

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

Module 5

**Rigorous and responsible conduct of
intervention optimization research**

Lesson 8: How to prevent protocol deviations



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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



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In the previous lesson you learned how to:

- Avoid accidental contamination between experimental conditions



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In this lesson you will learn how to:

- Prevent protocol deviations



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Protocol deviations occur when

- A participant who was randomly assigned to a treatment is not provided with that treatment
- A participant who was not randomly assigned to a treatment is provided with that treatment
- A treatment is delivered in a manner other than the intended manner

Protocol deviations can occur in...

- ...an optimization trial OR an evaluation trial
- But the potential is greater in experiments with a higher number of conditions

The difference between protocol deviations and contamination

- Protocol deviations occur because experimental procedures (protocol) are not followed
- Contamination occurs when uncontrolled contact between participants leads to sharing of information and resources
- It is possible to have contamination even when experimental protocols are followed to the letter

Accidental protocol deviations

- These occur when a mistake is made because, e.g.:
 - Staff are insufficiently trained or monitored
 - Instructions are confusing or incomplete
 - There are mix-ups about which experimental condition a participant has been assigned to
 - A computer program causes the wrong treatment to be delivered

Deliberate protocol deviations occur when

- Staff take it upon themselves to provide or withhold treatment rather than follow the prescribed experimental protocol
- This is usually done with the best of intentions

Example: A participant is randomly assigned to condition 3.

A project staff member notices this participant is highly anxious, and believes the ethical course of action is to provide the mindfulness meditation component to this participant.

Experimental condition	<i>MI</i>	<i>PEER</i>	<i>TEXT</i>	<i>MIND</i>	<i>Outcome</i>
1	No	No	No	No	\bar{Y}_1
2	No	No	No	Yes	\bar{Y}_2
3	No	No	Yes	No	\bar{Y}_3
4	No	No	Yes	Yes	\bar{Y}_4
5	No	Yes	No	No	\bar{Y}_5
6	No	Yes	No	Yes	\bar{Y}_6
7	No	Yes	Yes	No	\bar{Y}_7
8	No	Yes	Yes	Yes	\bar{Y}_8
9	Yes	No	No	No	\bar{Y}_9
10	Yes	No	No	Yes	\bar{Y}_{10}
11	Yes	No	Yes	No	\bar{Y}_{11}
12	Yes	No	Yes	Yes	\bar{Y}_{12}
13	Yes	Yes	No	No	\bar{Y}_{13}
14	Yes	Yes	No	Yes	\bar{Y}_{14}
15	Yes	Yes	Yes	No	\bar{Y}_{15}
16	Yes	Yes	Yes	Yes	\bar{Y}_{16}

The delicate balance

- Staff have to believe in the candidate components if they are to deliver them well.
- AT THE SAME TIME they also have to believe it is appropriate to withhold any candidate component that is not included in the assigned treatment.

The delicate balance

- Thus they have to maintain two opposing points of view
- Doing this successfully will require training in
 - The scientific method, i.e. random assignment
 - Clinical equipoise

Avoiding protocol deviations

- Remember that optimization trials are more complex than RCTs, so the staff will require much more training
- Use technology (e.g. REDCap) to manage the experiment

Avoiding protocol deviations

- Monitor staff
 - Record all sessions, randomly select for a thorough review periodically throughout the study
 - Go over the reviews with staff
- Stay in close touch with staff
 - Meet regularly with staff to address questions, including ethical concerns
 - Encourage open discussion of any protocol deviations

Avoiding protocol deviations

- It may help to have each staff person responsible for delivery of only one component
 - As opposed to a variety of experimental conditions
- Use technology to automate delivery of components where it makes sense to do so
 - BUT remember mistakes can be made here too

Avoiding protocol deviations

- Adopt the “aviation approach”
 - Everything important done or checked by at least 2 different people independently
- Connect with others who have successfully run optimization trials

Keep a log of all protocol deviations

- Encourage staff to be open about any deviations that occur
- Discuss how they can be avoided in the future
- Record them for later reference

In this lesson you learned how to:

- Prevent protocol deviations



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In the next lesson you will:

- Review what you have learned in Module 5



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