② Adaptive FWER control

2.1 Known dependence

Gaussian case with $\boxed{\text{known}}$ Γ, but arbitrary with $\Gamma_{ii}=1$ for all i:

Let us work with test statistics $T_j(X) = \begin{cases} X_j & \text{(one sided)} \\ |X_j| & \text{(two sided)} \end{cases}$, $1 \leq j \leq m$

Consider the threshold $S_\alpha(\Gamma) = \min\left\{ x \in \mathbb{R} : \mathbb{P}_{Z \sim \mathcal{N}(0,\Gamma)}\left(\max_{1 \leq j \leq m} T_j(Z) \leq x \right) \geq 1-\alpha \right\}$

↑ quantile computed under the full null.

Proposition: In the Gaussian setting (either one-sided or two-sided)

$$\forall P \in \mathcal{P}, \ \text{FWER}(S_\alpha(\Gamma), P) \leq \alpha$$

And there exists P_0 with $\text{FWER}(S_\alpha(\Gamma), P_0) = \alpha$.

Proof:

$$\text{FWER}(S_\alpha(\Gamma), P) = \mathbb{P}\left(\exists j \in \mathcal{H}_0(P) : T_j(X) > S_\alpha(\Gamma) \right)$$
$$= \mathbb{P}\left(\sup_{j \in \mathcal{H}_0(P)} \{T_j(X)\} > S_\alpha(\Gamma) \right)$$

Since $\forall j \in \mathcal{H}_0(P)$, $T_j(X) \leq T_j(X-\mu)$ (both one-sided or two-sided)

The latter is $\leq \mathbb{P}\left(\sup_{j \in \mathcal{H}_0(P)} \{T_j(X-\mu)\} > S_\alpha(\Gamma) \right) \leq \mathbb{P}\left(\sup_{1 \leq j \leq m} \{T_j(\underbrace{X-\mu}_{= Z \sim \mathcal{N}(0,\Gamma)})\} > S_\alpha(\Gamma) \right) \leq \alpha$

Moreover, for P_0 such that $\mu = 0$ (full null)

$$\text{FWER}(S_\alpha(\Gamma), P) = \mathbb{P}\left(\sup_{1 \leq j \leq m} \{T_j(X-\mu)\} > S_\alpha(\Gamma) \right) = \alpha$$ because $\sup_j T_j(X-\mu)$ has a continuous distribution

□

Examples: ① $\Gamma = \begin{pmatrix} 1 & & (\rho) \\ & \ddots & \\ (\rho) & & 1 \end{pmatrix}$ ρ-equicorrelated with $\rho \geq 0$, say one-sided

$Z \sim \mathcal{N}(0,\Gamma)$ can be realized as $Z_j = \sqrt{\rho}\, W + \sqrt{1-\rho}\, \xi_j$ where $W, \xi_1 \dots \xi_m$ iid $\mathcal{N}(0,1)$

Hence we can compute $S_\alpha(\Gamma)$ more explicitly via:

$$\mathbb{P}_{Z \sim \mathcal{N}(0,\Gamma)}\left(\max_{1 \leq j \leq m} T_j(Z) \leq x \right) = \mathbb{P}\left(\sqrt{1-\rho}\, \max_j \xi_j \leq x - \sqrt{\rho}\, W \right) = \begin{cases} \int \left[\Phi\left(\frac{x - \sqrt{\rho}\, w}{\sqrt{1-\rho}} \right) \right]^m \phi(w)\, dw & \text{if } \rho < 1 \\ \Phi(x) & \text{if } \rho = 1 \end{cases}$$

② Linear model (standard): $\underset{n\times1}{Y} = \underset{n\times p}{M}\ \underset{p\times1}{\beta} + \underset{n\times1}{\varepsilon}$, $\varepsilon \sim \mathcal{N}(0, I_n)$, M full rank $(n \geq p)$

$[(M^tM)^{-1}]_{jj} = 1 \quad \forall j$

OLS $\underbrace{\hat{\beta}}_{=X} = (M^tM)^{-1}M^tY \sim \mathcal{N}(\underbrace{\beta}_{=\mu}, \underbrace{(M^tM)^{-1}}_{=\Gamma})$

for $Z \sim \mathcal{N}(0, (M^tM)^{-1})$, distribution of $\max_{1\leq j\leq m}\{Z_j\}$ can be approached by Monte-Carlo algorithm

2.2 unknown dependence: the randomization trick

[Westfall and Young (1993)]
[Romano and Wolf (2005)]

Consider the two-group model and Student statistics $T_j(X) = \frac{1}{\sqrt{1/n_0 + 1/n_1}} \frac{|\hat{\mu}_{0j} - \hat{\mu}_{1j}|}{\hat{\sigma}_j}$
although we do not assume that Q is Gaussian nor known

An essential property here is called the randomization property

$$(T_j(X))_{j\in\mathcal{H}_0} \sim (T_j(X^\sigma))_{j\in\mathcal{H}_0} \quad \text{for any } \sigma \in \mathfrak{S}_n$$

true here!

Generate $\sigma_1 \ldots \sigma_B$ iid uniform on $\mathfrak{S}_n$

Consider the threshold $s_\alpha(X) = \min\left\{ x \in \mathbb{R} : \frac{1}{B+1}\left(1 + \sum_{b=1}^{B} \mathbb{1}\{\max_{1\leq j\leq m} T_j(X^{\sigma_b}) \leq x\}\right) \geq 1-\alpha \right\}$

(also called 'max T' procedure)

$\rightarrow$ mimics the distribution of the max under the null

$\boxed{\text{Proposition: In the two-group setting } \forall P \in \mathcal{P},\ \mathrm{FWER}(s_\alpha(X), P) \leq \alpha}$

Proof: first, let us consider the 'ideal threshold'

$$s_\alpha^0(X) = \min\left\{ x \in \mathbb{R} : \frac{1}{B+1}\left(1 + \sum_{b=1}^{B} \mathbb{1}\{\max_{j\in\mathcal{H}_0(P)} T_j(X^{\sigma_b}) \leq x\}\right) \geq 1-\alpha \right\}$$

Obviously $s_\alpha^0(X) \leq s_\alpha(X)$

First, $\forall t > S_\alpha(X)$, $t > S^\circ_\alpha(X)$, and thus by def of the quantile $S^\circ_\alpha(X)$,

$$\frac{1}{B+1}\left(1+\sum_{b=1}^{B} \mathbb{1}\left\{\max_{j\in\mathcal{H}_0(P)} T_j(X^{\sigma_b}) \geq t\right\}\right) \leq \frac{1}{B+1}\left(1+\sum_{b=1}^{B} \mathbb{1}\left\{\max_{j\in\mathcal{H}_0(P)} T_j(X^{\sigma_b}) > S_\alpha(X)\right\}\right) \leq \alpha$$

Hence,

$$FWER(S_\alpha, P) = \mathbb{P}\left(\max_{j\in\mathcal{H}_0(P)} \{T_j(X)\} > S_\alpha(X)\right) = \mathbb{P}\left(\frac{1}{B+1}\sum_{b=0}^{B} \mathbb{1}\{Y_b \geq Y_0\} \leq \alpha\right)$$

where $Y_0 = \max_{j\in\mathcal{H}_0(P)} \{T_j(X)\}$ and $Y_b = \max_{j\in\mathcal{H}_0(P)} \{T_j(X^{\sigma_b})\}$

Now, by the randomization hypo, we can show that $(Y_0, \dots, Y_B)$ is exchangeable

We can conclude the proof by the same argument as in Part I ② $\square$

③ Step down refinement

[Westfall and Young (1993)] [Romano and Wolf (2005)]

Remember: $FWER(R^{Bonf}, P) \leq \alpha \frac{m_0(P)}{m}$ may be not close to α

In fact: same phenomenon with the previous $S_\alpha(\tau)$ or $S_\alpha(X)$

because the max is taken under the full null, as if $\mathcal{H}_0(P) = \{1, \dots, m\}$

Idea: if A_0 is the set accepted nulls, aply the same method in restriction to A_0

this gives a new set of rejection. Iterate until convergence.

Formally consider $R_\mathcal{C}$ rejected set and $A_\mathcal{C} = \{1 \dots m\} \setminus R_\mathcal{C}$ for some arbitrary $\mathcal{C} \subset \underset{\mathcal{H}}{\underset{\shortparallel}{\{1, \dots, m\}}}$

SD algorithm:

* step 0: let $\mathcal{C}_0 = \mathcal{H}$
* step $j \geq 1$: let $\mathcal{C}_j = A_{\mathcal{C}_{j-1}}$ if $\mathcal{C}_j = \mathcal{C}_{j-1}$ stop and let $\hat{\mathcal{C}} = \mathcal{C}_j$
  otherwise go to step $j+1$

Proposition: In a multiple testing framework consider a family $(R_\mathcal{C})_{\mathcal{C}\subset\mathcal{H}}$ of multiple testing procedures satisfying (i) $\forall P \in \mathcal{P}$, for $\mathcal{C} = \mathcal{H}_0(P)$, $FWER(R_\mathcal{C}, P) \leq \alpha$

(ii) $\forall \mathcal{C}, \mathcal{C}' \subset \mathcal{H}$, $\mathcal{C} \subset \mathcal{C}' \Rightarrow A_\mathcal{C} \subset A_{\mathcal{C}'}$

Then $\forall P \in \mathcal{P}$, $FWER(R_{\hat{\mathcal{C}}}, P) \leq \alpha$

Proof: On an event with proba $\geq 1-\alpha$ we have $\mathcal{H}_0(P) \subset A_{\mathcal{H}_0(P)}$ by (i)
On this event, we can show that $\mathcal{H}_0(P) \subset A_{\hat{\mathcal{C}}}$ by the following argument:
for all $j \geq 0$, $\mathcal{H}_0(P) \subset \mathcal{C}_j$ implies $A_{\mathcal{H}_0(P)} \subset A_{\mathcal{C}_j} = \mathcal{C}_{j+1}$ by (ii) and thus $\mathcal{H}_0(P) \subset \mathcal{C}_{j+1}$
since $\mathcal{H}_0(P) \subset \mathcal{C}_0 = \mathcal{H}$ we have $\mathcal{H}_0(P) \subset \mathcal{C}_j$ for all j $\square$

Application 1: Bonferroni type $R_{\mathcal{C}} = \{1 \leq j \leq m : p_j(X) \leq \frac{\alpha}{|\mathcal{C}|}\}$ satisfies (i) and (ii)
This provides the Holm procedure (= SD version of Bonferroni)

Application 2: Gaussian model with known covariance Γ
(i) and (ii) satisfied with the RW-type $R_{\mathcal{C}} = \{1 \leq j \leq m : T_j(X) > S_{\mathcal{C}}(\Gamma)\}$

where $$S_{\mathcal{C}}(\Gamma) = \min\left\{x \in \mathbb{R} : \mathbb{P}_{Z \sim \mathcal{N}(0,\Gamma)}\left(\max_{j \in \mathcal{C}}\{T_j(Z)\} \leq x\right) \geq 1-\alpha\right\}$$

This provides a step down procedure that incorporates the knowledge of Γ.
This improves the 'single step' procedure of section 2.1

Exercise: simplified formulation
Let us define the step down procedure with critical values τ_ℓ, $1 \leq \ell \leq m$
as rejecting the nulls corresponding to $p_{(1)} \leq \dots \leq p_{(\hat{\ell})}$
for the stopping rule $\hat{\ell} = \max\{\ell \in \{0,..,m\} : \forall \ell' \leq \ell,\ p_{(\ell')} \leq \tau_{\ell'}\}$ (#)

(mind the conventions $p_{(0)}=0$, $\tau_0=0$)

1. Show that the Holm procedure corresponds to the step down procedure with critical values $\tau_\ell = \frac{\alpha}{m-\ell+1}$, $1 \leq \ell \leq m$

2. In the Gaussian equicorrelated with known equi-correlation $\rho \in [0,1]$ (say two-sided) show that the RW step down procedure corresponds to the step down procedure with the critical values

$$\tau_\ell(\Gamma) = \min\left\{x \in \mathbb{R} : \mathbb{P}_{Z \sim \mathcal{N}(0,\Gamma)}\left(\min_{1 \leq j \leq m-\ell+1}\{2\bar{\Phi}(|X_j|)\} \leq x\right) \geq 1-\alpha\right\}, \quad 1 \leq \ell \leq m$$

Aplication 3 Two-group case with unknown dependence

(i) and (ii) satisfied with the RW-type $R_{\mathcal{C}} = \{ 1 \leq j \leq m : T_j(X) > S_{\mathcal{C}}(X) \}$

$$S_{\mathcal{C}}(X) = \min \left\{ x \in \mathbb{R} : \frac{1}{B+1} \left(1 + \sum_{b=1}^{B} \mathbb{1}\{ \max_{j \in \mathcal{C}} T_j(X^{\pi_b}) \leq x \} \right) \geq 1 - \alpha \right\}$$

This improves the 'single-step' procedure found in 2.2 especially when many signal