EFSPI
EUROPEAN FEDERATION OF STATISTICIANS IN THE PHARMACEUTICAL INDUSTRY
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Testing procedure for multiple treatments and multiple outcomes

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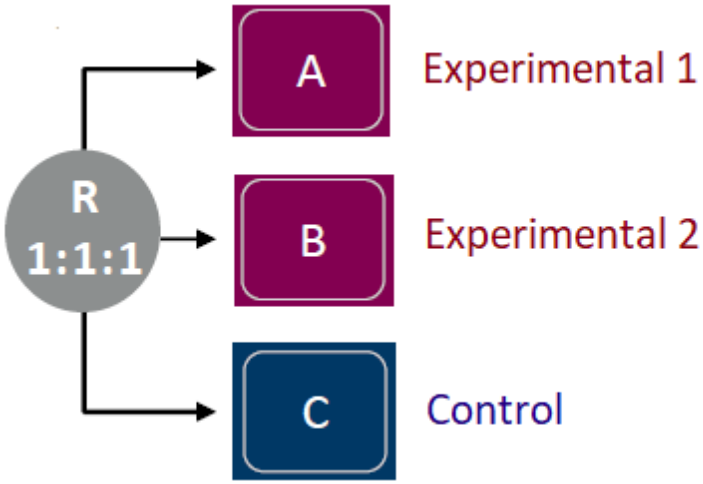
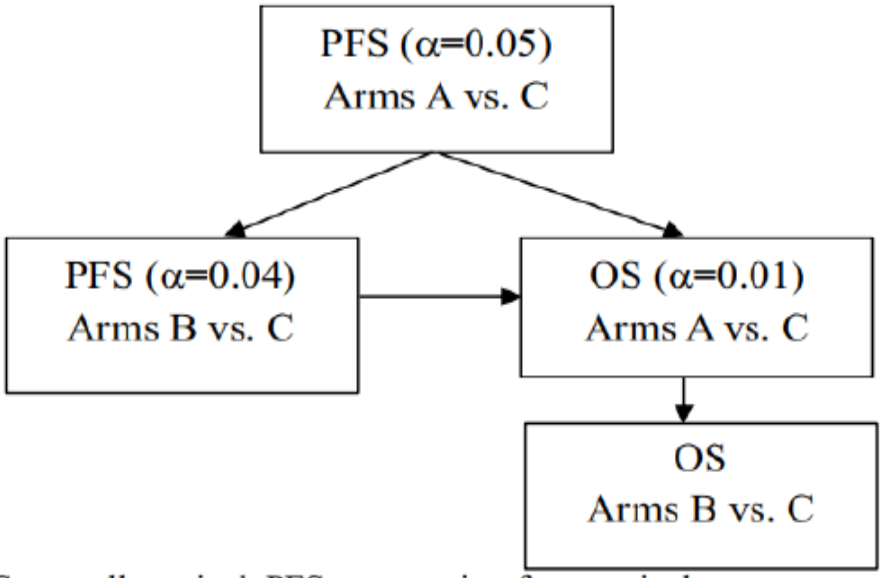
Clinical Trial Design (Advanced Cancer)



Comparisons: A vs. C (Experimental 1, preferred)
B vs. C (Experimental 2)
A vs. B (Not powered)

Outcomes: Primary: PFS
Secondary: OS

Multiple Testing Procedure



α=0.01 if PFS (B vs. C) is not positive
α=0.05 if both PFS analyses are positive

α=0.01 if PFS (B vs. C) is not positive, and
OS (B vs. C) is positive
α=0.05 if all previous analyses are positive

OS, overall survival; PFS, progression-free survival.

Issues:

1. OS tested *only* if PFS of A vs. C statistically significant
2. OS of A vs. C (preferred) tested at 0.05 *only* if PFS of B vs. C statistically significant

Alternative: Generalized Pairwise Comparisons

1. Instead of PFS (time to first outcome), use prioritized outcomes (time to worst outcome):
   - Time to death (OS)
   - Time to tumor progression (TTP)

2. Analyze time to worst outcome using GPC for the 2 comparisons (A vs. C and A vs. B)

3. Use powerful procedure (Holms or Hochberg) to account for multiplicity

Is this alternative approach preferable?