The Multiphase Optimization Strategy (MOST) for developing more effective, efficient, economical, and scalable behavioral and biobehavioral interventions

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Overview

- Brief orientation to the multiphase optimization strategy (MOST)
- An example of the application of MOST
- Some MOST fundamentals
- Choosing an experimental design based on the resource management principle
- Factorial experiments and multilevel data
- Concluding remarks and open discussion
Brief orientation to the multiphase optimization strategy (MOST)
Multicomponent behavioral and biobehavioral interventions (BBIs)

- May be aimed at prevention or treatment
- May be aimed at health, social, behavioral, or educational outcomes
- May include both behavioral and pharmaceutical components (biobehavioral interventions)
- May include components aimed at individuals, family, school, community
- Examples of multicomponent BBIs
  - Smoking cessation treatment
  - Treatment for depression
  - School-based drug abuse prevention
  - Prevention/treatment of obesity
Scenario 1: Cancer prevention: Developing a smoking cessation BBI

- Goal: choose from set of components/component levels to maximize probability of successful quitting
Definition: intervention components

- Intervention components: *Any aspects of an intervention that can be separated out for study*
  - Parts of intervention content
    - e.g., topics in a curriculum
  - Features that promote compliance/adherence
    - e.g., reminder phone calls or text messages
  - Features aimed at improving fidelity
    - e.g., enhanced teacher training
Scenario 1: Cancer prevention: Developing a smoking cessation intervention

- Goal: choose from set of components/component levels to maximize probability of successful quitting
Scenario 1: Cancer prevention: Developing a smoking cessation intervention

- **Goal**: choose from set of components/component levels to maximize probability of successful quitting

- **Components**:
  - Precession nicotine patch (No, Yes)
  - Precession nicotine gum (No, Yes)
  - Precession in-person counseling (No, Yes)
  - Cessation in-person counseling (Minimal, Intensive)
  - Cessation phone counseling (Minimal, Intensive)
  - Maintenance medication duration (Short, Long)
Scenario 1: Cancer prevention: Developing a smoking cessation intervention

- How to build a BBI out of these components?
- Construct new intervention by setting each component at highest level, put them together
  - Intervention = precessation patch and gum and counseling, intensive cessation in-person and phone counseling, long medication duration
- Then compare to control group via RCT
- Possibly conduct post-hoc analyses
- Let’s call this the **classical treatment package approach**
Scenario 2: Developing a way to manufacture truck leaf springs

- Goal: Choose from set of components/component levels to optimize amount of variability in length of leaf springs (less variability is better)

Leaf Spring: part of truck suspension system

Scenario 2: Developing a way to manufacture truck leaf springs

- **Goal:** Choose from set of components/component levels to optimize amount of variability in length of leaf springs (less variability is better)
- **Components** (suppose for each one higher hypothesized to be better):
  - Furnace temperature (lower, higher)
  - Heating time (shorter, longer)
  - Transfer time on conveyor belt (shorter, longer)
  - Hold down time in high pressure press (shorter, longer)
  - Quench oil temperature range (lower temps, higher temps)
Scenario 2: If engineers thought like behavioral scientists

- Would use the classical treatment package approach
- Construct new manufacturing process = higher furnace temp, longer heating time, longer conveyor belt time, longer time in high pressure press, higher temp quench oil
- Compare this process as a package to the old way, see if it is demonstrably better
- Conduct post-hoc analyses
Scenario 2: Developing a way to manufacture truck leaf springs

- But an engineer would not use the classical treatment package approach, because:
  - If the new process IS better, doesn’t indicate which components make a difference
  - If the new process IS NOT better, doesn’t indicate which (if any) of the components did effect an improvement
  - When repeated, no guarantee of systematic incremental improvement, so not a good long-run strategy
  - Does not take cost or other constraints into account
Scenario 2: Developing a way to manufacture truck leaf springs

- What WOULD an engineer do?
- Start with a clear idea of the goal, including constraints
  - e.g. Least variability AND must cost less than $1/spring
- Using the resources available, design an efficient experiment to gather needed information (e.g. individual effects of components)
- Based on the results of experiment, choose components and component levels to achieve stated goal. THIS IS optimization
- THEN compare new process to old process
Back to Scenario 1: If behavioral scientists thought like engineers

- We might want to **optimize** the smoking cessation intervention
- Using an approach that
  - Indicates which components are active
  - Ensures an incremental improvement, and therefore is the fastest way to the best intervention IN THE LONG RUN
  - Readily incorporates costs/constraints of any kind
  - Enables optimization using any desired criterion
Desiderata for BBIs

- **Effectiveness**
  - Extent to which the BBI does more good than harm (under real-world conditions, Flay (1986))

- **Efficiency**
  - Extent to which BBI avoids wasting time, money, or other valuable resources

- **Economy**
  - Extent to which BBI is effective without exceeding budgetary constraints, and offers a good value

- **Scalability**
  - Extent to which the BBI can be implemented widely with fidelity
Definition of optimization of a BBI

- Optimization of a BBI is the process of identifying a BBI that provides the best expected outcome obtainable within key constraints imposed by the need for efficiency, economy, and/or scalability.

- Note:
  - Process
  - Key constraints
  - Best expected level obtainable
Comparison of evaluation and optimization

- Evaluation requires comparison of intervention package to control
  - RCT the way to do this

- Optimization requires examination of individual components
  - In a RCT all components are confounded
  - Requires a different experimental design
The multiphase optimization strategy (MOST)

- A comprehensive strategy for optimization and evaluation
- Engineering-inspired framework
  - First, estimate individual contributions of intervention components, and interactions between components where anticipated (or feared)
  - Decide which to retain, at what levels/settings
  - THEN assemble into an intervention, and evaluate in a RCT
MOST: A comprehensive strategy for optimization and evaluation

- MOST is not
  - An off-the-shelf procedure that is identical for every application
  - A particular experimental design
MOST: A comprehensive strategy for optimization and evaluation

- MOST is
  - A framework for thinking through how to optimize a behavioral intervention
  - A practical way of approaching the engineering of behavioral interventions so that they meet specific optimization criteria
  - Designed to make the best use of available resources
  - Very new, and still an open area! Not everything is figured out
An example of the application of MOST
Example: Clinic-based smoking cessation study funded by the National Cancer Institute (part of the US National Institutes of Health)

Timothy Baker, Ph.D.  
Michael Fiore, M.D.  
University of Wisconsin  
Center for Tobacco Research and Intervention  
*Purpose of intervention: To help people quit smoking successfully*
Baker and Fiore’s model of the smoking cessation process: Phases

- From Baker et al. (2011)
Component 1: Precessation nicotine patch

- **Background**: Research suggests nicotine patch may be helpful during precessation (as opposed to cessation where it is always used).
- **Decision**: Should intervention include use of the nicotine patch during precessation?
- **Research question**: Does precessation use of the nicotine patch improve initial cessation outcomes relative to no precessation use of the nicotine patch?
- **Intervention component**: precessation nicotine patch.
- **Levels**: patch, no patch.
Component 2: Precessation nicotine gum

- **Background**: Research suggests that use of self-administered nicotine gum ad lib (as needed) may be helpful during precessation.
- **Decision**: Should intervention include use of ad lib nicotine gum during precessation?
- **Research question**: Does precessation use of nicotine gum improve initial cessation outcomes relative to no precessation use of nicotine gum?
- **Intervention component**: precessation nicotine gum.
- **Levels**: nicotine gum, no nicotine gum.
Component 3: Precessation counseling

- **Background**: Research indicates that counseling addressing issues such as how to develop skills for coping with withdrawal may be helpful during precessation.
- **Decision**: Should intervention include precessation counseling?
- **Research question**: Does precessation counseling improve initial cessation outcomes relative to no precessation counseling?
- **Intervention component**: Precessation counseling.
- **Levels**: Intensive, none.
Component 4: Cessation counseling

- **Background:** It is known that counseling during the cessation phase is efficacious, but the minimal effective level is not known. Given the expense of counseling, this is an important question.

- **Decision:** Should intervention include intensive or minimal level of counseling?

- **Research question:** Does intensive counseling (defined as three 20-min sessions) during the cessation phase improve initial cessation outcomes relative to minimal counseling (one 3-min session, level based on the 2008 PHS Guideline recommendations for brief clinician counseling)?

- **Intervention component:** Cessation counseling.

- **Levels:** intensive, minimal.
Component 5: Cessation telephone counseling

- **Background**: Delivering counseling over the telephone (e.g. cessation quitline) during cessation is very efficient. The minimal effective level is unknown.

- **Decision**: Should intervention include intensive or minimal level of telephone-delivered counseling during cessation?

- **Research question**: Does intensive phone counseling during cessation (defined as three 15-min sessions) improve initial cessation outcomes relative to minimal counseling (defined as one 10-min session)?

- **Intervention component**: cessation phone counseling.

- **Levels**: intensive, minimal.
Component 6: Duration of cessation NRT

- **Background:** It is standard to recommend use of NRT for eight weeks past the quit date. There is mixed evidence that a longer duration may improve outcomes.
- **Decision:** Should intervention include standard or extended period of cessation NRT?
- **Research question:** Does an extended duration of NRT (defined as 16 weeks) improve long-term cessation outcomes more than the standard 8-week duration?
- **Intervention component:** duration of cessation NRT.
- **Levels:** 16 weeks, 8 weeks.
Classical treatment package approach

- Create an intervention that includes all components at most intensive levels:
  - During precessation, patient uses a nicotine patch and ad lib nicotine lozenges or gum (depending on patient preference). Patient gets intensive in-person counseling.
  - During cessation, patient gets both intensive in-person and intensive phone counseling.
  - During maintenance, patient continues NRT for 16 weeks.
- Evaluate via RCT
Classical treatment package approach

- This RCT would evaluate whether the treatment has a statistically significant effect
- It would NOT show
  - Which components are active
  - Which component levels should be selected
Instead, MOST

- FIRST build an optimized smoking cessation intervention, and THEN evaluate the optimized intervention
- A simple criterion: intervention comprising components with empirically demonstrated effects
- We will come back to optimization criteria
Some MOST fundamentals
Resource management principle

- How engineers think, Lesson 1
  - This is what I need to find out: ______
  - These are the resources I have: ______
  - How can I manage my resources strategically to find out what I need to know?
Resource management principle

- Logic: huge (e.g. 64-arm) RCT would be definitive, but is not feasible to power
- Instead, manage research resources strategically to:
  - Gain the most information
  - Gain the most reliable information
  - Move science forward fastest
- Decide what information most important, and target resources there
- Choose designs for efficiency
- Take calculated risks
Resource management principle

- Note that the starting point is the resources you have
- By definition, MOST does not require an increase in research resources
- But in most cases will require a realignment of research resources
Continuous optimization principle

- How engineers think, Lesson 2:
  - I have finished developing this product and it is ready to market.
  - Now I am going to start developing the new, improved product.
  - Optimization is a **cyclic process**
Overview of experimentation to examine individual intervention components

- Objective is to identify the most promising components and levels/settings
- NOT to compare each combination to a control or against each other
Overview of experimentation to examine individual intervention components

- Conduct a *component screening experiment*

- Objectives:
  - For each component, determine whether there is a difference between the highest and lowest levels
  - This information to be used in making decisions about selection of components and levels for intervention package
Overview of experimentation to examine individual intervention components

- For nicotine patch, nicotine gum, precessation counseling
  - Comparison of On vs. Off
  - Experiment must provide evidence of whether or not each has an effect on outcomes
  - If yes, consider including in intervention package
  - Depending on optimization criterion, effect size may be considered in relation to:
    - Cost
    - Time
Overview of experimentation to examine individual intervention components

- For cessation counseling, cessation phone counseling
  - Comparison of Minimal vs. Intensive
  - Experiment must provide evidence of whether Intensive is doing more than Minimal
    - If Intensive NOT > Minimal, select Minimal
    - If Intensive > Minimal, consider selecting intensive
  - Depending on optimization criterion, effect size may be considered in relation to
    - Cost
    - Time
Overview of experimentation to examine individual intervention components

- For duration of cessation/maintenance NRT
  - Comparison of 8 weeks vs. 16 weeks
  - Experiment must provide evidence of whether 16 weeks is doing more than 8 weeks
  - If 16 weeks NOT > 8 weeks, select 8 weeks
  - If 16 weeks > 8 weeks, consider selecting 16 weeks
  - Depending on optimization criterion, effect size may be considered in relation to
    - Cost
    - Time
Assembly of optimized intervention

- Experimentation has provided empirical data about effects of each intervention component
- Based on this information, identify combination of components and level/doses that meets optimization criterion
- This forms the optimized intervention
Deciding on your optimization criterion

- This is the goal you want to achieve
- Constraints are
  - Set of intervention components under consideration
  - Limitations on
    - Cost to deliver intervention
    - Time to deliver intervention
    - Etc.
Possible optimization criteria

- No inactive components
- Most effective intervention that can be implemented for less than some $$$
- Most cost-effective
- Most effective intervention that can be completed in less than some upper limit on time
Choosing an experimental design based on the resource management principle
Groundwork before selecting an experimental design

- **OBJECTIVE**: To gather information that will be used in decision making
  - Primarily, main effects
  - Secondarily, interactions
- Less interested in precise estimates of every possible effect
- Instead, need as much practical information as possible
- **STARTING POINT**: What decisions do I need to make?
Choice of design for component screening experiment is critical

- Any experimental design is a possibility BUT...
- ...must be selected based on Resource Management Principle!!!
The resource management principle says:

- The investigator must carefully choose an experimental design so as to
  - Gather the information needed...
  - ...while making the most of (but not exceeding) the available resources
The resource management principle says:

- Thus the experimenter must
  - Have a clearly specified set of research questions
  - Know what resources are available
  - Know what resources are required by each design under consideration
    - Different designs require different resources
The component screening experiment

- Purpose: efficient screening of intervention components
  - Weed out underperforming components
  - Get a sense of magnitude of each component’s effect
  - Examine whether effect of a component is augmented or reduced in presence of another

- This information is then used to optimize the intervention
Resource management principle

- To select a design, consider several, and examine
  - The scientific information each will provide
    - And whether it is what you want!
  - What each design costs
    - Number of subjects
    - Number of experimental conditions
- NOTE that the starting point is the resources you have
Design option A: Six individual treatment/control experiments

1. Patch vs. no patch
2. Gum vs. no gum
3. Precessation counseling vs. no precessation counseling
4. Intensive cessation counseling vs. minimal
5. Intensive cessation phone counseling vs. minimal
6. 16 weeks of NRT during cessation/maintenance vs. 8 weeks
Design option B: Comparative treatment experiment

Experimental conditions:

<table>
<thead>
<tr>
<th>Treatment conditions</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precess. Patch = yes</td>
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<tr>
<td></td>
<td>All = low</td>
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<tr>
<td>Precess. gum = yes</td>
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<td>= 16 wks</td>
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<td>Cessation phone</td>
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<td>all others=low</td>
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<td>all others=low</td>
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<td>Control</td>
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<tr>
<td>All = low</td>
<td></td>
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Design option C

- $2^6$ factorial experiment
- This will have 64 experimental conditions
Design option D: Fractional factorial experiment

- A special type of factorial experiment
- Specially selected subset of experimental conditions is run
What are fractional factorial (FF) designs?

- Factorial designs in which only a \textit{subset} of experimental conditions are run
- But not just any subset! Carefully chosen to preserve balance properties
- FF designs require at most \( \frac{1}{2} \) the cells of a complete factorial, often many fewer
- Statisticians have developed many FF designs to choose from; software can be used to select one
Why run just a subset of conditions?

- Economy
- A lot of factors = REALLY a lot of conditions
  - $2^6 = 64$; $2^7 = 128$; $2^8 = 256$; etc.
- Example: using a FF designs it is possible to conduct a $2^8$ experiment with only 16 conditions
- BUT there are important tradeoffs
Choosing an experimental design: Comparison of options

- We chose a fractional factorial design requiring 32 conditions
Experimental design used to examine components of smoking cessation intervention

- This is a factorial experiment with six factors.
- It is a $2^{6-1}$ fractional factorial.
- The design has 32 experimental conditions.

<table>
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<tr>
<th>Condition</th>
<th>Precession Medication Type (Patch vs. none)</th>
<th>Precession Medication Type (Ad Lib NRT vs. none)</th>
<th>Precession Counseling (Intensive vs. none)</th>
<th>In-Person Counseling (Minimal vs. Intensive)</th>
<th>Phone Counseling (Minimal vs. Intensive)</th>
<th>Medication (8 weeks vs. 16 weeks)</th>
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You might be interested in knowing...

- When used to address suitable research questions, balanced factorial experimental designs often require many FEWER subjects than alternative designs.
- It is often possible to add one or more factors to a factorial experiment and maintain the same level of power WITHOUT ANY INCREASE IN THE NUMBER OF SUBJECTS.
- The primary motivation for conducting a factorial experiment may be economy rather than examination of interactions.
- When effect coding is used to analyze data from a balanced factorial experiment, all effect estimates are uncorrelated.
Powering factorial experiments

- Power for main effects: sample size requirements for a $k$-factor experiment about the same as for a $t$-test
- Power the experiment for the smallest effect size
- Adding a factor generally does not increase sample size requirements, unless that factor is expected to have a smaller effect size
- For component screening experiments, power the study for the smallest effect size that you would accept for inclusion in the intervention
Powering factorial experiments

- A resource to help you do a power analysis when planning a factorial experiment:
- Go to http://methodology.psu.edu/downloads
- Look for the macro FactorialPowerPlan
Factorial experiments and multilevel data
Can I use a factorial design if I have multilevel data?

- Two different situations:
  - Within-cluster randomization
    - e.g., clinic-based research
  - Individuals assigned to experimental conditions
    - Not worried about contamination
    - Effects at individual level
  - Replicate experiment within each cluster

- (see Dziak, Nahum-Shani, & Collins, 2012)
Can I use a factorial design if I have multilevel data?

Two different situations:

- Between-cluster randomization (often called cluster randomization)
  - e.g. school-based research
- Entire clusters (e.g. schools) assigned to treatment conditions
  - Contamination would be potential issue with individual assignment
  - May be effects at cluster level in addition to individual effects
- Question: Will I have enough units to assign to conditions?
- Question: Is power loss so great that examination of individual components is impractical?
Can I use a factorial design if I have multilevel data?

- The concern: any two individuals sampled from within a unit tend to be more alike than any two individuals sampled from different units.
- The measure of this is the intraclass correlation.
- Can reduce power, sometimes severely.
Can I use a factorial design if I have multilevel data?

- Cluster randomization:
  - Question: Will I have enough units to assign to experimental conditions?
    - With a complete factorial, maybe no
    - With a fractional factorial, maybe yes
      - In fact, this may be the only option
  - Question: Is power loss due to the design effect so great that examination of individual components is impossible?
• Low ICC=.05
• Medium ICC=.15
• High ICC=.30
• For main effects, $d = .2$
• 5 factors

From Dziak, Nahum-Shani, & Collins (2012)
Can I use a factorial design if I have multilevel data?

- YES!
- It has often been assumed you would not have enough power. NOT NECESSARILY TRUE!
- Situation is challenging though
- In a component screening experiment, may consider raising Type I error rate
Concluding remarks
## Some Differences in Perspective Between the Classical Approach and MOST

<table>
<thead>
<tr>
<th></th>
<th>Classical Approach</th>
<th>MOST</th>
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</thead>
<tbody>
<tr>
<td><strong>Objective</strong></td>
<td>To develop a BBI that demonstrates a statistically and clinically significant effect in an RCT</td>
<td>To engineer BBI that meets specific predetermined standards of effectiveness, efficiency, cost-effectiveness, and/or scalability, AND demonstrates a statistically and clinically significant result in an RCT</td>
</tr>
<tr>
<td><strong>Next steps after identification and pilot testing of components</strong></td>
<td>BBI assembled and then evaluated as a package</td>
<td>Optimized BBI engineered then evaluated as a package if sufficiently promising</td>
</tr>
<tr>
<td><strong>Experimental designs used</strong></td>
<td>Primarily the RCT</td>
<td>For optimization, experimental designs selected based on resource management principle; for evaluation of BBI as a package, primarily RCT</td>
</tr>
<tr>
<td><strong>Examination of effectiveness of individual components</strong></td>
<td>Relatively low priority; primarily via post-hoc analyses on data from RCT of BBI</td>
<td>High priority; primarily via experimental manipulation of components</td>
</tr>
<tr>
<td><strong>Examination of interactions between intervention components</strong></td>
<td>Low priority</td>
<td>High priority; experimental designs selected to enable this</td>
</tr>
<tr>
<td><strong>Inert/counterproductive components</strong></td>
<td>Generally tolerated as long as overall effectiveness of BBI can be demonstrated</td>
<td>Generally not tolerated</td>
</tr>
<tr>
<td><strong>Cost-effectiveness of BBI</strong></td>
<td>Assessed during or after evaluation</td>
<td>BBI engineered to meet specific standard before evaluation</td>
</tr>
<tr>
<td><strong>Scalability of BBI</strong></td>
<td>Dealt with after evaluation of BBI, sometimes via ad hoc modifications</td>
<td>BBI engineered to meet specific key criteria before evaluation</td>
</tr>
<tr>
<td><strong>Research aimed at measureable incremental improvement of BBIs over time</strong></td>
<td>Not emphasized</td>
<td>Emphasized in continuous optimization principle</td>
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</tbody>
</table>
For more information:

- http://methodology.psu.edu
  - Sign up for eNews
  - Section on MOST with
    - Suggested readings
    - FAQ
    - Advice for people writing grant proposals involving MOST
- TED talk online (search for Collins TED talk)
- Consider joining SBM Special Interest Group (OBI)
- WATCH FOR 2 books to be published in early 2018 (Springer)
- I HOPE: One-week training on optimization of behavioral and biobehavioral interventions in 2018
  - To receive an announcement about how to apply, sign up for The Methodology Center’s e-news