

A general introduction to adjustment for multiple comparisons

Chen, S.-Y., Feng, Z., & Yi, X. (2017). A general introduction to adjustment for multiple comparisons. *Journal of Thoracic Disease*, 9(6), 1725–1729. <https://doi.org/10.21037/jtd.2017.05.34>

A general introduction to adjustment for multiple comparisons

Common Methods for adjustment

- Bonferroni adjustment
- Holm adjustment
- Hochberg adjustment
- Hommel adjustment
- Benjamini-Hochberg (BH) adjustment
- Benjamini and Yekutieli (BY) adjustment

Reasons for multiple adjustment

the statistical inference of committing at least one incorrect rejection will become inevitable even when 100 hypotheses are individually tested at significance level $\alpha = 0.05$

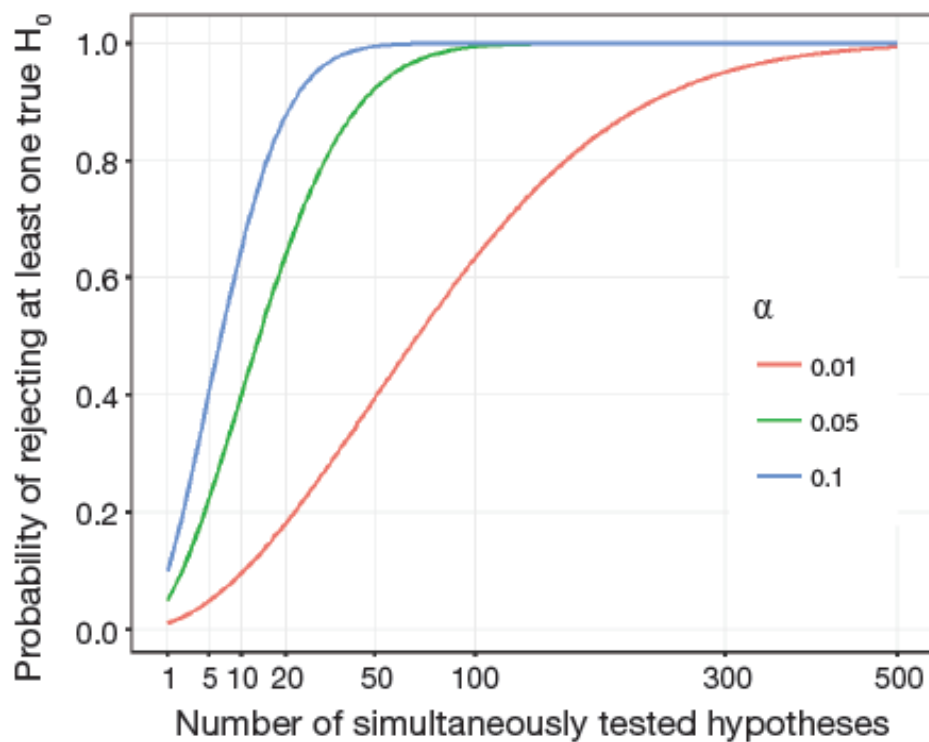


Figure 1 The increased error rate of multiple comparisons.

Table 1 Framework of simultaneous hypotheses testing

Null hypothesis, H_0	H_0 rejected (significant)	H_0 not rejected (non-significant)
Total, m	R	$m-R$
True, m_0	U	m_0-U
False, $m-m_0$	$R-U$	$m-R-(m_0-U)$

Two ways for adjusting the statistical inference of multiple comparisons

- adjust the observed p value
- adjust the cut-off value

Measures accounting for Type I error rates

per-comparison error rate = $E(U)/m$

- the expected proportion of variable U among all simultaneously tested hypotheses of m

familywise error rate = $P(U > 0)$

- jointly consider all hypotheses as a family for controlling Type I error; and therefore the most stringent criterion is to guarantee that not any H_0 is incorrectly rejected.

false discovery rate = $E(U/R)$ if $R > 0$; $= 0$ if $R = 0$

- expected proportion of incorrectly rejected H_0 among all rejections

Common Methods for adjustment

example: Let $m = 6$ and $\alpha = 0.05$; and the initially computed P values corresponding to six hypotheses are $p_1 = 0.1025$, $p_2 = 0.0085$, $p_3 = 0.0045$, $p_4 = 0.0658$, $p_5 = 0.0201$ and $p_6 = 0.0304$, respectively.

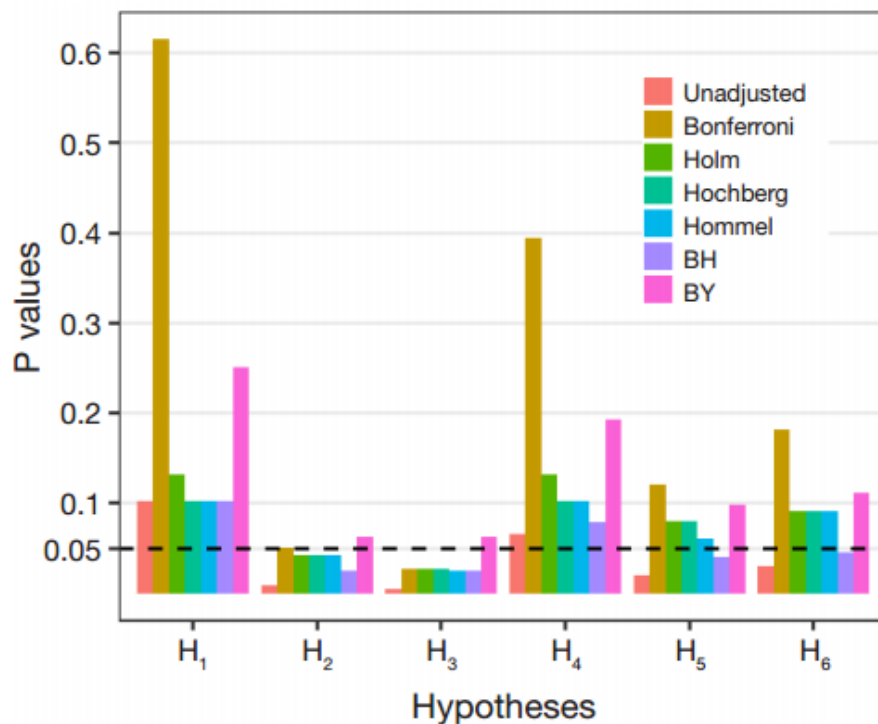


Figure 2 Differences of the adjusted P values among various methods. The dashed horizontal line denotes the pre-specified significance level.

Bonferroni adjustment

familywise error rate

adjusted p value = $\min\{p_i \cdot m, 1\}$ ($i \in [1, m]$)

much conservative

Holm adjustment

based on Bonferroni method, less conservative

in a stepwise way, computes the significance levels depending on the P value based rank of hypotheses.

each hypothesis will be tested in order from the smallest to largest P values

$$\alpha_i = \alpha / (m - i + 1)$$

Step 1: $H_{(1)} = H_3$ $p_{(1)} = 0.0045$ $\alpha'_{(1)} = \frac{0.05}{6 - 1 + 1} = 0.0083$

$\because p_{(1)} < \alpha'_{(1)}$

$\therefore H_3$ is rejected and declared significant at $\alpha = 0.05$.

Step 2: $H_{(2)} = H_2$ $p_{(2)} = 0.0085$ $\alpha'_{(2)} = \frac{0.05}{6 - 2 + 1} = 0.01$

$\because p_{(2)} < \alpha'_{(2)}$

$\therefore H_2$ is rejected and declared significant at $\alpha = 0.05$.

Step 3: $H_{(3)} = H_5$ $p_{(3)} = 0.0201$ $\alpha'_{(3)} = \frac{0.05}{6 - 3 + 1} = 0.0125$

$\because p_{(3)} > \alpha'_{(3)}$

$\therefore H_5$ is not rejected and declared non-significant at $\alpha = 0.05$.

\therefore Stop

Conclusion:

H_3 and H_2 are declared significant at $\alpha = 0.05$.

H_5, H_6, H_4 and H_1 are declared non-significant at $\alpha = 0.05$.

Figure 3 Schematic illustration for Holm adjustment

Hochberg adjustment

similar to holm method, but start with the largest P ($i=m$)

$$\alpha_i = \alpha / (m - i + 1)$$

Hommel adjustment

Simes [1986] modified Bonferroni method and proposed a global test of m hypotheses, however, could not be

used for assessing the individual hypothesis $H_i : p_i \leq i\alpha/m$

$$j = \max\{i \in \{1, \dots, m\} : p_{m-i+k} > k\alpha/i, k=1, \dots, i\}$$

if j does not exist, reject all the hypothesis

if j exist, reject all the hypothesis with $p_i \leq \alpha/j$

p.adjust() function in R stats package.

Benjamini-Hochberg (BH) adjustment

false discovery rate

Let q be the pre-specified upper bound of FDR (e.g., $q = 0.05$), the first step is to compute index k :

$$k = \max\{i : p_i \leq i * q/m\}$$

Benjamini and Yekutieli (BY) adjustment

Similar to BH method, a more conservative adjustment was further proposed for controlling FDR by Benjamini

and Yekutieli [2001]

$$k = \max \left\{ i : p_{(i)} \leq \frac{i}{m} \tilde{q} \right\} \text{ with } \tilde{q} = \frac{q}{\sum_{i=1}^m \frac{1}{i}}.$$

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