Submitted to the Annals of Statistics

FURTHER RESULTS ON CONTROLLING THE FALSE DISCOVERY PROPORTION

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The probability of false discovery proportion (FDP) exceeding $\gamma \in [0, 1)$, defined as γ-FDP, has received much attention as a measure of false discoveries in multiple testing. Although this measure has received acceptance due to its relevance under dependency, not much progress has been made yet advancing its theory under such dependency in a non-asymptotic setting, which motivates our research in this article. We provide a larger class of procedures containing the stepup analog of, and hence more powerful than, the stepdown procedure in Lehmann and Romano (2005) controlling the γ-FDP under the same positive dependence condition assumed in that paper. We offer better alternatives of the stepdown and stepup procedures in Romano and Shaikh (2006a, b) using pairwise joint distributions of the null p-values. We generalize the notion of γ-FDP making it appropriate in many practical situations where one is willing to tolerate a few false rejections or, due to high dependency some false rejections are inevitable and provide methods that control this generalized γ-FDP in three different scenarios - (i) no assumption is made about dependence and only the marginal p-values are being used, (ii) no assumption is made about the dependence but common pairwise joint distributions of the null p-values are available, and (iii) a positive dependence condition holds among the null p-values and the common pairwise joint distributions of the null p-values are available. Our theoretical findings are being supported through numerical studies.

1. Introduction. The idea of improving the traditional and often too conservative notion of familywise error rate (FWER) has been one of the main motivations behind much of the methodological developments taking place in modern multiple testing. One particular direction in which this idea has flourished is generalizing the FWER from its original definition of the probability of at least one false discovery or a non-zero fraction of false discoveries to one that allows more, yet tolerable, number or fraction of false discoveries and developing procedures that control these generalized error rates. The rationale behind taking this direction is that in many situations

[*]The research of Wenge Guo is supported by NSF Grant DMS-1006021.

[†]The research of Li He is supported by Merck Research Fellowship.

[‡]The research of Sanat Sarkar is supported by NSF Grant DMS-1006344.

AMS 2000 subject classifications: Primary 62J15

Keywords and phrases: γ-FDP, generalized γ-FDP, multiple testing, pairwise correlations, positive dependence, stepup procedure, stepdown procedure

where a large number of hypotheses are tested one is often willing to tolerate more than one false discovery, controlling of course too many of them. Moreover, due to high positive dependency among a group or groups of p-values corresponding to true null hypotheses, as in microarray experiments where the genes involved in the same biological process or pathway are highly dependent on each other and exhibit similar expression patterns, it is extremely unlikely that exactly one null p-value will be significant given that at least one of them will be significant. In such cases, a procedure controlling the probability of at least k false discoveries, the k-FWER, for some fixed $k > 1$, or the probability of the false discovery proportion (FDP) exceeding γ, the γ-FDP, for some fixed $0 < \gamma < 1$, will have a better ability to detect more false null hypotheses than the corresponding FWER procedure (i.e., when $k = 1$ or $\gamma = 0$).

Thus, the consideration of the k-FWER or γ-FDP seems more relevant than that of the FWER when controlling false discoveries in multiple testing of a large number of hypotheses under dependency. In fact, it has been noted that the dependency gets naturally factored into the constructions of procedures controlling the k-FWER or γ-FDP. For instance, the k-dimensional joint distributions of the null p-values can be explicitly used while constructing procedures controlling the k-FWER [Sarkar (2007, 2008a)]. Also, since the variability of the FDP increases with increasing dependence among the p-values [Efron (2007), Kim and van de Wiel (2008), Korn, Troendle, McShane and Simon (2004), Owen (2005), Schwartzman and Lin (2011)], by controlling the tail end probabilities of the FDP, the γ-FDP, one considers controlling a quantity that is more relevant under dependency than the expected FDP, the false discovery rate (FDR) [Benjamini and Hochberg (1995)], which is even less conservative than the FWER.

A number of papers have been written over the years on k-FWER and γ-FDP [Dudoit et al. (2004), Genovese and Wasserman (2004), Guo and Rao (2010), Guo and Romano (2007), Hommel and Hoffmann (1987), Korn and Freidlin (2008), Korn, Troendle, McShane and Simon (2004), Lehmann and Romano (2005), Romano and Shaikh (2006a, b), Romano and Wolf (2005), Roquain and Villers (2011), Sarkar (2007, 2008a) and van der Laan, Dudoit, and Pollard (2004)]. Among these, Lehmann and Romano (2005), and Romano and Shaikh (2006a, b) are worth mentioning as they have made some fundamental contributions to the development of theory and methodology of γ-FDP. A part of our research is motivated by these papers, and aims at extending, and often improving, some results in those papers under certain dependence situations. The motivation of the other part of our research comes from the realization that if one indeed is willing to tolerate a few false rejections, the premise under which one would seek to use a generalized error rate, the notion of γ-FDP does not completely take that into account unless it is further generalized accordingly. In other words, one should consider in this case a generalized form of the FDP that accounts for k or more false rejections, and control the probability of this generalized FDP, rather than the original FDP, exceeding γ. So, we introduce such a generalized notion of γ-FDP and propose procedures that control it under different dependence scenarios in this paper.

We organize the paper as follows. We provide some preliminaries in Section 2, including the definition of our proposed generalized version of the γ-FDP. In Section 3, we present a number of new results on γ-FDP. We construct a larger class of procedures controlling the γ-FDP under positive dependence than the stepdown procedure given in Lehmann and Romano (2005). This class includes the stepup analog of and hence powerful than the Lehmann-Romano stepdwon procedure. We offer better alternatives of the stepdown and stepup procedures in Romano and Shaikh (2006a, b), given pairwise joint distributions of the null p-values. Section 4 contains results on procedures controlling generalized γ-FDP we develop under the following three scenarios - (i) only the marginal p-values are available, (ii) the common pairwise joint distributions of the null p-values are given, and (iii) a positive dependence condition holds among the null p-values and the common pairwise joint distributions of the null p-values are given. We also provide numerical support to our theoretical findings. Concluding remarks are made in Section 5. Proofs of some supporting results are given in Appendix.

2. Preliminaries. Suppose that $H_i, i = 1, \ldots, n$, are the n null hypotheses to be tested based on their respective p-values $P_i, i = 1, \ldots, n$. Let $P_{(1)} \leq \cdots \leq P_{(n)}$ be the ordered versions of all the p-values and $H_{(1)}, \ldots, H_{(n)}$ be their corresponding null hypotheses. There are n_0 null hypotheses that are true. For notational convenience, the p-values corresponding to these true null hypotheses will be denoted by $\hat{P}_i, i = 1, \cdots, n_0$, and their ordered versions by $\hat{P}_{(1)} \leq \ldots \leq \hat{P}_{(n_0)}$.

Multiple testing is typically carried out using a stepwise or single-step procedure. Given a non-decreasing set of critical values $0 < \alpha_1 \leq \cdots \leq \alpha_n < 1$, a stepdown procedure rejects the set of null hypotheses $\{H_{(i)}, i \leq i^*_{SD}\}$, where $i^*_{SD} = \max\{1 \leq i \leq n : P_{(j)} \leq \alpha_j \ \forall j \leq i\}$ if the maximum exists, otherwise accepts all the null hypotheses. A stepup procedure, on the other hand, rejects the set of null hypotheses $\{H_{(i)}, i \leq i^*_{SU}\}$, where $i^*_{SU} = \max\{1 \leq i \leq n : P_{(i)} \leq \alpha_i\}$ if the maximum exists, otherwise accepts all the null hypotheses. A stepdown or stepup procedure with the same critical values is referred to as a single-step procedure.

Let V be the number of falsely rejected and R be the total number of rejected null hypotheses. Then, with V/R, which is zero if $R = 0$, defining the false discovery proportion (FDP), and given a fixed $\gamma \in (0, 1)$, the γ-FDP is defined as the probability of the FDP exceeding γ; i.e., γ-FDP $= \Pr(FDP > \gamma)$. Its generalized version introduced in this paper, which we call γ-kFDP, is defined as follows: Let

$$\mathrm{kFDP} = \begin{cases} \frac{V}{R} & \text{if } V \geq k \\ 0 & \text{otherwise} \end{cases}$$

Then γ-kFDP $= \Pr(\mathrm{kFDP} > \gamma)$. Since γ-kFDP is 0, and hence trivially controlled, for any procedure if $n_0 < k$, we assume throughout that $k \leq n_0 \leq n$ when controlling this error rate.

The distributional assumptions we make in this paper only relate to the null p-values. The following is the basic assumption regarding the marginal distributions of the p-values made throughout the whole paper:

Assumption 1. $\hat{P}_i \sim U(0, 1)$.

3. Improved procedures controlling the γ-FDP. In this section, we present results improving some previous work on controlling the γ-FDP under both positive dependence and arbitrary dependence conditions on the p-values (Lehmann and Romano, 2005; Romano and Shaikh, 2006a, b).

Under a positive dependence assumption, Lehmann and Romano (2005) gave a stepdown procedure controlling the γ-FDP. We improve this work in two different ways. First, we consider the stepup analog of this stepdown procedure, which is known to be always more powerful in the sense of discovering more, and prove that it also controls the γ-FDP under the same assumption. Second, we offer larger class of stepdown and stepup procedures controlling the γ-FDP under this assumption.

Under arbitrary dependence, Romano and Shaikh (2006a, b) developed stepdown and stepup procedures controlling the γ-FDP in terms of the marginal p-values. However, often there is information about correlations among the null p-values that could potentially be used to improve these procedures. So, to that end, we also present some results in this section.

3.1. *Procedures under positive dependence.* Let us make the following assumption characterizing a positive dependence structure among the null p-values:

ASSUMPTION 2. *The conditional expectation* $E\left\{\phi(\hat{P}_1,\ldots,\hat{P}_{n_0}) \mid \hat{P}_i \le u\right\}$ *is non-decreasing in* $u \in (0,1)$ *for each* $\hat{P}_i$ *and any non-decreasing (coordinate-wise) function* ϕ.

This is slightly weaker than that characterized by the property:

$$E\left\{\phi(\hat{P}_1,\ldots,\hat{P}_n) \mid \hat{P}_i = u\right\} \uparrow u \in (0,1),$$

which is referred to as the the positive dependence through stochastic ordering (PDS) condition by Block, Savits and Shaked (1985); see also Sarkar (2008b).

THEOREM 3.1. *The stepup or stepdown procedure with the critical constants*

$$\alpha_i = \frac{(\lfloor \gamma i \rfloor + 1)\alpha}{n + \lfloor \gamma i \rfloor + 1 - i},\ i = 1,\ldots,n, \tag{1}$$

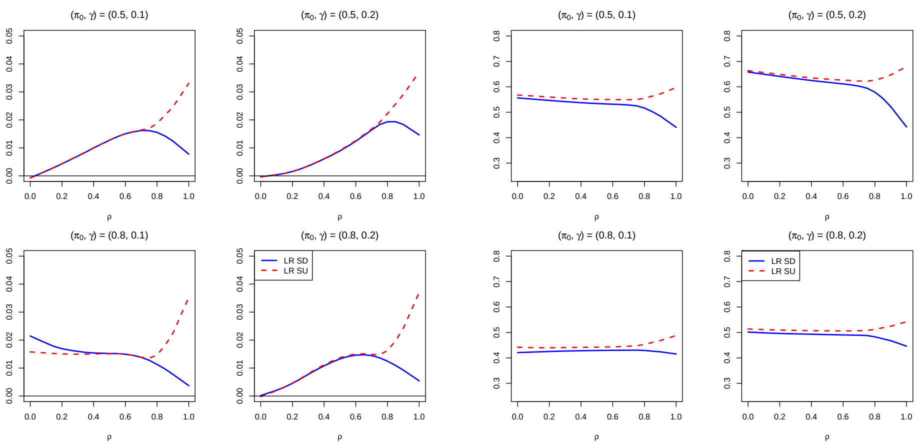
controls the γ*-FDP at* α *under Assumptions 1 and 2.*

Proof. Let $g(R) = \lfloor \gamma R \rfloor + 1$. Then, first note that

$$\begin{aligned}
\{V \ge g(R)\} &= \bigcup_{v=1}^{n_0} \left\{\hat{P}_{(v)} \le \alpha_R,\ g(R) \le v,\ V = v\right\} \\
&= \bigcup_{v=1}^{n_0} \left\{\hat{P}_{(v)} \le \frac{g(R)\alpha}{n - R + g(R)},\ g(R) \le v,\ V = v\right\} \\
&\subseteq \bigcup_{v=1}^{n_0} \left\{\hat{P}_{(v)} \le \frac{v\alpha}{n - R + v},\ V = v\right\} \\
&\subseteq \bigcup_{v=1}^{n_0} \left\{\hat{P}_{(v)} \le \frac{v\alpha}{n_0},\ V = v\right\} \subseteq \bigcup_{v=1}^{n_0} \left\{\hat{P}_{(v)} \le \frac{v\alpha}{n_0}\right\}. \qquad (2)
\end{aligned}$$

The probability of the event in the right-hand side of (2) is known to be less than or equal to α under Assumptions 1 and 2 from the so-called Simes' inequality (Simes, 1986; Sarkar, 1998; Sarkar and Chang, 1997). Thus, we get the desired result noting that γ-FDP $= \Pr(V \ge g(R))$. ■

REMARK 3.1. Lehmann and Romano (2005) proposed only the stepdown procedure considered in Theorem 3.1 under the same assumptions. Thus, Theorem 3.1 provides an improvement of the Lehamann-Romano result, since we now have an alternative procedure under the same assumptions, the step-up one, which is theoretically known to be more powerful.



(a) Simulated γ-FDP. (b) Simulated average power.

FIG 1. *Simulated γ-FDP's and average powers of the original Lehmann-Romano stepdown procedure (LR SD) and its stepup analogue (LR SU) for simultaneous testing of $\mu_i = 0$ against $\mu_i = 3$ in $n = 100$ normal random variables $N(\mu_i, 1)$ with a common correlation ρ at level $\alpha = 0.05$, for different values of ρ and $(\pi_0, \gamma) = (0.5, 0.1), (0.5, 0.2), (0.8, 0.1)$, and $(0.8, 0.2)$, where $\pi_0 = n_0/n$. (Runs per simulation = 2,000.)*

Moreover, not only our proof of the γ-FDP control is much simpler but also it covers both ours and the Lehmann-Romano original stepdown procedures. Our simulation studies indicate that this power improvement can often be quite significant when the underlying test statistics are moderately or highly correlated (see Figure 1).

There are more general results than Theorem 3.1 in terms of deriving procedures controlling the γ-FDP under Assumptions 1 and 2. More specifically, we have the following two theorems.

THEOREM 3.2. *With $n_1 = n - n_0$, let $M = \min\{n_0, \lfloor \gamma n_1/(1-\gamma) \rfloor + 1\}$, and $m(i) = \max\{1 \le j \le n_1 : \lfloor \gamma j/(1-\gamma) \rfloor + 1 = i\}$, for each $i = 1, \ldots, M$, where $m(0) = 0$. Then, given any set of constants $0 = \alpha'_0 \le \alpha'_1 \le \cdots \le \alpha'_n$, consider the stepdown procedure with the critical values $\alpha_i = \alpha\alpha'_i / C^{(1)}_{n,SD}$, $i = 1, \ldots, n$, where*

$$C^{(1)}_{n,SD} = \max_{1 \le n_0 \le n} \max_{1 \le i \le M} \left\{ \frac{n_0 \alpha'_{i+m(i)}}{i} \right\}.$$

It controls the γ-FDP at α under Assumptions 1 and 2.

THEOREM 3.3. *Let $\tilde{m}(i) = \min\{m(i), i + n_1\}$, where $m(i) = \max\{1 \leq j \leq n : \lfloor \gamma j \rfloor + 1 \leq i\}$, for each $i = 1, \ldots, n_0$, and $m(0) = 0$. Then, given any set of constants $0 = \alpha'_0 \leq \alpha'_1 \leq \cdots \leq \alpha'_n$, consider the stepup procedure with the critical values $\alpha_i = \alpha\alpha'_i / C^{(1)}_{n,SU}$, $i = 1, \ldots, n$, where*

$$C^{(1)}_{n,SU} = \max_{1 \leq n_0 \leq n} \max_{1 \leq j \leq n_0} \left\{ \frac{n_0 \alpha'_{\tilde{m}(j)}}{j} \right\}.$$

It controls the γ-FDP at α under Assumptions 1 and 2.

Proof of Theorem 3.2. With S denoting the number of rejected false null hypotheses, we first note that

$$\begin{aligned} I\left(V > \gamma R\right) &= I\left(V > \gamma(V+S)\right) = I\left(V \geq \lfloor \gamma S/(1-\gamma) \rfloor + 1\right) \\ &= \sum_{i=1}^{M} I\left(V \geq i,\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) . \qquad (3) \end{aligned}$$

Also, for a stepdown procedure with the critical constants α_i, $i = 1, \ldots, n$, we have

$$\begin{aligned} & I\left(V \geq i,\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ = \ & I\left(R \geq i + S,\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ = \ & I\left(P_{(1)} \leq \alpha_1, \ldots, P_{(i+S)} \leq \alpha_{i+S},\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ \leq \ & I\left(\hat{P}_{(1)} \leq \alpha_{1+S}, \ldots, \hat{P}_{(i)} \leq \alpha_{i+S},\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ \leq \ & I\left(\hat{P}_{(1)} \leq \alpha_{1+m(i)}, \ldots, \hat{P}_{(i)} \leq \alpha_{i+m(i)},\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ \leq \ & I\left(\hat{P}_{(i)} \leq \alpha_{i+m(i)},\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right). \qquad (4) \end{aligned}$$

Taking expectations of both sides of (3) after using (4) in it, we have

$$\begin{aligned} & \gamma\text{-FDP} = \Pr\left\{V > \gamma R\right\} \\ \leq \ & \sum_{i=1}^{M} \Pr\left(\hat{P}_{(i)} \leq \alpha_{i+m(i)}, \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ \leq \ & \sum_{j=1}^{n_0} \sum_{i=1}^{M} \frac{1}{i} \Pr\left(\hat{P}_j \leq \alpha_{i+m(i)}, \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\ = \ & \sum_{j=1}^{n_0} \sum_{i=1}^{M} \frac{\alpha_{i+m(i)}}{i} \Pr\left(\lfloor \gamma S/(1-\gamma) \rfloor + 1 = i \middle| \hat{P}_j \leq \alpha_{i+m(i)}\right) \\ = \ & \max_{1 \leq i \leq M} \left\{ \frac{\alpha_{i+m(i)}}{i} \right\} \sum_{j=1}^{n_0} \sum_{i=1}^{M} \Pr\left(\lfloor \gamma S/(1-\gamma) \rfloor + 1 = i \middle| \hat{P}_j \leq \alpha_{i+m(i)}\right), \qquad (5) \end{aligned}$$

with the second inequality following from this:

$$I\left(\hat{P}_{(i)} \le t\right) \quad \le \quad \frac{1}{i}\sum_{j=1}^{n_0} I\left(\hat{P}_j \le t\right) \text{ for any constant } 0 < t < 1, \tag{6}$$

which will be proved in Appendix.

Now, for each $1 \le j \le n_0$, we have

$$\begin{aligned}
& \sum_{i=1}^{M} \Pr\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 = i \middle| \hat{P}_j \le \alpha_{i+m(i)}\right) \\
= & \sum_{i=1}^{M} \Pr\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \ge i \middle| \hat{P}_j \le \alpha_{i+m(i)}\right) - \\
& \quad \sum_{i=1}^{M} \Pr\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \ge i+1 \middle| \hat{P}_j \le \alpha_{i+m(i)}\right) \\
\le & \sum_{i=1}^{M} \Pr\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \ge i \middle| \hat{P}_j \le \alpha_{i+m(i)}\right) - \\
& \quad \sum_{i=1}^{M} \Pr\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \ge i+1 \middle| \hat{P}_j \le \alpha_{i+1+m(i+1)}\right) \\
\le & \Pr\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \ge 1 \middle| \hat{P}_j \le \alpha_{1+m(1)}\right) = 1. \qquad (7)
\end{aligned}$$

The first inequality follows from Assumption 2. Applying (7) to (5), we have

$$\gamma\text{-FDP} \quad \le \quad \max_{1\le i\le M}\left\{\frac{n_0\alpha_{i+m(i)}}{i}\right\} \le \alpha \max_{1\le i\le M}\left\{\frac{n_0\alpha'_{i+m(i)}}{i}\right\}\Big/ C^{(1)}_{n,SD} \le \alpha,$$

which proves the theorem. ■

Proof of Theorem 3.3. Since $V \ge R - n_1$, we have

$$\begin{aligned}
& I\left(V > \gamma R\right) = I\left(V \ge \lfloor \gamma R\rfloor + 1, V \ge R - n_1\right) \\
= & \ I\left(\bigcup_{j=1}^{n_0}\left\{\hat{P}_{(j)} \le \alpha_R, V = j, \ \lfloor \gamma R\rfloor + 1 \le j, R \le j + n_1\right\}\right) \\
\le & \ I\left(\bigcup_{j=1}^{n_0}\left\{\hat{P}_{(j)} \le \alpha_R, R \le \tilde{m}(j)\right\}\right) \le I\left(\bigcup_{j=1}^{n_0}\left\{\hat{P}_{(j)} \le \alpha_{\tilde{m}(j)}\right\}\right). \qquad (8)
\end{aligned}$$

Let $\hat{R}_2$ be the number of rejections in a stepup procedure based on the p-values $\hat{P}_i$, $i = 1, \ldots, n_0$, and the critical values $\alpha_{\tilde{m}(i)}$, $i = 1, \ldots, n_0$. Then, by taking expectations of both sides in (8), we get

$$\begin{aligned}\gamma\text{-FDP} &\leq \Pr\left(\bigcup_{j=1}^{n_0}\left\{\hat{P}_{(j)} \leq \alpha_{\tilde{m}(j)}\right\}\right) = \sum_{l=1}^{n_0}\sum_{j=1}^{n_0}\frac{\Pr\left(\hat{P}_l \leq \alpha_{\tilde{m}(j)}, \hat{R}_2 = j\right)}{j} \\ &= \sum_{l=1}^{n_0}\sum_{j=1}^{n_0}\frac{\alpha_{\tilde{m}(j)}}{j}\Pr\left(\hat{R}_2 = j \big| \hat{P}_l \leq \alpha_{\tilde{m}(j)}\right).\end{aligned}$$

Making the same arguments as in (7), we note that

$$\sum_{j=1}^{n_0}\Pr\left(\hat{R}_2 = j \big| \hat{P}_l \leq \alpha_{\tilde{m}(j)}\right) \leq 1, \text{ for each } 1 \leq l \leq n_0.$$

Thus,

$$\gamma\text{-FDP} \leq \max_{1\leq i\leq n_0}\left\{\frac{n_0\alpha_{\tilde{m}(i)}}{i}\right\} \leq \alpha \max_{1\leq i\leq n_0}\left\{\frac{n_0\alpha'_{\tilde{m}(i)}}{i}\right\}\Big/ C_{n,SU}^{(1)} \leq \alpha,$$

which proves the theorem. ■

Remark 3.2. Theorems 3.2 and 3.3 provide a general approach to constructing stepdown and stepup γ-FDP controlling procedures under independence or positive dependence of the null p-values. If α_i''s are chosen according to (1), then both $C_{n,SD}^{(1)}$ and $C_{n,SU}^{(1)}$ can be seen to be equal to 1, implying that the original Lehmann-Romano stepdown procedure and its stepup analogue control the γ-FDP at α under Assumptions 1 and 2. However, there are other stepdown and stepup procedures, such as those obtained by re-scaling the critical values of the BH (Benjamini and Hochberg, 1995) stepup and the GBS (Gavrilov, Benjamini and Sarkar, 2009) stepdown methods, that can also control the γ-FDP under these assumptions.

3.2. *Procedures incorporating pairwise correlations.* What if Assumption 2 in Theorems 3.1 - 3.3 cannot be made? In this case, the stepup or stepdown procedure does no longer control the γ-FDP, but can be properly adjusted maintaining this control under any type of dependence structure. Romano and Shaikh (2006a, b) first developed such adjustments for a stepdown or stepup procedure based on the marginal p-values. However, in practice, the null p-values often have a known common pairwise joint distribution, and by explicitly utilizing such correlation information better adjustments can be made, potentially resulting in more powerful γ-FDP stepwise procedures. So, with that in mind, we present some results here under Assumption 1 and the following:

Assumption 3. *The null p-values $\hat{P}_1, \ldots, \hat{P}_{n_0}$ have a known common pairwise joint distribution function $F(u,v) = \Pr\left(\hat{P}_i \le u, \hat{P}_j \le v\right)$.*

Before presenting our main results in this subsection, let us introduce some relevant notations. With $m(i)$ defined in Theorem 3.2, for notational convenience, let $\overline{m}(i) = i + m(i)$, $i = 1, \ldots, M$. Given a sequence of constants $0 = \alpha'_0(\beta) \le \alpha'_1(\beta) \le \cdots \le \alpha'_n(\beta)$, for a fixed $\beta \in (0,1)$, let

$$
\begin{aligned}
C^{(2)}_{n,SD}(\beta) &= \max_{1 \le n_0 \le n} \min_{1 \le K \le n_0} \left\{ \sum_{i=1}^{K} \frac{n_0 \left(\alpha'_{\overline{m}(i)}(\beta) - \alpha'_{\overline{m}(i-1)}(\beta)\right)}{i} \right. \\
&+ \sum_{i=K+2}^{M} \frac{n_0(n_0-1)\left[F\left(\alpha'_{\overline{m}(i)}(\beta), \alpha'_{\overline{m}(i)}(\beta)\right) - F\left(\alpha'_{\overline{m}(i-1)}(\beta), \alpha'_{\overline{m}(i-1)}(\beta)\right)\right]}{i(i-1)} \\
&+ \left. \frac{n_0(n_0-1)F\left(\alpha'_{\overline{m}(K)}(\beta), \alpha'_{\overline{m}(K)}(\beta)\right)}{K(K+1)} - \frac{n_0 F\left(\alpha'_{\overline{m}(K)}(\beta), \alpha'_{\overline{m}(K+1)}(\beta)\right)}{K+1} \right\},
\end{aligned}
$$

and

$$
\begin{aligned}
C^{(2)}_{n,SU}(\beta) &= \max_{1 \le n_0 \le n} \min_{1 \le K \le n_0} \left\{ \sum_{r=1}^{K} \frac{n_0 \left(\alpha'_{\tilde{m}(r)}(\beta) - \alpha'_{\tilde{m}(r-1)}(\beta)\right)}{r} \right. \\
&+ \sum_{r=K+1}^{n_0} \left(\frac{n_0\left(\alpha'_{\tilde{m}(r)}(\beta) - \alpha'_{\tilde{m}(r-1)}(\beta)\right)}{r^2} + \sum_{s=r}^{n_0} \frac{n_0(n_0-1)\, G(\tilde{m}(r), \tilde{m}(s), \beta)}{rs} \right. \\
&+ \left. \left. \frac{n_0(n_0-1)\left(F(\alpha'_{\tilde{m}(r)}(\beta), \alpha'_{\tilde{m}(r)}(\beta)) - F(\alpha'_{\tilde{m}(r)}(\beta), \alpha'_{\tilde{m}(r-1)}(\beta))\right)}{r^2} \right) \right\},
\end{aligned}
$$

where

$$
\begin{aligned}
G(r,s,\beta) &= F\left(\alpha'_r(\beta), \alpha'_s(\beta)\right) - F\left(\alpha'_{r-1}(\beta), \alpha'_s(\beta)\right) \\
&\quad - F\left(\alpha'_r(\beta), \alpha'_{s-1}(\beta)\right) + F\left(\alpha'_{r-1}(\beta), \alpha'_{s-1}(\beta)\right).
\end{aligned}
$$

Theorem 3.4. *Given any sequence of critical constants $0 = \alpha'_0(\beta) \le \alpha'_1(\beta) \le \cdots \le \alpha'_n(\beta)$, for a fixed $\beta \in (0,1)$, the stepdown procedure with the critical values $\alpha_i, i = 1, \ldots, n$, satisfying $\alpha_i = \alpha'_i(\beta^*_{SD})$ and $C^{(2)}_{n,SD}(\beta^*_{SD}) = \alpha$, controls the γ-FDP at α under Assumptions 1 and 3.*

Theorem 3.5. *Given any sequence of critical constants $0 = \alpha'_0(\beta) \le \alpha'_1(\beta) \le \cdots \le \alpha'_n(\beta)$, for a fixed $\beta \in (0,1)$, the stepup procedure with the* *critical values $\alpha_i, i = 1, \ldots, n$, satisfying $\alpha_i = \alpha_i'(\beta^*_{SU})$ and $C^{(2)}_{n,SU}(\beta^*_{SU}) = \alpha$, controls the γ-FDP at α under Assumptions 1 and 3.*

Proof of Theorem 3.4. We will proceed as in proving Theorem 3.2, but not relying on any dependence condition and making use of the pairwise joint distributions of the null p-values whenever possible.

For each pre-specified K, where $1 \leq K \leq M$, we have from (3) and (4) that

$$
\begin{aligned}
& I\left(V > \gamma R\right) \\
\leq \; & \sum_{i=1}^{K}\sum_{j=1}^{n_0} \frac{1}{i} I\left(\hat{P}_j \leq \alpha_{\overline{m}(i)}\right) I\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 = i\right) + \\
& \sum_{i=K+1}^{M}\sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0} \frac{1}{i(i-1)} I\left(\max(\hat{P}_j, \hat{P}_l) \leq \alpha_{\overline{m}(i)}\right) I\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 = i\right) \\
\leq \; & \sum_{j=1}^{n_0}\sum_{i=1}^{K}\left[\frac{I\left(\hat{P}_j \leq \alpha_{\overline{m}(i)}\right)}{i} - \frac{I\left(\hat{P}_j \leq \alpha_{\overline{m}(i-1)}\right)}{i-1}\right] I\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \geq i\right) + \\
& \sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0}\sum_{i=K+2}^{M}\left[\frac{I\left(\max(\hat{P}_j, \hat{P}_l) \leq \alpha_{\overline{m}(i)}\right)}{i(i-1)} - \frac{I\left(\max(\hat{P}_j, \hat{P}_l) \leq \alpha_{\overline{m}(i-1)}\right)}{(i-1)(i-2)}\right] \\
& \qquad \times I\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \geq i\right) + \\
& \sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0}\left[\frac{I\left(\max(\hat{P}_j, \hat{P}_l) \leq \alpha_{\overline{m}(K+1)}\right)}{K(K+1)} - \frac{I\left(\hat{P}_j \leq \alpha_{\overline{m}(K)}\right)}{K(n_0-1)}\right] \\
& \qquad \times I\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 \geq K+1\right) \\
\leq \; & \sum_{j=1}^{n_0}\sum_{i=1}^{K} \frac{I\left(\alpha_{\overline{m}(i-1)} < \hat{P}_j \leq \alpha_{\overline{m}(i)}\right)}{i} + \\
& \sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0}\sum_{i=K+2}^{M} \frac{I\left(\alpha_{\overline{m}(i-1)} < \max(\hat{P}_j, \hat{P}_l) \leq \alpha_{\overline{m}(i)}\right)}{i(i-1)} + \\
& \sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0}\left[\frac{(n_0-K-1) I\left(\hat{P}_j \leq \alpha_{\overline{m}(K)}, \hat{P}_l \leq \alpha_{\overline{m}(K+1)}\right)}{K(K+1)(n_0-1)}\right. \\
& \qquad \left. + \frac{I\left(\alpha_{\overline{m}(K)} < \hat{P}_j \leq \alpha_{\overline{m}(K+1)}, \hat{P}_l \leq \alpha_{\overline{m}(K+1)}\right)}{K(K+1)}\right], \qquad (9)
\end{aligned}
$$

(with $I(\hat{P}_j \leq \alpha_{\bar{m}(0)})/0 = 0$). Here, the first inequality follows from (6) and the following inequality which will be proved in Appendix:

$$I\left(\hat{P}_{(i)} \le t\right) \quad \le \quad \frac{1}{i(i-1)} \sum_{j=1}^{n_0} \sum_{j'(\neq j)=1}^{n_0} I\left(\max\{\hat{P}_j, \hat{P}_{j'}\} \le t\right), \tag{10}$$

for any fixed i such that $2 \le i \le n_0$ and a constant $0 < t < 1$.

Taking expectations of both sides in (9), we get

$$\begin{aligned}
\gamma\text{-FDP} \quad \le \quad & \sum_{i=1}^{K} \frac{n_0\left(\alpha_{\overline{m}(i)} - \alpha_{\overline{m}(i-1)}\right)}{i} + \\
& \sum_{i=K+2}^{M} \frac{n_0(n_0-1)\left[F\left(\alpha_{\overline{m}(i)}, \alpha_{\overline{m}(i)}\right) - F\left(\alpha_{\overline{m}(i-1)}, \alpha_{\overline{m}(i-1)}\right)\right]}{i(i-1)} \\
& + \frac{n_0(n_0-1)F\left(\alpha_{\overline{m}(K)}, \alpha_{\overline{m}(K)}\right)}{K(K+1)} - \frac{n_0 F\left(\alpha_{\overline{m}(K)}, \alpha_{\overline{m}(K+1)}\right)}{K+1}.
\end{aligned} \tag{11}$$

Taking the minimum with respect to K and then the maximum with respect to n_0 in (11), we have

$$\gamma\text{-FDP} \le C_{n,SD}(\beta^*_{SD}) = \alpha,$$

which proves the theorem. ■

Proof of Theorem 3.5. Let $\hat{R}_2$ be the number of rejections in a stepup procedure based on the p-values $\hat{P}_i$, $i = 1, \ldots, n_0$, and the critical values $\alpha_{\tilde{m}(i)}$, $i = 1, \ldots, n_0$. Then, as in proving Theorem 3.3, we first have, for each prespecified $1 \le K \le n_0$,

$$\begin{aligned}
& I\left(V > \gamma R\right) \le \sum_{j=1}^{n_0} \sum_{r=1}^{n_0} \frac{I\left(\hat{P}_j \le \alpha_{\tilde{m}(r)}, \hat{R}_2 = r\right)}{r} \\
= \quad & \sum_{j=1}^{n_0} \sum_{r=1}^{n_0} \frac{I\left(\hat{P}_j \le \alpha_{\tilde{m}(r)}, \hat{R}_2 \ge r\right)}{r} - \sum_{j=1}^{n_0} \sum_{r=1}^{n_0} \frac{I\left(\hat{P}_j \le \alpha_{\tilde{m}(r)}, \hat{R}_2 \ge r+1\right)}{r} \\
\le \quad & \sum_{j=1}^{n_0} \sum_{r=1}^{n_0} \frac{I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \le \alpha_{\tilde{m}(r)}, \hat{R}_2 \ge r\right)}{r} \\
\le \quad & \sum_{j=1}^{n_0} \sum_{r=1}^{K} \frac{I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \le \alpha_{\tilde{m}(r)}\right)}{r} + \\
& \sum_{j=1}^{n_0} \sum_{r=K+1}^{n_0} \frac{I\left(\hat{R}_2 \ge r\right) I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \le \alpha_{\tilde{m}(r)}\right)}{r}.
\end{aligned} \tag{12}$$

We now apply the following inequality (to be proved in Appendix) to (12):

(13)
$$I\left(\hat{R}_2 \geq r\right) \leq \sum_{l=1}^{n_0}\left(\sum_{s=r+1}^{n_0} \frac{I\left(\alpha_{\tilde{m}(s-1)} < \hat{P}_l \leq \alpha_{\tilde{m}(s)}\right)}{s} + \frac{I\left(\hat{P}_l \leq \alpha_{\tilde{m}(r)}\right)}{r}\right).$$

Thus, we get

$$\begin{aligned}
& I\left(V > \gamma R\right) \\
\leq & \sum_{j=1}^{n_0}\sum_{r=1}^{K} \frac{I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \leq \alpha_{\tilde{m}(r)}\right)}{r} + \sum_{j=1}^{n_0}\sum_{r=K+1}^{n_0} \frac{I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \leq \alpha_{\tilde{m}(r)}\right)}{r^2} \\
+ & \sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0}\sum_{r=K+1}^{n_0}\sum_{s=r+1}^{n_0} \frac{I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \leq \alpha_{\tilde{m}(r)},\ \alpha_{\tilde{m}(s-1)} < \hat{P}_l \leq \alpha_{\tilde{m}(s)}\right)}{rs}
\end{aligned}$$

(14)
$$+ \sum_{j=1}^{n_0}\sum_{l(\neq j)=1}^{n_0}\sum_{r=K+1}^{n_0} \frac{I\left(\alpha_{\tilde{m}(r-1)} < \hat{P}_j \leq \alpha_{\tilde{m}(r)},\ \hat{P}_l \leq \alpha_{\tilde{m}(r)}\right)}{r^2}.$$

Taking expectation of both sides of (14), we have

$$\begin{aligned}
\gamma\text{-FDP} \quad \leq \quad & \sum_{r=1}^{K} \frac{n_0\left(\alpha_{\tilde{m}(r)} - \alpha_{\tilde{m}(r-1)}\right)}{r} + \sum_{r=K+1}^{n_0} \frac{n_0\left(\alpha_{\tilde{m}(r)} - \alpha_{\tilde{m}(r-1)}\right)}{r^2} \\
& + \sum_{r=K+1}^{n_0}\sum_{s=r+1}^{n_0} \frac{n_0\left(n_0-1\right) G\left(\tilde{m}(r), \tilde{m}(s), \beta^*_{SU}\right)}{rs} \\
& + \sum_{r=K+1}^{n_0} \frac{n_0\left(n_0-1\right)\left(F(\alpha_{\tilde{m}(r)}, \alpha_{\tilde{m}(r)}) - F(\alpha_{\tilde{m}(r)}, \alpha_{\tilde{m}(r-1)})\right)}{r^2}. \qquad (15)
\end{aligned}$$

Taking the minimum with respect to K and then the maximum with respect to n_0 in (15), we have

$$\gamma\text{-FDP} \leq C^{(2)}_{n,SU}(\beta^*_{SU}) = \alpha,$$

which proves the theorem. ■

Remark 3.3. Romano and Shaikh proved the following two results in (2006a) and (2006b), respectively: Given null p-values having any type of dependence structure, the γ-FDP of the stepdown procedure with critical values $\alpha_i, i = 1, \ldots, n$, satisfies

$$\gamma\text{-FDP} \quad \leq \quad \max_{1\leq n_0\leq n} \left\{ n_0 \sum_{i=1}^{M} \frac{\alpha_{\overline{m}(i)} - \alpha_{\overline{m}(i-1)}}{i} \right\}; \tag{16}$$

whereas, the γ-FDP of the stepup procedure with the same set of critical values satisfies

$$\gamma\text{-FDP} \quad \leq \quad \max_{1\leq n_0\leq n} \left\{ n_0 \sum_{i=1}^{n_0} \frac{\alpha_{\tilde{m}(i)} - \alpha_{\tilde{m}(i-1)}}{i} \right\}. \tag{17}$$

These upper bounds are generally always larger than the corresponding upper bounds of the γ-FDP we derive here, as seen by letting $K = M$ in (11) and $K = n_0$ in (15), respectively. Thus, theoretically, the stepdown and stepup γ-FDP controlling procedures introduced in Theorems 3.4 and 3.5, respectively, are generally always more powerful than the corresponding ones given by Romano and Shaikh in (2006a) and (2006b), respectively. Numerically also, we see from Figure 2, the stepdown and stepup γ-FDP procedures in Theorems 3.4 and 3.5, respectively, have larger critical constants than the corresponding Romano-Shaikh stepdown and stepup procedures, respectively, and are therefore more powerful than these existing procedures, although the new stepdown procedure has only the same critical constants as the existing one when the test statistics are highly correlated.

4. Procedures controlling the γ-kFDP. In this section, we present some γ-kFDP controlling procedures. As pointed out in the introduction, consideration of γ-kFDP, instead of γ-FDP, allows one to increase the power of a procedure controlling the FDP exceeding γ at the cost of tolerating a few more than one false rejection and/or by utilizing the dependence structure of the null p-values through their joint distributions of order more than one. Often this dependence structure is completely unknown and one has to rely only on the marginal p-values to construct these γ-kFDP procedures. Sometimes, a measure of dependence among the p-values may be available in the form of pairwise correlations, which then can be utilized to develop these procedures. In some situations, however, the dependence structure may be known up to the extent of whether it is of a positive type or not and allows one to utilize the correlations through the pairwise joint distributions. Our procedures cover all these three scenarios.

4.1. *Procedures based on the marginal p-values.*

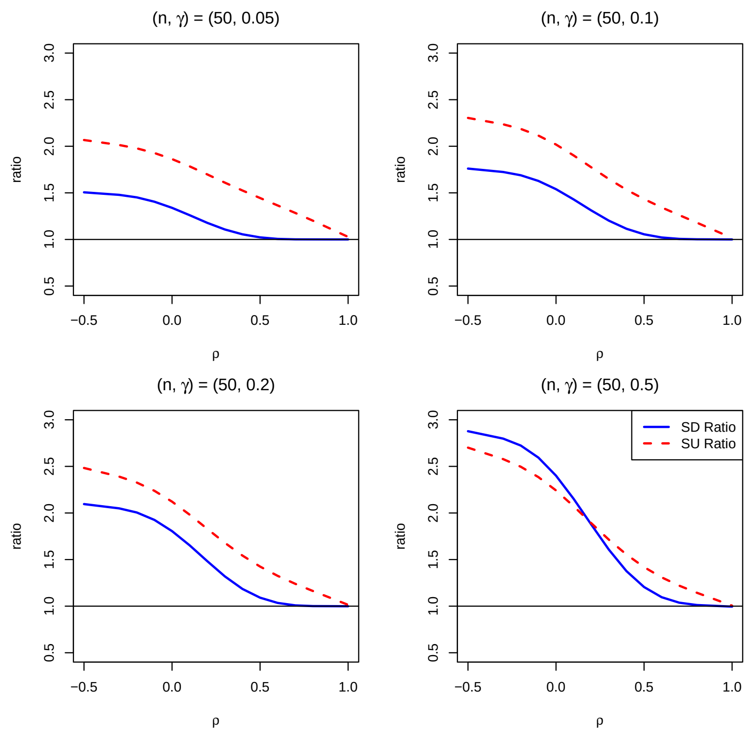


Fig 2. *Ratios of the critical values of the stepdown and stepup γ-FDP procedures in Theorems 3.4 and 3.5, respectively, to those of the corresponding Romano-Shaikh stepdown and stepup procedures provided by the upper bounds in (16) and (17), respectively, all of which are obtained by starting from the Lehmann-Romano type critical constants, for simultaneous testing of $\mu_i \leq 0$ against $\mu_i > 0$ in $n = 50$ normal random variables $N(\mu_i, 1)$ with a common correlation ρ at level $\alpha = 0.05$, for different values of ρ, and $\gamma = 0.05, 0.1, 0.2, 0.5$. (SD Ratio - Ratio for stepdown; SU Ratio - Ratio for stepup)*

THEOREM 4.1. *Let $m(i)$ be defined as in Theorem 3.2 for $i = 1, \ldots, M$. Then, given any set of constants $\alpha'_k \le \cdots \le \alpha'_n$, consider the stepdown procedure with the critical values $\alpha_i = \alpha\alpha'_{i\vee k}/C^{(3)}_{n,SD}$, $i = 1, \ldots, n$, where*

$$C^{(3)}_{n,SD} \quad = \quad \max_{k \le n_0 \le n} \left\{ n_0 \left(\frac{\alpha'_{k+m(k)}}{k} + \sum_{i=k+1}^{M} \frac{\alpha'_{i+m(i)} - \alpha'_{i-1+m(i-1)}}{i} \right) \right\}.$$

It controls the γ-kFDP at α under Assumption 1.

Proof. With $g(R)$ and S respectively defined in proving Theorems 3.1 and 3.2, following the line of arguments used in proving Theorem 3.2, we have

$$\begin{aligned}
&I\left(V \ge \max[g(R), k]\right) = I\left(V > \gamma(V+S),\ V \ge k\right) \\
&= I\left(V \ge \max\{\lfloor \gamma S/(1-\gamma) \rfloor + 1, k\}\right) = \sum_{i=k}^{M} I\left(V \ge i,\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\
&\le \sum_{i=k}^{M} I\left(\hat{P}_{(i)} \le \alpha_{i+m(i)},\ \lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\
&\le \sum_{j=1}^{n_0} \sum_{i=k}^{M} \frac{I\left(\hat{P}_j \le \alpha_{i+m(i)}\right)}{i} I\left(\lfloor \gamma S/(1-\gamma) \rfloor + 1 = i\right) \\
&= \sum_{j=1}^{n_0} \frac{I\left(\hat{P}_j \le \alpha_{k+m(k)}\right)}{k} I\left(\lfloor \gamma S/(1-\gamma) \rfloor + 1 \ge k\right) + \\
&\quad \sum_{j=1}^{n_0} \sum_{i=k+1}^{M} \left[\frac{I\left(\hat{P}_j \le \alpha_{i+m(i)}\right)}{i} - \frac{I\left(\hat{P}_j \le \alpha_{i-1+m(i-1)}\right)}{i-1} \right] \\
&\qquad \times I\left(\lfloor \gamma S/(1-\gamma) \rfloor + 1 \ge i\right)
\end{aligned}$$

(18)

$$\le \sum_{j=1}^{n_0} \left(\frac{I\left(\hat{P}_j \le \alpha_{k+m(k)}\right)}{k} + \sum_{i=k+1}^{M} \frac{I\left(\alpha_{i-1+m(i-1)} < \hat{P}_j \le \alpha_{i+m(i)}\right)}{i} \right),$$

if $n_0 \ge k$; otherwise, $I\left(V \ge \max[g(R), k]\right) = 0$. So, assuming $n_0 \ge k$, and taking expectations of both sides in (18), we get

$$\begin{aligned}
&\gamma\text{-kFDP} = \Pr\{V \geq \max[g(R), k]\} \\
\leq\ & n_0 \left(\frac{\alpha_{k+m(k)}}{k} + \sum_{i=k+1}^{M} \frac{\alpha_{i+m(i)} - \alpha_{i-1+m(i-1)}}{i} \right) \\
=\ & \alpha \left\{ n_0 \left(\frac{\alpha'_{k+m(k)}}{k} + \sum_{i=k+1}^{M} \frac{\alpha'_{i+m(i)} - \alpha'_{i-1+m(i-1)}}{i} \right) \right\} / C^{(3)}_{n,SD} \leq \alpha,
\end{aligned}$$

which proves the theorem. ■

THEOREM 4.2. *Let $\tilde{m}(i)$ be defined as in Theorem 3.3 for $i = 1, \ldots, n_0$. Then, given any set of constants $\alpha'_k \leq \cdots \leq \alpha'_n$, the stepup procedure with the critical values $\alpha_i = \alpha\alpha'_{i\vee k}/C^{(3)}_{n,SU}$, $i = 1, \ldots, n$, where*

$$C^{(3)}_{n,SU} = \max_{k \leq n_0 \leq n} \left\{ n_0 \left(\frac{\alpha'_{\tilde{m}(k)}}{k} + \sum_{i=k+1}^{n_0} \frac{\alpha'_{\tilde{m}(i)} - \alpha'_{\tilde{m}(i-1)}}{i} \right) \right\},$$

controls the γ-kFDP at α under Assumption 1.

Proof. Here, we will use the arguments similar to those used in proving Theorem 3.3.

$$\begin{aligned}
&I(V \geq \max[g(R), k]) = I(V \geq \lfloor \gamma R \rfloor + 1, V \geq k, V \geq R - n_1) \\
=\ & I\left(\bigcup_{j=k}^{n_0} \left\{ \hat{P}_{(j)} \leq \alpha_R, V = j,\ \lfloor \gamma R \rfloor + 1 \leq j, R \leq j + n_1 \right\} \right) \\
\leq\ & I\left(\bigcup_{j=k}^{n_0} \left\{ \hat{P}_{(j)} \leq \alpha_R, R \leq \tilde{m}(j) \right\} \right) \leq I\left(\bigcup_{j=k}^{n_0} \left\{ \hat{P}_{(j)} \leq \alpha_{\tilde{m}(j)} \right\} \right) \\
\leq\ & \sum_{j=1}^{n_0} \frac{I\left(\hat{P}_j \leq \alpha_{\tilde{m}(k)}\right)}{k} + \sum_{i=k+1}^{n_0} \sum_{j=1}^{n_0} \frac{I\left(\alpha_{\tilde{m}(i-1)} < \hat{P}_j \leq \alpha_{\tilde{m}(i)}\right)}{i}, \qquad (19)
\end{aligned}$$

if $n_0 \geq k$; otherwise, $I(V \geq \max[g(R), k]) = 0$. The third inequality follows from (13). So, assuming that $n_0 \geq k$, and taking expectations of both sides in (19), we have

$$\begin{aligned}
\gamma\text{-kFDP} &= \Pr\{V \geq \max[g(R), k]\} \leq n_0 \left(\frac{\alpha_{\tilde{m}(k)}}{k} + \sum_{i=k+1}^{n_0} \frac{\alpha_{\tilde{m}(i)} - \alpha_{\tilde{m}(i-1)}}{i} \right) \\
&= \alpha \left\{ n_0 \left(\frac{\alpha'_{\tilde{m}(k)}}{k} + \sum_{i=k+1}^{n_0} \frac{\alpha'_{\tilde{m}(i)} - \alpha'_{\tilde{m}(i-1)}}{i} \right) \right\} / C^{(3)}_{n,SU} \leq \alpha,
\end{aligned}$$

which proves the theorem. ■

REMARK 4.1. When $k = 1$, the results in Theorems 4.1 and 4.2 reduce to those given by Romano and Shaikh in (2006a) and (2006b), respectively, although our expressions of the upper bounds given in these theorems are different from theirs. Thus, our results can be regarded as a generalization of Romano and Shaikh's results. Moreover, we should emphasize that we provide alternative, much simpler proofs for these results.

4.2. *Procedures incorporating pairwise correlations.*

THEOREM 4.3. *Let $H(u) = F(u,u)$. Define $m(i)$ as in Theorem 3.2 for $i = 1,\ldots,M$. Then, given any set of constants $\alpha'_k \le \cdots \le \alpha'_n$, the step-down procedure with the critical values α_i, $i = 1,\ldots,n$, satisfying $H(\alpha_i) = \alpha H(\alpha'_{i\vee k})/C^{(4)}_{n,SD}$, $i = 1,\ldots,n$, where*

$$\begin{aligned} C^{(4)}_{n,SD} &= \max_{k\le n_0\le n}\left\{ n_0(n_0-1)\left(\frac{H(\alpha'_{k+m(k)})}{k(k-1)}\right.\right. \\ &\qquad \left.\left. + \sum_{i=k+1}^{M}\frac{H(\alpha'_{i+m(i)}) - H(\alpha'_{i-1+m(i-1)})}{i(i-1)}\right)\right\}, \end{aligned}$$

controls the γ-kFDP at α under Assumptions 1 and 3.

Proof. We proceed as in proving Theorem 4.1. Applying the inequality (10) and arguing as in (18), we get the following:

$$\begin{aligned} & I\left(V \ge \max[g(R),k]\right) \\ \le & \sum_{j=1}^{n_0}\sum_{j'(\neq j)=1}^{n_0}\sum_{i=k}^{M}\frac{I\left(\max(\hat{P}_j,\hat{P}_{j'}) \le \alpha_{i+m(i)}\right)}{i(i-1)} I\left(\lfloor \gamma S/(1-\gamma)\rfloor + 1 = i\right) \\ \le & \sum_{j=1}^{n_0}\sum_{j'(\neq j)=1}^{n_0}\left(\frac{I\left(\max(\hat{P}_j,\hat{P}_{j'}) \le \alpha_{k+m(k)}\right)}{k(k-1)}\right. \\ & \left. + \sum_{i=k+1}^{M}\frac{I\left(\alpha_{i-1+m(i-1)} < \max(\hat{P}_j,\hat{P}_{j'}) \le \alpha_{i+m(i)}\right)}{i(i-1)}\right), \end{aligned} \tag{20}$$

if $n_0 \ge k$; otherwise, $I\left(V \ge \max[g(R),k]\right) = 0$. So, assuming that $n_0 \ge k$, and taking expectations of both sides in (20), we get

$$
\begin{aligned}
& \gamma\text{-kFDP} = \Pr\left\{V \geq \max[g(R), k]\right\} \\
\leq\ & \left\{ n_0(n_0-1)\left(\frac{H(\alpha_{k+m(k)})}{k(k-1)} + \sum_{i=k+1}^{M} \frac{H(\alpha_{i+m(i)}) - H(\alpha_{i-1+m(i-1)})}{i(i-1)} \right) \right\} \\
=\ & \alpha \left\{ n_0(n_0-1)\left(\frac{H(\alpha'_{k+m(k)})}{k(k-1)} \right.\right. \\
& \qquad \left.\left. + \sum_{i=k+1}^{M} \frac{H(\alpha'_{i+m(i)}) - H(\alpha'_{i-1+m(i-1)})}{i(i-1)} \right) \right\} / C^{(4)}_{n,SD} \\
\leq\ & \alpha.
\end{aligned}
$$

Thus, the theorem is proved. ■

THEOREM 4.4. *Let $\tilde{m}(i)$ be defined as in Theorem 3.3 for $i = 1, \ldots, n_0$. Then, given any set of constants $\alpha'_k \leq \cdots \leq \alpha'_n$, the stepup procedure with the critical values α_i, $i = 1, \ldots, n$, satisfying $H(\alpha_i) = \alpha H(\alpha'_{i \vee k})/C^{(4)}_{n,SU}$, for $i = 1, \ldots, n$, where*

$$
C^{(4)}_{n,SU} = \max_{k \leq n_0 \leq n} \left\{ n_0(n_0-1)\left(\frac{H(\alpha'_{\tilde{m}(k)})}{k(k-1)} + \sum_{i=k+1}^{n_0} \frac{H(\alpha'_{\tilde{m}(i)}) - H(\alpha'_{\tilde{m}(i-1)})}{i(i-1)} \right) \right\},
$$

controls the γ-kFDP at α under Assumptions 1 and 3.

Proof. Proceeding as in proving Theorem 4.2 and using the following inequality (to be proved in Appendix):

$$
\begin{aligned}
I\left(\bigcup_{j=i}^{n_0} \hat{P}_{(j)} \leq \alpha_j \right) \leq & \sum_{j=1}^{n_0} \sum_{j'(\neq j)=1}^{n_0} \left(\frac{I\left(\max(\hat{P}_j, \hat{P}_{j'}) \leq \alpha_i\right)}{i(i-1)} \right. \\
& \left. + \sum_{r=i+1}^{n_0} \frac{I\left(\alpha_{r-1} < \max(\hat{P}_j, \hat{P}_{j'}) \leq \alpha_r\right)}{r(r-1)} \right), \qquad (21)
\end{aligned}
$$

for any fixed i such that $2 \leq i \leq n_0$ and a set of constants $0 < \alpha_i \leq \cdots \leq \alpha_{n_0}$, we have

$$
\begin{aligned}
& I\left(V \geq \max[g(R), k]\right) \\
= \; & I\left(\bigcup_{j=k}^{n_0}\left\{\hat{P}_{(j)} \leq \alpha_R, V=j,\ \lfloor \gamma R\rfloor + 1 \leq j,\ R \leq j+n_1\right\}\right) \\
\leq \; & \left(\bigcup_{j=k}^{n_0}\left\{\hat{P}_{(j)} \leq \alpha_{\tilde{m}(j)}\right\}\right) \\
\leq \; & \sum_{j=1}^{n_0}\sum_{j'(\neq j)=1}^{n_0}\left(\frac{I\left(\max(\hat{P}_j, \hat{P}_{j'}) < \alpha_{\tilde{m}(k)}\right)}{k(k-1)}\right. \\
& \left. + \sum_{r=k+1}^{n_0}\frac{I\left(\alpha_{\tilde{m}(r-1)} < \max(\hat{P}_j, \hat{P}_{j'}) < \alpha_{\tilde{m}(r)}\right)}{r(r-1)}\right).
\end{aligned}
$$

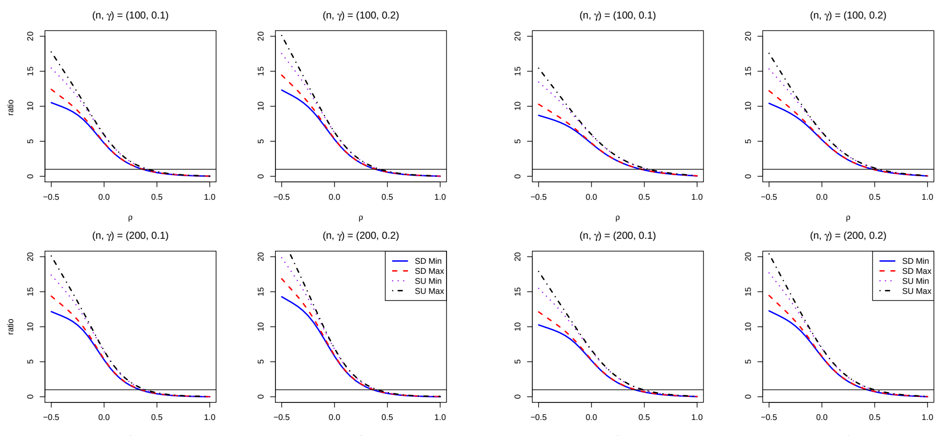
This proves

$$
\begin{aligned}
& \gamma\text{-kFDP} = \Pr\left\{V \geq \max[g(R), k]\right\} \\
\leq \; & n_0(n_0-1)\left(\frac{H(\alpha_{\tilde{m}(k)})}{k(k-1)} + \sum_{i=k+1}^{n_0}\frac{H(\alpha_{\tilde{m}(i)}) - H(\alpha_{\tilde{m}(i-1)})}{i(i-1)}\right) \\
= \; & \alpha\left\{n_0(n_0-1)\left(\frac{H(\alpha'_{\tilde{m}(k)})}{k(k-1)} + \sum_{i=k+1}^{n_0}\frac{H(\alpha'_{\tilde{m}(i)}) - H(\alpha'_{\tilde{m}(i-1)})}{i(i-1)}\right)\right\}/C_{n,SU}^{(4)} \\
\leq \; & \alpha,
\end{aligned}
$$

the desired result. ■

REMARK 4.2. As seen form Figure 3, the critical values of the γ-kFDP stepdown and stepup procedures (in Theorems 4.3 and 4.4, respectively) that utilize the pairwise correlation information are much larger than the corresponding critical values (in Theorems 4.1 and 4.2, respectively) that do not use this information when the underlying test statistics are negatively correlated or slightly or moderately positively correlated. However, when the test statistics are highly positively correlated, utilizing the pairwise correlation information is not helpful for improving the performance of the γ-kFDP methods.

4.3. *Procedures under positive dependence and incorporating pairwise correlations.* We make the following assumption regarding the positive dependence structure among the null p-values:



(a) k = 2 (b) k = 4

FIG 3. *Minimum and maximum ratios of the critical values of the stepdown and stepup γ-kFDP procedures in Theorems 4.3 and 4.4, respectively, to those of the corresponding stepdown and stepup γ-kFDP procedures in Theorems 4.1 and 4.2, respectively, all of which are based on the Lehmann-Romano type critical constants, for simultaneous testing of $\mu_i \leq 0$ against $\mu_i > 0$ in n normal random variables $N(\mu_i, 1)$ with a common correlation ρ at level $\alpha = 0.05$, for different values of ρ, $k = 2$ and 4, and $(n, \gamma) = (100, 0.1), (100, 0.2), (200, 0.1),$ and $(200, 0.2)$. (SD Min - Minimum ratio for stepdown; SD Max - Maximum ratio for stepdown; SU Min - Minimum ratio for stepup; SU Max - Maximum ratio for stepup)*

ASSUMPTION 4. *The null p-values $\hat{P}_1, \ldots, \hat{P}_{n_0}$ are positively dependent in the sense that the conditional expectation* $\mathrm{E}\left\{\psi\left(\hat{P}_1, \ldots, \hat{P}_{n_0}\right) \mid P_i \le u, P_j \le v\right\}$ *is non-decreasing in (u, v) for each (i, j) and any non-decreasing (coordinatewise) function ψ.*

Distributions satisfying the multivariate totally positive of order two (MTP_2) condition of Karlin and Rinott (1980) and are exchangeable under null hypotheses are among the distributions of the p-values, or the test statistics from which they are generated, that satisfy Assumptions 3 and 4. For example, the p-values obtained from the multivariate normal distributions with a common variance and a nonnegative common correlation, or, in general, certain mixtures of independent distributions, commonly considered in multiple testing, satisfy this MTP_2 condition. The definition of MTP_2 and several important related results related to it have been recalled from Karlin and Rinott (1980) in Sarkar (2008b).

THEOREM 4.5. *Let $H(u) = F(u, u)$. Then, the stepup or stepdown procedure with the critical constants α_i, $i = 1, \ldots, n$, satisfying*

$$H(\alpha_i) = \begin{cases} \frac{(k-1)k\alpha}{(n+k-i-1)(n+k-i)} & \text{for } i \text{ such that } 1 \le \lfloor \gamma i \rfloor + 1 \le k \\ \frac{\lfloor \gamma i \rfloor (\lfloor \gamma i \rfloor + 1)\alpha}{(n+\lfloor \gamma i \rfloor - i)(n+\lfloor \gamma i \rfloor + 1 - i)} & \text{for } i \text{ such that } \lfloor \gamma i \rfloor + 1 > k, \end{cases}$$

for any fixed $2 \le k \le n_0$, controls the γ-kFDP at α under Assumptions 1, 3 and 4.

Proof. A proof of this theorem relies on the following lemma that follows from Theorem 5.2 of Sarkar (2008b):

LEMMA 4.1. *Let $\hat{R}$ denote the number of rejections in the stepup procedure based on all the n_0 null p-values and the critical values α_i satisfying*

$$H(\alpha_i) = \frac{i \vee k(i \vee k - 1)\alpha}{n_0(n_0 - 1)}, \ i = 1, \ldots, n_0,$$

where $i \vee k = \max(i, k)$. Then, for any fixed $2 \le k \le n_0$, $\Pr\left(\hat{R} \ge k\right) \le \alpha$ *under Assumptions 1, 3 and 4.*

Proceeding as in our proof of Theorem 3.1, we note that

$$\{V \geq \max[g(R), k]\} = \bigcup_{v=k}^{n_0} \left\{\hat{P}_{(v)} \leq \alpha_R,\ V \geq \max[g(R), k],\ V = v\right\}$$

$$\subseteq \bigcup_{v=k}^{n_0} \left\{\hat{P}_{(v)} \leq \frac{V(V-1)\alpha}{(n-R+V)(n-R+V-1)},\ V \geq \max[g(R), k],\ V = v\right\}$$

$$\subseteq \bigcup_{v=k}^{n_0} \left\{\hat{P}_{(v)} \leq \frac{V(V-1)\alpha}{n_0(n_0-1)},\ V \geq \max[g(R), k],\ V = v\right\}$$

(22)

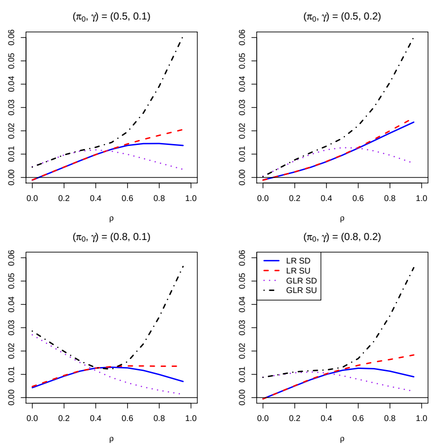
$$\subseteq \bigcup_{v=k}^{n_0} \left\{\hat{P}_{(v)} \leq \frac{v(v-1)\alpha}{n_0(n_0-1)}\right\}.$$

The fact that the probability of the event in the right-hand side of (22) is less than or equal to α under Assumptions 1, 3 and 4 follows from Lemma 4.1. Thus, we get the desired result noting that γ-kFDP $= \Pr\left(V \geq \max\{g(R), k\}\right)$. ■

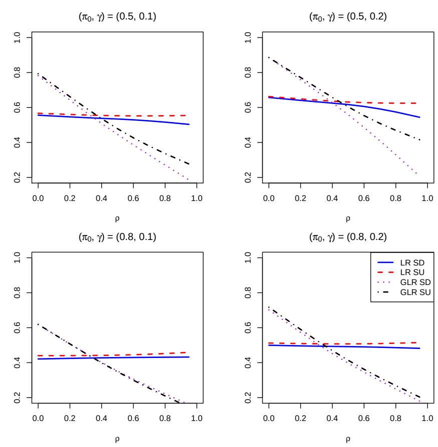
REMARK 4.3. As seen from Figure 4, by tolerating only up to one false rejection, one can significantly improve powers of the Lehmann-Romano stepdown γ-FDP procedure and its stepup analogue when the underlying test statistics are slightly or moderately correlated. However, when the test statistics are highly correlated, generalizing these Lehmann-Romano stepwise γ-FDP procedures to those controlling the γ-2FDP do not seem to work well.

5. Conclusion. This paper is mostly devoted to advancing the theory and methodology of the FDP control. First, we have considered the existing notion of γ-FDP and developed newer results extending and often improving what is available so far in the literature. Second, we have generalized the notion of γ-FDP to make it more appropriate and enhance the power of an existing γ-FDP procedure, and have given procedures controlling this generalized error rate under different dependence scenarios. We have given numerical evidence to show that the proposed methods can continue to have superior performance compared to the ones they intend to improve under some dependence situations.

6. Appendix. Proof of (6). Consider a single-step test based on the p-values $\hat{P}_1, \ldots, \hat{P}_{n_0}$ and the constant threshold t. Let $\hat{R}_1$ denote the number



(a) Simulated γ-kFDP.



(b) Simulated average power.

FIG 4. *Simulated γ-kFDP's and average powers of the original Lehmann-Romano stepdown procedure (LR SD) and its stepup analog (LR SU), and their generalizations (GLR SD and GLR SU, respectively) controlling the γ-2FDP for simultaneous testing of $\mu_i = 0$ against $\mu_i = 3$ in $n = 100$ normal random variables $N(\mu_i, 1)$ with a common correlation ρ at level $\alpha = 0.05$, for different values of ρ and $(\pi_0, \gamma) = (0.5, 0.1), (0.5, 0.2), (0.8, 0.1)$, and $(0.8, 0.2)$. (Runs per simulation = 2,000.)*

of rejections. Then, we have

$$\begin{aligned} I\left(\hat{P}_{(i)} \le t\right) &= I\left(\hat{R}_1 \ge i\right) = \sum_{j=1}^{n_0}\sum_{r=i}^{n_0} \frac{I\left(\hat{R}_1 = r, \hat{P}_j \le t\right)}{r} \\ &\le \frac{1}{i}\sum_{j=1}^{n_0} I\left(\hat{P}_j \le t, \hat{R}_1 \ge i\right) \le \frac{1}{i}\sum_{j=1}^{n_0} I\left(\hat{P}_j \le t\right), \end{aligned}$$

the desired result. ■

Proof of (10). With $\hat{R}_1$ defined in proving (6), we have for each $i = 2, \ldots, n_0$,

$$\begin{aligned} I\left(\hat{P}_{(i)} \le t\right) &= I\left(\hat{R}_1 \ge i\right) \le I\left(\hat{R}_1(\hat{R}_1 - 1) \ge i(i-1)\right) \\ &\le \frac{1}{i(i-1)} \sum_{j=1}^{n_0} \sum_{l(\neq j)=1}^{n_0} I\left(\hat{P}_j \le t, \hat{P}_l \le t\right), \end{aligned}$$

which proves the desired inequality. ■

Proof of (13). Let us define $\hat{R}_2$ as the number of rejections in the stepup procedure based on the p-values $\hat{P}_i$, $i = 1, \ldots, n_0$, and the critical values α_i, $i = 1, \ldots, n_0$. Then,

$$\begin{aligned} & I(\hat{R}_2 \ge k) \\ &= I\left(\bigcup_{r=k}^{n_0}\left\{\hat{P}_{(r)} \le \alpha_r\right\}\right) = \sum_{j=1}^{n_0}\sum_{r=k}^{n_0} \frac{I\left(\hat{R}_2 = r, \hat{P}_j \le \alpha_r\right)}{r} \\ &= \sum_{j=1}^{n_0}\sum_{r=k}^{n_0} \frac{I\left(\hat{R}_2 \ge r, \hat{P}_j \le \alpha_r\right)}{r} - \sum_{j=1}^{n_0}\sum_{r=k}^{n_0-1} \frac{I\left(\hat{R}_2 \ge r+1, \hat{P}_j \le \alpha_r\right)}{r} \\ &= \sum_{j=1}^{n_0}\sum_{r=k}^{n_0} \frac{I\left(\hat{R}_2 \ge r, \hat{P}_j \le \alpha_r\right)}{r} - \sum_{j=1}^{n_0}\sum_{r=k+1}^{n_0} \frac{I\left(\hat{R}_2 \ge r, \hat{P}_j \le \alpha_{r-1}\right)}{r-1} \\ &\le \sum_{j=1}^{n_0} \frac{I\left(\hat{R}_2 \ge k, \hat{P}_j \le \alpha_k\right)}{k} + \sum_{j=1}^{n_0}\sum_{r=k+1}^{n_0} \frac{I\left(\alpha_{r-1} < \hat{P}_j \le \alpha_r\right) I\left(\hat{R}_2 \ge r\right)}{r} \\ &\le \sum_{j=1}^{n_0} \frac{I\left(\hat{P}_j \le \alpha_k\right)}{k} + \sum_{j=1}^{n_0}\sum_{r=k+1}^{n_0} \frac{I\left(\alpha_{r-1} < \hat{P}_j \le \alpha_r\right)}{r}, \end{aligned}$$

the desired result. ■

Proof of (21). A proof of this is similar to that of (13). For any fixed i such that $2 \le i \le n_0$, first we note that

$$I\left(\bigcup_{r=i}^{n_0}\left\{\hat{P}_{(r)} \le \alpha_r\right\}\right) = I(\hat{R}_2 \ge i)$$

$$= \sum_{j=1}^{n_0}\sum_{j'(\neq j)=1}^{n_0}\sum_{r=i}^{n_0}\frac{I\left(\hat{R}_2 = r, \max(\hat{P}_j, \hat{P}_{j'}) \le \alpha_r\right)}{r(r-1)}. \tag{23}$$

As in the proof of (13), the right-hand side of (23) can be shown to be less than or equal to the following:

$$\sum_{j=1}^{n_0}\sum_{j'(\neq j)=1}^{n_0}\left(\frac{I\left(\max(\hat{P}_j, \hat{P}_{j'}) \le \alpha_i\right)}{i(i-1)} + \sum_{r=i+1}^{n_0}\frac{I\left(\alpha_{r-1} < \max(\hat{P}_j, \hat{P}_{j'}) \le \alpha_r\right)}{r(r-1)}\right).$$

This proves the inequality. ■

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