Interim analysis tool

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INTERFACULTY CENTER
DATA PROCESSING
& STATISTICS

INTERIM ANALYSIS

DATA COLLECTION

- All data at once

18 data points (e.g 18 mice)

- Not all data at once

Example 1

6 data points	6 data points	6 data points

Example 2

2	4	3	3	1	5

Interim analysis 1 (after 4) · Interim analysis 2 (after 3) · Final analysis

Purpose:
Stop data collection early,
in case of sufficient evidence

INTERIM ANALYSIS

APPROACH

What groups on this campus often do:

Allowed chance for a false positive = α

Interim analysis 1: $p < \alpha$?

Interim analysis 2: $p < \alpha$?

Final analysis: $p < \alpha$?

Problem 1: Total probability of a false positive > α
Problem 2: Influence on the power?

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INTERIM ANALYSIS

APPROACH

Step 1: perform the power analysis in Gpower as you would without interim analysis

determine a first approximation of the sample size

Step 2: use our tool

determine interim specific alpha’s and total sample size

Ex.: control group, experimental condition 1 & 2

Group means: 1, 2, 3

SD: 1.25

We can process 6 mice at a time

Stages: 6; 12; 18; 24; 27

Mice per group: 2; 4; 6; 8; 9

2 mice per group in a one way ANOVA is not reasonable

→ no interim analysis here

F tests - ANOVA: Fixed effects, omnibus, one-way

Analysis: A priori: Compute required sample size

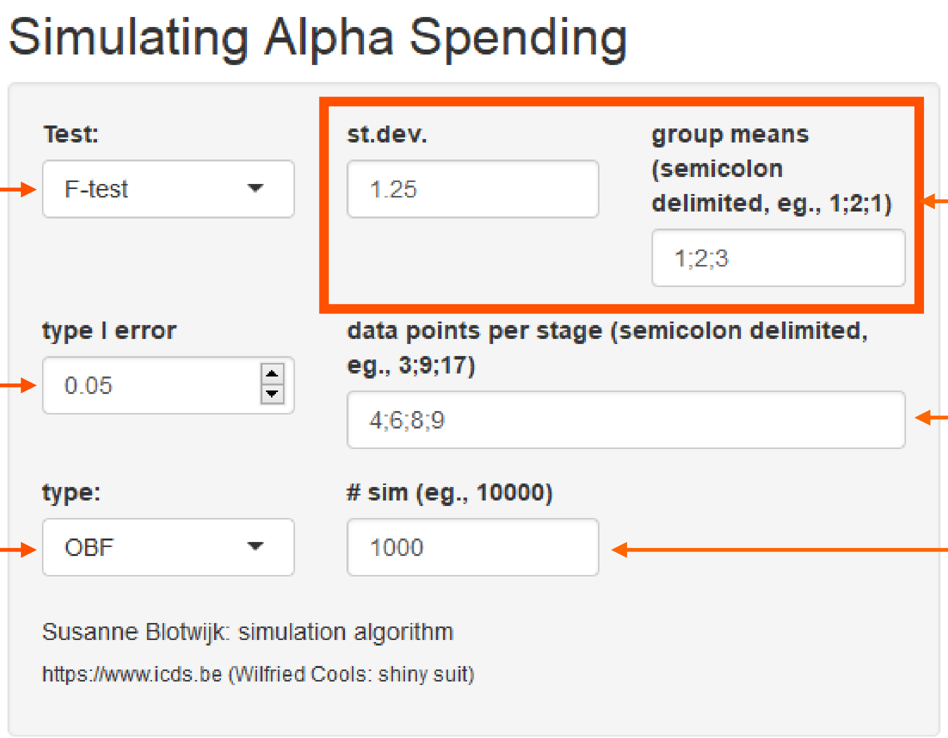
Input:	Effect size f	=	0.6531973
	α err prob	=	0.05
	Power (1-β)	=	0.8
	Number of groups	=	3
Output:	Noncentrality	=	11.5200012
	Critical F	=	3.4028261
	Numerator df	=	2
	Denominator df	=	24
	Total sample size	=	27
	Actual power	=	0.8210086

INTERIM ANALYSIS
TOOL: INPUT

T-test of one-way ANOVA

alpha

Alpha spending function, leave it as is



Same group parameters as the ones you used for the Gpower calculation

Number of mice per group at each interim analysis

Number of simulations
Higher number: takes more time
Lower number: lower accuracy and precision

INTERIM ANALYSIS

TOO LITTLE POWER

	test 1	test 2	test 3	test 4	
cumulative power	0.0691	0.378	0.6891	0.7879	
alphas	0.0034	0.014	0.0285	0.032	
cumulative alpha	0.0033	0.0164	0.0376	0.05	
target cumulative alpha	0.0033	0.0164	0.0376	0.05	
expected number					22.2503
expected stop					2.8638

Total power: decreases by adding interim analyses.

Type I errors for each test (all < .05)

In case of insufficient power (< 0.8), there are two options:

1) Add an extra mouse to the final stage

2) Remove one of the interim analyses

INTERIM ANALYSIS

TOOL: OUTPUT

Simulating Alpha Spending

Test: F-test

st.dev. 1.25

group means (semicolon delimited, eg., 1;2;1) 1;2;3

type I error 0.05

data points per stage (semicolon delimited, eg., 3;9;17) 4;6;8;10

type: OBF

sim (eg., 10000) 100000

Susanne Blotwijk: simulation algorithm

https://www.icds.be (Wilfried Cools: shiny suit)

We add one mouse to our original number, so 9+1 = 10. We have 3 groups, so in total 3*10 = 30.

SIMULATE the alpha spending function sample sizes

	test 1	test 2	test 3	test 4
cumulative power	0.0431	0.3273	0.6512	0.8414
alphas	0.0019	0.0102	0.0228	0.0352
cumulative alpha	0.002	0.0114	0.0284	0.05
target cumulative alpha	0.0019	0.0114	0.0284	0.05
expected number				23.8699
expected stop				2.9783

Total Power

Alpha values you should apply at each analysis

Total chance of a type I error at each analysis

Expected number of used mice

INTERIM ANALYSIS

TOO FEW SIMULATIONS

	test 1	test 2	test 3	test 4	
cumulative power	0.07	0.39	0.71	0.82	
alphas	0	0.02	0.03	0.04	
cumulative alpha	0	0.02	0.04	0.05	
target cumulative alpha	0	0.02	0.04	0.05	
expected number					22.11
expected stop					2.83

These two rows differ too much
→ accuracy is too low → more simulations needed

At least one number here is 0
→ precision is too low→ more simulations needed

1) Two numbers in this part of the column differ too much
→ accuracy is too low → more simulations needed

2) Less than two significant digits
→ precision is too low → more simulations needed