

Design of Optimization Trials

Bonnie Spring, Northwestern University Linda Collins, Penn State University



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Part 1: Introduction to the multiphase optimization strategy (MOST) for building more effective, efficient, economical, and scalable interventions



Linda M. Collins, Ph.D. The Methodology Center and Department of Human Development & Family Studies Presented at the SPHeRE seminar series Health Research Board, Royal College of Surgeons Ireland 19 April 2019

Outline of Part 1



- Definitions
- What's wrong with business as usual?
- What is MOST? What is optimization?
- OK, how do you do this?
- Resources

ومراجعتها ومحمد والبلا بالمأتين والمتناقين والمتعالية والمعرف أمراجهم ومناقاتها والمعروف فالأناف

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...

والمحاجبة التقاري ويتحجب أرجر المحجج وحاداته التبار

• ...using a strategy that at least in part aims to modify attitudes, cognitions, or behavior.

What is a behavioral/biobehavioral intervention?



• Examples:

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- Smoking cessation
- School-based drug abuse prevention
- Program to help children who are behind grade level in reading
- 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 antriretrovirals
- Most behavioral/biobehavioral interventions are made up of multiple components.

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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

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What is an intervention component?

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- Some components may be pharmaceutical (e.g. NRT; PrEP)
- Components can be defined at any level: individual, family, school, etc.

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• Can impact efficacy, effectiveness, efficiency, economy, scalability

Outline

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How behavioral/biobehavioral inventions are typically developed and evaluated

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- 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*

Classical treatment package approach



The RCT is best suited for



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



Classical treatment package approach



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

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What the RCT cannot not tell us

An RCT that finds a <u>non-significant</u> 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

Outline

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The multiphase optimization strategy (MOST)



- Alternative to the classical treatment package approach
- An engineering-inspired framework for development, optimization, and evaluation of behavioral and biobehavioral interventions
- Using MOST it is possible to engineer an intervention to meet a specific criterion



Multiphase optimization strategy (MOST)



Desiderata for behavioral/ biobehavioral interventions

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- 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 in the intended setting exactly as evaluated

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Definition of optimization of a behavioral/biobehavioral intervention

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- Optimization of a behavioral/biobehavioral intervention is
 - the process of identifying the intervention that provides the best expected outcome obtainable...
 - ...within key constraints imposed by the need for efficiency, economy, and/or scalability.
- Note tension between effectiveness and the other three desiderata

Continual optimization principle



Resource management principle

Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

Phases of MOST: **Preparation**, optimization, evaluation

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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

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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

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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.

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- <u>Suppose</u> to reduce waste of time and money, the investigators want to be confident that every component is necessary.
- Achieve this by selecting <u>only active intervention components</u>.

Another possible optimization criterion



- Key constraint: Money
- Most effective intervention that can be delivered for ≤ some amount of money
- CONSIDER a clinic-based smoking cessation intervention.
 - <u>Suppose</u> the health service 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 <u>most</u> <u>effective intervention that can be delivered for $\leq 500 \notin$ /person</u>.



Other possible optimization criteria

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- Time
- 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

Continual optimization principle



Resource management principle

Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

Phases of MOST: Preparation, **optimization**, evaluation

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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 <u>efficient</u> <u>randomized experiments</u>
 - Based on information gathered, select components and levels that meet optimization criterion.

Continual optimization principle



Resource management principle

Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

Phases of MOST: Preparation, optimization, evaluation Evaluation

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 Objective: To establish whether the optimized intervention has a statistically significant effect compared to a control or alternative intervention

• Conduct an RCT

Continual optimization principle



Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

Two fundamental principles



- Resource management principle
 - When conducting research in the optimization and evaluation phases, make the best use of available resources

- Continual optimization principle
 - MOST provides the opportunity to keep improving an intervention incrementally



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Continual optimization principle



Resource management principle

Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

Example: Clinic-based smoking cessation study



- Pls: Mike Fiore and Tim Baker, University of Wisconsin
- Funded by the United States National Cancer Institute (part of the National Institutes of Health)



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


Choosing an efficient design for the optimization trial*

	Approximate	Number of	Can
	N to achieve	experimental	interactions
	power≥.85	conditions	be examined?
Design	(Cohen's <i>d</i> =.27)		
Option A: Six individual experiments			
Option B: Comparative treatment			
Option C: Factorial experiment			

*We are developing a fixed intervention, so we are considering traditional factorial experimental designs

Design option A: Six individual treatment/control experiments internationa hehavioural trials network

- 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

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Choosing an efficient design for the optimization trial

	Approximate N to achieve	Number of experimental	Can interactions
Desire	power≥.85	conditions	be examined?
Design	(Cohen's $d=.27$)		
Option A: Six individual experiments	3,072	12	None
Option B: Comparative treatment			
Option C: Factorial experiment			

Design option B: Comparative treatment experiment



Experimental conditions:

Treatment conditions					Control	
Precessation patch = yes	Precessation gum = <i>yes</i>	Precessation counseling = <i>yes</i>	Cessation counseling = <i>intensive</i>	Cessation phone counseling = <i>intensive</i>	Cessation NRT = 16 weeks	All = <i>low</i>
All others = low	All others = low	All others = low	All others = low	All others = low	All others = low	

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Choosing an efficient design for the optimization trial

	Approximate N to achieve	Number of experimental	Can interactions
Design	(Cohen's <i>d</i> =.27)	conditions	be examined.
Option A: Six individual experiments	3,072	12	None
Option B: Comparative treatment	1,792	7	None
Option C: Factorial experiment			

Design option C



- 2⁶ factorial experiment
- This will have 64 experimental conditions



Choosing an efficient design for the optimization trial

Design	Approximate N to achieve power≥.85	Number of experimental conditions	Can interactions be examined?
	(concir s d=.27)		
Option A: Six individual experiments	3,072	12	None
Option B: Comparative treatment	1,792	7	None
Option C: Factorial experiment	512	64	Yes, all

Factorial experiments 101



• Example: 2 X 2, or 2², factorial design

	Component A			
Component B	Off	On		
Off	A,B off	A on, B off		
On	A off, B on	A,B on		

- Factorial experiments can have
 - ≥ 2 factors
 - ≥ 2 levels per factor
- On the next slide is a 2⁴ factorial design



Experimental conditions in a 2⁴ factorial experiment

Experimental condition	Factor A	Factor B	Factor C	Factor D
1	Off	Off	Off	Off
2	Off	Off	Off	On
3	Off	Off	On	Off
4	Off	Off	On	On
5	Off	On	Off	Off
6	Off	On	Off	On
7	Off	On	On	Off
8	Off	On	On	On
9	On	Off	Off	Off
10	On	Off	Off	On
11	On	Off	On	Off
12	On	Off	On	On
13	On	On	Off	Off
14	On	On	Off	On
15	On	On	On	Off
16	On	On	On	On

What are we trying to estimate with a factorial experiment?

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- 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):
 - ½ ((effect of Factor A at level 1 of Factor B) (effect of Factor A at level 2 of Factor B))

 MAIN EFFECT OF FACTOR A is mean of conditions 1-8 vs. mean of conditions 9-16

Experimental	Factor A	Factor B	Factor C	Factor D
condition				
1	Off	Off	Off	Off
2	Off	Off	Off	On
3	Off	Off	On	Off
4	Off	Off	On	On
5	Off	On	Off	Off
6	Off	On	Off	On
7	Off	On	On	Off
8	Off	On	On	On
9	On	Off	Off	Off
10	On	Off	Off	On
11	On	Off	On	Off
12	On	Off	On	On
13	On	On	Off	Off
14	On	On	Off	On
15	On	On	On	Off
16	On	On	On	On

 MAIN EFFECT OF FACTOR B is mean of conditions 5—8 and 13—16 vs. mean of conditions 1—4 and 9—12

Experimental condition	Factor A	Factor B	Factor C	Factor D
1	Off	Off	Off	Off
2	Off	Off	Off	On
3	Off	Off	On	Off
4	Off	Off	On	On
5	Off	On	Off	Off
6	Off	On	Off	On
7	Off	On	On	Off
8	Off	On	On	On
9	On	Off	Off	Off
10	On	Off	Off	On
11	On	Off	On	Off
12	On	Off	On	On
13	On	On	Off	Off
14	On	On	Off	On
15	On	On	On	Off
16	On	On	On	On

 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

Experimental	Factor A	Factor B	Factor C	Factor D
1	Off	Off	Off	Off
2	Off	Off	Off	On
3	Off	Off	On	Off
4	Off	Off	On	On
5	Off	On	Off	Off
6	Off	On	Off	On
7	Off	On	On	Off
8	Off	On	On	On
9	On	Off	Off	Off
10	On	Off	Off	On
11	On	Off	On	Off
12	On	Off	On	On
13	On	On	Off	Off
14	On	On	Off	On
15	On	On	On	Off
16	On	On	On	On

- 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

Experimental	Factor A	Factor B	Factor C	Factor D
1	Off	Off	Off	Off
2	Off	Off	Off	On
3	Off	Off	On	Off
4	Off	Off	On	On
5	Off	On	Off	Off
6	Off	On	Off	On
7	Off	On	On	Off
8	Off	On	On	On
9	On	Off	Off	Off
10	On	Off	Off	On
11	On	Off	On	Off
12	On	Off	On	On
13	On	On	Off	Off
14	On	On	Off	On
15	On	On	On	Off
16	On	On	On	On

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.
- When effect coding is used to analyze data from a balanced factorial experiment, all effect estimates are uncorrelated.



If you would like to read more about this optimization trial:



Piper, M.E., Fiore, M.C., Smith, S.S., Fraser, D., Bolt, D.M., Collins, L.M., Mermelstein, R., Schlam, T.R., Cook. J.W., Jorenby, D.E., Loh, W.-Y., & Baker, T.B. (2016). Identifying effective intervention components for smoking cessation: A factorial screening experiment. *Addiction*, *111*, 129-141.

This trial actually used a *fractional factorial* experimental design.

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Using data from the experiment to optimize

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- 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
 - Developing ways of doing this is an active research area

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Components examined in Wisc	onsin smoking cessation study	ihtn
Component	Levels	international
Experiment 1	: Motivation	behavioural
Nicotine patch	On vs off	LI Idis network
Nicotine gum	On vs off	
Motivational interviewing	On vs off	
Behavioral reduction counseling	On vs off	
Experiment	2: Cessation	
Preparation nicotine patch	On vs off	
Preparation oral NRT	On	
Preparation counseling	On vs off	
Cessation in-person counseling	Intensive	
Cessation phone counseling	Intensive vs minimal	
Duration of medication	16 weeks vs 8 weeks	
Experiment 3:	Maintenance	
Extended medication	26 weeks	
Maintenance counseling	Counseling via telephone	
Medication adherence counseling	2 10-min sessions vs none	and the second second
Automated adherence calls	On	
Helping Hand ("MEMS" device) with counseling	Printout, feedback, counseling vs none (all received Helping Hand)	

Components/levels selected based on screening experiment



Based on the results of experimentation on 15 components, 5 "winners":

- 1. Pre-cessation oral NRT (lozenge)
- 2. 26-week postquit combination NRT (patch + mini-lozenge)
- 3. Intensive in-person counseling during cessation phase
- 4. Counseling calls during maintenance phase
- 5. Automated adherence calls

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Continual optimization principle



Resource management principle

Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

The evaluation phase



- Conduct an RCT comparing the optimized intervention to a suitable control
- Why is this necessary?
 - Factorial experiment does not provide direct comparison of treatment package to control
 - Treatment package may not even appear in experiment
 - Control for an RCT is often different



These components were combined into a treatment package and evaluated in an RCT

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- Comparison group: "modern usual care"
 - 8 weeks of nicotine patch starting at the quit day
 - Brief 10-minute counseling session
 - Faxed referral to the Wisconsin Tobacco Quit Line with a time for the quit line to call the participant for a counseling session
 - Instructions for downloading a free smoking cessation app (QUITNOW)

Some results of RCT



	Percent Abstinent				
	Modern	Optimized	OR	95% CI	p-value
	Usual Care	Treatment	(95% CI)		
Week 4	28.6	43.8	1.95	1.40, 2.72	< 0.001
Week 8	23.8	46.4	2.77	1.97, 3.91	< 0.001
Week 16	24.4	49.7	3.05	2.17, 4.29	<0.001
Week 26	18.4	39.0	2.83	1.96, 4.08	< 0.001
Post-week 26	6.0	15.9	2.95	1.69, 5.14	< 0.001
(CO-confirmed;					
< 6 ppm)					

Piper, M.E., et al. (in press). A randomized controlled trial of an optimized smoking cessation intervention delivered in primary care. *Annals of Behavioral Medicine*.

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For more information:

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- http://methodology.psu.edu
 - Sign up for eNews
 - Section on MOST with
 - Suggested reading
 - FAQ
 - Advice for people writing grant proposals involving MOST
 - One intro video (more to come)
 - Apply for free consulting on MOST https://methodology.psu.edu/publications/news/mostconsulting

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Books

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• Available now



 Available sometime Fall 2018: Collins, L.M. & Kugler, K.C. (in press). **Optimization of** Behavioral, Biobehavioral, and **Biomedical Interventions:** Advanced Topics.

Northwestern Medicine®

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Optimizing weight loss treatment: Design and implementation of the Opt-IN study

Bonnie Spring, PhD Northwestern University Director, Center for Behavior and Health

Overview

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- Obesity as public health problem
- Gold standard obesity treatments: challenges to scalability
- What components to include in the treatment package?
- Treatment optimization by factorial experiment:
 - Conceptual model, intervention components, optimization criteria
 - The Opt-IN study
- One optimization experiment: Tips, tricks, and a workaround



Obesity – The Public Health Problem

• **Prevalence**:

U.S: 30% obese; 69% overweight/obese (CDC, 2008)World: 1.4 bill overweight/obese (WHO, 2013)

• U.S. employer annual cost of obesity-related medical expense, absenteeism, and presenteeism for full-time workers



The Intervention Challenge

- ibtn
- Effective treatment (intensive lifestyle treatment e.g., DPP, Look AHEAD) produces 7% sustained weight loss and metabolic improvement but burdensome (16-36 sessions) and costly (\$1800/patient)



Diabetes Prevention Program, Diabetes Care, 2012

ENGAGED: <u>E-N</u>etworking <u>G</u>uiding <u>A</u>dherence to <u>G</u>oals in <u>Exercise and Diet (RC1DK087126)</u>



Can we cut treatment intensity in half but preserve weight loss by using mHealth to reconfigure treatment components?

N= 96 obese adults, RCT, 6 month intervention, Outcomes assessed at 3, 6 and 12 months

(1) Self-Guided (1 group session; Group Lifestyle Balance DVD; record by paper and pencil, no coaching)
(2) Standard (8 weekly group sessions; phone coaching: weekly mos 0-3, monthly mos 3-6; record by paper and pencil)

(3) **Technology** (8 weekly group sessions; phone coaching weekly mos 0-3, monthly mos 3-6; <u>record by app &</u> <u>wireless accelerometer, social media</u>)

• All receive team weight loss incentives

يحرجهم أألبه والمناقلين بجامعه أمرا سيمرجن الكافات ومراجع

والمستجمعة المتحلط أستناقص والأسرين والمستجمعا والمستخصص والمستحد المراجع

Treatment Package Approach: The ENGAGED Trial

Reduce DPP treatment intensity by half; reconfigure components to increase efficiency

- 1. 8 in-person treatment sessions
- 2. Telephone coaching
- 3. Peer support (groups, message board, adherence info)
- 4. Incentives
- 5. Technology (app, accelerometer, texts)



Happy Birthday,Philly! May you eat well, but

stay within the Fan Meter safe zone...[©]"

"Love Shimmer – so reinforcing!"







Spring et al, Obesity, 2017

Weight Change (% of Baseline body weight) at 3, 6, and 12 Months

Bars reflect +/- 1 Standard Error





What don't we know at end of RCT?

If Treatment > Control

- Which components are making positive contribution
- Whether all components are needed
- Which components' contribution to effect offsets its cost
- How to make intervention
 more effective

If Treatment < Control

- Whether any components are worth retaining
- Whether one component had a negative effect that offset a positive effect
- Explicitly what went wrong and how to do it better next time

Courtesy of Kari Kugler and Linda Collins

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Opt-In Study



Optimization of Remotely Delivered Intensive Lifestyle Treatment for Obesity



Principal Investigators

Bonnie Spring, Ph.D. (Northwestern University) Linda Collins, Ph.D (Pennsylvania State University)



Funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK R01 DK097364)

والمتناكين ويتمجو أمرار
Primary Aim 1

Identify which components/component levels, contribute most to

- a) average weight loss
- b) percent achieving ≥ 5-7 % weight loss
 among overweight and obese adults over a
 6-month period.

Five components

- 1. Coaching Intensity
 - 12 v. 24 phone sessions
- 2. Text Messaging
 - No v. Yes
- 3. Progress Reports for PCP
 - No v. Yes
- 4. Recommendations to use meal replacements
 - No v. Yes
- 5. Training participants' self selected buddies to be supportive
 - No v. Yes



Primary Aim 2



• Apply these results to build an optimized intervention strategy

• Made up of only <u>active</u> components

• Intervention package < \$500 dollars (scalable)

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Step 1: Opt-IN Conceptual Model







Implemented Design

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Table 3. Experimental Conditions							
Exp. Cond- ition	CORE	# Coaching Sessions	Report to PCP	Texts	Meal Repl.	Buddy Training	
1	Yes	12	res	NO	No	No	
2	Yes	12	Yes	No	Yes	Yes	
3	Yes	12	Yes	res	No	Yes	
4	Yes	12	Yes	Yes	Yes	No	
5	Yes	12	NO	No	No	Yes	
6	Yes	12	No	No	Yes	No	
7	Yes	12	No	Yes	No	No	
8	Yes	12	No	Yes	Yes	Yes	
9	Yes	24	res	No	No	No	
10	Yes	24	Yes	No	Yes	Yes	
11	Yes	24	Yes	Yes	No	Yes	
12	Yes	24	Voc	Yes	Yes	No	
13	Yes	24	NO	No	No	Yes	
14	Yes	24	No	No	Yes	No	
15	Yes	24	No	Yes	No	No	
16	Yes	24	No	Yes	Yes	Yes	



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Table 2- Estimated Cost of Lowest vs. Highest Level of Intervention							
Components							
Intervention Component Levels	Cost/person	Cost/person					
	Lowest Level	Highest Level					
1. Dhana Cassiana: 12 ar 24	<u>ФОС БО</u>	¢170.04					
1. Phone Sessions: 12 of 24	φδ0.5Z	φ173.04					
2. PCP: no reports or reports	\$0	\$34,88					
	~ ~	<i>\$</i> 01100					
3. Texts: no or yes	\$0	\$33.60					
4. Meal Replacements: no or yes	\$0	\$29.96					
5 Buddy Training: no or yes	\$0	\$48.82					
3. Duddy Hanning. no or yes	ΨΟ	ψ-0.02					
+. Core intervention cost	\$281.67	\$281.67					
	Minimum	Maximum					
	cost	cost					
	¢ 000 40	# 004.07					
	\$ 368.19	\$601.97					

Enrollment Criteria

Inclusion

- 18-60 years (at least half \geq 45)
- BMI 25-39.9 kg/m^{2*}
- Weight stable
- Must have Android or iPhone smartphone
- No other major medical concerns
- Willing to use smartphone app

Exclusion

- Unstable medical conditions
- History of diabetes w/insulin, CVD, Crohn's, sleep apnea (CPAP)
- Previous hospitalization for psychiatric reasons in past 5 yrs.

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- At risk for cardiovascular events with MVPA or use assistive device for mobility
- Taking weight loss/gain meds
- Meet criteria for eating disorders or substance abuse
- Pregnant, trying to get pregnant, or lactating
- Living with another Opt-IN participant**
- Plantar fasciitis diagnosed by physician or podiatrist***

*Extended BMI range from 30-39.9 to 25-39.9 on 8/26/14 **Approved 9/21/15 ***Approved 11/16/15



Core Treatment (All receive)

- Behavioral Coaching and Curriculum
 - Online lessons
 - Phone coaching (12 vs. 24)
- Self-Monitoring Tool
 - Smartphone application
- Dietary Intervention
 - Calorie/fat goals, feedback
- Physical Activity Intervention
 - Moderate intensity (brisk walking) physical activity goal, increasing duration over time



Pellegrini CA, Hoffman SA, Collins LM, Spring B. Optimization of remotely delivered intensive lifestyle treatment for obesity using the multiphase optimization strategy: Opt-in study protocol. *Contemporary clinical trials*. 2014;38:251-259

Intervention Components

- 1. Coaching Calls over 6 Months
 - 12 calls
 - 24 calls
- 2. <u>Progress Report Mailed to Primary Care Physician</u>
 - Report mailed at 3- and 6-months to participant and Provider
 - Outlines weight loss progress, behavioral recommendations
- 3. <u>Text Messages</u>
 - Encouraging words, personalized feedback based on selfmonitoring
 - Automated messages in real-time

وي والمنظلية المنهجين أور المحمد وتباليك فالكون والأشار

NUMERATURE LANGER	NORTHWESTER
Phone (\$11) 808-7814 Fax (\$11) 808-8388	
Thursday, April 04, 2013	
«Physician_Name» «Address» «City», «State» «Zip»	
RE: Primary Care Provider Progress Report for Opt-IN Research Northwestern University Dear «Physician_Name»,	Study (IRB#STU00066546) at
Your patient, «Patient_Name» DOB: «Patient_DOB», is participat conducted in the Department of Preventive Medicine at Northwa	ting in the Opt-IN research study bein estem University. Opt-IN is a 6-mont!
behavioral telephone-based weight loss program that encourage low-fat diet and to encage in a moderate level of physical activity	s participants to follow a low-calorie, /. such as brisk walking. As part of the
behavioral telephone-based weight loss program that encourage low/st: diet and to engage in a moderate level of physical activity study, we are sending you quarterly reports on your patients' pro	s participants to follow a low-calorie, γ, such as brisk walking. As part of the ogress.
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Intervention Components (continued)

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- 4. Meal Replacement Recommendations
 - Provided with one week's supply at randomization session
 - Recommendations to continue use made by coach throughout intervention
- 5. Buddy Training
 - One telephone training session
 - Four 30-45 minute online webinar sessions
 - Buddies receive \$5 for each session complete and additional \$20 for completing 3 out of 4 webinars





Behind the Scenes: Implementation



How to explain this to participants...

- Ensure they know the 5 components
- Show them the 16 different conditions
- Highlight:
 - No control group
 - Everyone gets something
- Study staff & coaches have no idea which conditions/components yield greatest weight loss

<u>Condition</u>	Opt-IN Study Components	<u>uddy</u> aining				
1		No				
2	• You <i>will</i> receive:	Yes				
3	 Personalized weight, calorie, and physical activity goals to promote weight loss 	Yes				
4	- Online handouts and lessons on diet, physical activity,	No				
5	and behavioral strategies	Yes				
6	 Opt-IN study smartphone application to monitor your diet, activity, and weight daily 	No				
7	- Coaching calls (12 or 24 total) over the 6 month program	No				
8	Additionally, you MAY receive a combination of these weight loss					
9	components:	No				
10	 Text Messaging 	Yes				
11	 Progress Reports to PCP 	Yes				
12	 Meal Replacement Recommendations 					
13	- Buddy Support	Yes				
14		No				
15	🛛 💒 🔊 🔏 📲 🌋 🎎	No				
16	7 🖤 💯 🚟 🏎	Yes				
	opt-in@northwestern.edu Phone: 773-234-6711					
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How to Implement a Study with 16 Conditions? ibtn

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Checks, double checks, and triple checks!



Sample visual aids in coaching folder









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□ PCP 3- or 6-month report time?

Yes

🗆 No

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□ Review use of meal replacements over the last 2 weeks:

Participant informed report has or will be sent

Number of meal replacements _____

□ Using no meal replacements



□ Confirm that participant received text messages over last week from coach:

Inquire about buddy support:

Buddy providing support

□ Buddy not providing support

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The Corrigendum

- Copy Paste Error implemented design (proposed in R01) did not match intended fractional factorial Resolution V design
- Error discovered when enrollment almost halfway completed
- Solution: expand the design to a complete 2⁵ factorial with 32 experimental conditions
 - Eliminates aliasing of effects among experimental factors and enables us to examine interactions among all five components
- Does not require randomization of additional subjects

Table 2 Full Factorial Design with 32 conditions

Condition	Constitute	Descet	Treet	Marl Davis and	Dudda
Condition	Coaching	keport	lext	Meal Replacement	Buddy
	Sessions	to PCP	messages	Recommendations	Training
1	12	YES	NO	NO	NO
2	12	YES	NO	YES	YES
3	12	YES	YES	NO	YES
4	12	YES	YES	YES	NO
5	12	NO	NO	NO	YES
6	12	NO	NO	YES	NO
7	12	NO	YES	NO	NO
8	12	NO	YES	YES	YES
9	24	YES	NO	NO	NO
10	24	YES	NO	YES	YES
11	24	YES	YES	NO	YES
12	24	YES	YES	YES	NO
13	24	NO	NO	NO	YES
14	24	NO	NO	YES	NO
15	24	NO	YES	NO	NO
16	24	NO	YES	YES	YES
17	12	NO	NO	NO	NO
18	12	NO	NO	YES	YES
19	12	NO	YES	NO	YES
20	12	NO	YES	YES	NO
21	12	YES	NO	NO	YES
22	12	YES	NO	YES	NO
23	12	YES	YES	NO	NO
24	12	YES	YES	YES	YES
25	24	NO	NO	NO	NO
26	24	NO	NO	YES	YES
27	24	NO	YES	NO	YES
28	24	NO	YES	YES	NO
29	24	YES	NO	NO	YES
30	24	YES	NO	YES	NO
31	24	YES	YES	NO	NO
32	24	YES	YES	YES	YES

Pellegrini CA,.....Collins, L., Spring B. Corrigendum Contemporary clinical trials. 2015;45:468-469

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Randomization by Study Condition*

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Condition	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
	18	18	18	18	18	18	18	18	19	18	18	18	18	18	18	18
Condition	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
	17	18	17	16	16	17	17	18	17	16	18	17	18	17	17	17
	*No significant differences between conditions *No differential dropout								ions							

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Results



CONSORT





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Demographics (n=562) ibtn						
Female (n=459)	81.7%					
White (n=417)	74.2%					
Not Hispanic or Latinx (n=489)	87%					
M (SD) Age	38.7 (11.8) years					
M (SD) Baseline Weight	198.5 (30) lbs.					
M (SD) BMI	32.3 (3.6) kg/m ²					

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	Retention	ibtn international behavioural			
	3-month assessment	6-month assessment			
Randomized	562 (460 female, 102 male)				
Assessments Completed	509	473			
Retention Rate	90.6%	84.2%			

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Opt-IN Baseline to 6-month Weight Loss

Component	No/Yes Lo/High	<i>M</i> (SD)
Coaching	12-call 24-call	
PCP Report	No Yes	*
Text Messaging	No Yes	*
Meal Replacement Recommendations	No Yes	*
Buddy Training	No Yes	

N = 562



But...DON'T make a decision simply based on the main effects!



Decision by Regression Equation Including Interactions



- Parsimonious regression model:
- $\hat{Y} = -.96(bud) + .80(coach \times pcp \times meal) + .91(pcp \times text \times bud) .84(coach \times pcp \times text \times bud) .83(coach \times pcp \times meal \times bud)$

$$\hat{Y} = -.96(1) + .80(-1)(-1)(-1)(-1) + .91(-1)(-1)(1) - .84(-1)(-1)(-1)(1) - .83(-1)(-1)(-1)(1) = -.96 - .8 + .91 + .84 + .83 = .82$$

 $\hat{Y} = -.96(1) + .80(-1)(1)(-1) + .91(1)(-1)(1) - .84(-1)(1)(-1)(1) - .83(-1)(1)(-1)(1) = -.96 + .8 - .91 - .84 - .83 = -2.74$

8 Presentation or Section Tile 1 Presentation of Section Tile 1

Potential Next Steps



• RCT of the optimized intervention

• Further optimization of weight loss initiation treatment

• Optimization of weight loss maintenance treatment



Optimization Phase Takeaways



- Factorial experiments are possible to implement if you plan ahead
- Evidence-based intervention design: genuine equipoise
- Appealing to ppts: no inert control
- Some implementation challenges, but manageable
- Error highlights design's efficiency (no additional ppts needed), flexibility, ability to course correct
- DON'T make a conclusion based on main effects alone. DO embrace interactions!

