New Developments in East: Design and Simulation of Trials with Multiple Treatment Arms

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Outline of Presentation

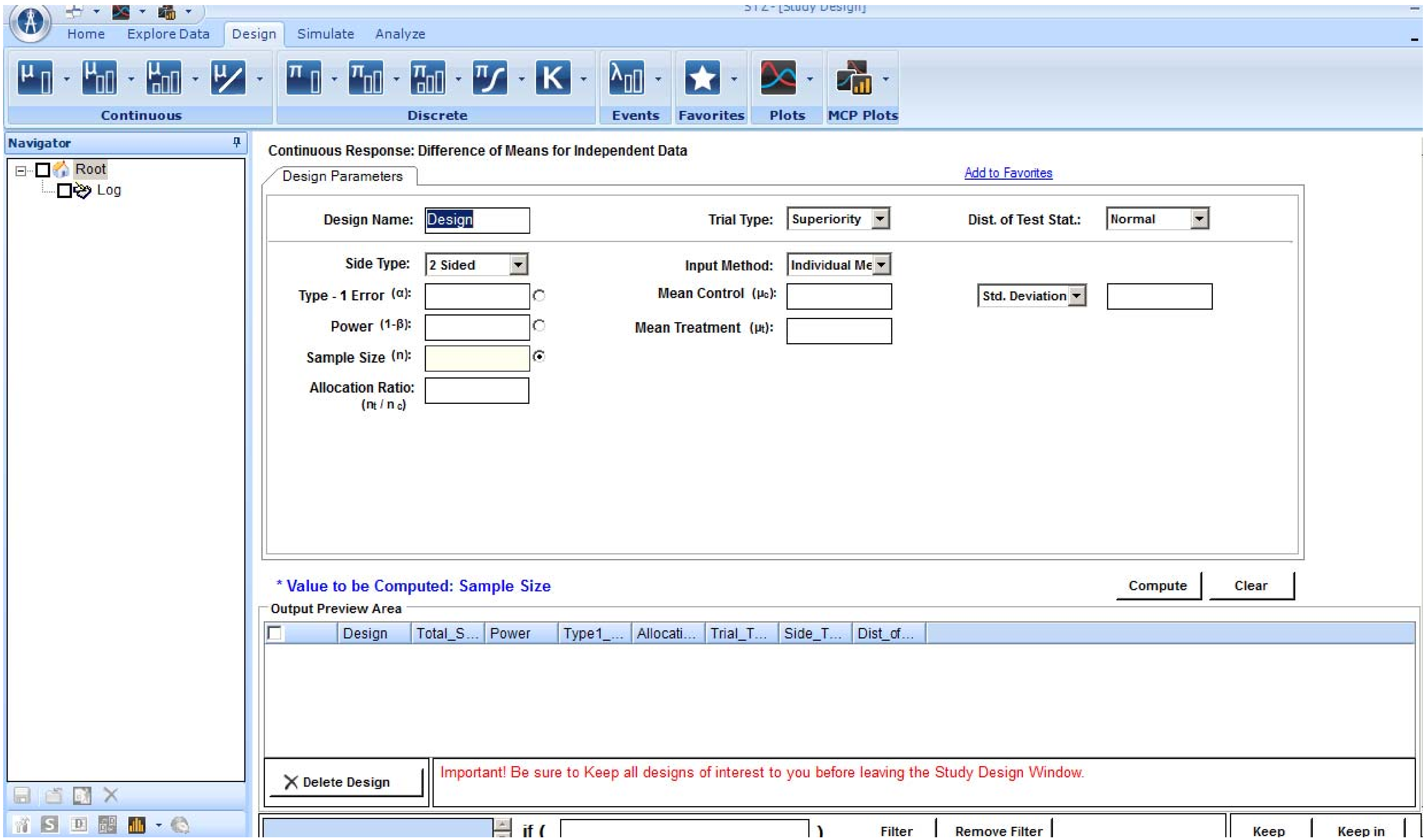
Multiple Comparisons Procedures in SiZ(™)

- Overview of SiZ(™)
- Brief introduction to MCP and MCP module in SiZ(™)
- Motivating example: Alzheimers disease
- Parametric tests (Dunnett, Step-Down Dunnett)
- Nonparametric tests (Bonferroni, Holms, Hochberg, Hommel, Fixed Sequence, Fall Back)
- Principle of closed testing
- Short-cuts to closed testing

New Architecture for East-6

- Integration of SiZ(™), East(R) and modules for adaptive multi-arm trials into one unified platform

Quick Overview of SiZ



Some Sources of Multiplicity

- Repeated significance tests
- Multiple treatment arms
- Multiple endpoints
- Subgroup analysis
- Variable selection in regression models

Error Rates for Multiplicity Problems

- There is a 'family' of m inferences
- Parameters are $\delta_1, \delta_2, \ldots \delta_m$
- Null hypotheses are $H_1, H_2, \ldots H_m$
- Comparisonwise error rate applies to an individual hypothesis; offers 'local control' of type-1 error

$$\text{CER}_j = P(\text{reject } H_j | H_j \text{ is true})$$

- Familywise error rate applies to the entire family

$$\text{FWER} = P(\text{reject at least one true null hypotheses})$$

- Usually wish to control FWER at some level α

Strong and Weak Control of FWER

- Control of FWER at level α means that

$$P(\text{reject at least one true null hypotheses}) \leq \alpha \quad (1)$$

- **Strong Control** of FWER means that (1) is satisfied under all partial null hypotheses of the type $H_I = \cap_{i \in I} H_i$ for all subsets $I \subseteq \{1, 2, \ldots m\}$
- **Weak Control** of FWER means that (1) is satisfied only under some H_I, typically $I = \{1, 2, \ldots m\}$
- Strong control of FWER is a regulatory requirement if multiple statements about product efficacy are to be included in the product label

Motivation for MCP Design Software

- Many confirmatory trials have multiple arms or multiple endpoints
- Software to perform multiplicity adjusted analyses for such trials exists (in R and SAS)
- Sample size software for such designs is, however, limited
- SiZ can evaluate the operating characteristics of the different MCPs and choose the best one for the study

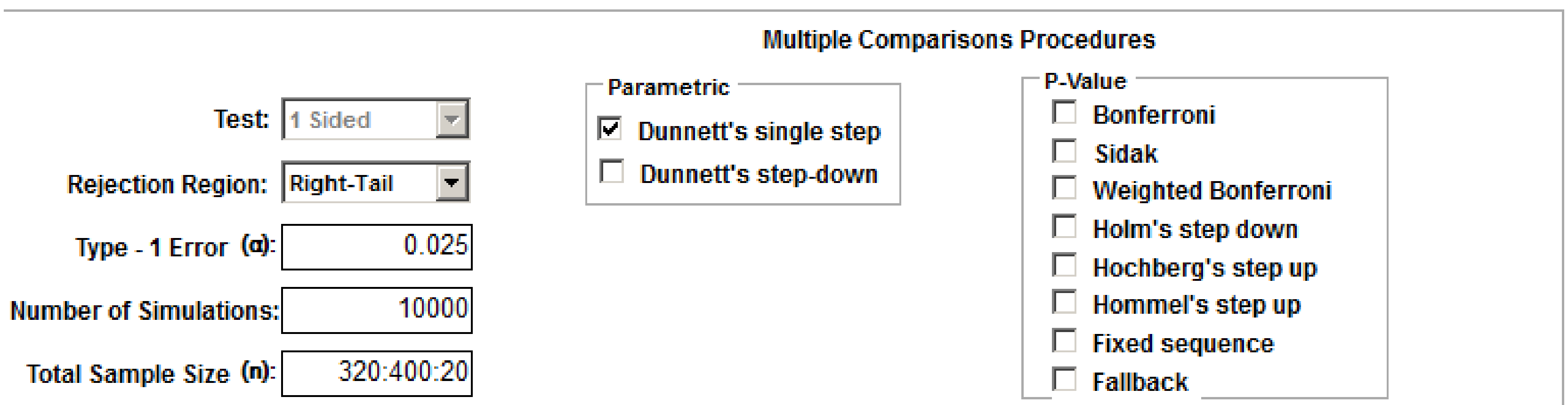
Motivating Example: Alzheimer's Disease

- Randomized, double-blind, placebo controlled, parallel group trial
- Three doses (0.3 mg, 1 mg, 2 mg) compared to placebo
- Primary endpoint: change from baseline in ADAS-cog-11 at week 24
- Difference from placebo expected to be between 1.5 and 2.5 units with common standard deviation $\sigma = 5$

Multiplicity arises because the trial is considered successful if at least one dose is declared statistically significant

The MCP Module in SiZ

- **Simulation based sample size calculations**
- **Parametric Tests: Single-step Dunnett and step-down Dunnett**
- **Nonparametric Tests: Bonferroni, Sidak, Weighted Bonferroni, Holm, Hochberg, Hommel, Fixed-sequence, Fall-back**



Dunnett's Procedure

- Let $Y_{ij} \sim N(\mu_i, \sigma^2)$ be response of subject $j = 1, 2, \ldots n$ on treatment $i = 0, 1, 2, \ldots m$, where $i = 0$ denotes the control arm
- The marginal t-statistic for ith treatment effect is

$$t_i = \frac{\overline{y}_i - \overline{y}_0}{s\sqrt{2/n}}$$

- Denote the cumulative distribution function for the maximum t_i by

$$F(x|m, \nu) = P\left\{\max(T_1, T_2, \ldots T_m) \leq x\right\}$$

- Under H_0: $\mu_i - \mu_0 = 0$ for all i, $F(x|m, \nu)$ is multivariate-t with $\nu = (m+1)(n-1)$ degrees of freedom
- Compute $q_{\alpha,m}$, the $(1-\alpha)$ quantile of F, defined by

$$F(q_{\alpha,m}|m, \nu) = 1 - \alpha$$

The critical value $q_{\alpha,m}$ is evaluated by numerical integration

Single-Step Dunnett

Reject every null hypothesis

$$H_i\text{: } \mu_i - \mu_0 = 0$$

for which $t_i \geq q_{\alpha,m}$

Simulations of Single-Step Dunnett

Design | Treatment Parameters

☐ Generate Means through DR Curve

☑ Common Standard Deviation 5

Arm	Mean	Std.Dev.	Allocation Ratio
Control	0	5	1
1	1.5	5	1
2	2.5	5	1
3	2	5	1

Output Preview Area

☑	Scenario ID	MCP	Global_ Power	Disjunctive _Power	Conjunctive _Power	FWER	Alpha	Total_Sample _Size
☑	Scenario1	Dunnett_Single_Step	0.8581	0.8581	0.2508	0	0.025	320
☑	Scenario2	Dunnett_Single_Step	0.8784	0.8784	0.273	0	0.025	340
☑	Scenario3	Dunnett_Single_Step	0.899	0.899	0.289	0	0.025	360
☑	Scenario4	Dunnett_Single_Step	0.9118	0.9118	0.3089	0	0.025	380
☑	Scenario5	Dunnett_Single_Step	0.9272	0.9272	0.3373	0	0.025	400

- **A total sample size of 360 patients produces the desired 90% global power with Dunnett's single-step procedure**

Power Definitions for Multiplicity Problems

Global Power: Probability of rejecting at least one null hypothesis

Disjunctive Power: Probability of rejecting at least one null hypothesis that is false

Conjunctive Power: Probability of rejecting all null hypotheses that are false

Global and Disjunctive power are usually almost the same

Step-Down Dunnett

Key Idea: Because the test statistics $T_1, T_2, \ldots T_m$ are positively correlated, if you reject a hypothesis, the rejection criteria for the remaining hypotheses can be weakened

Accordingly let:

$q_{\alpha,m}$ satisfy $F(q_{\alpha,m}|m,\nu) = \alpha$; denote it by c_1

$q_{\alpha,m-1}$ satisfy $F(q_{\alpha,m-1}|m-1,\nu) = \alpha$; denote it by c_2

$\vdots$

$q_{\alpha,1}$ satisfy $F(q_{\alpha,1}|1,\nu) = \alpha$; denote it by c_m

Step-Down Dunnett, contd.

Let $T_{(1)} \geq T_{(2)} \geq \cdots \geq T_{(m)}$ denote the m order statistics

- Step 1. If $t_{(1)} \geq c_1$, reject $H_{(1)}$ and go to the next step. Otherwise retain all hypotheses and stop.
- Steps $i = 2, \ldots, m-1$. If $t_{(i)} \geq c_i$, reject $H_{(i)}$ and go to the next step. Otherwise retain $H_{(i)}, \ldots H_{(m)}$ and stop.
- Step m. If $t_{(m)} \geq c_m$ reject $H_{(m)}$. Otherwise retain $H_{(m)}$.

Since $c_1 > c_2 > \cdots > c_m$, step-down Dunnett rejects at least as many (and sometimes more) hypotheses as single step

Simulations of Step-Down Dunnett

Output Preview Area

☑	Scenario ID	MCP	Global_ Power	Disjunctive _Power	Conjunctive _Power	FWER	Alpha	Total_Sample _Size	#_Arms	#
☑	Scenario1	Dunnett_Single_Step	0.8966	0.8966	0.2875	0	0.025	360	4	
☑	Scenario2	Dunnett_Step_Down	0.8966	0.8966	0.4376	0	0.025	360	4	

- **The step-down test improves the conjunctive power**
- **Global and disjunctive power are the same in this example since all null hypotheses are false**

Advantages and Limitations of Dunnett

Advantages

- More powerful than nonparametric procedures if assumptions are met
- Generates multiplicity adjusted confidence intervals for individual treatment effects

Limitations

- Relies on normality assumption
- Relies on homoscedasticity assumption

Dunnett's FWER under unequal variance

☐ Generate Means through DR Curve

☐ Common Standard Deviation

Arm	Mean	Std.Dev.	Allocation Ratio
Control	0	5	1
1	0	5	1
2	0	5	1
3	0	10	1

Output Preview Area

☑	Scenario ID	MCP	Global_Power	Disjunctive_Power	Conjunctive_Power	FWER	Alpha	Total_Sample_Size	#_Arms	#_Simulations_Requested
☑	Scenario1	Dunnett_Single_Step	0.02618	0	0	0.02618	0.025	360	4	100000
☑	Scenario2	Dunnett_Step_Down	0.02575	0	0	0.02575	0.025	360	4	100000
☑	Scenario3	Bonferroni	0.02346	0	0	0.02346	0.025	360	4	100000
☑	Scenario4	Sidak	0.02325	0	0	0.02325	0.025	360	4	100000

In 100,000 simulations FWER was not preserved for Dunnett but was preserved for Bonferroni and Sidak (two non-parametric MCPs)

Nonparametric MCPs

- **Do not require any distributional assumptions**
- **Bonferroni and Sidak are single-step MCPs**
- **Holms is a step-down MCP (start with the biggest effect and work your way down)**
- **Hochberg and Hommel are step-up MCPs (start with the smallest effect and work your way up)**
- **Fixed Sequence and Fall Back procedures test each individual hypothesis in a pre-specified order**

Bonferroni Procedure

- Let $p_1, p_2, \ldots p_m$ be the m marginal p-values
- The Bonferroni procedure rejects any H_i for which

$$p_i \leq \frac{\alpha}{m}$$

Comparing Dunnett and Bonferroni

Design | Treatment Parameters

☐ Generate Means through DR Curve

☐ Common Standard Deviation

Arm	Mean	Std.Dev.	Allocation Ratio
Control	0	5	1
1	1.5	5	1
2	2.5	5	1
3	2	10	1

Compute Power

Create Scenario | Advanced | Clear

Output Preview Area

☑	Scenario ID	MCP	Global_Power	Disjunctive_Power	Conjunctive_Power	FWER	Alpha	Total_Sample_Size	#_Arms	#_Simulations_Requested
☑	Scenario1	Dunnett_Single_Step	0.7145	0.7145	0.0809	0	0.025	360	4	10000
☑	Scenario2	Dunnett_Step_Down	0.7122	0.7122	0.1706	0	0.025	360	4	10000
☑	Scenario3	Bonferroni	0.8603	0.8603	0.1185	0	0.025	360	4	10000
☑	Scenario4	Sidak	0.8699	0.8699	0.1147	0	0.025	360	4	10000

Dunnett loses power because of heteroscedasticity

The Weighted Bonferroni

- **Let $w_i < 1$ be the fraction of α allocated to testing H_i, where $\sum_{i=1}^{m} w_i = 1$**
- **The weighted Bonferroni procedure rejects any H_i for which**

$$p_i \leq w_i \alpha$$

Note: The regular Bonferroni is a special case of the weighted Bonferroni in which $w_i = \frac{1}{m}$ for all i

Can we improve on Bonferroni for testing individual hypotheses?

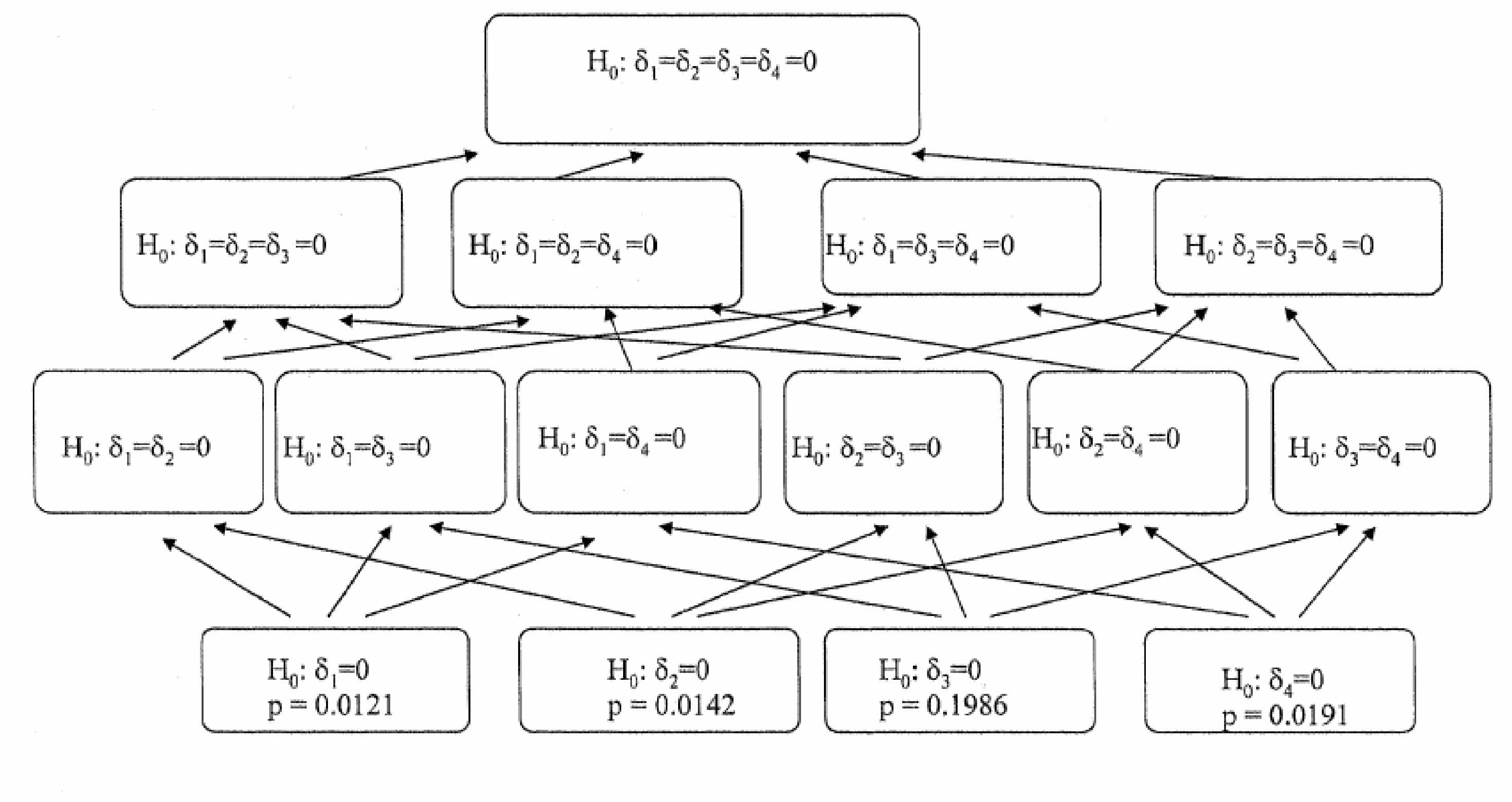
- Suppose we are testing m individual hypotheses
- Let $p_1, p_2, \ldots p_i$ be the individual p-values
- The Bonferrioni procedure rejects each H_i for which $p_i \leq \frac{\alpha}{m}$. Can we do better than a single cut-off?
- Yes! By applying closed testing, we don't require the same strict criterion for every individual hypothesis

Closed Testing of Individual Hypotheses

Given individual hypotheses $H_1, H_2, \ldots H_m$:

1. Construct the closed set consisting of all possible intersections of the individual hypotheses of the form $H_{i_1} \cap H_{i_2} \cap \cdots \cap H_{i_q}$ for all $q = 1, 2, \ldots m$
2. Specify a local level-α test for each member of the closed set
3. An individual H_i may be rejected with strong control of FWER at level α if both these conditions hold:
   - H_i is rejected by its local level-α test
   - All intersection hypotheses that contain H_i are also rejected by their local level-α tests

Example of Closed Testing



Acknowledgement: **This slide has been taken from Peter Westfall's notes**

Testing the Intersection Hypotheses

The key difference between one closed testing procedure and another is the method used to test intersection hypotheses of the form $H_{i_1} \cap H_{i_2} \cap \cdots \cap H_{i_q}$. There are many candidates

- Use Dunnetts test for the intersection hypotheses
  Short Cut: Step-down Dunnett procedure
- Use the Bonferroni test for the intersection hypotheses
  Short Cut: Step-down Holms procedure
- Using Simes test for the intersection hypotheses
  Short Cut: Step-up Hommel procedure
- Using Hochberg's test for the intersection hypotheses
  Short Cut: Step-up Hochberg procedure

Level-α Tests of $H_1 \cap H_2 \cap \cdots H_m$

Let $p_{(1)} \leq p_{(2)} \leq \ldots \leq p_{(m)}$ be the ordered p-values

Bonferroni: Reject if $p_{(1)} \leq \alpha / m$

Hochberg: Reject if

$$p_{(m)} \leq \alpha \text{ or } p_{(m-1)} \leq \frac{\alpha}{2} \text{ or } p_{(m-2)} \leq \frac{\alpha}{3} \text{ or } \ldots \text{ or } p_{(1)} \leq \frac{\alpha}{m}$$

Simes: Reject if

$$p_{(m)} \leq \alpha \text{ or } p_{(m-1)} \leq \frac{(m-1)\alpha}{m} \text{ or } p_{(m-2)} \leq \frac{(m-2)\alpha}{m} \text{ or } \ldots \text{ or } p_{(1)} \leq \frac{\alpha}{m}$$

Hochberg is more powerful than Bonferroni. Simes is more powerful than Hochberg. Simes is only valid if the p-values are positively correlated

Holm's Procedure

- Order the p-values for the individual hypotheses in ascending order as $p_{(1)} \leq p_{(2)} \leq \cdots \leq p_{(m)}$
- If $p_{(1)} \leq \alpha/m$ reject $H_{(1)}$ and continue testing; else stop
- If $p_{(2)} \leq \alpha/(m-1)$ reject $H_{(2)}$ and continue testing; else stop
- In general, reject $p_{(i)}$ if $p_{(i)} \leq \alpha/(m-i+1)$ and $H_{(1)}, H_{(2)}, \ldots H_{(i-1)}$ have already been rejected

Power Comparison: Bonferroni vs Holms

Output Preview Area

☑	Scenario ID	MCP	Global_ Power	Disjunctive _Power	Conjunctive _Power	FWER	Alpha	Total_Sample _Size	#_Arms	#_Simulations _Requested
☑	Scenario1	Bonferroni	0.8869	0.8869	0.2729	0	0.025	360	4	10000
☑	Scenario2	Holm_Step_Down	0.8869	0.8869	0.4338	0	0.025	360	4	10000

Global and disjunctive power are equal; global power for Bonferroni and Holm are equal but big differences in conjunctive and individual power

Arm	Mean	Std.Dev.	Allocation Ratio
Control	0	5	1
1	1.5	5	1
2	2.5	5	1
3	2	5	1

Pure Bonferroni

Arm	Power
Control	N.A.
1	0.3484
2	0.8255
3	0.609

Bonferroni-Holms

Arm	Power
Control	N.A.
1	0.4726
2	0.8435
3	0.6782

Hochberg's Procedure

- Order the p-values in ascending order as $p_{(1)} \leq p_{(2)} \cdots \leq p_{(m)}$
- If $p_{(m)} \leq \alpha$, reject all m hypotheses and stop; otherwise retain $H_{(m)}$ and continue testing
- If $p_{(m-1)} \leq \alpha/2$, reject all $m-1$ hypotheses and stop; otherwise retain $H_{(m-1)}$ and continue testing
- If $p_{(m-2)} \leq \alpha/3$, reject all $m-2$ hypotheses and stop; otherwise retain $H_{(m-1)}$ and continue testing
- In general, at any step $i = 1, 2, \ldots m$, if

$$p_{(m-i+1)} \leq \frac{\alpha}{i}$$

reject all $m-i+1$ hypotheses and stop; otherwise retain $H_{(m-i+1)}$ and continue testing

Hommel's Procedure

- Order the p-values in ascending order as $p_{(1)} \leq p_{(2)} \cdots \leq p_{(m)}$
- If $p_{(m)} \leq \alpha$, reject all m hypotheses and stop; otherwise retain $H_{(m)}$ and continue testing
- If $p_{(m)} \leq \alpha$ or $p_{(m-1)} \leq \alpha/2$, reject all $m-1$ hypotheses and stop; otherwise retain $H_{(m-1)}$ and continue testing
- If $p_{(m)} \leq \alpha$ or $p_{(m-1)} \leq 2\alpha/3$ or $p_{(m-2)} \leq \alpha/3$, reject all $m-2$ hypotheses and stop; otherwise retain $H_{(m-2)}$ and continue testing
- In general, at any step $i = 1, 2, \ldots m$, if

$$p_{(m)} \leq \frac{i\alpha}{i} \text{ or } p_{(m-1)} \leq \frac{(i-1)\alpha}{i} \text{ or } p_{(m-2)} \leq \frac{(i-2)\alpha}{i} \ldots p_{(m-i+1)} \leq \frac{\alpha}{i}$$

reject all $m-i+1$ hypotheses and stop; otherwise retain $H_{(m-i+1)}$ and continue testing

Hommel versus Hochberg

- **Hommel's procedure is clearly more powerful than Hochberg's since it gives more chances for rejection at each step**
- **But it is rarely used in practice because it is perceived to be too complicated**
- **Hochberg is very simple to explain and use, hence more popular**

Comparing Power for Bonferroni, Holms, Hochberg and Hommel Procedures

Output Preview Area

☑	Scenario ID	MCP	Global_ Power	Disjunctive _Power	Conjunctive _Power	FWER	Alpha	Total_Sample _Size	#_Arms	#_Simulations _Requested
☑	Scenario1	Bonferroni	0.6489	0.6489	0.1004	0.0104	0.025	360	6	10000
☑	Scenario2	Holm_Step_Down	0.6489	0.6489	0.1409	0.02	0.025	360	6	10000
☑	Scenario3	Hochberg_Step_Up	0.6512	0.6512	0.1444	0.0215	0.025	360	6	10000
☑	Scenario4	Hommel_Step_Up	0.659	0.659	0.1449	0.0221	0.025	360	6	10000

Pure Bonferroni

Arm	Power
Control	N.A.
1	0.35058
2	0.82962
3	0.60603

Bonferroni-Holms

Arm	Power
Control	N.A.
1	0.47823
2	0.84946
3	0.68022

Hochberg

Arm	Power
Control	N.A.
1	0.49421
2	0.85649
3	0.69625

Hommel

Arm	Power
Control	N.A.
1	0.49374
2	0.85722
3	0.69663

Fixed Sequence Testing

- Assume $H_1, H_2, ..., H_m$ are ordered hypotheses; i.e., $\mu_i \geq \mu_{i-1}$, $i = 1, 2, \ldots m$
- Let $p_1, p_2, ..., p_m$ be the associated raw p-values
  - Step 1. If $p_1 < \alpha$, reject H_1 and go to the next step. Otherwise retain all hypotheses and stop
  - Step $i = 2, \ldots, m-1$. If $p_i < \alpha$, reject H_i and go to the next step. Otherwise retain all the remaining hypotheses and stop
  - Step m. If $p_m < \alpha$, reject H_m; otherwise retain it.
- More powerful than other procedures if ordering is correct
- Closed under fixed sequence testing of each intersection hypotheses

Example 1: Testing sequence is correct

Design | Treatment Parameters

☐ Generate Means through DR Curve

☑ Common Standard Deviation 5

Arm	Mean	Std.Dev.	Allocation Ratio	Test Sequence
Control	0	5	1	
1	1.5	5	1	3
2	2.5	5	1	1
3	2	5	1	2

Compute Power

Create Scenario | Advanced | Clear

Output Preview Area

☑	Scenario ID	MCP	Global_Power	Disjunctive_Power	Conjunctive_Power	FWER	Alpha	Total_Sample_Size	#_Arms	#_Simulations_Requested
☑	Scenario1_1	Dunnett_Step_Down	0.8958	0.8958	0.4444	0	0.025	360	4	10000
☑	Scenario1_2	Bonferroni	0.8903	0.8903	0.2693	0	0.025	360	4	10000
☑	Scenario1_3	Holm_Step_Down	0.8905	0.8905	0.4408	0	0.025	360	4	10000
☑	Scenario1_4	Hochberg_Step_Up	0.8901	0.8901	0.4471	0	0.025	360	4	10000
☑	Scenario1_5	Hommel_Step_Up	0.8951	0.8951	0.4526	0	0.025	360	4	10000
☑	Scenario1_6	Fixed_Sequence	0.9177	0.9177	0.4548	0	0.025	360	4	10000

If the order of testing is correctly specified, the fixed sequence procedure is the most powerful

Example 2: Testing sequence is incorrect

Design | Treatment Parameters

☐ Generate Means through DR Curve

☑ Common Standard Deviation 5

Arm	Mean	Std.Dev.	Allocation Ratio	Test Sequence
Control	0	5	1	
1	1.5	5	1	1
2	2.5	5	1	2
3	2	5	1	3

Compute Power

Create Scenario | Advanced | Clear

Output Preview Area

☑	Scenario ID	MCP	Global_ Power	Disjunctive _Power	Conjunctive _Power	FWER	Alpha	Total_Sample _Size	#_Arms	#_Simulations _Requested
☑	Scenario1_1	Dunnett_Step_Down	0.8973	0.8973	0.4374	0	0.025	360	4	10000
☑	Scenario1_2	Bonferroni	0.8823	0.8823	0.2704	0	0.025	360	4	10000
☑	Scenario1_3	Holm_Step_Down	0.8939	0.8939	0.4433	0	0.025	360	4	10000
☑	Scenario1_4	Hochberg_Step_Up	0.8914	0.8914	0.4404	0	0.025	360	4	10000
☑	Scenario1_5	Hommel_Step_Up	0.8932	0.8932	0.4568	0	0.025	360	4	10000
☑	Scenario1_6	Fixed_Sequence	0.515	0.515	0.4454	0	0.025	360	4	10000

Fixed sequence procedure loses considerable power if testing sequence is incorrect

The Fall Back Procedure

- Assume $H_1, H_2, ..., H_m$ are ordered hypotheses, $w_1, w_2, \ldots w_m$ are pre-specified weights with $\sum_{i=1}^{m} w_i = 1$, and $p_1, p_2, ..., p_m$ are the associated raw p-values. The testing proceeds as follows:
  - Step 1. Test H_1 at $\alpha_1 = w_1\alpha$. If $p_1 \leq \alpha_1$, reject H_1; otherwise retain it and go to the next step.
  - Step $i = 2, \ldots, m$. Test H_i at $\alpha_i = \alpha_{i-1} + w_i\alpha$ if H_{i-1} is rejected and at $\alpha_i = w_i\alpha$ if H_{i-1} is retained. If $p_i \leq \alpha_i$, reject H_i; otherwise retain it and go to the next step.
- Provides option to continue even if a hypothesis is retained. Hence good insurance policy in case incorrect testing order was specified
- Specializes to fixed sequence test if $w_1 = 1$ and $w_2 = \cdots = w_m = 0$
- Was shown by Wiens and Dmitreinko (2005) to be a closed test

Example 3: Performance of Fall Back Test under Incorrect Testing Sequence

Arm	Mean	Std.Dev.	Allocation Ratio	Proportion of Alpha	Test Sequence
Control	0	5	1		
1	1.5	5	1	0.333	1
2	2.5	5	1	0.333	2
3	2	5	1	0.333	3

Test H_1 at level $\alpha_1 = \alpha/3$. If H_1 is rejected, test H_2 at level $\alpha_2 = \alpha_1 + \alpha/3$, otherwise test H_2 at level $\alpha_2 = \alpha/3$. If H_2 is rejected test H_3 at level $\alpha_2 + \alpha/3$, otherwise test H_3 at level $\alpha/3$

Output Preview Area

☑	Scenario ID	MCP	Global_ Power	Disjunctive _Power	Conjunctive _Power	FWER	Alpha	Total_Sample _Size	#_Arms	#_Simulations _Requested
☑	Scenario1_1	Hommel_Step_Up	0.899	0.899	0.4569	0	0.025	360	4	10000
☑	Scenario1_2	Fixed_Sequence	0.512	0.512	0.4463	0	0.025	360	4	10000
☑	Scenario1_3	Fallback	0.8888	0.8888	0.3145	0	0.025	360	4	10000

Fall back procedure is almost as good as Hommel despite guessing treatment order incorrectly

Example 4: Performance of Fall Back Test under Correct Testing Sequence

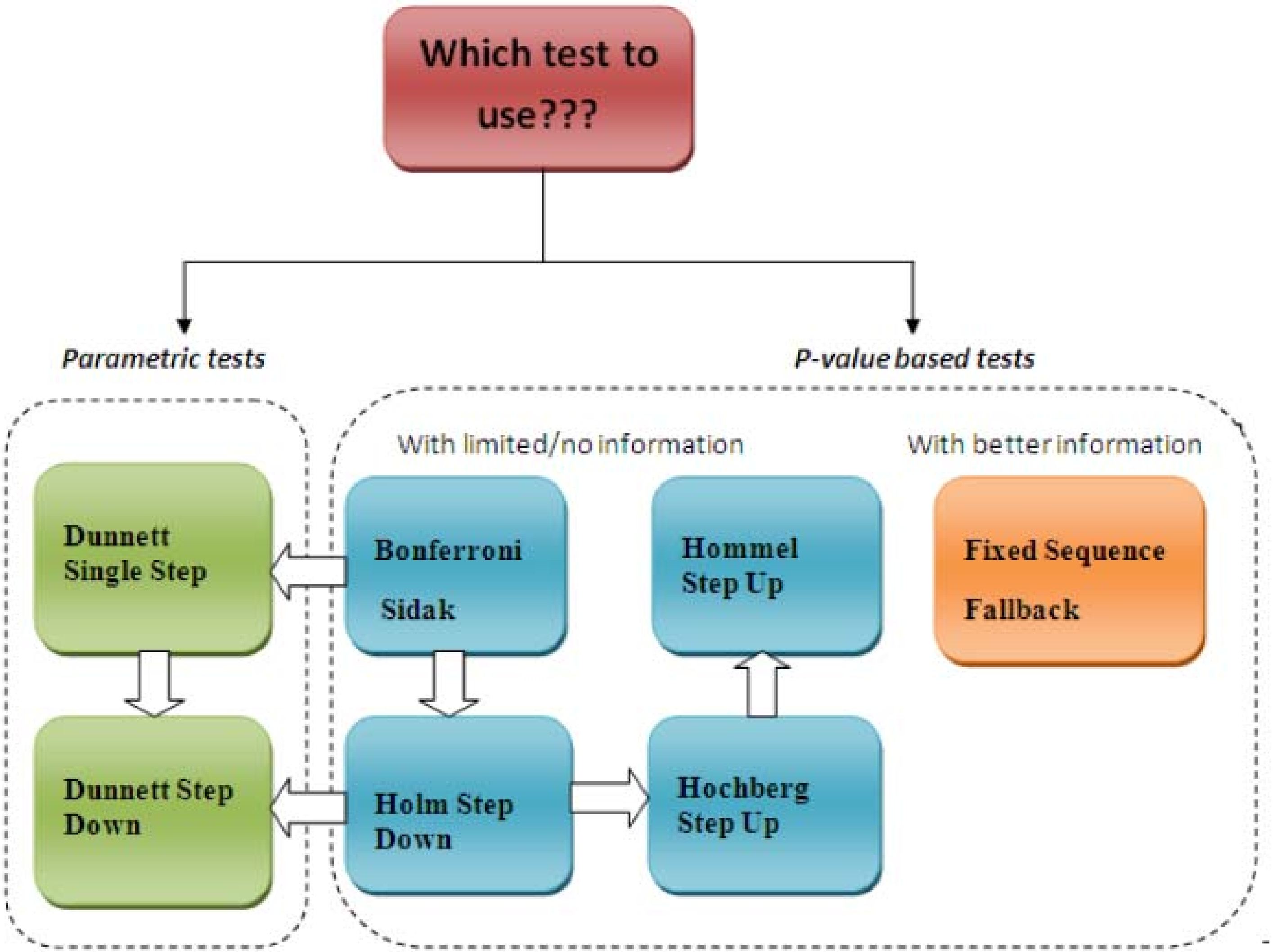
Arm	Mean	Std.Dev.	Allocation Ratio	Proportion of Alpha	Test Sequence
Control	0	5	1		
1	1.5	5	1	0.333	3
2	2.5	5	1	0.333	1
3	2	5	1	0.333	2

Output Preview Area

☑	Scenario ID	MCP	Global_Power	Disjunctive_Power	Conjunctive_Power	FWER	Alpha	Total_Sample_Size	#_Arms	#_Simulations_Requested
☑	Scenario1_1	Hommel_Step_Up	0.8956	0.8956	0.456	0	0.025	360	4	10000
☑	Scenario1_2	Fixed_Sequence	0.9178	0.9178	0.452	0	0.025	360	4	10000
☑	Scenario1_3	Fallback	0.8925	0.8925	0.4118	0	0.025	360	4	10000

In this example the fall back test is almost as good as the fixed sequence test when the ordering is correctly specified and is superior to the fixed sequence test when the ordering is incorrectly specified

Which Test to Use?



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