered in the theorem, first note that

$$
\begin{aligned}
&E\{\phi(X_{n_0+1},\dots,X_n)|X_{n_0:I_0}=x\}\\
&\quad=\sum_{k=1}^{n_0}E\{\phi(X_{n_0+1},\dots,X_n)|X_{n_0:I_0}=x,\ X_k=X_{n_0:I_0}\}\\
&\qquad\times P\{X_k=X_{n_0:I_0}|X_{n_0:I_0}=x\},
\end{aligned}
$$

which reduces to

$$
\frac{1}{n_0}\sum_{k=1}^{n_0}E\{\phi(X_{n_0+1},\dots,X_n)|X_{n_0:I_0}=x,\ X_k=X_{n_0:I_0}\} \tag{4.13}
$$

because of the exchangeability condition of the X_j's under the true hypotheses. Since the X_j's are also MTP_2 under any alternatives, each of the conditional expectations in (4.13), and hence that in (4.8), with nondecreasing ϕ is nondecreasing in x. This is because of Lemma 2.4. The condition (4.12), which is the positive quadrant dependence condition, is a consequence of the MTP_2 property [see, e.g., Karlin and Rinott (1980)]. Thus, the theorem is proved. □

REMARK 4.2. Multivariate distributions satisfying the properties stated in Theorem 4.2 include those of i.i.d. test statistics, and multivariate normal with nonnegative common correlations. For example, in many-to-one comparisons of means in a balanced one-way layout with one-sided alternatives and known variances, the Benjamini–Liu procedure controls the FDR.

It is to be noted that the step-down procedure with the critical values satisfying (4.11) actually provides a modification of the Benjamini–Liu procedure for the dependence case. If the joint distribution of $(X_1,\dots,X_j)$ is completely specified under $\bigcap_{i=1}^{j} H_i$, for all $j=1,\dots,n$, and the conditions stated in Theorem 4.2 hold, then it controls the FDR at α.

In the Benjamini–Liu procedure, $c_{j:n}=-\infty$ for $j\le[n\alpha]$. Therefore, if it continues up to $n-[n\alpha]$ steps without accepting any of the null hypotheses, it stops and declares all of them to be false. Some null hypotheses, even with extremely small values of the corresponding test statistics, may end up being rejected. This particular feature, as Benjamini and Liu (1999) have argued, is not quite unrealistic. Since the hypotheses are being tested simultaneously, a few false rejections are allowed in controlling the FDR when many correct rejections have already been made. One may, however, want to protect against rejecting a null hypothesis with a small value of the corresponding test statistic by restricting all the test statistics to have values more than a certain prespecified number. This is not going to inflate the FDR in the situations stated in Theorem 4.2 because the MTP_2 as well as the exchangeability conditions still holds for the conditional distribution on a set like $\{X_i\ge a,\ i=1,\dots,n\}$ for any fixed a.

APPENDIX

PROOF OF LEMMA 3.1. First note that the event $\{R = n - j\}$, that is, $A^r_{j,n}$, can be written as $\bigcup_J A_J$, where the union is taken over all $J \subseteq \{1, \dots, n\}$ such that $|J| = j$ and the A_J's are the following disjoint subsets:

$$A_J = \Big\{\max_{k\in J} X_k < c_{j:n},\ X_{1:J^c} \ge c_{j+1:n}, \dots, X_{r-j:J^c} \ge c_{n:n}\Big\} \qquad \text{for } j = 0, 1, \dots, r-1,$$

$$= \Big\{X_{r:J} < c_{r:n}, \dots, X_{j:J} < c_{j:n},\ \min_{k\in J^c} X_k \ge c_{j+1:n}\Big\} \qquad \text{for } j = r, \dots, n.$$

Since $\{X_i \ge c_{j+1:n}, A_J\} = A_J$ if $i \in J^c$ and $=\varnothing$ otherwise, we have

$$\begin{aligned}\sum_{i=1}^{n} P\{X_i \ge c_{j+1,n},\ R = n - j\} &= \sum_{i=1}^{n} \sum_{J:J^c \ni i} P\{A_J\} \\ &= \sum_{J} \sum_{i:i\in J^c} P\{A_J\} \\ &= (n-j) \sum_{J} P\{A_J\} \\ &= (n-j)P\{R = n-j\}.\end{aligned}$$

Thus, the lemma follows. □

PROOF OF LEMMA 3.2. First note that

$$\sum_{j=0}^{r-1} \frac{1}{n-j} P\{X_i \ge c_{j+1:n},\ R = n - j\}$$

$$= \sum_{j=1}^{r} \frac{1}{n-j+1} P\{X_i \ge c_{j:n},\ R \ge n-j+1\}$$

$$- \sum_{j=1}^{r-1} \frac{1}{n-j} P\{X_i \ge c_{j+1:n},\ R \ge n-j+1\} \tag{A.1}$$

$$= \frac{1}{n-r+1} P\{X_i \ge c_{r:n},\ R \ge n-r+1\}$$

$$+ \sum_{j=1}^{r-1} E\bigg[P\{R \ge n-j+1|X_i\}\bigg\{\frac{I(X_i \ge c_{j:n})}{n-j+1} - \frac{I(X_i \ge c_{j+1:n})}{n-j}\bigg\}\bigg]$$

$$= \frac{1}{n-r+1} P\{X_{r:n} \geq c_{r:n},\ X_i \geq c_{r:n}\}$$
$$+ \sum_{j=1}^{r-1} E\Big[P\{X_{j:n} \geq c_{j:n}, \ldots, X_{r:n} \geq c_{r:n} | X_i\}$$
$$\times \Big\{ \frac{I(X_i \geq c_{j:n})}{n-j+1} - \frac{I(X_i \geq c_{j+1:n})}{n-j} \Big\}\Big].$$

The last equality follows from (4.5). Also,

$$\sum_{j=r}^{n-1} \frac{1}{n-j} P\{X_i \geq c_{j+1:n},\ R = n-j\}$$
$$= \sum_{j=r}^{n-1} \frac{1}{n-j} P\{X_i \geq c_{j+1:n},\ R \leq n-j\}$$
$$- \sum_{j=r+1}^{n-1} \frac{1}{n-j+1} P\{X_i \geq c_{j:n},\ R \leq n-j\}$$
$$= \frac{1}{n-r+1} P\{X_i \geq c_{r:n},\ R \leq n-r\}$$
$$\text{(A.2)} \qquad - \sum_{j=r}^{n-1} E\Big[P\{R \leq n-j | X_i\}$$
$$\times \Big\{ \frac{I(X_i \geq c_{j:n})}{n-j+1} - \frac{I(X_i \geq c_{j+1:n})}{n-j} \Big\}\Big]$$
$$= \frac{1}{n-r+1} P\{X_{r:n} < c_{r:n},\ X_i \geq c_{r:n}\}$$
$$+ \sum_{j=r}^{n-1} E\Big[P\{X_{r:n} < c_{r:n}, \ldots, X_{j:n} < c_{j:n} | X_i\}$$
$$\times \Big\{ \frac{I(X_i \geq c_{j+1:n})}{n-j} - \frac{I(X_i \geq c_{j:n})}{n-j+1} \Big\}\Big].$$

Again, (4.5) is used in the last equality of (A.2). Combining (A.1) and (A.2), we get the proof of Lemma 3.2. □

PROOF OF LEMMA 3.3. The FDR of the step-down procedure with critical values $c_{1:n} \leq \cdots \leq c_{n:n}$ is given by

$$\text{(A.3)} \qquad \text{FDR} = \sum_{i=1}^{n_0} \sum_{j=0}^{n-1} \frac{1}{n-j} P\{X_i \geq c_{j+1:n},\ R = n-j\},$$

with R still representing the total number of rejections. From Lemma 3.1, we note that (A.3) reduces to $P\{X_{n:n} \geq c_{n:n}\}$ if we extend the first summation up to $i = n$.

Therefore, we can write (A.3) as

$$\text{(A.4)}\quad \text{FDR} = P\{X_{n:n} \ge c_{n:n}\} - \sum_{i=n_0+1}^{n} \sum_{j=0}^{n-1} \frac{1}{n-j} P\{X_i \ge c_{j+1:n},\ R = n-j\}.$$

The first probability in (A.4) can be expressed as

$$\text{(A.5)}\quad \begin{aligned} &P\{X_{n:n} \ge c_{n:n}\} \\ &\quad = P\{X_{n_1:I_1} \ge c_{n:n}\} + P\{X_{n_0:I_0} \ge c_{n:n},\ X_{n_1:I_1} < c_{n:n}\}. \end{aligned}$$

Let R^* denote the total number of rejections in the step-down procedure based on $(X_{n_{0+1}}, \dots, X_n)$ and the critical values $(c_{n_{0+1}:n}, \dots, c_{n:n})$. Then the double summation in (A.4) can be written as

$$\text{(A.6)}\quad \sum_{k=0}^{n_1} \sum_{i=n_0+1}^{n} \sum_{j=0}^{n-1} \frac{1}{n-j} P\{X_i \ge c_{j+1:n},\ R = n-j,\ R^* = n_1 - k\}.$$

Since $c_{j+1:n} \le c_{n_0+k+1:n}$ for $j \le n_0 + k$, (A.6) is greater than or equal to

$$\text{(A.7)}\quad \begin{aligned} &\sum_{k=0}^{n_1-1} \sum_{i=n_0+1}^{n} \sum_{j=0}^{n_0+k} \frac{1}{n-j} P\{X_i \ge c_{n_0+k+1:n},\ R = n-j,\ R^* = n_1 - k\} \\ &\quad = \sum_{k=0}^{n_1-1} \sum_{j=0}^{n_0+k} \frac{n_1 - k}{n-j} P\{R = n-j,\ R^* = n_1 - k\}. \end{aligned}$$

The equality in (A.7) follows from the result

$$\sum_{i=n_0+1}^{n} P\{X_i \ge c_{n_0+k+1:n},\ R^* = n_1 - k | R\} = (n_1 - k) P\{R^* = n_1 - k | R\},$$

which can be proved as in Lemma 3.1.

We will now prove, using the following supporting result (Result A.1) on ordered random variables that (A.7) is greater than or equal to

$$\text{(A.8)}\quad P\{X_{n_1:I_1} \ge c_{n:n}\} - \sum_{k=0}^{n_1-1} \frac{n_0 + k}{n} P\{X_{n_0:I_0} \ge c_{n_0+k:n},\ R^* = n_1 - k\}.$$

Once it is proved, we can use (A.5) and (A.8) in (A.4) to obtain

$$\begin{aligned} \text{FDR} \le &\sum_{k=0}^{n_1-1} \frac{n_0 + k}{n} P\{X_{n_0:I_0} \ge c_{n_0+k:n},\ R^* = n_1 - k\} \\ &+ P\{X_{n_0:I_0} \ge c_{n:n},\ R^* = 0\}, \end{aligned}$$

proving the lemma. □

RESULT A.1. *For any fixed* $a_1 \le \cdots \le a_n$ *and* $J \subseteq \{1, \ldots, n\}$,

$$\{Y_{1:n} \ge a_1, \ldots, Y_{n:n} \ge a_n,\ Y_{1:J^c} \ge a_{|J|+1}, \ldots, Y_{|J^c|:J^c} \ge a_n\}$$
$$= \{Y_{1:J} \ge a_1, \ldots, Y_{|J|:J} \ge a_{|J|},\ Y_{1:J^c} \ge a_{|J|+1}, \ldots, Y_{|J^c|:J^c} \ge a_n\}.$$

PROOF. To prove the desired inequality, that is, that (A.7) is greater than or equal to (A.8), we first note that, given $B_{k,I_1} = \{R^* = n_1 - k\}$, k of the n_1 random variables $X_{n_0+1}, \ldots, X_n$ are all less than $c_{n_0+k:n}$ and the ordered components of the remaining $n_1 - k$ random variables are greater than or equal to $c_{n_0+k+1:n}, \ldots, c_{n:n}$, respectively. Therefore, for every fixed $k = 0, \ldots, n_1 - 1$, we have

$$\begin{aligned}
&\sum_{j=0}^{n_0+k} \frac{n_1 - k}{n - j} P\{R = n - j,\ R^* = n_1 - k\} \\
&\quad= \sum_{j=0}^{n_0+k} \frac{n_1 - k}{n - j} \sum_{J:|J|=k} P\Big\{X_{j:n} < c_{j:n},\ X_{j+1:n} \ge c_{j+1:n}, \ldots, X_{n:n} \ge c_{n:n}, \\
&\qquad\qquad \max_{i \in J} X_i < c_{n_0+k:n},\ X_{1:I_1 \setminus J} \ge c_{n_0+k+1:n}, \ldots, \\
&\qquad\qquad X_{n_1-k:I_1 \setminus J} \ge c_{n:n}\Big\} \\
&\quad= \sum_{j=0}^{n_0+k} \frac{n_1 - k}{n - j} \sum_{J:|J|=k} P\{X_{j:I_0 \cup J} < c_{j:n},\ X_{j+1:I_0 \cup J} \ge c_{j+1:n}, \ldots, \\
&\qquad\qquad X_{n_0+k:I_0 \cup J} \ge c_{n_0+k:n},\ R^* = n_1 - k\},
\end{aligned} \tag{A.9}$$

where $J \subseteq I_1$, $I_1 \setminus J = I_1 - J$ and, for each J with $|J| = k$, $X_{1:I_0 \cup J} \le \cdots \le X_{n_0+k:I_0 \cup J}$ are the ordered components of the $(n_0 + k)$-dimensional set containing $(X_1, \ldots, X_{n_0})$ and $(X_i,\ i \in J)$. Then

$$\begin{aligned}
&\{X_{j:n} \ge c_{j:n}, \ldots, X_{n:n} \ge c_{n:n}, X_{1:I_1 \setminus J} \ge c_{n_0+k+1:n}, \ldots, X_{n_1-k:I_1 \setminus J} \ge c_{n:n}\} \\
&\quad= \{X_{j:I_0 \cup J} \ge c_{j:n}, \ldots, X_{n_0+k:I_0 \cup J} \ge c_{n_0+k:n}, \\
&\qquad X_{1:I_1 \setminus J} \ge c_{n_0+k+1:n}, \ldots, X_{n_1-k:I_1 \setminus J} \ge c_{n:n}\}
\end{aligned}$$

for $j = 0, \ldots, n_0 + k - 1$, which is obtained from Result A.1 with $a_i = -\infty$ for $i = 1, \ldots, j$ and $= c_{i:n}$ for $i = j + 1, \ldots, n$, provides the last step in (A.9). The summation in (A.9) without the $(n_0 + k)$th term is greater than or equal to

$$\begin{aligned}
&\frac{n_1 - k}{n} \sum_{j=0}^{n_0+k-1} \sum_{J:|J|=k} P\{X_{j:I_0 \cup J} < c_{j:n},\ X_{j+1:I_0 \cup J} \ge c_{j+1:n}, \ldots, \\
&\qquad\qquad X_{n_0+k:I_0 \cup J} \ge c_{n_0+k:n},\ R^* = n_1 - k\} \\
&\quad= \frac{n_1 - k}{n} \sum_{J:|J|=k} P\{X_{n_0+k:I_0 \cup J} \ge c_{n_0+k:n},\ R^* = n_1 - k\} \\
&\quad= \frac{n_1 - k}{n} P\{X_{n_0:I_0} \ge c_{n_0+k:n},\ R^* = n_1 - k\},
\end{aligned} \tag{A.10}$$

whereas, from the last expression in (A.9), we see that the (n_0+k)th term is

$$\sum_{J:|J|=k} P\Big\{X_{n_0:I_0} < c_{n_0+k:n},\ \max_{i\in J} X_i < c_{n_0+k:n},\ R^* = n_1 - k\Big\}$$
$$= P\{X_{n_0:I_0} < c_{n_0+k:n},\ R^* = n_1 - k\}. \tag{A.11}$$

The last equality in (A.10) follows from the fact that

$$\Big\{X_{n_0+k:I_0\cup J} \ge c_{n_0+k:n},\ \max_{i\in J} X_i < c_{n_0+k:n}\Big\}$$
$$= \Big\{X_{n_0:I_0} \ge c_{n_0+k:n},\ \max_{i\in J} X_i < c_{n_0+k:n}\Big\}.$$

Applying (A.10) and (A.11) to (A.9), we get that (A.7) is greater than or equal to

$$\sum_{k=0}^{n_1-1} P\{X_{n_0:I_0} < c_{n_0+k:n},\ R^* = n_1 - k\}$$
$$+ \sum_{k=0}^{n_1-1} \frac{n_1-k}{n} P\{X_{n_0:I_0} \ge c_{n_0+k:n},\ R^* = n_1 - k\}$$
$$= \sum_{k=0}^{n_1-1} P\{R^* = n_1 - k\}$$
$$- \sum_{k=0}^{n_1-1} \left(1 - \frac{n_1-k}{n}\right) P\{X_{n_0:I_0} \ge c_{n_0+k:n},\ R^* = n_1 - k\}$$
$$= P\{X_{n_1:I_1} \ge c_{n:n}\} - \sum_{k=0}^{n_1-1} \frac{n_0+k}{n} P\{X_{n_0:I_0} \ge c_{n_0+k:n},\ R^* = n_1 - k\},$$

which is (A.8). This proves the desired inequality and finally Lemma 3.3. □

PROOF OF LEMMA 3.4. Let $f(x_1,\dots,x_n)$ denote the joint density of $(X_1,\dots,X_n)$. If f is MTP_2, then, for any fixed $1 \le k \le n_0$, the joint density of $(X_{n_0:I_0}, X_{n_0+1},\dots,X_n)$, conditionally given $X_k = X_{n_0:I_0} = x$, which is proportional to

$$\int\cdots\int f(x_1,\dots,x_{k-1},x,x_{k+1},\dots,x_n) \prod_{j=1(\ne k)}^{n_0} I(x_j \le x) \prod_{j=1(\ne k)}^{n_0} dx_j, \tag{A.12}$$

is also MTP_2. This is because of the fact that the integrand in (A.12) is MTP_2, as both $\prod_{j=1(\ne k)}^{n_0} I(x_j \le x)$ and f are MTP_2, and the property that an integral of an MTP_2 function is also MTP_2 [see, e.g., Karlin and Rinott (1980)]. □

Acknowledgments. The author thanks two referees for their constructive comments and numerous suggestions, which greatly improved the presentation of the paper.

REFERENCES

ABRAMOVICH, F. and BENJAMINI, Y. (1996). Adaptive thresholding of wavelets coefficients. *Comput. Statist. Data Anal.* **22** 351–361.

ABRAMOVICH, F., BENJAMINI, Y., DONOHO, D. L. and JOHNSTONE, I. M. (2000). Adapting to unknown sparsity by controlling the false discovery rate. Technical Report 2000-19, Dept. Statistics, Stanford Univ.

BASFORD, K. E. and TUKEY, J. W. (1997). Graphical profiles as an aid to understanding plant breeding experiments. *J. Statist. Plann. Inference* **57** 93–107.

BENJAMINI, Y. and HOCHBERG, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. Roy. Statist. Soc. Ser. B* **57** 289–300.

BENJAMINI, Y. and LIU, W. (1999). A step-down multiple hypotheses testing procedures that controls the false discovery rate under independence. *J. Statist. Plann. Inference* **82** 163–170.

BENJAMINI, Y. and YEKUTIELI, D. (2001). The control of the false discovery rate in multiple testing under dependency. *Ann. Statist.* **29** 1165–1188.

DRIGALENKO, E. I. and ELSTON, R. C. (1997). False discoveries in genome scanning. *Gen. Epidem.* **14** 779–784.

FINNER, H. (1999). Stepwise multiple test procedures and control of directional errors. *Ann. Statist.* **27** 274–289.

FINNER, H. and ROTERS, M. (1998). Asymptotic comparison of step-down and step-up multiple test procedures based on exchangeable test statistics. *Ann. Statist.* **26** 505–524.

FINNER, H. and ROTERS, M. (1999). Asymptotic comparisons of the critical values of step-down and step-up multiple comparison procedures. *J. Statist. Plann. Inference* **79** 11–30.

KARLIN, S. and RINOTT, Y. (1980). Classes of orderings of measures and related correlation inequalities I. *J. Multivariate Anal.* **10** 467–498.

LIU, W. (1996). Multiple tests of a non-hierarchical finite family of hypotheses. *J. Roy. Statist. Soc. Ser. B* **58** 455–461.

SARKAR, S. K. (1998). Some probability inequalities for ordered MTP_2 random variables: a proof of the Simes conjecture. *Ann. Statist.* **26** 494–504.

SARKAR, S. K. and CHANG, C.-K. (1997). The Simes method for multiple hypothesis testing with positively dependent test statistics. *J. Amer. Statist. Assoc.* **92** 1601–1608.

SIMES, R. J. (1986). An improved Bonferroni procedure for multiple tests of significance. *Biometrika* **73** 751–754.

TAMHANE, A. C., LIU, W. and DUNNETT, C. W. (1998). A generalized step-up–down multiple test procedure. *Canad. J. Statist.* **26** 353–363.

WILLIAMS, V. S. L., JONES, L. V. and TUKEY, J. W. (1999). Controlling error in multiple comparisons with examples from state-to-state differences in educational achievement. *J. Edu. Behav. Statist.* **24** 42–69.

DEPARTMENT OF STATISTICS
TEMPLE UNIVERSITY
PHILADELPHIA, PENNSYLVANIA 19122
E-MAIL: sanat@sbm.temple.edu