Introduction to the Multiphase Optimization Strategy (MOST)

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New Experimental Approaches to Designing Effective Multi-Component Interventions
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The Methodology Center

PennState

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 antriretrovirals
- 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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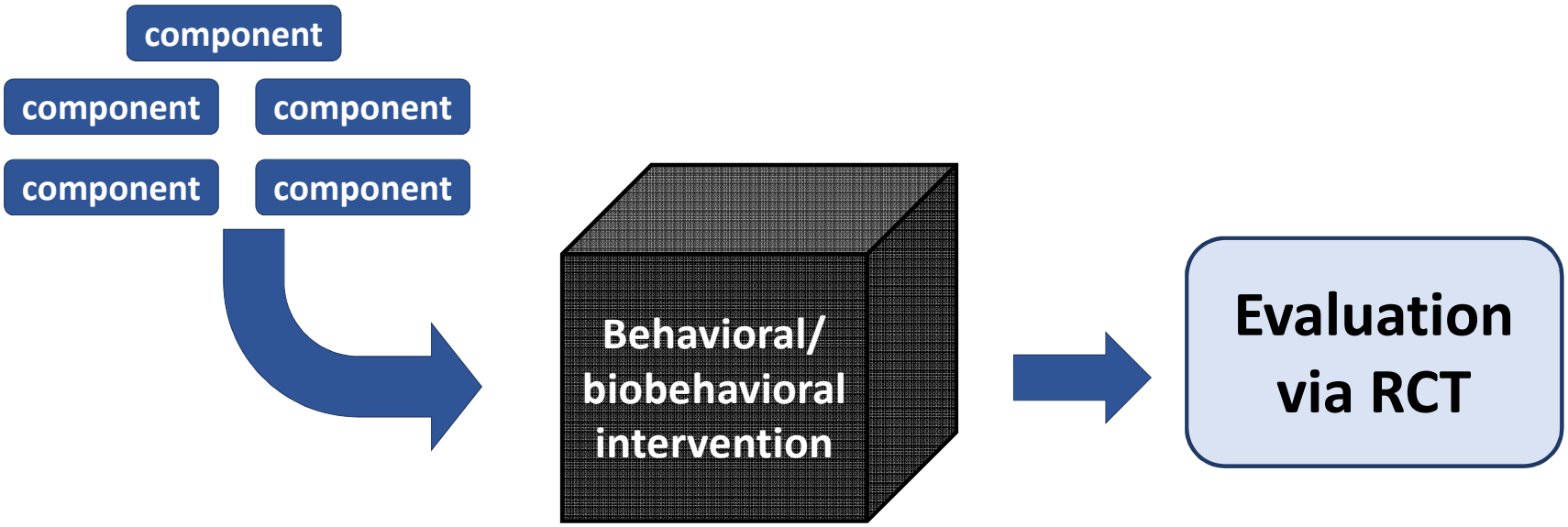
How behavioral/biobehavioral inventions are typically developed and evaluated

- 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



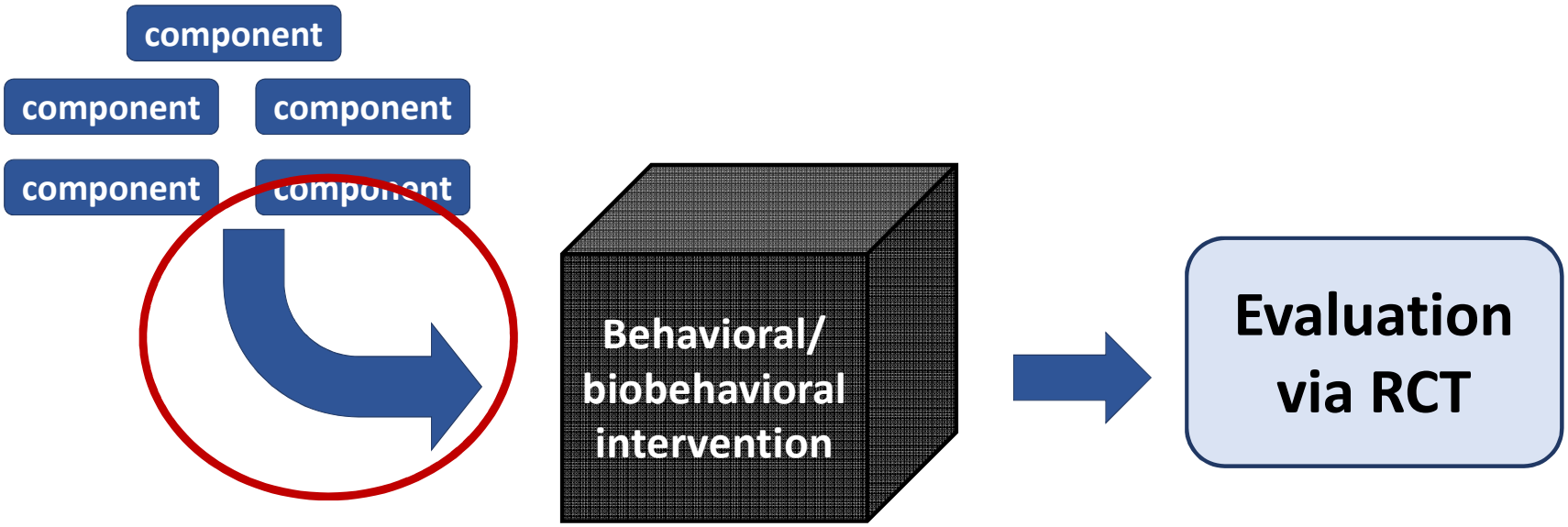
What is wrong with evaluating a treatment package via an RCT?

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



What the RCT cannot not tell us

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

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

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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

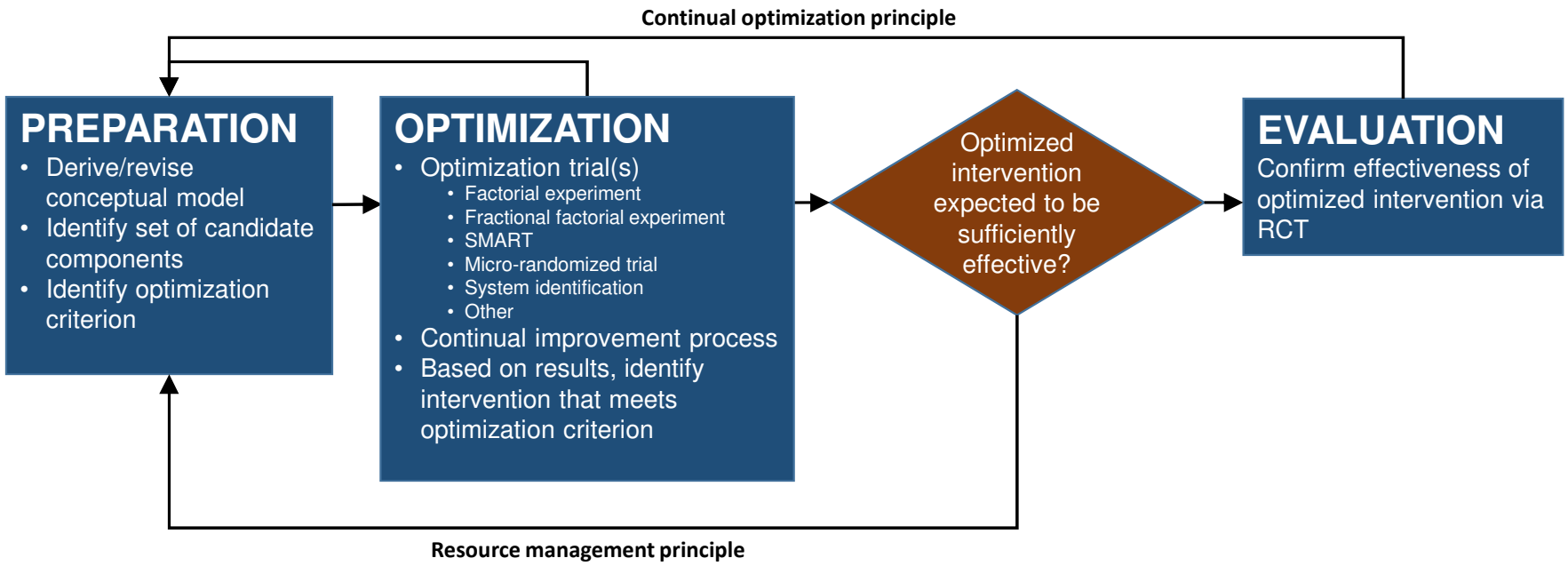
Desiderata for behavioral/ biobehavioral interventions

- 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

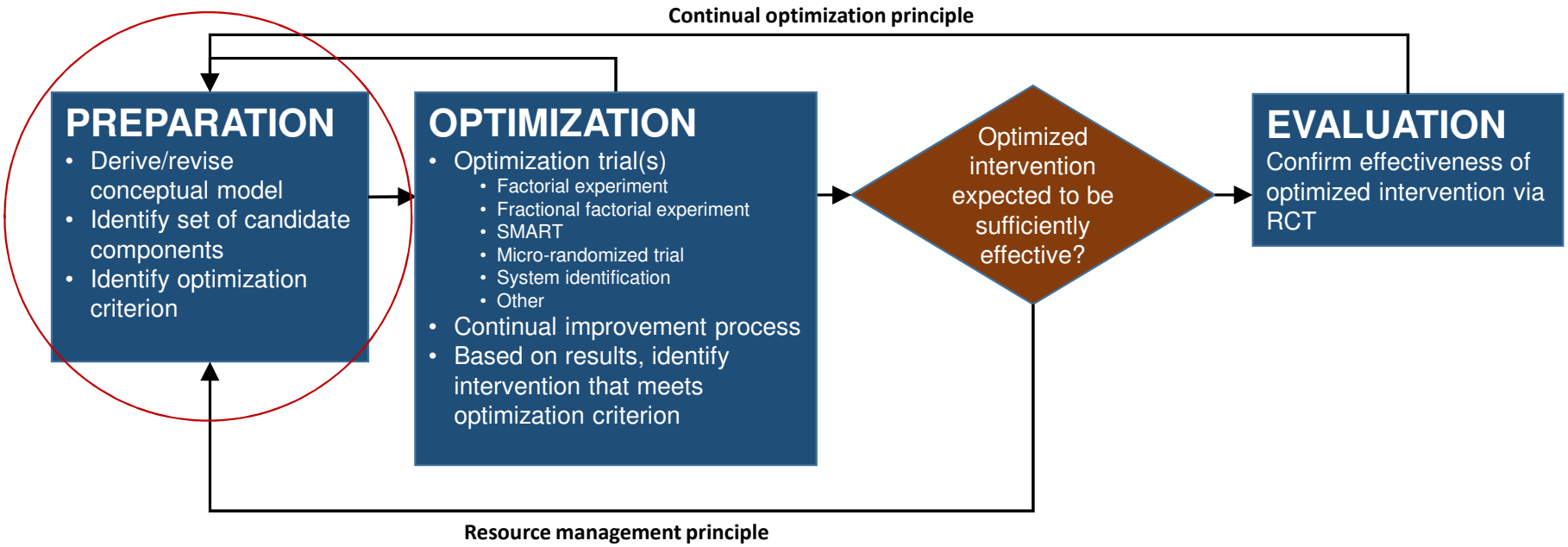
Definition of optimization of a behavioral/biobehavioral intervention

- *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)



The Multiphase Optimization Strategy (MOST)



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 ≤ 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 ≤ $500/person.

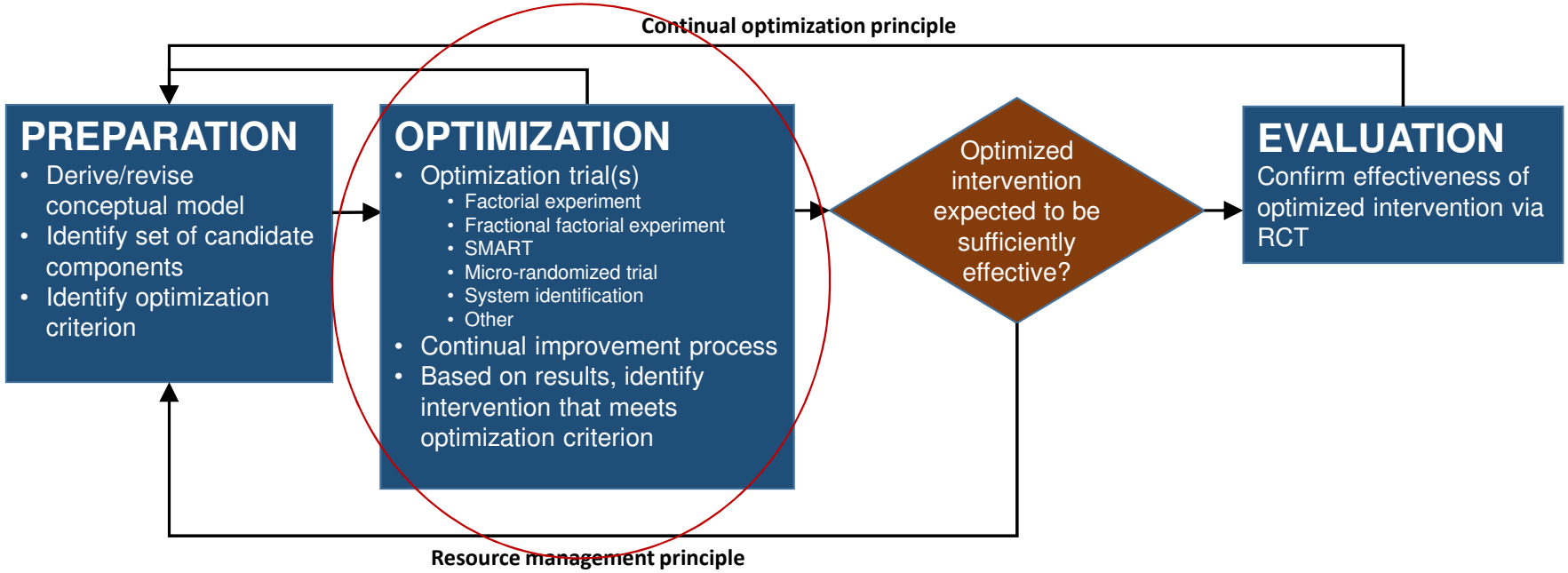
Another possible optimization criterion

- 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.

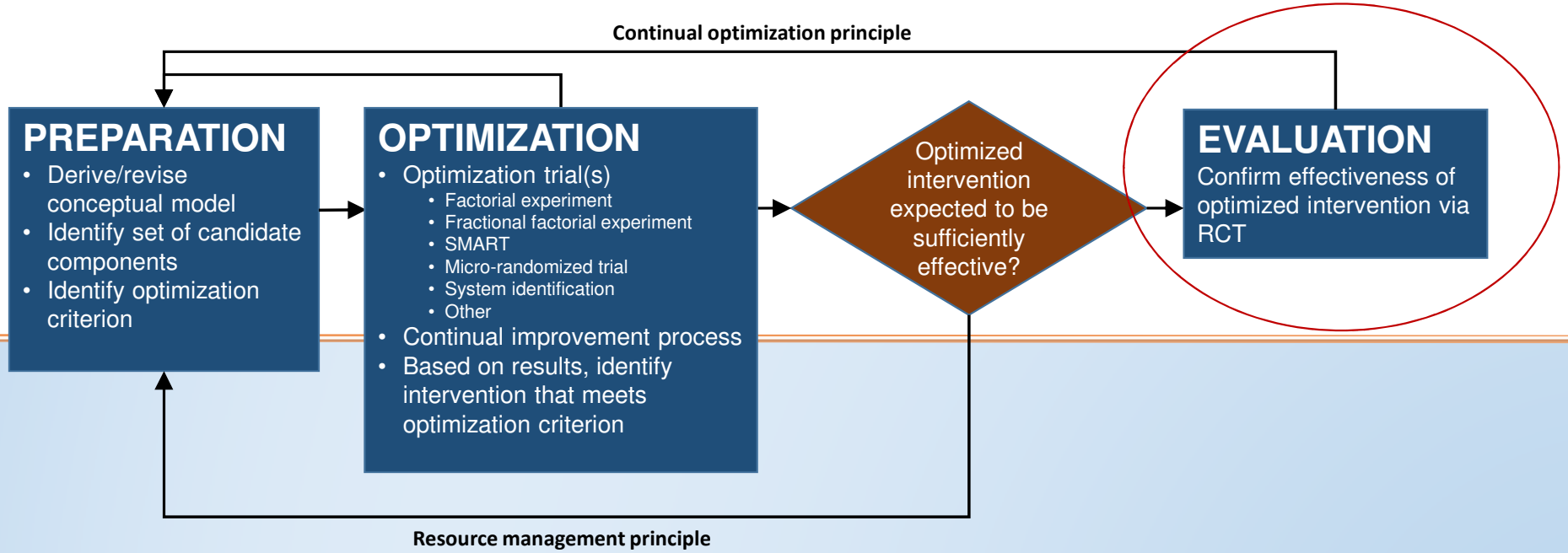
Phases of MOST: Preparation, optimization, evaluation

Different approaches to collecting the necessary information:

- Factorial experiment (Linda)
- Fractional factorial experiment (Linda)
- SMART (Billie)
- Micro-randomized trial (Susan)
- System identification
- Other…????

Number of decision points in intervention	Intensity of adaptation of intervention	Particularly relevant approaches for an optimization trial
0 (Fixed MBI)		Factorial Fractional factorial
1		Factorial Fractional factorial SMART
2 or more	Lower intensity of adaptation	
↕	↕	
∞	Higher intensity of adaptation	System identification experiment Micro-randomized trial

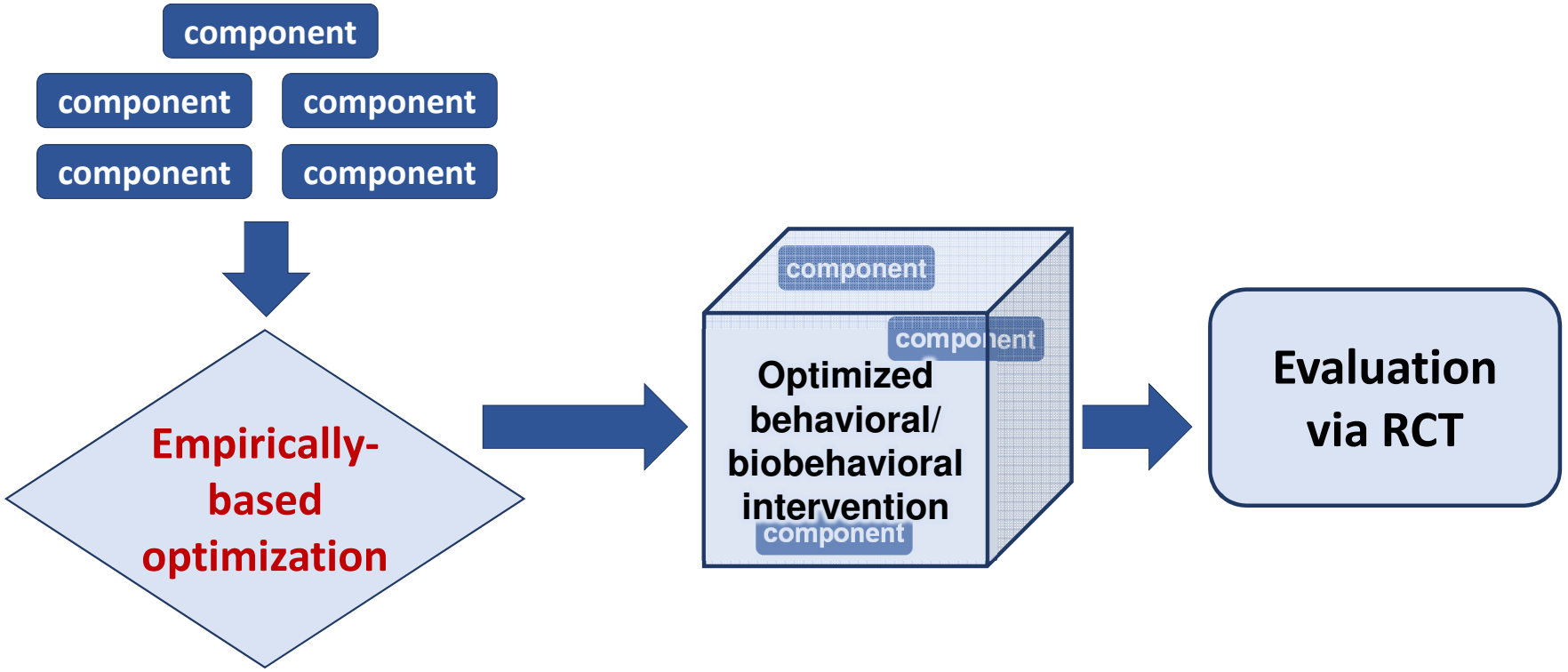
The Multiphase Optimization Strategy (MOST)



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)



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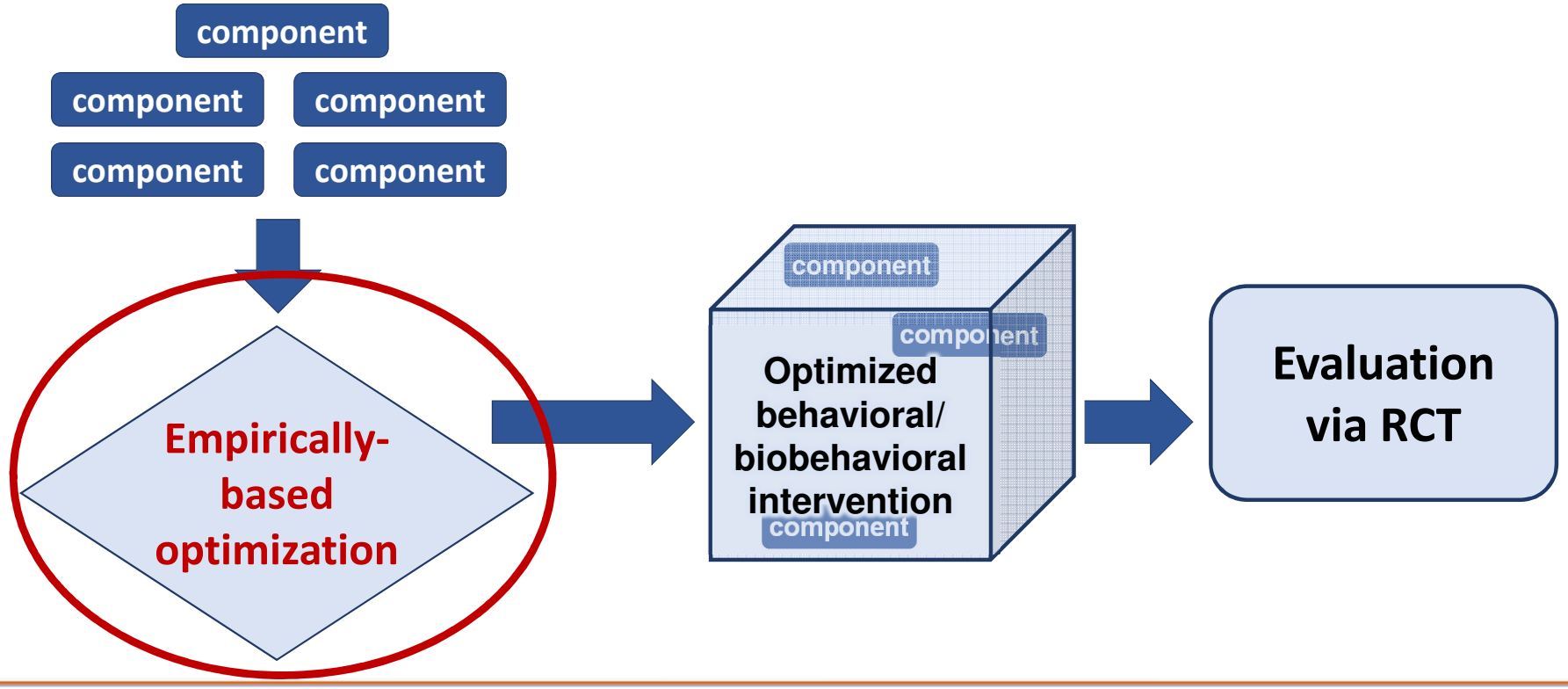

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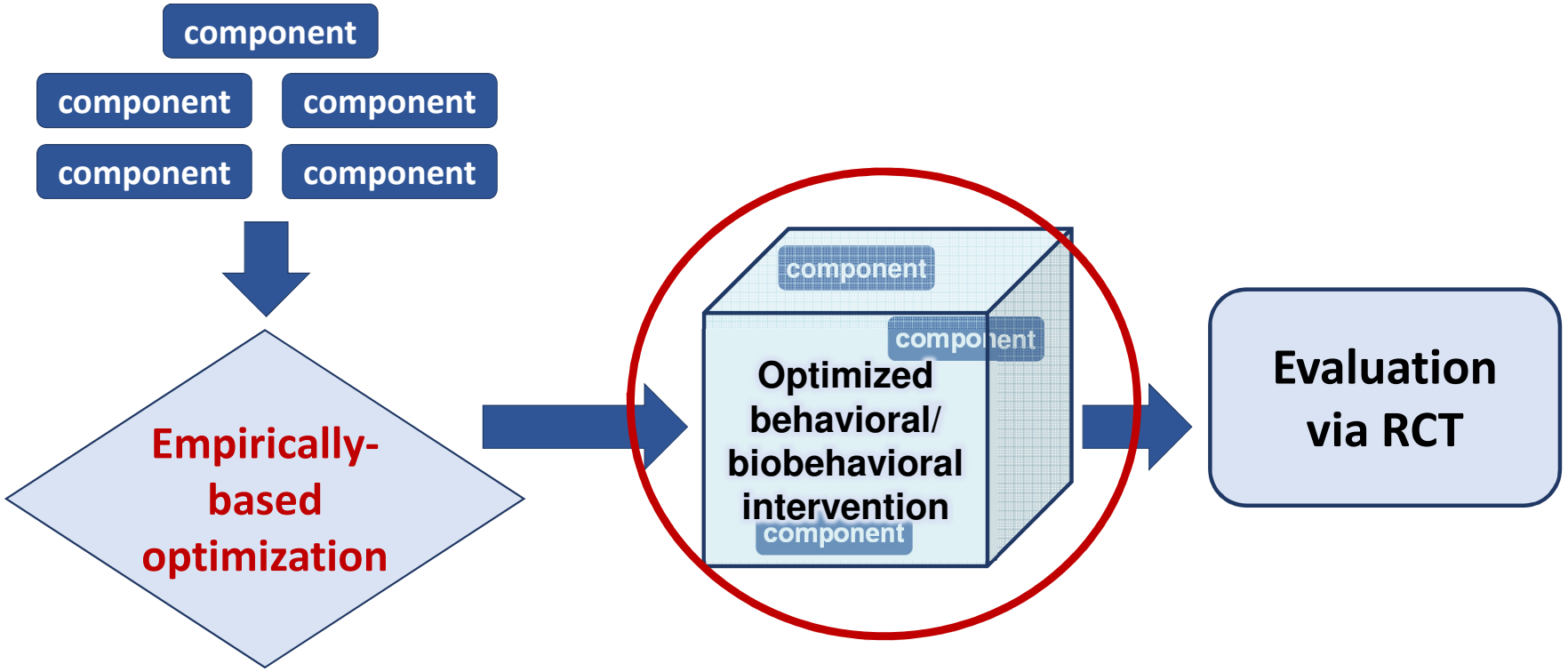

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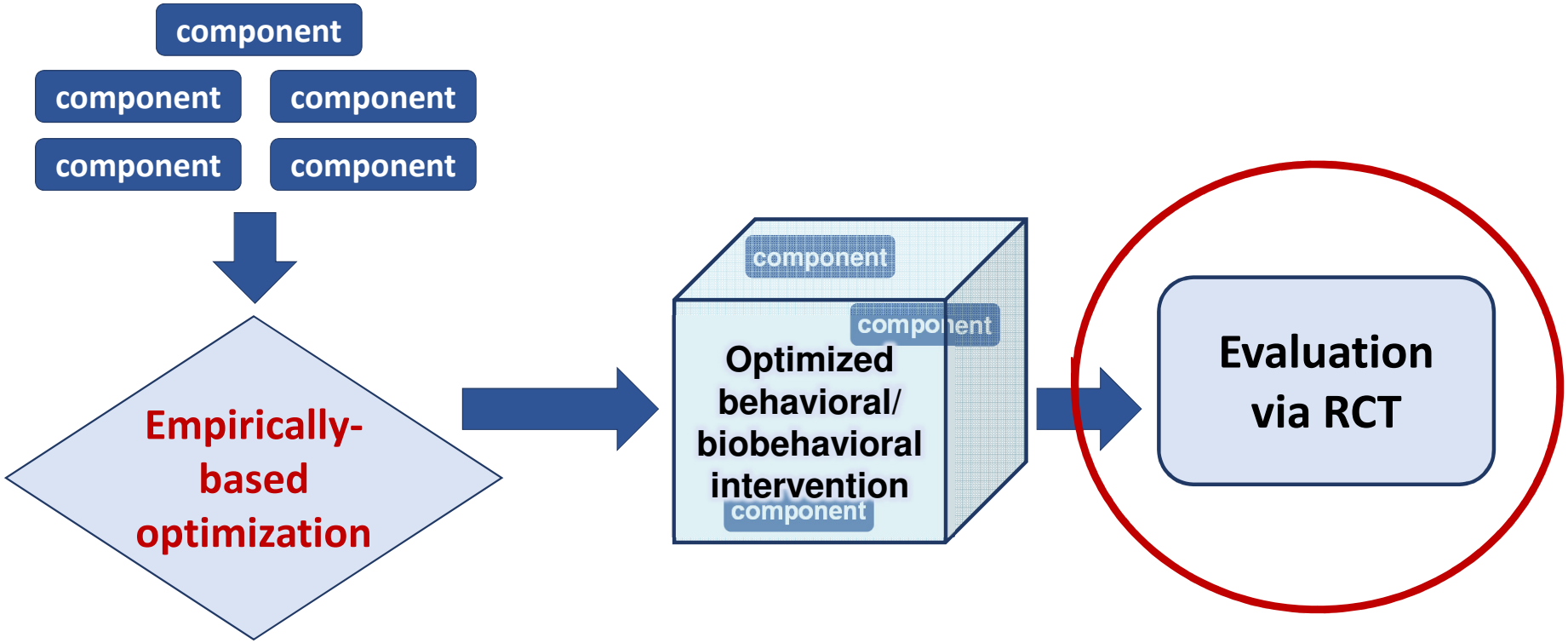

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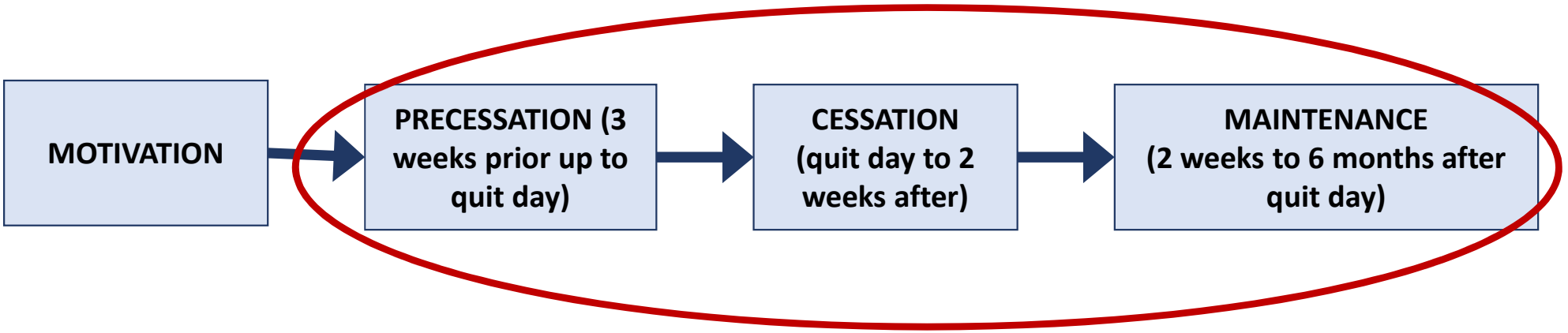
Example: Clinic-based smoking cessation study

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

- Part of a P01; PIs: Mike Fiore and Tim Baker, University of Wisconsin
- Funded by the National Cancer Institute

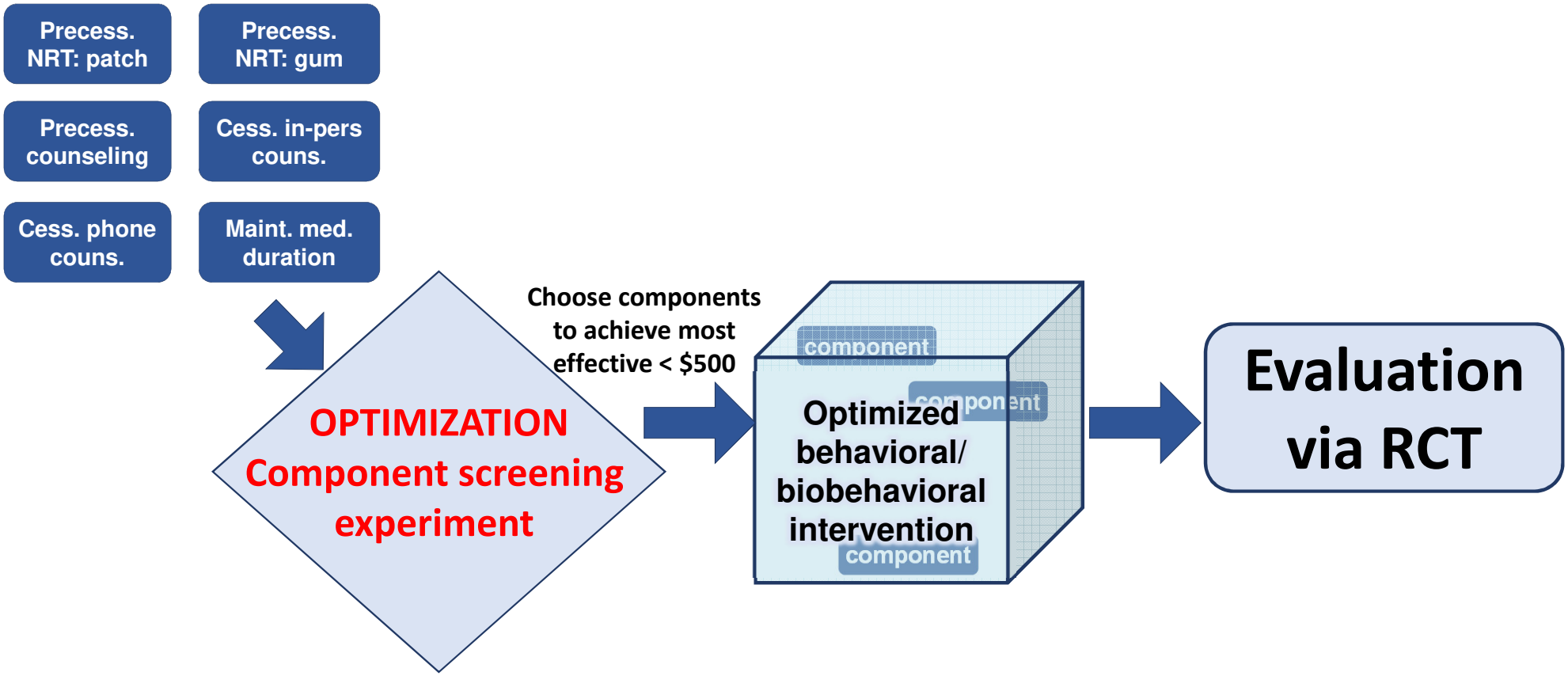
Baker & Fiore's phase-based model of the smoking cessation process



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



Choosing an efficient design for the component screening experiment

Design	N to achieve power≥.8	Number of experimental conditions	Can interactions be examined?
Option 1: Six individual experiments			
Option 2: Comparative treatment			
Option 3: Factorial experiment			
Option 4: Fractional factorial experiment			

Choosing an efficient design for the component screening experiment

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

Option 2: Comparative treatment experiment

Experimental conditions:

Treatment conditions						Control
Precessation patch = *yes* All others = low	Precessation gum = *yes* All others = low	Precessation counseling = *yes* All others = low	Cessation counseling = *intensive* All others = low	Cessation phone counseling = *intensive* All others = low	Cessation NRT = *16 weeks* All others = low	All = *low*

Choosing an efficient design for the component screening experiment

Design	N to achieve power≥.8	Number of experimental conditions	Can interactions be examined?
Option 1: Six individual experiments	3,072	12	None
Option 2: Comparative treatment	1,792	7	None
Option 3: Factorial experiment			
Option 4: Fractional factorial experiment			

Choosing an efficient design for the component screening experiment

Design	N to achieve power≥.8	Number of experimental conditions	Can interactions be examined?
Option 1: Six individual experiments	3,072	12	None
Option 2: Comparative treatment	1,792	7	None
Option 3: Factorial experiment	512	64	Yes, all
Option 4: Fractional factorial experiment			

Choosing an efficient design for the component screening experiment

Design	N to achieve power≥.8	Number of experimental conditions	Can interactions be examined?
Option 1: Six individual experiments	3,072	12	None
Option 2: Comparative treatment	1,792	7	None
Option 3: Factorial experiment	512	64	Yes, all
Option 4: Fractional factorial experiment	512	8, 16, or 32 depending on design chosen	Yes, selected subset

Factorial experiments 101

- Example: 2 X 2, or 2^2, 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 2^4 factorial design

Experimental conditions in a factorial experiment with four factors

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?

- 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 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 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 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 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 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

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 ½ 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)

The logic behind FF designs

- 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

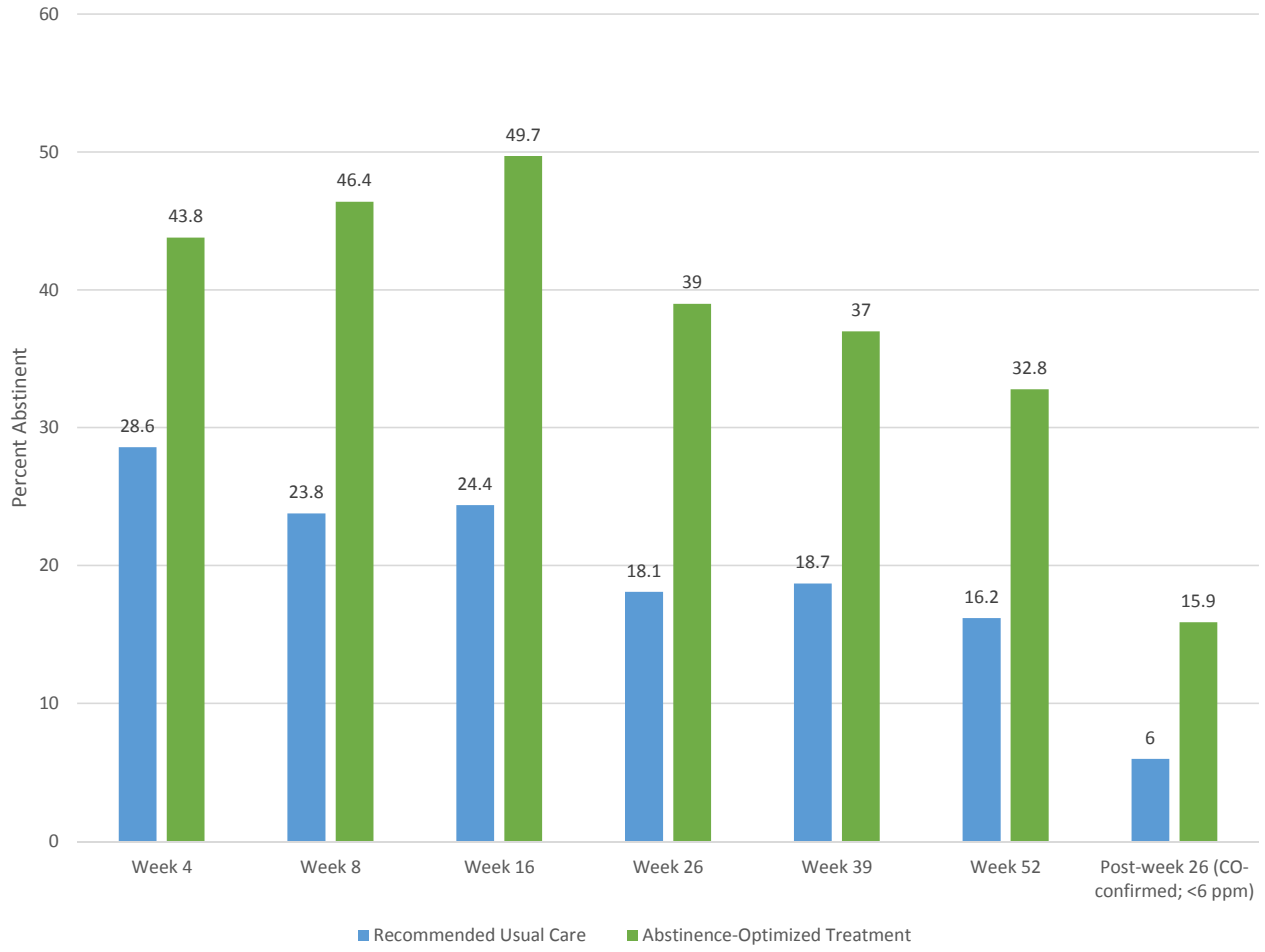
- Factorial experiment with six factors.
- It is a 2^{6-1} fractional factorial.
- The design has 32 experimental conditions.
- Each main effect aliased with one 5-way interaction; each 2-way aliased with one 4-way; each 3-way with one 3-way
- HEY! Where is the control group???

Table 1. Experimental Conditions

	Precessation Interventions			Pericessation Interventions		
Condition	Precessation Medication Type (Patch vs. none)	Precessation Medication Type (Ad Lib NRT vs. none)	Precessation Counseling (Intensive vs. none)	In-Person Counseling (Minimal vs. Intensive)	Phone Counseling (Minimal vs. Intensive)	Medication (8 weeks vs. 16 weeks)
1	Patch	Ad Lib	Intensive	Minimal	Minimal	Standard
2	Patch	Ad Lib	Intensive	Minimal	Intensive	Long-term
3	Patch	Ad Lib	Intensive	Intensive	Minimal	Long-term
4	Patch	Ad Lib	Intensive	Intensive	Intensive	Standard
5	Patch	Ad Lib	None	Minimal	Minimal	Long-term
6	Patch	Ad Lib	None	Minimal	Intensive	Standard
7	Patch	Ad Lib	None	Intensive	Minimal	Standard
8	Patch	Ad Lib	None	Intensive	Intensive	Long-term
9	Patch	None	Intensive	Minimal	Minimal	Long-term
10	Patch	None	Intensive	Minimal	Intensive	Standard
11	Patch	None	Intensive	Intensive	Minimal	Standard
12	Patch	None	Intensive	Intensive	Intensive	Long-term
13	Patch	None	None	Minimal	Minimal	Standard
14	Patch	None	None	Minimal	Intensive	Long-term
15	Patch	None	None	Intensive	Minimal	Long-term
16	Patch	None	None	Intensive	Intensive	Standard
17	None	Ad Lib	Intensive	Minimal	Minimal	Long-term
18	None	Ad Lib	Intensive	Minimal	Intensive	Standard
19	None	Ad Lib	Intensive	Intensive	Minimal	Standard
20	None	Ad Lib	Intensive	Intensive	Intensive	Long-term
21	None	Ad Lib	None	Minimal	Minimal	Standard
22	None	Ad Lib	None	Minimal	Intensive	Long-term
23	None	Ad Lib	None	Intensive	Minimal	Long-term
24	None	Ad Lib	None	Intensive	Intensive	Standard
25	None	None	Intensive	Minimal	Minimal	Standard
26	None	None	Intensive	Minimal	Intensive	Long-term
27	None	None	Intensive	Intensive	Minimal	Long-term
28	None	None	Intensive	Intensive	Intensive	Standard
29	None	None	None	Minimal	Minimal	Long-term
30	None	None	None	Minimal	Intensive	Standard
31	None	None	None	Intensive	Minimal	Standard
32	None	None	None	Intensive	Intensive	Long-term

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)

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- Definitions
- What's wrong with business as usual?
- What is MOST? What is optimization?
- OK, how do you do this?
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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, R01DA 029084)
- 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)