CONTROL OF DIRECTIONAL ERRORS IN FIXED SEQUENCE MULTIPLE TESTING

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Supplementary Material

S1 Proofs

Proof of Lemma 1. Let T and P denote the test statistic and the corresponding p-value for testing H, respectively. When testing H, a type 3 error occurs if H is rejected and $\theta T < 0$. Then, the type 3 error rate is given by $Pr(P \leq \alpha, \theta T < 0)$.

When $\theta > 0$, we have

$$
\begin{aligned}
& Pr(P \leq \alpha, \theta T < 0) = Pr(2F_0(T) \leq \alpha, T < 0) \\
= \;& Pr\left(T \leq F_0^{-1}\left(\frac{\alpha}{2}\right)\right) = F_\theta\left(F_0^{-1}\left(\frac{\alpha}{2}\right)\right) \\
\leq \;& F_0\left(F_0^{-1}\left(\frac{\alpha}{2}\right)\right) = \frac{\alpha}{2}.
\end{aligned}
$$

The inequality follows from the assumption that F_θ is stochastically increasing in θ. Similarly, when $\theta < 0$, we can also prove that $Pr(P \leq \alpha, \theta T < 0) \leq \frac{\alpha}{2}$. □

Proof of Theorem 1(i). Induction will be used to show that Procedure 1 strongly controls the mdFWER at level α. First consider the case of $n = 2$. We show control of the mdFWER of Procedure 1 in all possible combinations of true and false null hypotheses while testing two hypotheses H_1 and H_2.

Case I: H_1 is true. Type 1 or type 3 error occurs only when H_1 is rejected.

$$\text{mdFWER} = Pr(P_1 \leq \alpha) \leq \alpha.$$

Case II: Both H_1 and H_2 are false. We have no type 1 errors but only type 3 errors.

$$\begin{aligned} & \text{mdFWER} \\ = \; & Pr(\{P_1 \leq \alpha, T_1\theta_1 < 0\} \cup \{P_1 \leq \alpha, T_1\theta_1 \geq 0, P_2 \leq \alpha/2, T_2\theta_2 < 0\}) \\ \leq \; & Pr(P_1 \leq \alpha, T_1\theta_1 < 0) + Pr(P_2 \leq \alpha/2, T_2\theta_2 < 0) \\ \leq \; & \frac{\alpha}{2} + \frac{\alpha}{4} = \frac{3\alpha}{4}. \end{aligned}$$

The first inequality follows from Bonferroni inequality and the second follows from Lemma 1.

Case III: H_1 is false and H_2 is true. The mdFWER is bounded above by

$$
\begin{aligned}
& Pr(\text{ make type 3 error when testing } H_1) \\
& \quad + Pr(\text{ make type 1 error when testing } H_2) \\
\leq\ & Pr(P_1 \leq \alpha, T_1\theta_1 < 0) + Pr(P_2 \leq \alpha/2) \\
\leq\ & \frac{\alpha}{2} + \frac{\alpha}{2} = \alpha.
\end{aligned}
$$

The first inequality follows from Bonferroni inequality and the second follows from Lemma 1 and $P_2 \sim U(0,1)$ since H_2 is true.

Now assume the inductive hypothesis that the mdFWER is bounded above by α when testing at most $n-1$ hypotheses by using Procedure 1 at level α. In the following, we prove the mdFWER is also bounded above by α when testing n hypotheses $H_1, \ldots, H_n$. Without loss of generality, assume H_1 is a false null (if H_1 is a true null, the desired result directly follows by using the same argument as in Case I of $n = 2$). Then, the mdFWER is bounded above by

$$
\begin{aligned}
& Pr(\text{ make type 3 error when testing } H_1) \\
+\ & Pr(\text{ make at least one type 1 or type 3 errors when testing } H_2, \ldots, H_n) \\
\leq\ & \frac{\alpha}{2} + \frac{\alpha}{2} = \alpha.
\end{aligned}
$$

The inequality follows from the induction assumption, noticing that $H_2, \ldots, H_n$ are tested by using Procedure 1 at level $\alpha/2$. Thus, the desired result follows.

(ii). We now prove that the critical constants are unimprovable. For instance, when H_1 is true, it is easy to see that the first critical constant, α, is unimprovable. For each given $k = 2, \ldots, n$, when $\theta_i > 0, i = 1, \ldots, k-1$ and $\theta_k = 0$, that is, $H_i, i = 1, \ldots, k-1$ are false and H_k is true, we present a simple joint distribution of the test statistics $T_1, \ldots, T_k$ to show that the kth critical constant of this procedure is also unimprovable.

Define $Z_k \sim N(0,1)$ and $Z_i = \Phi^{-1}(|2\Phi(Z_{i+1}) - 1|), i = 1, \ldots, k-1$, where $\Phi(\cdot)$ is the cdf of N(0, 1). Let q_i denote Z_i's upper $\alpha/2^i$ quantile. It is easy to check that for each $i = 1, \ldots, k$, $Z_i \sim N(0,1)$. Thus, $-q_i$ is Z_i's lower $\alpha/2^i$ quantile. In addition, by the construction of Z_i's, it is easy to see that the event $Z_i \geq q_i$ is equivalent to the event $Z_{i+1} \notin (-q_{i+1}, q_{i+1})$.

Let $T_i = Z_i + \theta_i, i = 1, \ldots, k$, thus $T_i \sim N(\theta_i, 1)$. Then, as $\theta_i \to 0+$ for $i = 1, \ldots, k-1$, we have

$$
\begin{aligned}
\text{mdFWER} &= \sum_{j=1}^{k-1} Pr(T_1 \geq q_1, \ldots, T_{j-1} \geq q_{j-1}, T_j \leq -q_j) \\
&\quad + Pr(T_1 \geq q_1, \ldots, T_{k-1} \geq q_{k-1}, T_k \notin (-q_k, q_k)) \\
&= \sum_{j=1}^{k-1} Pr(Z_1 \geq q_1, \ldots, Z_{j-1} \geq q_{j-1}, Z_j \leq -q_j) \\
&\quad + Pr(Z_1 \geq q_1, \ldots, Z_{k-1} \geq q_{k-1}, Z_k \notin (-q_k, q_k)) \\
&= \sum_{j=1}^{k-1} Pr(Z_j \leq -q_j) + Pr(Z_k \notin (-q_k, q_k))
\end{aligned}
$$

$$= \sum_{j=1}^{k-1} \frac{\alpha}{2^j} + \frac{\alpha}{2^{(k-1)}} = \alpha.$$

Thus, the kth critical constant of Procedure 1 is unimprovable and hence each critical constant of Procedure 1 is unimprovable under arbitrary dependence. □

PROOF OF LEMMA 2. Note that when $\theta_1 > 0$ and $\theta_2 = 0$, we have

$$\begin{aligned}
& \text{mdFWER} \\
= \;& Pr\left(P_1 \leq \alpha, \theta_1 T_1 < 0\right) + Pr\left(P_1 \leq \alpha, \theta_1 T_1 \geq 0, P_2 \leq \alpha\right) \\
= \;& Pr\left(P_1 \leq \alpha, T_1 < 0\right) + Pr\left(P_1 \leq \alpha, T_1 \geq 0, P_2 \leq \alpha, T_2 > 0\right) \\
& + Pr\left(P_1 \leq \alpha, T_1 \geq 0, P_2 \leq \alpha, T_2 \leq 0\right) \\
= \;& Pr\left(2F_0(T_1) \leq \alpha\right) + Pr\left(2(1 - F_0(T_1)) \leq \alpha, 2(1 - F_0(T_2)) \leq \alpha\right) \\
& + Pr\left(2(1 - F_0(T_1)) \leq \alpha, 2F_0(T_2) \leq \alpha\right) \\
= \;& Pr\left(T_1 \leq c_1\right) + Pr\left(T_1 \geq c_2, T_2 \geq c_2\right) + Pr\left(T_1 \geq c_2, T_2 \leq c_1\right) \\
= \;& F_{\theta_1}(c_1) + 1 - F_{\theta_1}(c_2) - F_0(c_2) + F_{(\theta_1,0)}(c_2, c_2) + F_0(c_1) - F_{(\theta_1,0)}(c_2, c_1) \\
= \;& \alpha + F_{\theta_1}(c_1) - F_{\theta_1}(c_2) + F_{(\theta_1,0)}(c_2, c_2) - F_{(\theta_1,0)}(c_2, c_1). \qquad \text{(S1.1)}
\end{aligned}$$

Specifically, under Assumption 1 (independence), (S1.1) can be simplified as,

$$\begin{aligned}
& \alpha + F_{\theta_1}(c_1) - F_{\theta_1}(c_2) + F_{\theta_1}(c_2)F_0(c_2) - F_{\theta_1}(c_2)F_0(c_1) \\
= \;& \alpha + F_{\theta_1}(c_1) - \alpha F_{\theta_1}(c_2).
\end{aligned}$$

Similarly, when $\theta_1 < 0$ and $\theta_2 = 0$, we can prove that

$$\text{mdFWER} = 1 + F_{\theta_1}(c_1) - F_{\theta_1}(c_2) + F_{(\theta_1,0)}(c_1, c_1) - F_{(\theta_1,0)}(c_1, c_2). \qquad \square$$

Proof of Lemma 3. By using the same arguments as in Theorem 1, we can easily prove control of the mdFWER of Procedure 2 in the case of $n = 2$ when H_1 is true or both H_1 and H_2 are false. In the following, we prove the desired result also holds when H_1 is false and H_2 is true.

Note that H_1 is false and H_2 is true imply $\theta_1 \neq 0$ and $\theta_2 = 0$. To show that the mdFWER is controlled for $\theta_1 > 0$ and $\theta_2 = 0$, we only need to show by Lemma 2 that $\alpha + F_{\theta_1}(c_1) - \alpha F_{\theta_1}(c_2) \leq \alpha$. This is equivalent to show

$$F_{\theta_1}(c_2)\left(F_0(c_2) - F_0(c_1)\right) \leq F_{\theta_1}(c_2) - F_{\theta_1}(c_1). \qquad \text{(S1.2)}$$

For proving (S1.2), it is enough to prove the following, as $0 \leq F_0(c_2) \leq 1$,

$$F_{\theta_1}(c_2)\left(F_0(c_2) - F_0(c_1)\right) \leq F_0(c_2)\left(F_{\theta_1}(c_2) - F_{\theta_1}(c_1)\right). \qquad \text{(S1.3)}$$

Dividing both sides of (S1.3) by $F_{\theta_1}(c_2)F_0(c_2)$, we see that we only need to prove,

$$1 - \frac{F_0(c_1)}{F_0(c_2)} \leq 1 - \frac{F_{\theta_1}(c_1)}{F_{\theta_1}(c_2)},$$

which follows directly from (3.5) and Assumption 2 (MLR).

Similarly, to show that the mdFWER is controlled for $\theta_1 < 0$ and $\theta_2 = 0$, we only need to show by Lemma 2 that $1 + \alpha F_{\theta_1}(c_1) - F_{\theta_1}(c_2) \leq \alpha$. This is equivalent to showing

$$(1-\alpha)\left(1 - F_{\theta_1}(c_1)\right) \leq F_{\theta_1}(c_2) - F_{\theta_1}(c_1).$$

Writing $1-\alpha$ as $(1 - F_0(c_1)) - (1 - F_0(c_2))$ and writing $F_{\theta_1}(c_2) - F_{\theta_1}(c_1)$ as

$(1 - F_{\theta_1}(c_1)) - (1 - F_{\theta_1}(c_2))$, we get that it is equivalent to prove

$$\left[(1 - F_0(c_1)) - (1 - F_0(c_2))\right](1 - F_{\theta_1}(c_1)) \leq (1 - F_{\theta_1}(c_1)) - (1 - F_{\theta_1}(c_2)) \quad \text{(S1.4)}$$

Since $0 \leq 1 - F_0(c_1) \leq 1$, to prove inequality (S1.4), it is enough to prove the following,

$$\begin{aligned} & (1 - F_{\theta_1}(c_1))\left[(1 - F_0(c_1)) - (1 - F_0(c_2))\right] \\ \leq\ & (1 - F_0(c_1))\left[1 - F_{\theta_1}(c_1)\right] - \left[1 - F_{\theta_1}(c_2)\right]. \end{aligned} \quad \text{(S1.5)}$$

Dividing both sides of (S1.5) by $(1 - F_{\theta_1}(c_1))(1 - F_0(c_1))$, we see that proving (S1.4) is equivalent to showing

$$\frac{1 - F_{\theta_1}(c_2)}{1 - F_{\theta_1}(c_1)} \leq \frac{1 - F_0(c_2)}{1 - F_0(c_1)}, \quad \text{(S1.6)}$$

which follows directly from (3.6) and Assumption 2 (MLR). By combining the arguments of the above two cases, the desired result follows. □

Proof of Theorem 2. The proof is by induction on number of hypotheses n. We already proved strong control of the mdFWER for $n = 2$ in Lemma 3. Let us assume the result holds for testing any $n = k$ hypotheses, that is, mdFWER $\leq \alpha$ while testing any k pre-ordered hypotheses. We now argue that is will hold for $n = k+1$ hypotheses. Without loss of generality, assume H_1 is a false null, as in the proof of Theorem 1.

Let $V_{k+1}^{(-1)}$ denote the total number of type 1 or type 3 errors committed while testing $H_2, \ldots, H_{k+1}$ and excluding H_1. Then, by the inductive hypothesis, the mdFWER while testing the k hypotheses $H_2, \ldots, H_{k+1}$ is $Pr(V_{k+1}^{(-1)} > 0) \leq \alpha$. Then, the mdFWER of testing $k+1$ hypotheses $H_1, \ldots, H_{k+1}$ is defined by

$$\begin{aligned}
& Pr\left(\{P_1 \leq \alpha, T_1\theta_1 < 0\} \cup \{P_1 \leq \alpha, T_1\theta_1 \geq 0, V_{k+1}^{(-1)} > 0\}\right) \\
= \;& Pr\left(P_1 \leq \alpha, T_1\theta_1 < 0\right) + Pr\left(P_1 \leq \alpha, T_1\theta_1 \geq 0\right) \cdot Pr\left(V_{k+1}^{(-1)} > 0\right) \\
\leq \;& Pr\left(P_1 \leq \alpha, T_1\theta_1 < 0\right) + \alpha \; Pr\left(P_1 \leq \alpha, T_1\theta_1 \geq 0\right). \qquad \text{(S1.7)}
\end{aligned}$$

The equality follows by Assumption 1 (independence) and the inequality follows by the inductive hypothesis. Note that (S1.7) is the same as (3.8) under independence, which is equal to the mdFWER of Procedure 2 in the case of two hypotheses. So again by applying Lemma 3, we get that mdFWER $\leq \alpha$ for $n = k+1$. Hence, the proof follows by induction. □

PROOF OF THEOREM 3 . Without loss of generality, we assume $\theta_i > 0$ if $\theta_i \neq 0$ for $i = 1, \ldots, n$. Also, if there exists an i with $\theta_i = 0$, by induction, we can simply assume $i_0 = n$. Thus, to prove the mdFWER control of Procedure 2, we only need to consider two cases:

(i) $\theta_i > 0$ for $i = 1, \ldots, n$;

(ii) $\theta_i > 0$ for $i = 1, \ldots, n-1$ and $\theta_n = 0$.

Case (i). Consider the general case of $\theta_i > 0, i = 1, \ldots, n$. By Assumption 3, the test statistics $T_1, \ldots, T_n$ are positively regression dependent. For $j = 1, \ldots, n-1$, let E_{n-j} denote the event of making at least one type 3 error when testing $H_{j+1}, \ldots, H_n$ using Procedure 2 at level α. By using induction, we prove the following two lemmas hold.

Lemma 1. *Assume the conditions of Theorem 3. For $j = 1, \ldots, n-1$, the following inequality holds.*

$$Pr(E_{n-j} | T_1 > c_2, \ldots, T_j > c_2) \leq \alpha. \tag{S1.8}$$

PROOF OF LEMMA 1. We prove the result by using reverse induction.

When $j = n-1$, we have

$$
\begin{aligned}
& Pr(E_{n-j}|T_1 > c_2, \ldots, T_j > c_2) \\
= \; & Pr(T_n < c_1|T_1 > c_2, \ldots, T_{n-1} > c_2) \\
= \; & \frac{Pr(T_n < c_1)Pr(T_1 > c_2, \ldots, T_{n-1} > c_2|T_n < c_1)}{Pr(T_1 > c_2, \ldots, T_{n-1} > c_2)} \\
\leq \; & Pr(T_n < c_1) \leq \alpha.
\end{aligned}
$$

The inequality follows from Assumption 3.

Assume the inequality (S1.8) holds for $j = m$. In the following, we prove that it also holds for $j = m-1$. Note that

$$
\begin{aligned}
& Pr(E_{n-m+1}|T_1 > c_2, \ldots, T_{m-1} > c_2) \\
= \; & Pr\left(\{T_m < c_1\} \bigcup \left(\{T_m > c_2\} \bigcap E_{n-m}\right) \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) \\
= \; & Pr\left(T_m < c_1 \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) \\
& + Pr\left(\{T_m > c_2\} \bigcap E_{n-m} \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) \\
= \; & Pr\left(T_m < c_1 \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) \\
& + Pr\left(T_m > c_2 \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) Pr\left(E_{n-m} \big| T_1 > c_2, \ldots, T_m > c_2\right) \\
\leq \; & Pr\left(T_m < c_1 \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) \\
& + \alpha Pr\left(T_m > c_2 \big| T_1 > c_2, \ldots, T_{m-1} > c_2\right) \\
\leq \; & \alpha.
\end{aligned}
$$

Therefore, the desired result follows. Here, the first inequality follows from the assumption of induction and the second follows from Lemma 2 below.

□

Lemma 2. *Assume the conditions of Theorem 3. For $j = 1, \dots, n-1$, the following inequality holds:*

$$\begin{aligned} & Pr\left(T_j < c_1 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right) \\ & \quad + \alpha Pr\left(T_j > c_2 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right) \le \alpha. \end{aligned} \tag{S1.9}$$

Specifically, for $j = 1$, we have

$$Pr\left(T_1 < c_1\right) + \alpha Pr\left(T_1 > c_2\right) \le \alpha.$$

Proof of Lemma 2. To prove the inequality (S1.9), it is enough to show that

$$Pr\left(T_j < c_1 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right) \le \alpha Pr\left(T_j < c_2 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right),$$

which is equivalent to

$$\begin{aligned} & (1-\alpha) Pr\left(T_j < c_2 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right) \\ \le \; & Pr\left(T_j < c_2 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right) - Pr\left(T_j < c_1 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right). \end{aligned}$$

Note that

$$1 - \alpha = Pr_{\theta_j=0}(T_j < c_2) - Pr_{\theta_j=0}(T_j < c_1).$$

Thus, the above inequality is equivalent to

$$Pr_{\theta_j=0}(T_j < c_2) - Pr_{\theta_j=0}(T_j < c_1) \le 1 - \frac{Pr\left(T_j < c_1 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right)}{Pr\left(T_j < c_2 \middle| T_1 > c_2, \dots, T_{j-1} > c_2\right)},$$

which in turn is implied by

$$\begin{aligned} & 1-\frac{Pr_{\theta_j=0}(T_j<c_1)}{Pr_{\theta_j=0}(T_j<c_2)} \\ \leq \quad & 1-\frac{Pr\left(T_j<c_1 \middle| T_1>c_2,\ldots,T_{j-1}>c_2\right)}{Pr\left(T_j<c_2 \middle| T_1>c_2,\ldots,T_{j-1}>c_2\right)}. \end{aligned} \tag{S1.10}$$

Note that by Assumption 2, we have

$$\frac{Pr(T_j<c_1)}{Pr(T_j<c_2)} \leq \frac{Pr_{\theta_j=0}(T_j<c_1)}{Pr_{\theta_j=0}(T_j<c_2)}.$$

Thus, to prove the inequality (S1.10), we only need to show that

$$\frac{Pr\left(T_j<c_1 \middle| T_1>c_2,\ldots,T_{j-1}>c_2\right)}{Pr\left(T_j<c_2 \middle| T_1>c_2,\ldots,T_{j-1}>c_2\right)} \leq \frac{Pr(T_j<c_1)}{Pr(T_j<c_2)},$$

which is equivalent to

$$Pr\left(T_1>c_2,\ldots,T_{j-1}>c_2 \middle| T_j<c_1\right) \leq Pr\left(T_1>c_2,\ldots,T_{j-1}>c_2 \middle| T_j<c_2\right),$$

which follows from Assumption 3. Therefore, the desired result follows.

□

Based on Lemmas 1 and 2, we have

$$\begin{aligned} & \text{mdFWER} = Pr(T_1<c_1)+\sum_{j=2}^{n} Pr(T_1>c_2,\ldots,T_{j-1}>c_2,T_j<c_1) \\ = \quad & Pr(T_1<c_1)+Pr(T_1>c_2)\sum_{j=2}^{n} Pr(T_2>c_2,\ldots,T_{j-1}>c_2,T_j<c_1|T_1>c_2) \\ = \quad & Pr(T_1<c_1)+Pr(T_1>c_2)Pr(E_{n-1}|T_1>c_2) \\ \leq \quad & Pr(T_1<c_1)+\alpha Pr(T_1>c_2) \\ \leq \quad & \alpha. \end{aligned}$$

Therefore, the mdFWER is controlled at level α for Case (i). Here, the first inequality follows from Lemma 1 and the second follows from Lemma 2.

Case (ii). Consider the general case of $\theta_i > 0, i = 1, \ldots, n-1$ and $\theta_n = 0$. Under Assumption 3, $T_i, i = 1, \ldots, n-1$ are positively regression dependent and under Assumption 4, T_n is independent of T_i's . Note that

$$
\begin{aligned}
& \text{mdFWER} \\
= \; & \sum_{j=1}^{n-1} Pr(T_1 > c_2, \ldots, T_{j-1} > c_2, T_j < c_1) \\
& \quad + Pr(T_1 > c_2, \ldots, T_{n-1} > c_2, T_n < c_1) + \; Pr(T_1 > c_2, \ldots, T_n > c_2) \\
= \; & \sum_{j=1}^{n-1} Pr(T_1 > c_2, \ldots, T_{j-1} > c_2, T_j < c_1) + \alpha Pr(T_1 > c_2, \ldots, T_{n-1} > c_2).
\end{aligned}
$$

The second equality follows from Assumption 4.

For $m = 1, \ldots, n-1$, define

$$
\Delta_m = \sum_{j=1}^{m} Pr(T_1 > c_2, \ldots, T_{j-1} > c_2, T_j < c_1) + \alpha Pr(T_1 > c_2, \ldots, T_m > c_2).
$$

Thus, mdFWER $= \Delta_{n-1}$. By using induction, we prove below that $\Delta_m \leq \alpha$ for $m = 1, \ldots, n-1$.

For $m = 1$, by using Lemma 2, we have

$$
\Delta_1 = Pr\left(T_1 < c_1\right) + \alpha Pr\left(T_1 > c_2\right) \leq \alpha.
$$

Assume $\Delta_m \le \alpha$. In the following, we show $\Delta_{m+1} \le \alpha$. Note that

$$
\begin{aligned}
& \Delta_{m+1} \\
= & \sum_{j=1}^{m+1} Pr(T_1 > c_2, \ldots, T_{j-1} > c_2, T_j < c_1) \\
& \quad + \alpha Pr(T_1 > c_2, \ldots, T_m > c_2, T_{m+1} > c_2) \\
= & \sum_{j=1}^{m} Pr(T_1 > c_2, \ldots, T_{j-1} > c_2, T_j < c_1) \\
& \quad + Pr(T_1 > c_2, \ldots, T_m > c_2) \left[Pr(T_{m+1} < c_1 | T_1 > c_2, \ldots, T_m > c_2) \right. \\
& \qquad \left. + \alpha Pr(T_{m+1} > c_2 | T_1 > c_2, \ldots, T_m > c_2) \right] \\
\le & \sum_{j=1}^{m} Pr(T_1 > c_2, \ldots, T_{j-1} > c_2, T_j < c_1) + \alpha Pr(T_1 > c_2, \ldots, T_m > c_2) \\
= & \Delta_m \le \alpha. \qquad \text{(S1.11)}
\end{aligned}
$$

The first inequality follows from Lemma 2 and the second follows from the inductive hypothesis. Thus, $\Delta_m \le \alpha$ for $m = 1, \ldots, n-1$. Therefore, mdFWER $= \Delta_{n-1} \le \alpha$, the desired result.

Combining the arguments of Cases (i) and (ii), the proof of Theorem 3 is complete. □

PROOF OF PROPOSITION 2. From the proof of Theorem 1 and by Lemma 1, it is easy to see that we only need to prove the mdFWER control of Procedure 2 when H_1 is false and H_2 is true, i.e., $\theta_1 \neq 0$ and $\theta_2 = 0$.

Case I: $\theta_1 > 0$ **and** $\theta_2 = 0$**.** By Lemma 2, the mdFWER of Procedure 2 is controlled at level α if we have the following:

$$F_{\theta_1}(c_1) - F_{\theta_1}(c_2) + F_{(\theta_1,0)}(c_2, c_2) - F_{(\theta_1,0)}(c_2, c_1) \leq 0.$$

After rewriting $F_{(\theta_1,0)}(x, y)$ as $Pr(T_1 \leq x, T_2 \leq y)$ and then dividing through by $Pr(T_1 \leq c_2)$, we get,

$$Pr\left(T_2 \leq c_2 | T_1 \leq c_2\right) - Pr\left(T_2 \leq c_1 | T_1 \leq c_2\right) \leq 1 - \frac{Pr(T_1 \leq c_1)}{Pr(T_1 \leq c_2)}.$$

Dividing by $Pr\left(T_2 \leq c_2 | T_1 \leq c_2\right)$, we get,

$$\begin{aligned} & 1 - \frac{Pr\left(T_2 \leq c_1 | T_1 \leq c_2\right)}{Pr\left(T_2 \leq c_2 | T_1 \leq c_2\right)} \\ \leq \; & \frac{1}{Pr\left(T_2 \leq c_2 | T_1 \leq c_2\right)} \left(1 - \frac{Pr(T_1 \leq c_1)}{Pr(T_1 \leq c_2)}\right). \end{aligned} \tag{S1.12}$$

For proving (S1.12), it is enough to prove the following inequality, as $\frac{1}{Pr(T_2 \leq c_2 | T_1 \leq c_2)} \geq 1$.

$$1 - \frac{Pr\left(T_2 \leq c_1 | T_1 \leq c_2\right)}{Pr\left(T_2 \leq c_2 | T_1 \leq c_2\right)} \leq 1 - \frac{Pr(T_1 \leq c_1)}{Pr(T_1 \leq c_2)}. \tag{S1.13}$$

By Assumption 2 and (3.5), it follows that $\frac{F_0(c_2)}{F_0(c_1)} \leq \frac{F_{\theta_1}(c_2)}{F_{\theta_1}(c_1)}$, which is equivalent to, $1 - \frac{Pr(T_2 \leq c_1)}{Pr(T_2 \leq c_2)} \leq 1 - \frac{Pr(T_1 \leq c_1)}{Pr(T_1 \leq c_2)}$. Thus for proving (S1.12), it is enough to prove the following:

$$1 - \frac{Pr\left(T_2 \leq c_1 | T_1 \leq c_2\right)}{Pr\left(T_2 \leq c_2 | T_1 \leq c_2\right)} \leq 1 - \frac{Pr(T_2 \leq c_1)}{Pr(T_2 \leq c_2)}\ . \tag{S1.14}$$

But, (S1.14) is equivalent to showing

$$Pr\left(T_1 \leq c_2 | T_2 \leq c_1\right) \geq Pr\left(T_1 \leq c_2 | T_2 \leq c_2\right),$$

which follows directly from Assumption 5.

Case II: $\theta_1 < 0$ and $\theta_2 = 0$. Similarly, by Lemma 2, the mdFWER of Procedure 2 is controlled at level α if we have the following:

$$1 + F_{\theta_1}(c_1) - F_{\theta_1}(c_2) + F_{(\theta_1,0)}(c_1, c_1) - F_{(\theta_1,0)}(c_1, c_2) \leq \alpha, \qquad \text{(S1.15)}$$

which after some rearrangement and rewriting $1-\alpha$ as $F_0(c_2)-F_0(c_1)$ gives,

$$\begin{aligned} & \big(F_0(c_2) - F_{(\theta_1,0)}(c_1, c_2)\big) - \big(F_0(c_1) - F_{(\theta_1,0)}(c_1, c_1)\big) \\ \leq \; & (1 - F_{\theta_1}(c_1)) - (1 - F_{\theta_1}(c_2)) \,. \end{aligned} \qquad \text{(S1.16)}$$

Thus, proving (S1.15) is equivalent to proving that

$$Pr\,(T_1 \geq c_1, T_2 \leq c_2) - Pr\,(T_1 \geq c_1, T_2 \leq c_1) \leq Pr\,(T_1 \geq c_1) - Pr\,(T_1 \geq c_2)\,.$$

Dividing through by $Pr(T_1 \geq c_1)$, we get

$$\begin{aligned} & Pr\,(T_2 \geq c_1 | T_1 \geq c_1) - Pr\,(T_2 \geq c_2 | T_1 \geq c_1) \\ \leq \; & 1 - \frac{Pr(T_1 \geq c_2)}{Pr(T_1 \geq c_1)}. \end{aligned} \qquad \text{(S1.17)}$$

Thus to prove (S1.15), it is enough to prove the following,

$$1 - \frac{Pr\,(T_2 \geq c_2 | T_1 \geq c_1)}{Pr\,(T_2 \geq c_1 | T_1 \geq c_1)} \leq 1 - \frac{Pr(T_1 \geq c_2)}{Pr(T_1 \geq c_1)},$$

which is equivalent to proving,

$$\frac{Pr\,(T_2 \geq c_2 | T_1 \geq c_1)}{Pr\,(T_2 \geq c_1 | T_1 \geq c_1)} \geq \frac{Pr(T_1 \geq c_2)}{Pr(T_1 \geq c_1)}. \qquad \text{(S1.18)}$$

By Assumption 2 and (3.6), it follows that for $\theta_1 < 0$, $\frac{Pr(T_1 \geq c_2)}{Pr(T_1 \geq c_1)} \leq \frac{Pr(T_2 \geq c_2)}{Pr(T_2 \geq c_1)}$. Thus to prove (S1.15), it is enough to prove the following,

$$\frac{Pr\left(T_2 \geq c_2 | T_1 \geq c_1\right)}{Pr\left(T_2 \geq c_1 | T_1 \geq c_1\right)} \geq \frac{Pr(T_2 \geq c_2)}{Pr(T_2 \geq c_1)}. \tag{S1.19}$$

But (S1.19) is equivalent to showing

$$Pr\left(T_1 \geq c_1 | T_2 \geq c_2\right) \geq Pr\left(T_1 \geq c_1 | T_2 \geq c_1\right), \tag{S1.20}$$

which follows directly from Assumption 5. By combining the arguments of the above two cases, the desired result follows. □

Proof of Proposition 3. By Corollary 1, without loss of generality, assume that $\theta_i > 0, i = 1, 2$ and $\theta_3 = 0$, that is, H_1 and H_2 are false and H_3 is true. Note that

$$\begin{aligned} & \text{mdFWER} \\ = \; & Pr(T_1 \leq c_1) + Pr(T_1 \geq c_2, T_2 \leq c_1) \qquad \text{(S1.21)} \\ & + Pr\left(T_1 \geq c_2, T_2 \geq c_2, T_3 \notin (c_1, c_2)\right). \end{aligned}$$

In the following, we prove that

$$\begin{aligned} & Pr(T_1 \geq c_2, T_2 \leq c_1) + Pr\left(T_1 \geq c_2, T_2 \geq c_2, T_3 \notin (c_1, c_2)\right) \\ \leq \; & Pr\left(T_1 \geq c_2, T_3 \notin (c_1, c_2)\right). \qquad \text{(S1.22)} \end{aligned}$$

To prove (S1.22), it is enough to show the following inequality:

$$\begin{aligned} & Pr(T_2 \leq c_1|T_1) + Pr\left(T_2 \geq c_2, T_3 \notin (c_1, c_2)|T_1\right) \\ \leq \; & Pr\left(T_3 \notin (c_1, c_2)|T_1\right). \end{aligned} \tag{S1.23}$$

Note that

$$\begin{aligned} & Pr\left(T_2 \geq c_2, T_3 \leq c_1|T_1\right) \\ = \; & Pr(T_3 \leq c_1|T_1) - Pr\left(T_2 < c_2, T_3 \leq c_1|T_1\right) \end{aligned} \tag{S1.24}$$

and

$$\begin{aligned} & Pr\left(T_2 \geq c_2, T_3 \geq c_2|T_1\right) \qquad \text{(S1.25)} \\ = \; & 1 - Pr(T_2 < c_2|T_1) - Pr(T_3 < c_2|T_1) + Pr\left(T_2 < c_2, T_3 < c_2|T_1\right). \end{aligned}$$

In addition, we have

$$Pr\left(T_3 \notin (c_1, c_2)|T_1\right) = 1 + Pr(T_3 \leq c_1|T_1) - Pr(T_3 < c_2|T_1). \tag{S1.26}$$

Thus, in order to show (S1.23), by combining (S1.24)-(S1.26), we only need to prove the following inequality:

$$\begin{aligned} & Pr\left(T_2 < c_2, T_3 < c_2|T_1\right) - Pr\left(T_2 < c_2, T_3 \leq c_1|T_1\right) \\ \leq \; & Pr(T_2 < c_2|T_1) - Pr(T_2 \leq c_1|T_1). \end{aligned} \tag{S1.27}$$

Note that (S1.27) can be rewritten as

$$
\begin{aligned}
& Pr\left(T_2 < c_2, T_3 < c_2 | T_1\right)\left[1 - \frac{Pr\left(T_2 < c_2, T_3 \le c_1 | T_1\right)}{Pr\left(T_2 < c_2, T_3 < c_2 | T_1\right)}\right] \\
\le\ & Pr(T_2 < c_2 | T_1)\left[1 - \frac{Pr(T_2 \le c_1 | T_1)}{Pr(T_2 < c_2 | T_1)}\right]. \qquad \text{(S1.28)}
\end{aligned}
$$

Thus, to prove (S1.27), it is enough to show

$$1 - \frac{Pr\left(T_2 < c_2, T_3 \le c_1 | T_1\right)}{Pr\left(T_2 < c_2, T_3 < c_2 | T_1\right)} \le 1 - \frac{Pr(T_2 \le c_1 | T_1)}{Pr(T_2 < c_2 | T_1)}. \qquad \text{(S1.29)}$$

That is,

$$\frac{Pr(T_2 \le c_1 | T_1)}{Pr(T_2 < c_2 | T_1)} \le \frac{Pr\left(T_2 < c_2, T_3 \le c_1 | T_1\right)}{Pr\left(T_2 < c_2, T_3 < c_2 | T_1\right)}. \qquad \text{(S1.30)}$$

By Assumption 6 (BMLR), we have

$$\frac{Pr(T_2 \le x_2 | T_1)}{Pr(T_3 \le x_2 | T_1)} \ge \frac{Pr(T_2 \le x_1 | T_1)}{Pr(T_3 \le x_1 | T_1)}. \qquad \text{(S1.31)}$$

By (S1.31), to prove (S1.30), it is enough to show

$$\frac{Pr(T_3 \le c_1 | T_1)}{Pr(T_3 < c_2 | T_1)} \le \frac{Pr\left(T_2 < c_2, T_3 \le c_1 | T_1\right)}{Pr\left(T_2 < c_2, T_3 < c_2 | T_1\right)}. \qquad \text{(S1.32)}$$

That is,

$$Pr\left(T_2 < c_2 | T_3 < c_2, T_1\right) \le Pr\left(T_2 < c_2 | T_3 < c_1, T_1\right). \qquad \text{(S1.33)}$$

The inequality (S1.33) holds under Assumption 5. Therefore, the inequality (S1.22) holds.

Based on (S1.21)-(S1.22) and Proposition 1, we have

$$\text{mdFWER} = Pr(T_1 \le c_1) + Pr\left(T_1 \ge c_2, T_3 \notin (c_1, c_2)\right) \le \alpha.$$

Thus, the desired result follows. $\square$

Proof of Theorem 4. By Corollary 1, without loss of generality, assume that $\theta_i > 0, i = 1, \ldots, n-1$ and $\theta_n = 0$, that is, $H_i, i = 1, \ldots, n-1$ are false and H_n is true. Note that

$$\begin{aligned} & \text{mdFWER} \\ = & \sum_{j=1}^{n-1} Pr(T_1 \geq c_2, \ldots, T_{j-1} \geq c_2, T_j \leq c_1) \\ & \quad + Pr(T_1 \geq c_2, \ldots, T_{n-1} \geq c_2, T_n \notin (c_1, c_2)). \end{aligned} \tag{S1.34}$$

In the following, we prove that

$$\begin{aligned} & Pr(T_1 \geq c_2, \ldots, T_{n-2} \geq c_2, T_{n-1} \leq c_1) \\ & \quad + Pr\left(T_1 \geq c_2, \ldots, T_{n-1} \geq c_2, T_n \notin (c_1, c_2)\right) \\ \leq & \; Pr\left(T_1 \geq c_2, \ldots, T_{n-2} \geq c_2, T_n \notin (c_1, c_2)\right). \end{aligned} \tag{S1.35}$$

To prove (S1.35), it is enough to show the following inequality:

$$\begin{aligned} & Pr(T_{n-1} \leq c_1 | T_1, \ldots, T_{n-2}) \\ & \quad + Pr\left(T_{n-1} \geq c_2, T_n \notin (c_1, c_2) | T_1, \ldots, T_{n-2}\right) \\ \leq & \; Pr\left(T_n \notin (c_1, c_2) | T_1, \ldots, T_{n-2}\right). \end{aligned} \tag{S1.36}$$

By using the same argument as in proving (S1.23) in the case of three hypotheses, we can prove that the inequality (S1.36) holds under Assumptions

5 and 7. Then, by combining (S1.34) and (S1.35), we have

$$\begin{aligned}
&\text{mdFWER} \\
\leq \; &\sum_{j=1}^{n-2} Pr(T_1 \geq c_2, \ldots, T_{j-1} \geq c_2, T_j \leq c_1) \qquad \text{(S1.37)} \\
&\quad + Pr(T_1 \geq c_2, \ldots, T_{n-2} \geq c_2, T_n \notin (c_1, c_2)).
\end{aligned}$$

Note that the right-hand side of (S1.37) is the mdFWER of Procedure 2 when testing $H_1, \ldots, H_{n-2},\ H_n$. By induction and Proposition 1, the mdFWER is bounded above by α, the desired result. □