Compatible simultaneous lower confidence bounds for the Holm procedure and other Bonferroni based closed tests

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Notation

Parameter of interest: $\vartheta = (\vartheta_1, \ldots, \vartheta_k) \in \Theta \subseteq R^k$

Data: $X \in \mathcal{X}$

Thresholds : $(\delta_1, \ldots, \delta_k) \in \Theta$

Hypotheses: $H_i : \vartheta_i \leq \delta_i, \; i \in I = \{1, \ldots, k\}$

Corresponding p-values : $p_i = p_i(X), \; i \in I$

The Closure Principle

Construct level-α tests for all intersection hypotheses

$$H_J = \bigcap_{j \in J} H_j \text{ with } \emptyset \neq J \subseteq I$$

Reject H_i, iff all H_J with $i \in J$ can be rejected.

Such closed test procedures control the familywise error rate (FWER) at level α.

A Class ($\mathcal{B}$) of Bonferroni Based Closed Tests

Basis: Local α-levels $\alpha_i(J) \geq 0,\ i \in I,\ J \subseteq I$ with

$$\sum_{i \in I} \alpha_i(J) \leq \alpha, \quad J \subseteq I.$$

An intersection hypothesis H_J is rejected, if

$$\min_{j \in J}(p_j - \alpha_j(J)) \leq 0.$$

Bonferroni's inequality ensures the control of the FWER at level α.

Closure test: Reject all those hypotheses H_i with

$$\max_{J: i \in J \subseteq I} \min_{j \in J}(p_j - \alpha_j(J)) \leq 0$$

Simultaneous Compatible Confidence Bounds

Let $R = R(x)$ be the index set of rejected hypotheses H_i

$$R = \{i \in I : \max_{J \subseteq I : i \in J} \min_{j \in J} (p_j - \alpha_j(J)) \leq 0\}$$

Problem: Find lower confidence bounds $L_i = L_i(X),\ i \in I,$

such that

$$P_\vartheta(L_i(X) < \vartheta_i, \text{ for all } i \in I) \geq 1 - \alpha$$

and

$$\forall x \in \mathcal{X} : \quad i \in R(x) \Rightarrow L_i(x) \geq \delta_i.$$

Examples

(Single-step) Bonferroni test

$R = \{i : p_i \leq \alpha/k\}$

Local α levels: $\alpha_i(J) = \alpha/k, \; i \in I, \; J \subseteq I$

(Step-down) Bonferroni-Holm test

Ordered p-values: $p_{(1)} \leq p_{(2)} \leq \cdots \leq p_{(k)}$

$R = \{(i) : \max_{j=1,\ldots,i}(k-j+1)p_{(j)} \leq \alpha\}$

Local α levels: $\alpha_i(J) = \begin{cases} \alpha/|J| & \text{if } i \in J, \\ 0 & \text{else .} \end{cases}$

Simultaneous confidence bounds?

Construction Principles

Bofinger (1987). Step down procedures for comparison with a control. Aust. J. Stat. 29, 348-364.

Finner (1994). Testing Multiple Hypotheses: General Theory, Specific Problems, and Relationships to Other Multiple Decision Procedures. Habilitationsschrift. Universität Trier, FB IV Mathematik/Statistik.

Finner & Straßburger (2006). On equivalence with the best in k-sample models. J. Am. Stat. Assoc. 101, 737-746.

Finner & Straßburger (2007). Step-up related simultaneous confidence intervals for MCC and MCB. Biometrical J 49, 40-5

Hayter & Hsu (1994). On the relationship between stepwise decision procedures and confidence sets. Journal of the American Statistical Association 89, 128-136.

Stefansson, Kim & Hsu (1988). On confidence sets in multiple comparisons. Statistical decision theory and related topics IV, Pap. 4th Purdue Symp.; West Lafayette/Indiana 1986, Vol. 2, 89-104

Basis: p-Value Compatible Local Confidence Bounds

For the construction of simultaneous confidence bounds one needs local, lower confidence bounds $L_i'(\alpha') = L_i'(X, \alpha')$ fulfilling:

For all $i \in I$ and $\alpha' \in [0, \alpha]$ it holds,

$$P_\vartheta(L_i'(X, \alpha') < \vartheta_i) \geq 1 - \alpha',$$

$$\forall x \in \mathcal{X} : \; L_i'(x, \alpha') \geq \delta_i \Leftrightarrow p_i(x) \leq \alpha'.$$

Compatible Confidence Bounds for Bonferroni Based Closure Tests

Compatible confidence bounds for multiple tests in $\mathcal{B}$ can be constructed as follows:

$$L_i = \begin{cases} \min_{J \in \mathcal{J}: i \notin J} \max\{\delta_i, L_i'(\alpha_i(J))\} & \text{if } i \in R \\ \min_{J \in \mathcal{J}: i \in J} L_i'(\alpha_i(J)) & \text{if } i \in I \setminus R, \end{cases}$$

where

$$\mathcal{J} = \{J \subseteq I : \min_{j \in J}(p_j - \alpha_j(J)) > 0\}.$$

$J \in \mathcal{J} \;\Leftrightarrow$ intersection hypothesis H_J can not be rejected

The Subclass ($\mathcal{SCB}$) of so Called “Short-Cut“ Procedures

Hommel, Bretz und Maurer (Stat. Med. 2007) showed

that there exists an easy implementable short-cut for all procedures in $\mathcal{B}$ with

$$\alpha_i(J) \le \alpha_i(J') \text{ for all } i \in I \text{ and all } J,\ J' \text{ with } i \in J' \subseteq J \subseteq I.$$

Examples: (weighted) Bonferroni-Holm test, Test of apriori ordered hypotheses, Fallback and Gatekeeping procedures.

Simplified Confidence Bounds for Short-Cut Procedures

Simultaneous compatible confidence bounds for multiple tests in $\mathcal{SCB}$ reduce to:

$$L_i = \begin{cases} \min_{J \subseteq I \setminus R} \max\{\delta_i, L_i'(\alpha_i(J))\} & \text{if } i \in R, \\ L_i'(\alpha_i(I \setminus R)) & \text{if } i \in I \setminus R. \end{cases}$$

Further Reduction for "α-Exhaustive Multiple Tests"

Necessary condition for maximizing the number of rejected hypotheses:

$$\alpha_i(J) = 0, \text{ for all } i, J \text{ with } i \notin J \text{ and } \emptyset \neq J \subseteq I.$$

Reduced confidence bounds:

$$L_i = \begin{cases} \max\{\delta_i, L_i'(\alpha_i(\emptyset))\} & \text{if } R = I, \\ \delta_i & \text{if } i \in R \neq I, \\ L_i'(\alpha_i(I \setminus R)) & \text{if } i \in I \setminus R. \end{cases}$$

In case of $i \in R \neq I$ the lower bound L_i only reflects the test decision $\vartheta_i > \delta_i$.

A Numerical Example

Observations: $X = (X_1, X_2, \ldots, X_5),\, X_i \sim N(\vartheta_i, 1)$

Hypotheses: $H_i : \vartheta_i \leq 0,\; i = 1, \ldots, 5$

FWER: $\alpha = 5\%$

p-Values: $p_i = 1 - \Phi(X_i)$

Loc. conf. bounds: $L_i'(\alpha') = X_i - u_{1-\alpha'}$

i	1	2	3	4	5
x_i	4.261	3.530	2.252	0.417	−1.338
p_i	0.00001	0.0002	0.0122	0.338	0.910

(Single-step) Bonferroni Test

Local levels: $\alpha_i(J) = 0.01, \quad i \in I, \; J \subseteq I$

i	1	2	3	4	5
x_i	4.261	3.530	2.252	0.417	−1.338
p_i	0.00001	0.0002	0.0122	0.338	0.910
α/k	0.01	0.01	0.01	0.01	0.01
L_i	1.935	1.203	−0.074	−1.909	−3.664

Rejected hypotheses: $R = \{1, 2\}$

Confidence bounds: $L_i = x_i - u_{1-\alpha/5} = x_i - 2.326$

(Step-down) Bonferroni-Holm Test

Local levels: $\alpha_i(J) = 0.05/|J|, \quad i \in I, \; J \subseteq I$

i	1	2	3	4	5
x_i	4.261	3.530	2.252	0.417	−1.338
p_i	0.00001	0.0002	0.0122	0.338	0.910
α/i	0.01	0.0125	0.0166	0.025	0.05
L_i	0	0	0	−1.543	−3.298

Rejected hypotheses: $R = \{1, 2, 3\}$

Confidence bounds: $\alpha_i(I \setminus R) = \alpha/|I \setminus R| = \alpha/2$

$$\Rightarrow L_i = \begin{cases} 0 & \text{if } i \in R \\ x_i - u_{1-\alpha/2} = x_i - 1.960 & \text{if } i \in I \setminus R \end{cases}$$

Comparison of Single-step & Step-down Confidence Bounds

i	1	2	3	4	5
Single-step L_i	1.935	1.203	−0.074	−1.909	−3.664
Step-down L_i	0	0	0	−1.543	−3.298

Step-down versus single-step bounds / Assets and drawbacks:

(+) H_3 can be rejected by the step-down procedure.

(+) (moderate) larger confidence bounds for $\vartheta_3, \ \vartheta_4$ and ϑ_5

(−) much smaller confidence bounds for ϑ_1 and ϑ_2