HOW TO APPLY THE MULTIPHASE OPTIMIZATION STRATEGY (MOST) IN YOUR INTERVENTION DEVELOPMENT RESEARCH

Module 3
Introduction to the optimization trial

Lesson 4: Why factorial experiments can be so economical

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In the previous lesson you learned how to:

- Express the fundamental differences between the logical underpinnings of an RCT and those of a factorial experiment

- Explain why the factorial experiment usually requires many fewer experimental participants than alternative designs

In this lesson you will learn how to:

- Explain why it is often possible to examine additional factors in a factorial experiment without the need to increase the number of participants to maintain power

- Explain why factorial experiments can have very small per-condition *n*'s and still be well-powered

Brief review of statistical power

- Type I error = rejecting H_0, given that H_0 is true = mistakenly concluding an effect exists when it does not
- α = Type I error rate = probability of rejecting H_0, given that H_0 is true

Brief review of statistical power

- Type II error = failing to reject H_0, given that H_0 is false = mistakenly overlooking an effect
- β = Type II error rate = probability of failing to reject H_0, given that H_0 is false
- Power = $1 - \beta$ = probability of correctly rejecting H_0, given that H_0 is false

Brief review of statistical power

- All else being equal, power depends on:
  - Effect size (larger = more power)
  - α selected (larger = more power)
  - N (larger = more power)

(When there is a cluster structure, the intra-class correlation may also be a consideration)

Reminder of how RCTs are powered

Treatment A *n*=150	Control *n*=150

Total *N* = 300

- Now suppose I decide to add another treatment that I want to compare to the control condition. Same expected effect size. Will dividing the *N*=300 among the 3 conditions maintain power?

Treatment B *n*=100	Treatment A *n*=100	Control *n*=100

Total *N* = 300

Reminder of how RCTs are powered

Treatment A	Control	
n=150	*n*=150	Total *N* = 300

- No – to maintain power it will be necessary to obtain 150 more participants.

Treatment B	Treatment A	Control	
n=150	*n*=150	*n*=150	Total *N* = 450

- Why? Because to maintain the same power each treatment-control comparison must be based on 300 participants.

Developing an intervention aimed at reducing viral load among HIV+ individuals who drink heavily

- Suppose there are 4 candidate components:
- Motivational interviewing (no, yes)
- Peer mentoring (no, yes)
- Text message support (no, yes)
- Mindfulness meditation (no, yes)

Choosing an experimental design: Comparison of options

Comparison of Features of Design Alternatives for Hypothetical HIV Study			
Design	**Number of Experimental Conditions**	**Number of Participants Needed to Maintain Power ≥ .8 (*d* = .3)**	**Can Interactions Be Estimated?**
Individual Experiments	8	1,408	No
Comparative Treatment	5	880	No
Factorial (main effect)	16	352	Yes

With N=352, the per-condition n=22.

How can this experiment be well-powered with only 22 per condition?

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*Outcome*
1	No	No	No	No	22
2	No	No	No	Yes	22
3	No	No	Yes	No	22
4	No	No	Yes	Yes	22
5	No	Yes	No	No	22
6	No	Yes	No	Yes	22
7	No	Yes	Yes	No	22
8	No	Yes	Yes	Yes	22
9	Yes	No	No	No	22
10	Yes	No	No	Yes	22
11	Yes	No	Yes	No	22
12	Yes	No	Yes	Yes	22
13	Yes	Yes	No	No	22
14	Yes	Yes	No	Yes	22
15	Yes	Yes	Yes	No	22
16	Yes	Yes	Yes	Yes	22

An important difference between the RCT and the factorial experiment

- With an RCT, a small per-condition *n* is usually an indication that the experiment has low, possibly unacceptable, power.

- By contrast, in a balanced factorial experiment a small per-condition n DOES NOT NECESSARILY INDICATE LOW POWER.

The logic behind powering factorial experiments

- In factorial experiments, per-condition *n* does not determine power
- What matters is the *N per level of each factor*
- Recall how main effects are calculated

MAIN EFFECT OF *MI* is mean of conditions 9—16 MINUS mean of conditions 1—8.

The *N* per level (No, Yes) = 176.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	Per-condition *n*
1	No	No	No	No	22
2	No	No	No	Yes	22
3	No	No	Yes	No	22
4	No	No	Yes	Yes	22
5	No	Yes	No	No	22
6	No	Yes	No	Yes	22
7	No	Yes	Yes	No	22
8	No	Yes	Yes	Yes	22
9	Yes	No	No	No	22
10	Yes	No	No	Yes	22
11	Yes	No	Yes	No	22
12	Yes	No	Yes	Yes	22
13	Yes	Yes	No	No	22
14	Yes	Yes	No	Yes	22
15	Yes	Yes	Yes	No	22
16	Yes	Yes	Yes	Yes	22

MAIN EFFECT OF *PEER* is mean of conditions 5—8 and 13—16 MINUS mean of conditions 1—4 and 9—12.

The *N* per level is still 176.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	Per-condition *n*
1	No	No	No	No	22
2	No	No	No	Yes	22
3	No	No	Yes	No	22
4	No	No	Yes	Yes	22
5	No	Yes	No	No	22
6	No	Yes	No	Yes	22
7	No	Yes	Yes	No	22
8	No	Yes	Yes	Yes	22
9	Yes	No	No	No	22
10	Yes	No	No	Yes	22
11	Yes	No	Yes	No	22
12	Yes	No	Yes	Yes	22
13	Yes	Yes	No	No	22
14	Yes	Yes	No	Yes	22
15	Yes	Yes	Yes	No	22
16	Yes	Yes	Yes	Yes	22

This works because this experiment is *balanced*:

(a) Each level of each factor appears same number of times (here, 4) at each level of every other factor.

This is an absolute requirement for balance.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*Outcome*
1	No	No	No	No	22
2	No	No	No	Yes	22
3	No	No	Yes	No	22
4	No	No	Yes	Yes	22
5	No	Yes	No	No	22
6	No	Yes	No	Yes	22
7	No	Yes	Yes	No	22
8	No	Yes	Yes	Yes	22
9	Yes	No	No	No	22
10	Yes	No	No	Yes	22
11	Yes	No	Yes	No	22
12	Yes	No	Yes	Yes	22
13	Yes	Yes	No	No	22
14	Yes	Yes	No	Yes	22
15	Yes	Yes	Yes	No	22
16	Yes	Yes	Yes	Yes	22

First, note that this experiment is *balanced*:

(b) Equal *ns* per experimental condition

This is a requirement for perfect balance; in practice, usually approximate balance

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*Outcome*
1	No	No	No	No	22
2	No	No	No	Yes	22
3	No	No	Yes	No	22
4	No	No	Yes	Yes	22
5	No	Yes	No	No	22
6	No	Yes	No	Yes	22
7	No	Yes	Yes	No	22
8	No	Yes	Yes	Yes	22
9	Yes	No	No	No	22
10	Yes	No	No	Yes	22
11	Yes	No	Yes	No	22
12	Yes	No	Yes	Yes	22
13	Yes	Yes	No	No	22
14	Yes	Yes	No	Yes	22
15	Yes	Yes	Yes	No	22
16	Yes	Yes	Yes	Yes	22

- Suppose you want to assess the performance of an additional candidate component:
- Motivational interviewing (no, yes)
- Peer mentoring (no, yes)
- Text message support (no, yes)
- Mindfulness meditation (no, yes)
- Behavioral skills training (low intensity, high intensity)

This is now a $2{\times}2{\times}2{\times}2{\times}2 = 2^5$ experiment.

The number of experimental conditions has DOUBLED to 32.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*SKILLS*	*Outcome*	Per-condition *n*
1	No	No	No	No	Low	$\overline{Y}_1$	
2	No	No	No	No	High	$\overline{Y}_2$	
3	No	No	No	Yes	Low	$\overline{Y}_3$	
4	No	No	No	Yes	High	$\overline{Y}_4$	
5	No	No	Yes	No	Low	$\overline{Y}_5$	
6	No	No	Yes	No	High	$\overline{Y}_6$	
7	No	No	Yes	Yes	Low	$\overline{Y}_7$	
8	No	No	Yes	Yes	High	$\overline{Y}_8$	
9	No	Yes	No	No	Low	$\overline{Y}_9$	
10	No	Yes	No	No	High	$\overline{Y}_{10}$	
11	No	Yes	No	Yes	Low	$\overline{Y}_{11}$	
12	No	Yes	No	Yes	High	$\overline{Y}_{12}$	
13	No	Yes	Yes	No	Low	$\overline{Y}_{13}$	
14	No	Yes	Yes	No	High	$\overline{Y}_{14}$	
15	No	Yes	Yes	Yes	Low	$\overline{Y}_{15}$	
16	No	Yes	Yes	Yes	High	$\overline{Y}_{16}$	
17	Yes	No	No	No	Low	$\overline{Y}_{17}$	
18	Yes	No	No	No	High	$\overline{Y}_{18}$	
19	Yes	No	No	Yes	Low	$\overline{Y}_{19}$	
20	Yes	No	No	Yes	High	$\overline{Y}_{20}$	
21	Yes	No	Yes	No	Low	$\overline{Y}_{21}$	
22	Yes	No	Yes	No	High	$\overline{Y}_{22}$	
23	Yes	No	Yes	Yes	Low	$\overline{Y}_{23}$	
24	Yes	No	Yes	Yes	High	$\overline{Y}_{24}$	
25	Yes	Yes	No	No	Low	$\overline{Y}_{25}$	
26	Yes	Yes	No	No	High	$\overline{Y}_{26}$	
27	Yes	Yes	No	Yes	Low	$\overline{Y}_{27}$	
28	Yes	Yes	No	Yes	High	$\overline{Y}_{28}$	
29	Yes	Yes	Yes	No	Low	$\overline{Y}_{29}$	
30	Yes	Yes	Yes	No	High	$\overline{Y}_{30}$	
31	Yes	Yes	Yes	Yes	Low	$\overline{Y}_{31}$	
32	Yes	Yes	Yes	Yes	High	$\overline{Y}_{32}$	

Suppose behavioral skills training has the same expected main effect magnitude as the others, and all else is equal.

How many more participants do you need?

NO ADDITIONAL PARTICIPANTS ARE REQUIRED to maintain power.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*SKILLS*	*Outcome*	Per-condition *n*
1	No	No	No	No	Low	$\overline{Y}_1$	11
2	No	No	No	No	High	$\overline{Y}_2$	11
3	No	No	No	Yes	Low	$\overline{Y}_3$	11
4	No	No	No	Yes	High	$\overline{Y}_4$	11
5	No	No	Yes	No	Low	$\overline{Y}_5$	11
6	No	No	Yes	No	High	$\overline{Y}_6$	11
7	No	No	Yes	Yes	Low	$\overline{Y}_7$	11
8	No	No	Yes	Yes	High	$\overline{Y}_8$	11
9	No	Yes	No	No	Low	$\overline{Y}_9$	11
10	No	Yes	No	No	High	$\overline{Y}_{10}$	11
11	No	Yes	No	Yes	Low	$\overline{Y}_{11}$	11
12	No	Yes	No	Yes	High	$\overline{Y}_{12}$	11
13	No	Yes	Yes	No	Low	$\overline{Y}_{13}$	11
14	No	Yes	Yes	No	High	$\overline{Y}_{14}$	11
15	No	Yes	Yes	Yes	Low	$\overline{Y}_{15}$	11
16	No	Yes	Yes	Yes	High	$\overline{Y}_{16}$	11
17	Yes	No	No	No	Low	$\overline{Y}_{17}$	11
18	Yes	No	No	No	High	$\overline{Y}_{18}$	11
19	Yes	No	No	Yes	Low	$\overline{Y}_{19}$	11
20	Yes	No	No	Yes	High	$\overline{Y}_{20}$	11
21	Yes	No	Yes	No	Low	$\overline{Y}_{21}$	11
22	Yes	No	Yes	No	High	$\overline{Y}_{22}$	11
23	Yes	No	Yes	Yes	Low	$\overline{Y}_{23}$	11
24	Yes	No	Yes	Yes	High	$\overline{Y}_{24}$	11
25	Yes	Yes	No	No	Low	$\overline{Y}_{25}$	11
26	Yes	Yes	No	No	High	$\overline{Y}_{26}$	11
27	Yes	Yes	No	Yes	Low	$\overline{Y}_{27}$	11
28	Yes	Yes	No	Yes	High	$\overline{Y}_{28}$	11
29	Yes	Yes	Yes	No	Low	$\overline{Y}_{29}$	11
30	Yes	Yes	Yes	No	High	$\overline{Y}_{30}$	11
31	Yes	Yes	Yes	Yes	Low	$\overline{Y}_{31}$	11
32	Yes	Yes	Yes	Yes	High	$\overline{Y}_{32}$	11

WHY?

Main effect of *MI* is the mean of Conditions 17—32 MINUS the mean of conditions 1—16.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*SKILLS*	*Outcome*	Per-condition *n*
1	No	No	No	No	Low	$\bar{Y}_1$	11
2	No	No	No	No	High	$\bar{Y}_2$	11
3	No	No	No	Yes	Low	$\bar{Y}_3$	11
4	No	No	No	Yes	High	$\bar{Y}_4$	11
5	No	No	Yes	No	Low	$\bar{Y}_5$	11
6	No	No	Yes	No	High	$\bar{Y}_6$	11
7	No	No	Yes	Yes	Low	$\bar{Y}_7$	11
8	No	No	Yes	Yes	High	$\bar{Y}_8$	11
9	No	Yes	No	No	Low	$\bar{Y}_9$	11
10	No	Yes	No	No	High	$\bar{Y}_{10}$	11
11	No	Yes	No	Yes	Low	$\bar{Y}_{11}$	11
12	No	Yes	No	Yes	High	$\bar{Y}_{12}$	11
13	No	Yes	Yes	No	Low	$\bar{Y}_{13}$	11
14	No	Yes	Yes	No	High	$\bar{Y}_{14}$	11
15	No	Yes	Yes	Yes	Low	$\bar{Y}_{15}$	11
16	No	Yes	Yes	Yes	High	$\bar{Y}_{16}$	11
17	Yes	No	No	No	Low	$\bar{Y}_{17}$	11
18	Yes	No	No	No	High	$\bar{Y}_{18}$	11
19	Yes	No	No	Yes	Low	$\bar{Y}_{19}$	11
20	Yes	No	No	Yes	High	$\bar{Y}_{20}$	11
21	Yes	No	Yes	No	Low	$\bar{Y}_{21}$	11
22	Yes	No	Yes	No	High	$\bar{Y}_{22}$	11
23	Yes	No	Yes	Yes	Low	$\bar{Y}_{23}$	11
24	Yes	No	Yes	Yes	High	$\bar{Y}_{24}$	11
25	Yes	Yes	No	No	Low	$\bar{Y}_{25}$	11
26	Yes	Yes	No	No	High	$\bar{Y}_{26}$	11
27	Yes	Yes	No	Yes	Low	$\bar{Y}_{27}$	11
28	Yes	Yes	No	Yes	High	$\bar{Y}_{28}$	11
29	Yes	Yes	Yes	No	Low	$\bar{Y}_{29}$	11
30	Yes	Yes	Yes	No	High	$\bar{Y}_{30}$	11
31	Yes	Yes	Yes	Yes	Low	$\bar{Y}_{31}$	11
32	Yes	Yes	Yes	Yes	High	$\bar{Y}_{32}$	11

There are still *N*=176 participants in each level of this factor.

Thus, all else being equal, power associated with estimation of the main effect of *MI* remains the same.

Main effect of *SKILLS* is the mean of the even-numbered conditions MINUS the mean of the odd-numbered conditions.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*SKILLS*	*Outcome*	Per-condition *n*
1	No	No	No	No	Low	$\bar{Y}_1$	11
2	No	No	No	No	High	$\bar{Y}_2$	11
3	No	No	No	Yes	Low	$\bar{Y}_3$	11
4	No	No	No	Yes	High	$\bar{Y}_4$	11
5	No	No	Yes	No	Low	$\bar{Y}_5$	11
6	No	No	Yes	No	High	$\bar{Y}_6$	11
7	No	No	Yes	Yes	Low	$\bar{Y}_7$	11
8	No	No	Yes	Yes	High	$\bar{Y}_8$	11
9	No	Yes	No	No	Low	$\bar{Y}_9$	11
10	No	Yes	No	No	High	$\bar{Y}_{10}$	11
11	No	Yes	No	Yes	Low	$\bar{Y}_{11}$	11
12	No	Yes	No	Yes	High	$\bar{Y}_{12}$	11
13	No	Yes	Yes	No	Low	$\bar{Y}_{13}$	11
14	No	Yes	Yes	No	High	$\bar{Y}_{14}$	11
15	No	Yes	Yes	Yes	Low	$\bar{Y}_{15}$	11
16	No	Yes	Yes	Yes	High	$\bar{Y}_{16}$	11
17	Yes	No	No	No	Low	$\bar{Y}_{17}$	11
18	Yes	No	No	No	High	$\bar{Y}_{18}$	11
19	Yes	No	No	Yes	Low	$\bar{Y}_{19}$	11
20	Yes	No	No	Yes	High	$\bar{Y}_{20}$	11
21	Yes	No	Yes	No	Low	$\bar{Y}_{21}$	11
22	Yes	No	Yes	No	High	$\bar{Y}_{22}$	11
23	Yes	No	Yes	Yes	Low	$\bar{Y}_{23}$	11
24	Yes	No	Yes	Yes	High	$\bar{Y}_{24}$	11
25	Yes	Yes	No	No	Low	$\bar{Y}_{25}$	11
26	Yes	Yes	No	No	High	$\bar{Y}_{26}$	11
27	Yes	Yes	No	Yes	Low	$\bar{Y}_{27}$	11
28	Yes	Yes	No	Yes	High	$\bar{Y}_{28}$	11
29	Yes	Yes	Yes	No	Low	$\bar{Y}_{29}$	11
30	Yes	Yes	Yes	No	High	$\bar{Y}_{30}$	11
31	Yes	Yes	Yes	Yes	Low	$\bar{Y}_{31}$	11
32	Yes	Yes	Yes	Yes	High	$\bar{Y}_{32}$	11

There are also *n*=176 participants in each level of this factor.

Thus, all else being equal, power is the same as for the other main effect estimates.

Please remember this

- All else being equal, adding one or more factors to a factorial experiment will increase the number of conditions in the experiment
- BUT it is very often possible to add one or more factors to a factorial experiment without the need to increase the sample size

Please remember this

- For this reason, it can be inefficient to conduct a factorial optimization trial with only 2 or 3 factors

Please remember this

- Factorial experiments can have very small per-condition *n*s and yet maintain a high degree of statistical power

This design has only n=11 per condition.

Yet it has as much power for detection of main effects as the design we saw before with n=22 per condition.

Experimental condition	*MI*	*PEER*	*TEXT*	*MIND*	*SKILLS*	*Outcome*	Per-condition *n*
1	No	No	No	No	Low	$\overline{Y}_1$	11
2	No	No	No	No	High	$\overline{Y}_2$	11
3	No	No	No	Yes	Low	$\overline{Y}_3$	11
4	No	No	No	Yes	High	$\overline{Y}_4$	11
5	No	No	Yes	No	Low	$\overline{Y}_5$	11
6	No	No	Yes	No	High	$\overline{Y}_6$	11
7	No	No	Yes	Yes	Low	$\overline{Y}_7$	11
8	No	No	Yes	Yes	High	$\overline{Y}_8$	11
9	No	Yes	No	No	Low	$\overline{Y}_9$	11
10	No	Yes	No	No	High	$\overline{Y}_{10}$	11
11	No	Yes	No	Yes	Low	$\overline{Y}_{11}$	11
12	No	Yes	No	Yes	High	$\overline{Y}_{12}$	11
13	No	Yes	Yes	No	Low	$\overline{Y}_{13}$	11
14	No	Yes	Yes	No	High	$\overline{Y}_{14}$	11
15	No	Yes	Yes	Yes	Low	$\overline{Y}_{15}$	11
16	No	Yes	Yes	Yes	High	$\overline{Y}_{16}$	11
17	Yes	No	No	No	Low	$\overline{Y}_{17}$	11
18	Yes	No	No	No	High	$\overline{Y}_{18}$	11
19	Yes	No	No	Yes	Low	$\overline{Y}_{19}$	11
20	Yes	No	No	Yes	High	$\overline{Y}_{20}$	11
21	Yes	No	Yes	No	Low	$\overline{Y}_{21}$	11
22	Yes	No	Yes	No	High	$\overline{Y}_{22}$	11
23	Yes	No	Yes	Yes	Low	$\overline{Y}_{23}$	11
24	Yes	No	Yes	Yes	High	$\overline{Y}_{24}$	11
25	Yes	Yes	No	No	Low	$\overline{Y}_{25}$	11
26	Yes	Yes	No	No	High	$\overline{Y}_{26}$	11
27	Yes	Yes	No	Yes	Low	$\overline{Y}_{27}$	11
28	Yes	Yes	No	Yes	High	$\overline{Y}_{28}$	11
29	Yes	Yes	Yes	No	Low	$\overline{Y}_{29}$	11
30	Yes	Yes	Yes	No	High	$\overline{Y}_{30}$	11
31	Yes	Yes	Yes	Yes	Low	$\overline{Y}_{31}$	11
32	Yes	Yes	Yes	Yes	High	$\overline{Y}_{32}$	11

AND it has as much power as a comparable *t*-test based on overall N=352.

Please remember this

- Factorial experiments can have very small per-condition *n*s and yet maintain a high degree of statistical power
- Power is driven primarily by the *N* per level of a factor
- This is a unique characteristic of the factorial experiment family

This can be counterintuitive

- An RCT with *n*=11 per condition would be extremely unlikely to be sufficiently powered
- Yet depending on circumstances, factorial experiments can have per-condition *n*s as low as 2 or 3 and still be sufficiently powered
    - Provided that the *N* per level is large enough

In this lesson you learned how to:

- Explain why it is often possible to examine additional factors in a factorial experiment without the need to increase the number of participants to maintain power
- Explain why factorial experiments can have very small per-condition *n*’s and still be well-powered

In the next lesson you will learn how to:

- Explain why increasing the number of levels of a factor to three or more—for even one factor—requires a substantial increase in the number of participants to maintain power