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

Module 3
Introduction to the optimization trial

Lesson 5: Why the 2^k experiment is so economical

NYU SCHOOL OF GLOBAL PUBLIC HEALTH

Intervention Optimization Initiative

This course was developed by

Linda M. Collins

School of Global Public Health

New York University

(narrator)

Kate Guastaferro

College of Health and Human Development

The Pennsylvania State University

In the previous lesson you learned how to:

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

In this 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.

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

Let's return to the example.

It has 4 factors:

MI with 2 levels
PEER with 2 levels
TEXT with 2 levels
MIND with 2 levels

So it's a 2×2×2×2, or 2^4

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

We showed that it is possible to add a factor (or more than one) to this experiment with NO ADDITIONAL PARTICIPANTS 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

This experiment is still adequately powered with N=352.

What would happen if instead of adding a factor, you wanted to add a *level* to a factor?

- e.g. *TEXT* would be No, Low, High

This still has 4 factors:

MI with 2 levels
PEER with 2 levels
***TEXT* with 3 levels**
MIND with 2 levels

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

So now it's a 2×2×3×2, or a $2^3 3$

Thus there are 2×2×3×2=24 experimental conditions

The 352 participants are divided among 24 conditions.

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

There is now slight variability in per-condition *n*; this is unimportant.

The main effect of *MI* = mean of conditions 13—24 MINUS mean of 1—12.

Each level of *MI* still *N*=176.

Power remains the same.

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

TEXT has 3 levels now, so two main effects: let's say High vs. No and Low vs. No

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

Let's look at High vs. No.

Assume this effect is expected to be no smaller than the other main effects.

This main effect is the mean of conditions 5, 6, 11, 12, 17, 18, 23, 24 MINUS the mean of conditions 1, 2, 7, 8, 13, 14, 19, 20.

This means the per-level $N \approx 120$.

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

All else being equal, power will be reduced.

Now let's consider the Low vs. No comparison.

This is also based on a per-level *N*≈120.

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

It is likely the Low vs. No comparison is expected to have a smaller effect size than High vs. Low.

If so, power will be reduced further.

How to bring power up to what it was before the addition of the 3rd level

- All else being equal, this requires obtaining more participants
- Suppose both main effects expected to be about the same size as the other (e.g. main effect of *MI*)

How to bring power up to what it was before the addition of the 3rd level

- It would be necessary to add about 176 more participants
- **This is an increase of 50%**

How to bring power up to what it was before the addition of the 3rd level

- But note that the Low vs. No comparison is likely to have a smaller effect size
- This would require even more participants

Conclusions

- It is possible to add one or more factors and maintain power without adding participants
- **So, adding one or more factors to a factorial optimization trial is often an efficient strategy**

Conclusions

- However, adding a *level* of a factor usually requires at least 50% more participants
- **So, adding even one level to a factor can be costly**

If you are considering including > 2 levels in a factor in an optimization trial:

- Remember: the 2^k factorial experiment is generally the most efficient
- Do you really need that in-between level?

If you are considering including > 2 levels in a factor in an optimization trial:

- One strategy:
  - Start by using 2 levels to ascertain that there is a difference between High and No
  - Then if there is, examine Low vs. No in a subsequent experiment
  - If there is no difference between High vs. No, do you care about Low vs. No?

In this lesson you learned 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.

In the next lesson you will learn how to:

- Explain the concept of experimental control in a factorial design.