On Weighted Hochberg Procedures

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1. Introduction

- Hypotheses: $H_1, H_2, \ldots, H_n$, p-values: $p_1, p_2, \ldots, p_n$, weights: $w_1, w_2, \ldots, w_n$
- Ordered p-values: $p_{(1)} \leq p_{(2)} \leq \cdots \leq p_{(n)}$
- Ordered hypotheses and weights: $H_{(1)}, H_{(2)}, \ldots, H_{(n)}$ and $w_{(1)}, w_{(2)}, \ldots, w_{(n)}$
- Later we will show that the weighted Hochberg procedure based on ordered weighted p-values: $p_i^* = p_i/w_i$ does not control the familywise error rate (FWER).

2. Weighted Procedures

- **Weighted Holm (WHM) Procedure:** Accept $H_{(i)}, H_{(i+1)}, \ldots, H_{(n)}$ & stop testing if

$$p_{(i)} > \frac{w_{(i)}}{\sum_{k=i}^{n} w_{(k)}}\alpha;$$

  otherwise reject $H_{(i)}$ and test $H_{(i+1)}$. Benjamini & Hochberg (1997)

- **Weighted Simes (WSM) Procedure:** Let $I = \{i_1, i_2, \ldots, i_m\} \subseteq \{1, 2, \ldots, n\}$ and let $p_{(i_1)} \leq p_{(i_2)} \leq \cdots \leq p_{(i_m)}$. Reject $H_I = \bigcap_{j=1}^{m} H_{i_j}$ at level α if

$$p_{(i_j)} \leq \frac{\sum_{k=1}^{j} w_{(i_k)}}{\sum_{k=1}^{m} w_{(i_k)}}\alpha \text{ for some } j = 1, 2, \ldots, m.$$

- **Weighted Closed (WCL) Procedure:** Use the WSM procedure to test all intersections and follow the closure principle.
- **Weighted Hochberg (WHC) Procedure:** Reject $H_{(i)}, H_{(i-1)}, \ldots, H_{(1)}$ and stop testing if

$$p_{(i)} \leq \frac{w_{(i)}}{\sum_{k=i}^{n} w_{(k)}} \alpha;$$

otherwise accept $H_{(i)}$ and test $H_{(i-1)}$.

3. Does WHC Control FWER?

3.1 Proof Using the Closure Method

- Show that rejection of any hypothesis by WHC implies its rejection by WLC.
- There is a gap in Hochberg's proof (for equally weighted hypotheses) where he omits showing that WLC rejects $H_{(j)}$ for $j < i$ if WHC rejects $H_{(i)}$ for $i < n$.
- The proof fails in this case for general weights, but works for equal weights (thus filling the gap in Hochberg's proof).

Counterexample

H_1	H_2	H_3
$p_1 = 0.03$	$p_2 = 0.035$	$p_3 = 0.1$
$w_1 = 0.2$	$w_2 = 0.6$	$w_3 = 0.2$
$c_1 = \frac{w_1}{w_1+w_2+w_3}\alpha = 0.01$	$c_2 = \frac{w_2}{w_2+w_3}\alpha = 0.0375$	$c_3 = \frac{w_3}{w_3}\alpha = 0.05$

- WHC rejects H_1 and H_2 since $p_3 > 0.05$ but $p_2 < 0.0375$.
- But WCL does not reject $H_1 \bigcap H_3$ since

$$p_3 > 0.05 \text{ and } p_1 > \frac{w_1}{w_1 + w_3}\alpha = 0.025.$$

  Hence it does not reject H_1.

3.2 Alternative Method of Proof

- A simpler proof (without using the closure principle) of Hochberg's procedure: If $H_1, \ldots, H_m$ are true and $H_{m+1}, \ldots, H_n$ are false then FWER is maximized when $p_{m+1}, \ldots, p_n \to 0$. Hence

$$\begin{aligned}
1 - \text{FWER} &= P\{\text{Accept } H_1, \ldots, H_m\} \\
&\geq P\left\{p_{(i_{n-m+j})} > \frac{\alpha}{n-(n-m)-j+1}, j = 1, \ldots, m\right\} \\
&\geq P\left\{p_{(i_j)} > \frac{\alpha}{m-j+1}, j = 1, \ldots, m\right\} \\
&\geq P\left\{p_{(i_j)} > \frac{j\alpha}{m}, j = 1, \ldots, m\right\} \\
&= 1 - \alpha \text{ by Simes identity.}
\end{aligned}$$

- This proof fails in the weighted case because FWER of WHC is not always maximized when false p-values $\to 0$.

- **Counterexample:** Suppose H_1 and H_3 are true and H_2 is false. WHC rejects H_1 and H_2, hence commits a type I error. Now let $p_2 \to 0$. Then $p_2 = 0 < p_1 = 0.03 < p_3 = 0.1$. The critical values equal

  $$c_2 = \frac{w_2}{w_1 + w_2 + w_3}\alpha = 0.03, c_1 = \frac{w_1}{w_1 + w_3}\alpha = 0.025, c_3 = \alpha = 0.05.$$

  WHC rejects only H_2 and hence does not commit a type I error.

  Therefore letting $p_2 \to 0$ does not maximize FWER.

4. Conservative Weighted Hochberg Procedure (CWHC)

Matrix of critical constants for WCL that uses WSM ($n = 3$):

$$\boldsymbol{C} = \begin{bmatrix} \alpha & & \\ \alpha & & \\ \alpha & & \\ \alpha & \frac{w_{(1)}}{w_{(1)}+w_{(2)}}\alpha & \\ \alpha & \frac{w_{(1)}}{w_{(1)}+w_{(3)}}\alpha & \\ \alpha & \frac{w_{(2)}}{w_{(2)}+w_{(3)}}\alpha & \\ \alpha & \frac{w_{(1)}+w_{(2)}}{w_{(1)}+w_{(2)}+w_{(3)}}\alpha & \frac{w_{(1)}}{w_{(1)}+w_{(2)}+w_{(3)}}\alpha \end{bmatrix}.$$

- Liu (1996) showed that if all column (row) entries of $\boldsymbol{C}$ are equal then the closure procedure has a step-up (step-down) shortcut with the last row (first column) as its critical constants.
- Make column entries equal by taking the minimum of each column, which results in a conservative step-up procedure.
- Need to take the minimum of only the top $\binom{n}{m}$ entries in the mth column, $m = 1, \ldots, n$.

$$\boldsymbol{C} = \begin{bmatrix} \alpha & & \\ \alpha & & \\ \alpha & & \\ \alpha & \frac{0.2}{0.2+0.6}\alpha & \\ \alpha & \frac{0.2}{0.2+0.2}\alpha & \\ \alpha & \frac{0.6}{0.6+0.2}\alpha & \\ \alpha & \frac{0.2+0.6}{1}\alpha & \frac{0.2}{1}\alpha \end{bmatrix} \Rightarrow \begin{bmatrix} \alpha & & \\ \alpha & 0.25\alpha & \\ \alpha & 0.25\alpha & 0.2\alpha \end{bmatrix}.$$

Example:

Step 1: Compare $p_{(3)} = 0.1$ with $\alpha = 0.05 \Rightarrow$ Do not reject $H_{(3)}$.

Step 2: Compare $p_{(2)} = 0.035$ with $0.25\alpha = 0.0125 \Rightarrow$ Do not reject $H_{(2)}$.

Step 3: Compare $p_{(1)} = 0.03$ with $0.2\alpha = 0.01 \Rightarrow$ Do not reject $H_{(1)}$.

5. Simulations

Table 1: Estimates of FWER ($n = 3$, Three True Hypotheses)

Weights	WHC	CWHC
(0.1, 0.45, 0.45)	0.0486	0.0480
(0.2, 0.4, 0.4)	0.0496	0.0492
(0.3, 0.35, 0.35)	0.0491	0.0491
(0.4, 0.3, 0.3)	0.0491	0.0489
(0.5, 0.25, 0.25)	0.0488	0.0485
(0.6, 0.2, 0.2)	0.0503	0.0498
(0.7, 0.15, 0.15)	0.0486	0.0476
(0.8, 0.1, 0.1)	0.0495	0.0480
(0.9, 0.05, 0.05)	0.0504	0.0486

$N = 100,000$, SE $= 0.00057$

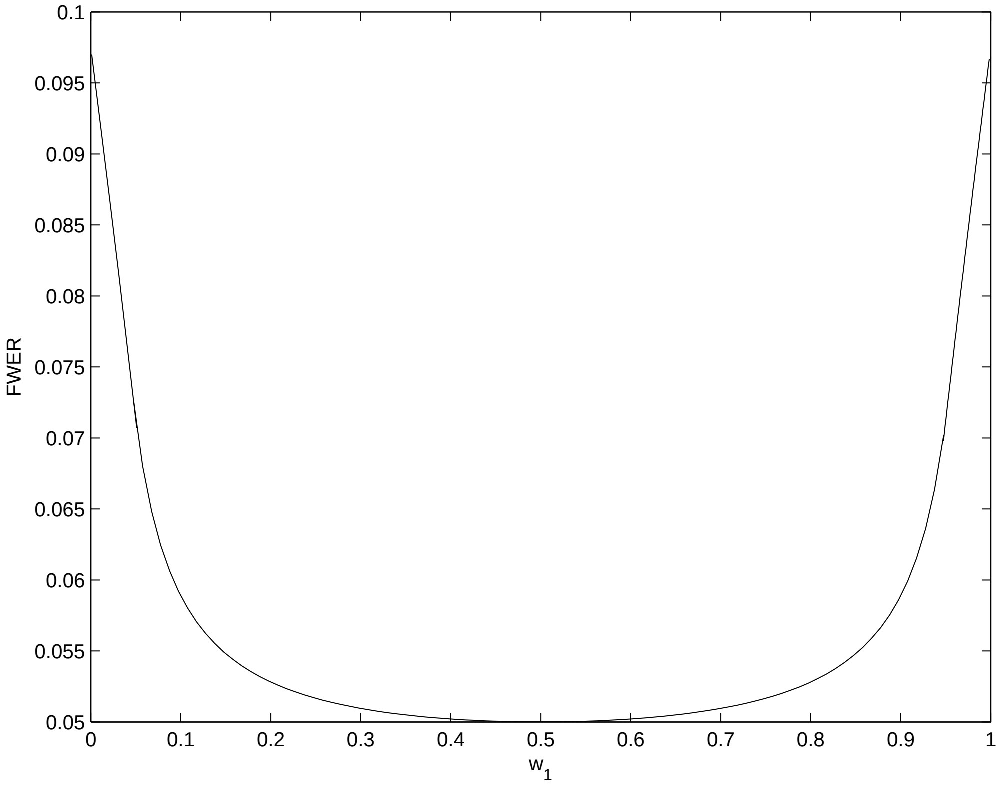
6. An Alternate Weighted Hochberg Procedure (WHC*)

- Order weighted p-values, $p_i^* = p_i/w_i$: $p^*_{(1)} \le p^*_{(2)} \le \cdots \le p^*_{(n)}$. Let $H^*_{(1)}, H^*_{(2)}, \ldots, H^*_{(n)}$ be the corresponding hypotheses and $w^*_{(1)}, w^*_{(2)}, \ldots, w^*_{(n)}$ the corresponding weights.
- Reject $H^*_{(i)}, H^*_{(i-1)}, \ldots, H^*_{(1)}$ and stop testing if

$$p^*_{(i)} \le \frac{\alpha}{\sum_{k=i}^{n} w^*_{(k)}};$$

  otherwise accept $H^*_{(i)}$ and continue to test $H^*_{(i-1)}$. (Based on weighted Holm procedure proposed by Holm (1979))

$$1 - \mathrm{FWER} = \begin{cases} 1 - \alpha + \alpha^2 - \frac{\alpha^2}{2}\left(\frac{w_1}{w_2} + \frac{w_2}{w_1}\right) & \text{if } \frac{\alpha}{1+\alpha} \leq w_1 \leq \frac{1}{2} \\ (1-\alpha)^2 + \frac{w_1}{2w_2}(1-\alpha^2) & \text{if } w_1 \leq \frac{\alpha}{1+\alpha}. \end{cases}$$



7. Conclusions

- Overall null appears to be the least favorable configuration (LFC) of WHC.
- Even in this LFC, WHC controls the FWER.
- CWHC guarantees conservative control of FWER.
- WHC* does not control the FWER.
- WHC is recommended.