Introduction to the Multiphase Optimization Strategy (MOST)

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New Experimental Approaches to Designing Effective Multi-Component Interventions
May 3, 2017
Outline

- Definitions
- What’s wrong with business as usual?
- What is MOST? What is optimization?
- OK, how do you do this?
- FAQ
What is a behavioral/biobehavioral intervention?

- A program with the objective of improving and maintaining human health and well-being, broadly defined...
- ...aimed at individuals, families, schools, organizations, or communities...
- ...using a strategy that at least in part aims to modify attitudes, cognitions, or behavior.
What is a behavioral/biobehavioral intervention?

- Examples:
  - Smoking cessation
  - School-based drug abuse prevention
  - Online intervention to prevent excessive drinking and risky sex in college students
  - Adult weight loss
  - Intervention to get HIV+ individuals into the health care system and treated with antiretrovirals

- Most behavioral/biobehavioral interventions are made up of multiple components.
- We could also include multicomponent biomedical interventions
What is an intervention component?

- Definition: *Any aspect of an intervention that can be separated out for study*
  - Parts of intervention content
    - e.g., each major topic to be covered
  - Features that promote compliance/adherence
    - e.g., MEMScaps
  - Features aimed at improving fidelity of delivery
    - e.g., 800 number for program delivery staff to call with questions
What is an intervention component?

- Some components may be pharmaceutical (e.g. NRT; PrEP)
- Components can be defined at any level: individual, family, school, etc.
- Can impact efficacy, effectiveness, efficiency, economy, scalability
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How behavioral/biobehavioral inventions are typically developed and evaluated

- Intervention components are chosen based on scientific theory, clinical experience, etc.
- Combined into a package
- Package is evaluated via a randomized controlled trial (RCT)
- Let’s call this the treatment package approach
Treatment package approach

Behavioral/biobehavioral intervention

Evaluation via RCT
What is wrong with evaluating a treatment package via an RCT?

Absolutely nothing!
The RCT is best suited for

- Determining whether a treatment package performs better than
  - A control or comparison group
  - An alternative intervention
Treatment package approach

Behavioral/biobehavioral intervention

Evaluation via RCT
What the RCT cannot not tell us

An RCT that finds a **significant** effect **DOES NOT** tell us

- Which components are making positive contributions to overall effect
- Whether the inclusion of one component has an impact on the effect of another
- Whether a component’s contribution offsets its cost
- How to make the intervention more effective, efficient, and scalable
What the RCT cannot not tell us

An RCT that finds a non-significant effect DOES NOT tell us

- Whether any components are worth retaining
- Whether one component had a negative effect that offset the positive effect of others
- Specifically what went wrong and how to do it better the next time
What’s the alternative?

- When engineers build products they take an approach that is
  - Systematic
  - Efficient
  - Focused on the clear objective of optimizing the product
- MOST integrates methodological perspectives from the behavioral and engineering sciences...
- ... to build optimized behavioral interventions
Outline

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The multiphase optimization strategy (MOST)

- An engineering-inspired framework for development, optimization, and evaluation of behavioral interventions
- Using MOST it is possible to engineer an intervention to meet a specific criterion
Desiderata for behavioral/ biobehavioral interventions

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

- Efficiency
  - Extent to which the intervention avoids wasting time, money, or other valuable resources

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

- Scalability
  - Extent to which the intervention can be implemented widely with fidelity
Definition of optimization of a behavioral/biobehavioral intervention

- Optimization of a behavioral/biobehavioral intervention is
  - the process of identifying the intervention that provides the highest expected level of effectiveness obtainable...
  - ...within key constraints imposed by the need for efficiency, economy, and/or scalability.

- Note tension between effectiveness and the other three desiderata
The Multiphase Optimization Strategy (MOST)

**PREPARATION**
- Derive/revise conceptual model
- Identify set of candidate components
- Identify optimization criterion

**OPTIMIZATION**
- Optimization trial(s)
  - Factorial experiment
  - Fractional factorial experiment
  - SMART
  - Micro-randomized trial
  - System identification
  - Other
- Continual improvement process
- Based on results, identify intervention that meets optimization criterion

**EVALUATION**
Confirm effectiveness of optimized intervention via RCT

Optimized intervention expected to be sufficiently effective?

Continual optimization principle

Resource management principle
The Multiphase Optimization Strategy (MOST)

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**EVALUATION**
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- **Continual optimization principle**
- **Resource management principle**

Optimized intervention expected to be sufficiently effective?
Phases of MOST: Preparation, optimization, evaluation

Preparation

- Purpose: to lay groundwork for optimization
  - Review prior research, take stock of clinical experience, conduct secondary analyses, etc.
  - Derive conceptual model
  - Select intervention components to examine
  - Conduct pilot/feasibility work
  - Identify clearly operationalized optimization criterion
Selecting an optimization criterion

- Optimization always involves a clearly stated *optimization criterion*
- This is the goal you want to achieve
- Once achieved, it is the bar that sets a standard for later efforts
One possible optimization criterion

- No specific key constraints BUT do not want waste
- Efficient intervention with no “dead wood”
- CONSIDER a clinic-based smoking cessation intervention.
  - Suppose to reduce waste of time and money, the investigators want to be confident that every component is necessary.
  - Achieve this by selecting only active intervention components.
Another possible optimization criterion

- Key constraint: Money
- Most effective intervention that can be delivered for $\leq$ some $$
- CONSIDER a clinic-based smoking cessation intervention.
  - Suppose insurers say they will pay for a program that costs no more than $500/person to implement, including materials and staff time.
  - Achieve this by selecting set of components that represents the most effective intervention that can be delivered for $\leq$ $500/person.
Another possible optimization criterion

- Key constraint: Time
- Most effective intervention that can be delivered in ≤ some amount of time
- CONSIDER a clinic-based smoking cessation intervention.
  - Suppose interviews with clinic staff suggest that the program has the best chance of being implemented well if it takes no more than a total of 90 minutes to deliver.
  - Achieve this by selecting set of components that represents the most effective intervention that can be delivered in ≤ 90 minutes.
Other possible optimization criteria

- Cost-effectiveness
- A criterion based on a combination of cost and time
- Most effective without exceeding a specified level of participant burden
- Or any other relevant criterion
The Multiphase Optimization Strategy (MOST)
Phases of MOST: Preparation, optimization, evaluation

Optimization

- Objective: To form a treatment package that meets the optimization criterion
  - Collect and analyze empirical data on performance of individual intervention components relying on efficient randomized experiments
  - Based on information gathered, select components and levels that meet optimization criterion.
Phases of MOST: Preparation, optimization, evaluation

Different approaches to collecting the necessary information:

- Factorial experiment (Linda)
- Fractional factorial experiment (Linda)
- SMART (Billie)
- Micro-randomized trial (Susan)
- System identification
- Other...????
<table>
<thead>
<tr>
<th>Number of decision points in intervention</th>
<th>Intensity of adaptation of intervention</th>
<th>Particularly relevant approaches for an optimization trial</th>
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</thead>
<tbody>
<tr>
<td>0 (Fixed MBI)</td>
<td>Lower intensity of adaptation</td>
<td>Factorial</td>
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<td>Higher intensity of adaptation</td>
<td>System identification experiment</td>
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<td>Micro-randomized trial</td>
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The Multiphase Optimization Strategy (MOST)

PREPARATION
- Derive/revise conceptual model
- Identify set of candidate components
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  - Other
- Continual improvement process
- Based on results, identify intervention that meets optimization criterion

EVALUATION
Confirm effectiveness of optimized intervention via RCT
Phases of MOST: Preparation, optimization, evaluation

- Evaluation
  - Objective: To establish whether the optimized intervention has a statistically significant effect compared to a control or alternative intervention
    - Conduct an RCT
Multiphase optimization strategy (MOST)

- Empirically-based optimization
- Optimized behavioral/biobehavioral intervention
- Evaluation via RCT
Multiphase optimization strategy (MOST)
Multiphase optimization strategy (MOST)
Multiphase optimization strategy (MOST)
Outline

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Example: Clinic-based smoking cessation study

Objective: Develop a smoking cessation intervention made up exclusively of active components

- Part of a Po1; PIs: Mike Fiore and Tim Baker, University of Wisconsin
- Funded by the National Cancer Institute
Baker & Fiore’s phase-based model of the smoking cessation process
Components being considered for the smoking cessation intervention

- Precessation nicotine patch (No, Yes)
- Precessation ad lib nicotine gum (No, Yes)
- Precessation in-person counseling (No, Yes)
- Cessation in-person counseling (Minimal, Intensive)
- Cessation phone counseling (Minimal, Intensive)
- Maintenance medication duration (Short, Long)
MOST as implemented in smoking cessation study

Optimized behavioral/biobehavioral intervention

Choose components to achieve most effective < $500

Precess. NRT: patch
Precess. NRT: gum
Precess. counseling
Cess. in-pers couns.
Cess. phone couns.
Maint. med. duration

Evaluation via RCT
Choosing an efficient design for the component screening experiment

<table>
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<th>Design</th>
<th>N to achieve power ≥ .8</th>
<th>Number of experimental conditions</th>
<th>Can interactions be examined?</th>
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<tbody>
<tr>
<td>Option 1: Six individual experiments</td>
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<td>Option 2: Comparative treatment</td>
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<td>Option 3: Factorial experiment</td>
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<tr>
<td>Option 4: Fractional factorial</td>
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<tr>
<td>Option 1: Six individual experiments</td>
<td>3,072</td>
<td>12</td>
<td>None</td>
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<tr>
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Option 2: Comparative treatment experiment

Experimental conditions:

<table>
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<th>Treatment conditions</th>
<th>Control</th>
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<tr>
<td>Precessation patch = yes</td>
<td>All = low</td>
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<tr>
<td>Precessation gum = yes</td>
<td>All others = low</td>
</tr>
<tr>
<td>Precessation counseling = yes</td>
<td>All others = low</td>
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<tr>
<td>Cessation counseling = intensive</td>
<td>All others = low</td>
</tr>
<tr>
<td>Cessation phone counseling = intensive</td>
<td>All others = low</td>
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<tr>
<td>Cessation NRT = 16 weeks</td>
<td>All others = low</td>
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## Choosing an efficient design for the component screening experiment

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<td>7</td>
<td>None</td>
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<td>512</td>
<td>64</td>
<td>Yes, all</td>
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<td>512</td>
<td>64</td>
<td>Yes, all</td>
</tr>
<tr>
<td>Option 4: Fractional factorial experiment</td>
<td>512</td>
<td>8, 16, or 32 depending on design chosen</td>
<td>Yes, selected subset</td>
</tr>
</tbody>
</table>
Factorial experiments 101

- Example: 2 X 2, or $2^2$, factorial design

<table>
<thead>
<tr>
<th>Component B</th>
<th>Component A</th>
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<tbody>
<tr>
<td>Off</td>
<td>Off</td>
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<tr>
<td>Off</td>
<td>A,B off</td>
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<tr>
<td>On</td>
<td>A off, B on</td>
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<tr>
<td>On</td>
<td>A,B on</td>
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</table>

- Factorial experiments can have
  - ≥ 2 factors
  - ≥ 2 levels per factor
- On the next slide is a $2^4$ factorial design
Experimental conditions in a factorial experiment with four factors

<table>
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<tr>
<th>Experimental condition</th>
<th>Factor A</th>
<th>Factor B</th>
<th>Factor C</th>
<th>Factor D</th>
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<tbody>
<tr>
<td>1</td>
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</table>
What are we trying to estimate with a factorial experiment?

- Most important for decision making: Main effect of each factor
  - DEFINITION OF MAIN EFFECT OF FACTOR A:
    - Effect of Factor A averaged across all levels of all other factors
- Also selected interactions
  - DEFINITION OF INTERACTION BETWEEN FACTOR A AND FACTOR B (assuming each factor has two levels):
    - $\frac{1}{2} \left( \text{effect of Factor A at level 1 of Factor B} - \text{effect of Factor A at level 2 of Factor B} \right)$
- MAIN EFFECT OF FACTOR A is mean of conditions 1-8 vs. mean of conditions 9-16
- **MAIN EFFECT OF FACTOR B** is mean of conditions 5—8 and 13—16 vs. mean of conditions 1—4 and 9—12

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</table>
- **MAIN EFFECT OF FACTOR C** is mean of conditions 3, 4, 7, 8, 11, 12, 15, and 16 vs. mean of conditions 1, 2, 5, 6, 9, 10, 13, and 14

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</tbody>
</table>
- MAIN EFFECT OF FACTOR D is mean of conditions 1,3,5,7,9,11,13,15 vs. mean of conditions 2,4,6,8,10,12,14,16.

<table>
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<th>Experimental condition</th>
<th>Factor A</th>
<th>Factor B</th>
<th>Factor C</th>
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Option 4: Fractional factorial (FF) design

- Factorial design in which only a 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 we will discuss shortly
When you might consider a FF design

- 5 or more factors
  - Although FF’s exist for 3 and 4 factors
- Overhead costs associated with new experimental conditions are relatively high
- You are primarily interested in main effects and lower-order interactions
- Most of the remaining effects are expected to be negligible in size
Let’s be clear which interactions we are talking about

- There are two categories of interactions of potential interest to intervention scientists
  - Interactions between the factors in a factorial experiment
  - Interactions between uncontrolled factors outside the experiment and experimental factors
    - e.g. Interaction between gender and an intervention component
- Here we are talking about interactions between factors
Remember this about power

- Using a FF design does NOT change required \( N \)
- FF designs are powered same as complete factorials
- Compared to the corresponding complete factorial, in a FF design
  - Each condition will have more subjects than the corresponding complete factorial
  - But each effect estimate based on SAME number of subjects
The logic behind FF designs

- OK, what would happen if we removed half of the experimental conditions from a $2^5$ factorial design, so that instead of 32 conditions there were 16?
- IT DEPENDS ON WHICH CONDITIONS YOU REMOVE, but one thing is certain:
- There will be aliasing
The logic behind FF designs

- What is aliasing?
  - This term refers to the combining of two or more effects, so that it is impossible to determine which effect is responsible for what has been observed.
  - Recall that in a complete $2^5$ there are 32 experimental conditions, so you can estimate 32 effects.
  - Once you remove half of the experimental conditions, you can estimate only 16 effects.
  - As a result, each of these 16 effects is a combination of two of the effects from the complete factorial.

- THIS IS NOT NECESSARILY ALL BAD
The logic behind FF designs

- Statisticians have figured out what aliasing occurs when different conditions are removed
- SO it follows that it is possible to select a FF design with conditions that produce characteristics we like!
- The idea: select a design in which effects of primary scientific interest (main effects, lower-order interactions) are aliased with effects expected to be negligible (higher-order interactions)
Some writers use the term “confounding” of effects

I prefer to reserve the term “confounding” for accidental combining of effects (such as in a nonexperimental or quasiexperimental study)...

...and to reserve the term “aliasing” for situations in which the combining of effects is done deliberately and strategically

- As it is in fractional factorial experiments
How do I select the experimental conditions to include in the design?

- Statisticians have developed many FF designs to choose from; different designs have different properties
- Starting point: An idea of which effects you are willing to assume are negligible
- Then software can be used to select a design, e.g.,
  - PROC FACTEX in SAS
  - FRF2 in R
Did you know…?

- 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.
Experimental design used to examine components of smoking cessation intervention

- Factorial experiment with six factors.
- It is a $2^{6-1}$ fractional factorial.
- The design has 32 experimental conditions.
- Each main effect aliased with one 5-way interaction; each 2-way aliased with one 4-way; each 3-way with one 3-way
- HEY! Where is the control group???
Using data from the experiment to optimize

- **IF YOU DID A FACTORIAL EXPERIMENT:**
  - Conduct an analysis of variance, obtain estimates of effects of each of the components
  - Use this information to select components
    - Discard components that do not perform adequately
    - Use size of effects in combination with other data (e.g., cost) or prediction model to select components that will make up optimized intervention
  - Alternative approaches to decision-making is an open research area
RCT of smoking cessation intervention (Piper et al., in preparation)
Outline

- Definitions
- What’s wrong with business as usual?
- What is MOST? What is optimization?
- OK, how do you do this?
- FAQ
Frequently asked questions

- Nice idea, but will it be fundable?
- Can this approach be carried out with the level of funding typically available?
- I don’t see how I can implement all the experimental conditions required by a factorial experiment.
- How might intervention science be different if MOST were widely used?
Imagine the state of the art if MOST were widely implemented

- A bar for effectiveness, efficiency, economy, and scalability would be set and then raised with each new evidence-based behavioral/biobehavioral intervention
- A coherent base of knowledge would be accumulated about what works
- Over time, increases in effectiveness, efficiency, economy, and scalability
For more information:

- http://methodology.psu.edu
  - Sign up for eNews
- TED talk online (search for Collins TED talk)
- 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
- WATCH FOR 2 books to be published in 2018 (Springer)
Some funded projects using MOST (that I know of)

- Smoking cessation intervention for adults (M. Fiore & T. Baker, U of Wisconsin, P01CA180945)
- Prevention of drug abuse and HIV in South Africa (L. Caldwell, PSU, R01DA029084)
- Substance use prevention program aimed at American Indian families (N. Whitesell, U. of Colorado, R01DA035111)
- Moderation of gestational weight gain (D. Downs, PSU, R01HL119245)
- Intervention to get HIV positive individuals into the health care system and on ART (M. Gwadz, NYU & L. Collins, PSU, R01DA040480)
Some funded projects using MOST (that I know of)

- Weight reduction program for adults (B. Spring, NWU and L. Collins, PSU, R01DK097364)
- Online intervention to prevent excessive alcohol use and risky sex in college students (L. Collins, PSU, R01AA022931)
- Positive psychology intervention for cardiac patients to improve health behaviors (J. Huffman, Harvard U, R01HL113272)
- Tobacco treatment for smokers getting lung cancer screening (J. Ostroff, Sloan-Kettering, R01CA207442)
Some funded projects using MOST (that I know of)

- Intervention to reduce fear of recurrence in breast cancer patients (L. Wagner, now at Wake Forest, R21CA173193)
- Intervention to prevent childhood obesity (L. Francis, USDA)
- Adherence intervention to promote use of insulin pumps among adolescents (K. Driscoll, U of Florida, K23DK091558)
- Maternal depression care-seeking (E. Fernandez y Garcia, UC Davis, K23MH101157)
- Physical activity for breast cancer survivors (S. Phillips, NWU, K07CA196840)