An Introduction to Optimization Trials for Behavioral Interventions

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International Behavioral Trials Network

- Simon Bacon (Concordia U) and Kim Lavoie (UQAM), co-leaders
- Free membership www.ibtnetwork.org
- Next IBTN Conference: May 28 to 30 2020, in Montreal (deadline for abstract submission Jan 20, 2020)

Linda Collins

Distinguished Professor, Department of Human Development and Family Studies
Director, The Methodology Center
The Pennsylvania State University

Co-led a workshop on Optimization Trials with Bonnie Spring (Northwestern U) at the 2018 IBTN conference

Slides available:
https://ibtnetwork.org/conference/

***several slides presented here taken with permission directly from the workshop presentation

Outline

- Definitions
- What's wrong with business as usual?
- What is optimization? What is MOST? How is it done?
- Examples of research applications with MOST
- Resources

What is a behavioral/biobehavioral intervention?

- A program with the objective of improving and maintaining human health and well-being
  - aimed at individuals, families, schools, organizations, communities…
  - using a strategy that at least in part aims to modify attitudes, cognitions, or behavior.

- Behavioral vs biobehavioral interventions

What is a behavioral/biobehavioral intervention?

- Examples:
  - 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
  - Lifestyle and weight management intervention
  - Cognitive behavioral therapy for the treatment of fear of cancer recurrence in cancer patients

- Most behavioral/biobehavioral interventions are made up of multiple components.

What is an intervention component?

- Any aspect of an intervention that can be separated out for study
  - Parts of intervention/program content
    - Each major topic to be covered (e.g., CBT, nutrition, mental health component)
    - Optimal dose of a behavioral intervention: duration, frequency, amount
  - Features that promote adherence or engagement
    - e.g., podometer, text/email reminders
  - Features aimed at improving fidelity of delivery or monitoring
    - e.g., 1-800 # for program delivery staff to call with questions
    - Who is delivering the intervention
- Components can be defined at any level: individual, family, school, etc.

Example

e-intervention for smoking cessation with 6 intervention components:

- 4 program components
  - Messages addressing the individual's expectations about what will happen if s/he quits smoking – present vs absent
  - Efficacy expectation messages addressing barriers to perceived self-efficacy – present vs absent
  - Message framing – positive vs negative
  - Testimonials from former smokers – present vs absent

- 2 delivery components (mode, frequency, duration, dose, intensity)
  - Exposure schedule – 1 long message vs 4 short messages
  - Source of message – Primary care physician vs HMO

Collins et al. 2007 Am J Prev Med

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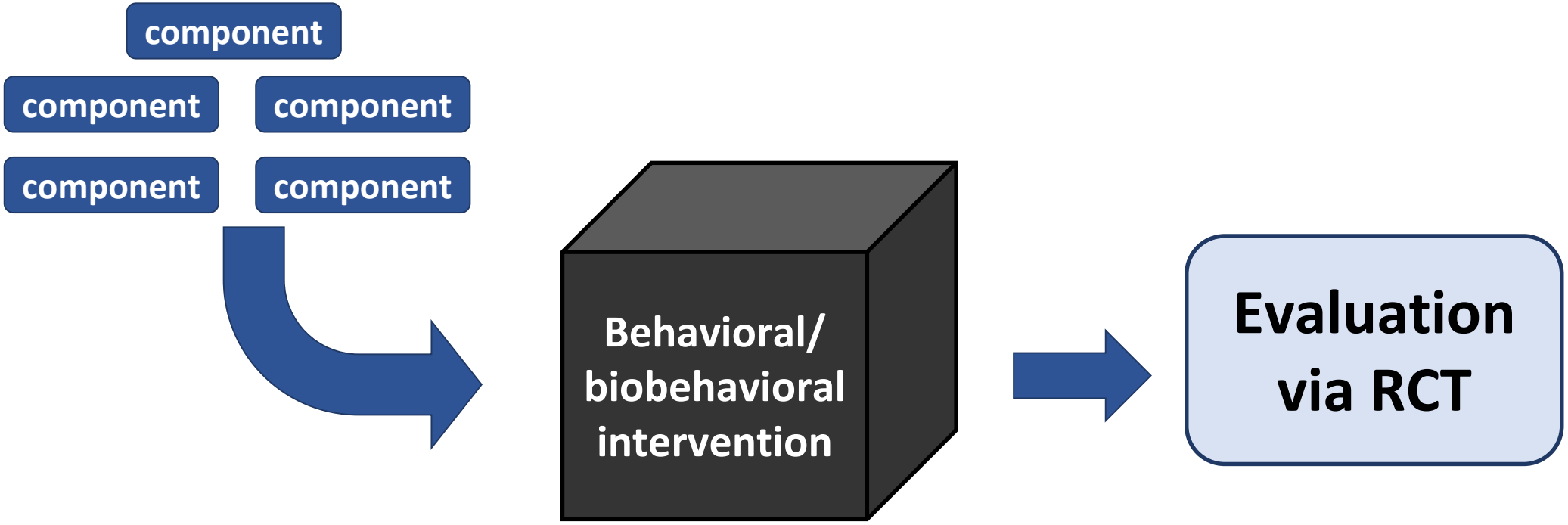
How behavioral/biobehavioral interventions are typically developed and evaluated

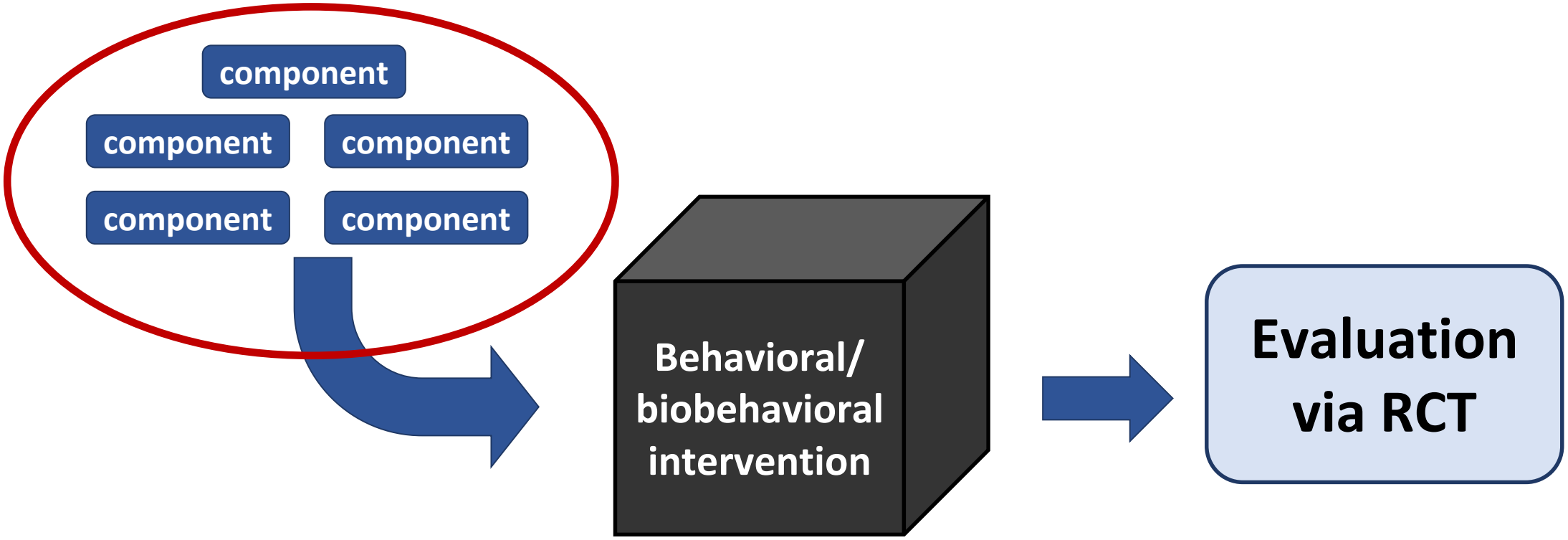
- Intervention components are chosen based on scientific theory, clinical experience, etc.
- Combined into a package
- Package is evaluated via a randomized controlled trial (RCT)
- Determining whether a treatment package performs better than
  - A control or comparison group or alternative intervention

treatment package approach

Classical treatment package approach



Classical 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 other components
- Specifically what went wrong and how to do it better the next time

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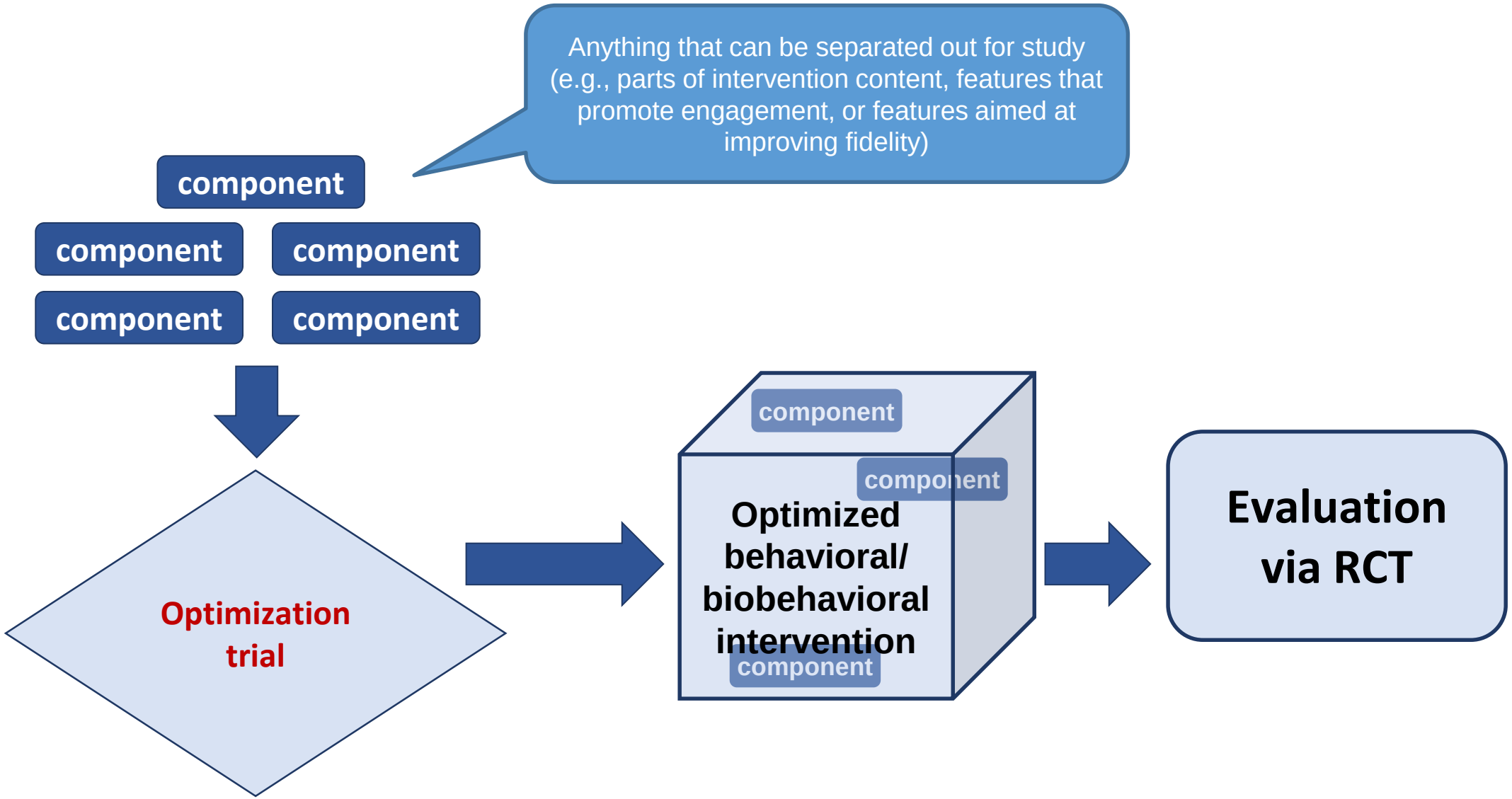
The multiphase optimization strategy (MOST)

- Alternative to the classical treatment package approach
- An engineering-inspired framework for development, optimization, and evaluation of multicomponent behavioral and biobehavioral interventions
  - Scientific research and discovery is an iterative process of deduction and induction

Multiphase optimization strategy (MOST)



Multiphase optimization strategy (MOST)

- The **process** of identifying the intervention that provides the **best expected outcome** obtainable within key constraints
  - **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

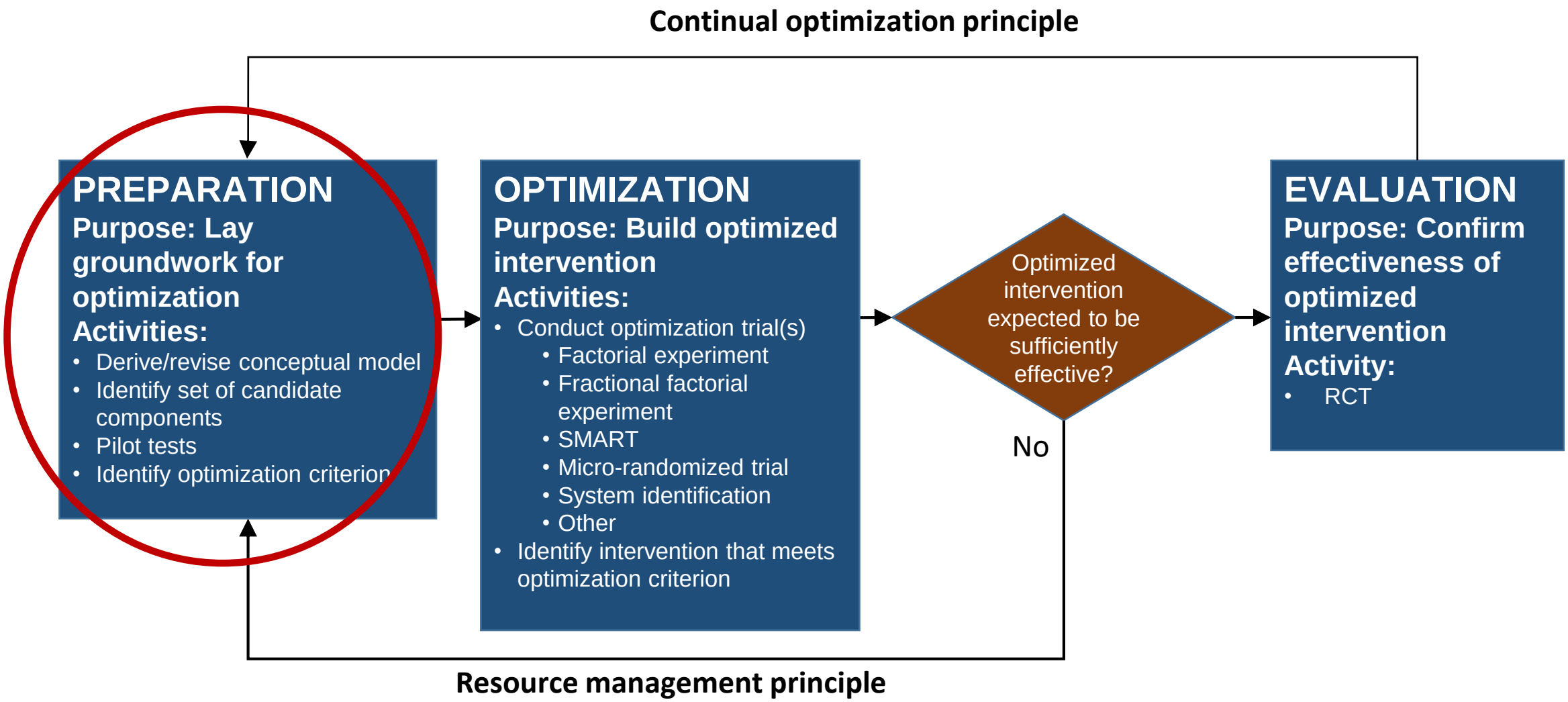


Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

Phases of MOST:
Preparation, optimization, evaluation

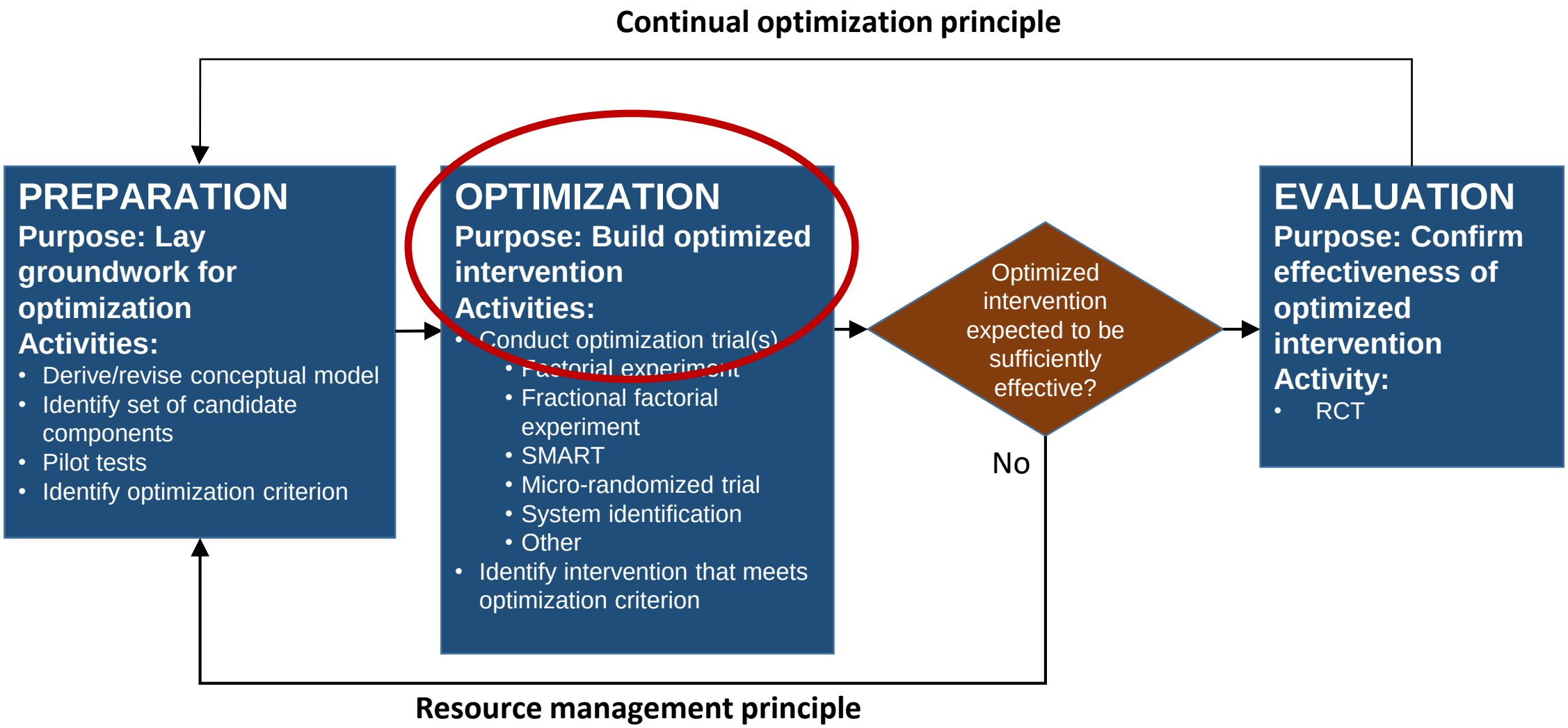
Preparation

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

- Possible criterion:
  - Only active intervention components (efficient but with no “dead wood”)
  - Most effective intervention that can be delivered for ≤ X$ / person
  - Most effective without exceeding a specified level of participant burden
  - Time
  - Cost-effectiveness
  - Or any other relevant criterion



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Phases of MOST: Preparation, optimization, evaluation

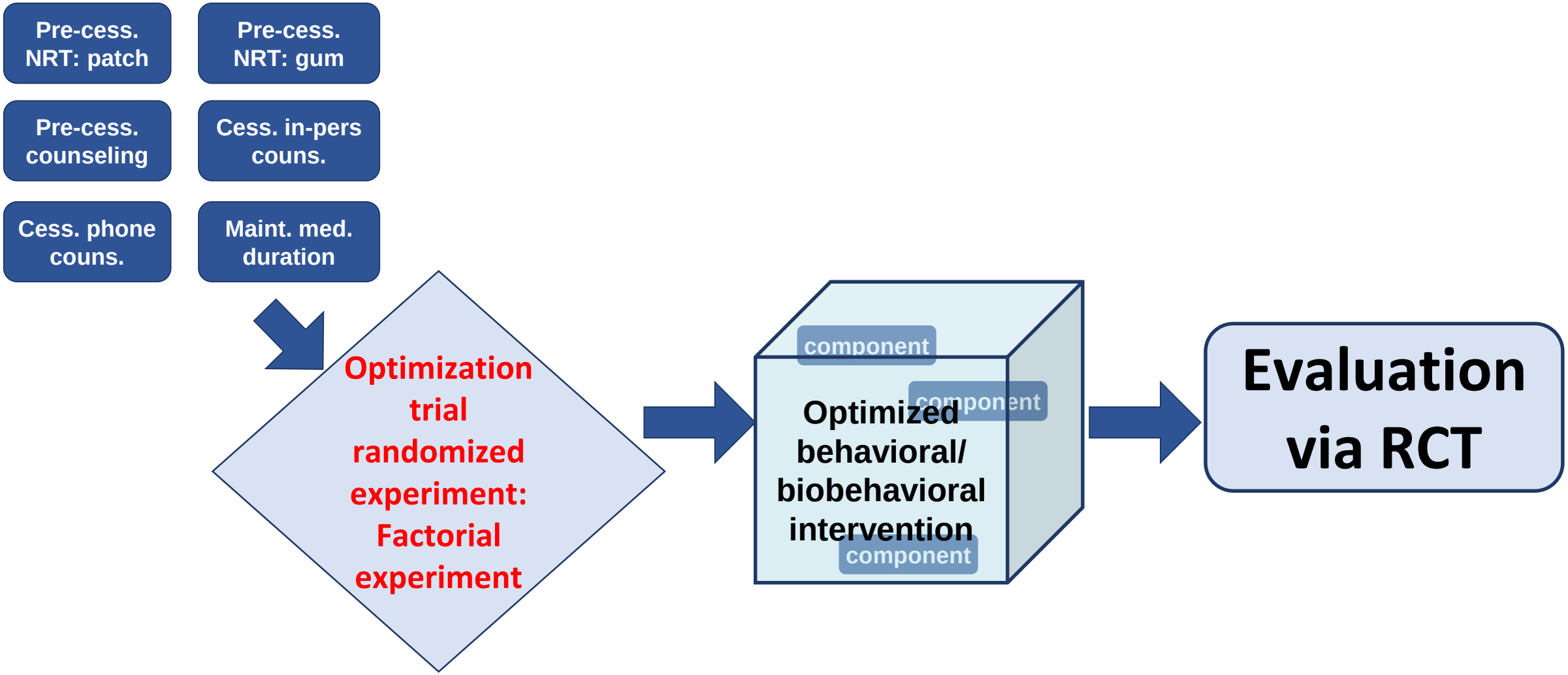
Optimization

- Objective: To form a treatment package that meets the optimization criterion
- *Optimization* is the process of identifying an intervention that provides the best expected outcome obtainable within key constraints
  - 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.

Example: Clinic-based smoking cessation study

- PIs: Mike Fiore and Tim Baker, University of Wisconsin, Funded by the United States National Cancer Institute
- 6 intervention components
  - Pre-cessation nicotine patch (No, Yes)
  - Pre-cessation ad lib nicotine gum (No, Yes)
  - Pre-cessation 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 optimization design

- **Design A:** Six individual treatment/control experiments
  1. Patch vs. no patch
  2. Gum vs. no gum, etc.

- **Design B:** Comparative treatment experiment

Treatment conditions						Control
Pre-cessation patch = *yes* All others = low	Pre-cessation gum = *yes* All others = low	Pre-cessation 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*

- **Design C:** Factorial experiment
  - 2^6 factorial experiment = 64 experimental conditions

Choosing an efficient design for the optimization trial

Design	Approximate N to achieve power≥.85 (Cohen's *d*=.27)	Number of experimental conditions	Can interactions be examined?
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

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

Components

	Factor A	
Factor 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 (components)
  - ≥ 2 levels per factor (e.g., low, moderate vs high dose for a given component)
- On the next slide is a 2^4 factorial design

Experimental conditions in a 2^4 factorial experiment

We can estimate **main effects** for each factor and **interaction effects** for each combination of 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

- For the **main effect of Factor A**: 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

- For the **main effect of Factor B:** 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

- For the **main effect of Factor B:** 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

- And so on for Factor D

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
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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

Using data from the factorial experiment

- Conduct an analysis of variance, obtain estimates of effects of each of the components
- Use this information to select components that make up the optimized intervention
  - Discard components that do not perform adequately
  - Discard components that do not perform optimally when delivered in combination with other components

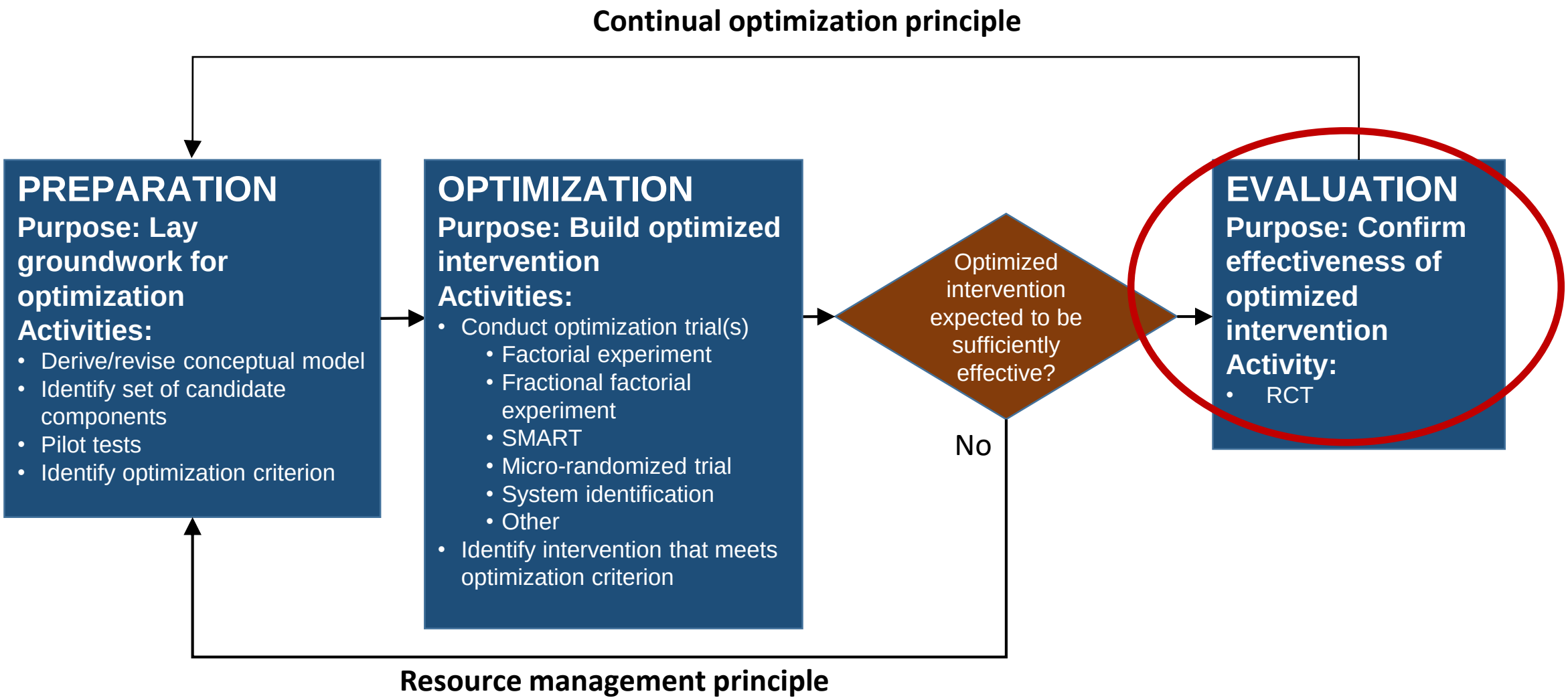
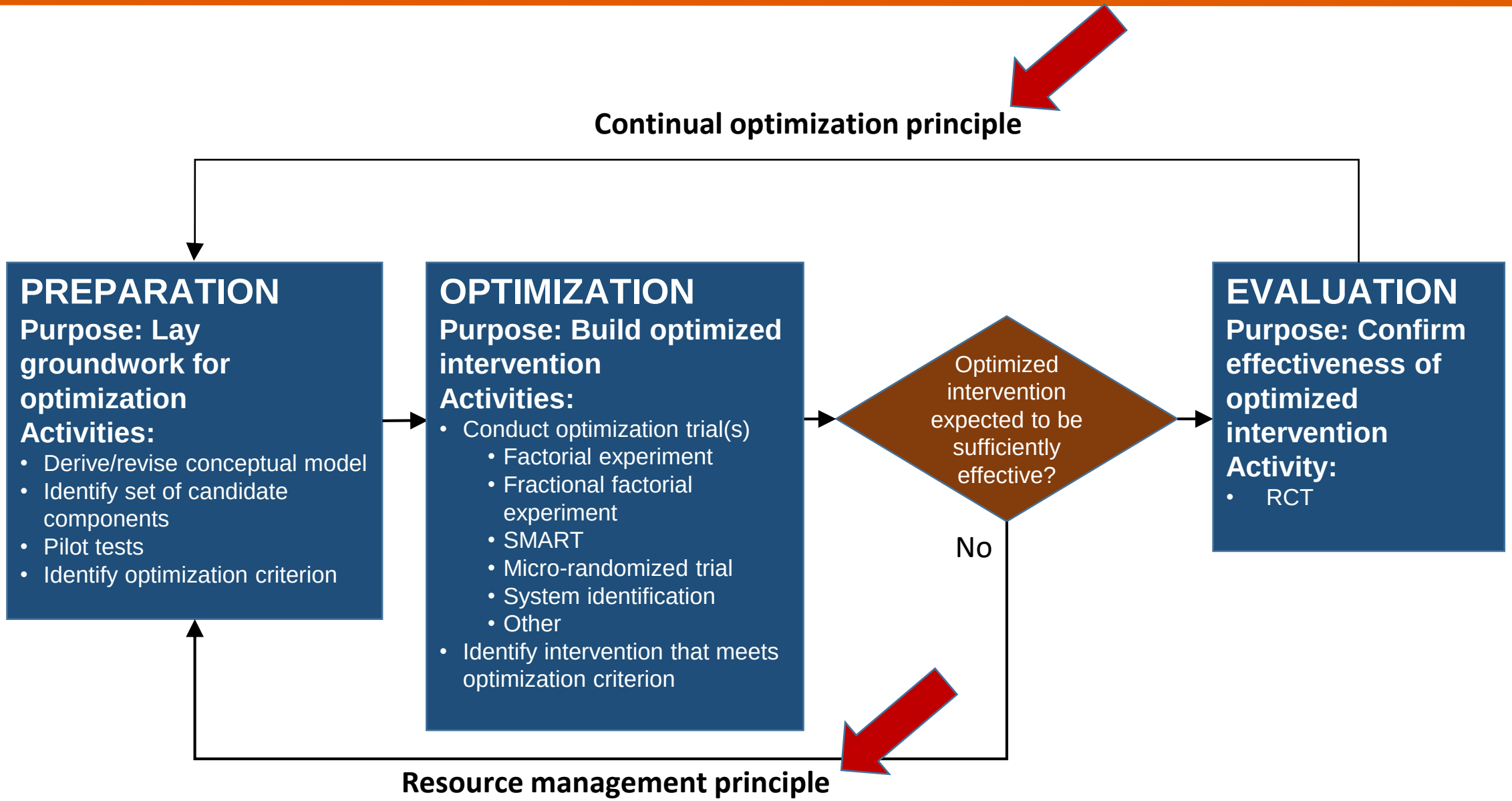


Figure 1.1. Flow chart of the three phases of the multiphase optimization strategy (MOST). Rectangle = action. Diamond = decision.

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

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

- 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 group for an RCT is often different a factorial experiment condition with all factors turned off



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- **Examples of research applications with MOST**
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Positive psychology intervention to promote health behaviors after an acute coronary syndrome (ACS)

Celano et al. 2018 Psychosomatic Medicine

- Individuals who have experienced an ACS may not succeed in achieving desirable health behaviors (eg. Physical activity)
- Lack of optimism is linked to reduced participation in health behaviors
- Design of a positive psychology-based intervention in post-ACS patients to promote physical activity
  - Positive Emotions After Acute Coronary Events III (PEACE-III)

Optimization trial

- 3 program components
  - Program content (PP vs. PP+MI)
  - Frequency of PP exercice (weekly vs. daily)
  - Booster session (no vs. yes)

- Optimization criterion: which of these components are associated with the greatest improvements in physical activity (MVPA) and self-reported health behavior adherence
- n=128 patients hospitalised post ACS

Factorial design

Condition	Program content	PP exercise frequency	Booster sessions
1	PP only	Weekly	No
2	PP only	Daily	No
3	PP + MI	Weekly	No
4	PP + MI	Daily	No
5	PP only	Weekly	Yes
6	PP only	Daily	Yes
7	PP + MI	Weekly	Yes
8	PP + MI	Daily	Yes

Results

- Physical activity (MVPA)
  - Adding MI did not improve outcome
  - Adding a booster session improved outcome
  - No difference whether PP exercise is done weekly or daily
- Adherence to health behaviors
  - Adding MI improved outcome
  - Adding booster session led to a non-statistically significant improvement
  - No difference whether PP exercise is done weekly or daily

Implementation of an evidence-based, community-delivered survivorship program for young adults with cancer (IMPACT)

PURPOSE

- To develop and optimize an intervention to improve post-traumatic growth (PTG) in AYA cancer survivors

STUDY DESIGN

- Partial preference randomized controlled trial (RCT) with multiphase optimization strategy (MOST)

GOAL: Make strategic choices based on theory (PTG) & prior knowledge to inform design decisions & reduce resource demands

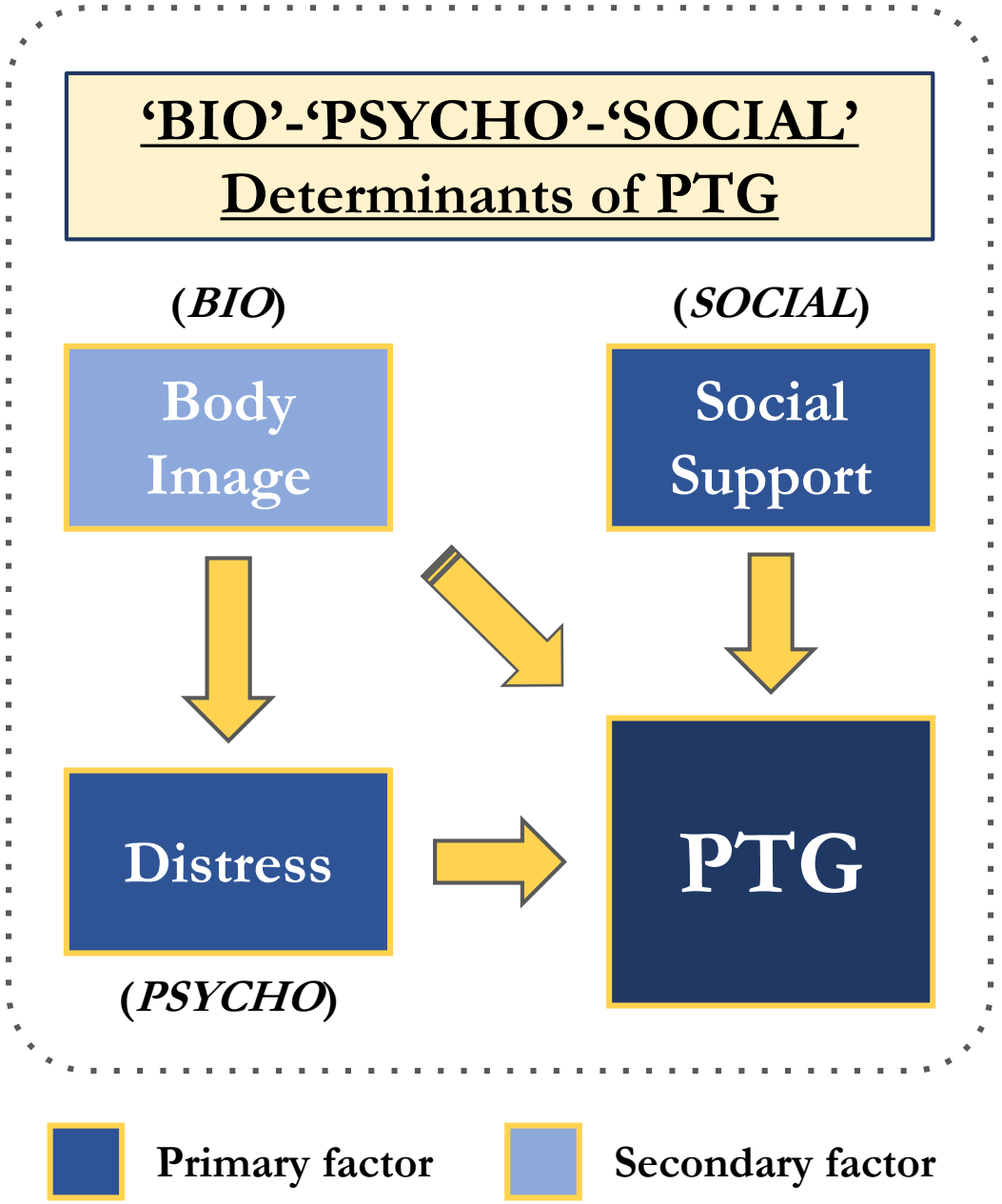
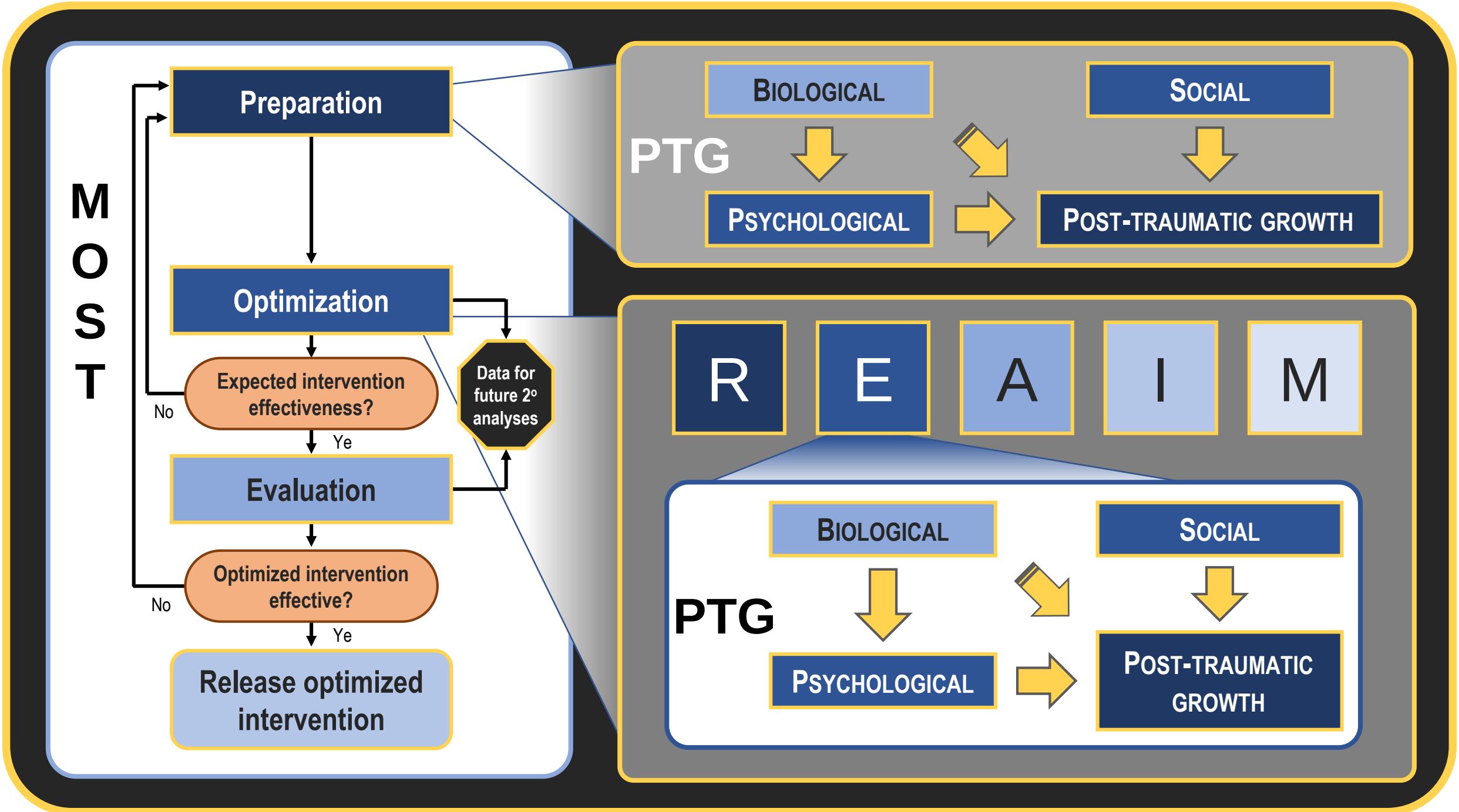


Figure 1: PRIME+ Methodological & Theoretical Frameworks



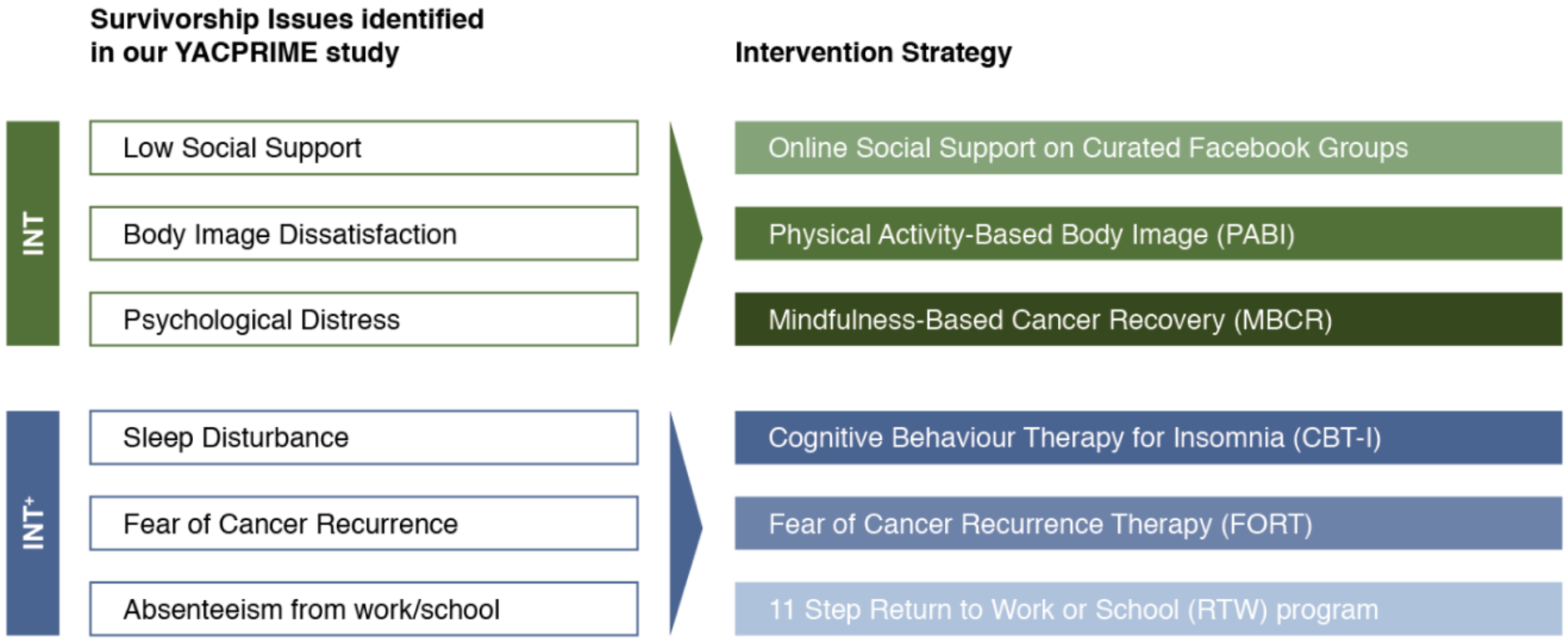


Figure 4: Survivorship issues to intervention strategies

Table 2: Interventions summary

Anxiety/Depression Body Image social support return to work fear of recurrence Insomnia

	MBCR	PABI	Social Support	RTW	FORT	CBT-I
Participants per group	5	5	5	5	5	5
Session duration	90 min	30 min	60 min	60 min	120 min	60 min
Session per week	1	1	1	1	1	1
Number of weeks	8	8	8	8	6	6
Intervention setting	online	online	online	online or telephone	online	online
Components	- Theory on relaxation, meditation, body-mind connection - Group meditation, yoga, personnal practice - Group support to increase performance, interpersonnal support	- Web-based education and PA prescription - Self-directed PA participation - Remote (cellphone application/web) PA coaching	- Emotional support - Instrumental support - Informational support - Appraisal support	- Vocational rehabilitation assessment - Barriers and facilitators identification relative to work stage - Formulation of RTW goals - Formulation of strategies to overcome barriers and enhance facilitator - Strategies for communicating with healthcare team and employer - Support to build a RTW or Return to School plan	- Web-based education of models of FCR, cognitive restructuring, siymptoms of possible recurrence, and relaxation techniques with the assistance of audio recording. - Self directed CR participation in the context of FCR triggers - Weekly guidance on how to manage worries, and building plan of action for FCR triggers, and when to seek medical assistance. Existential review exercise with exposure to worst case scenario. Group support to build future plans.	- Education about sleep - Time in Bed Restriction - Stimulus Control - Cognitive restructuring

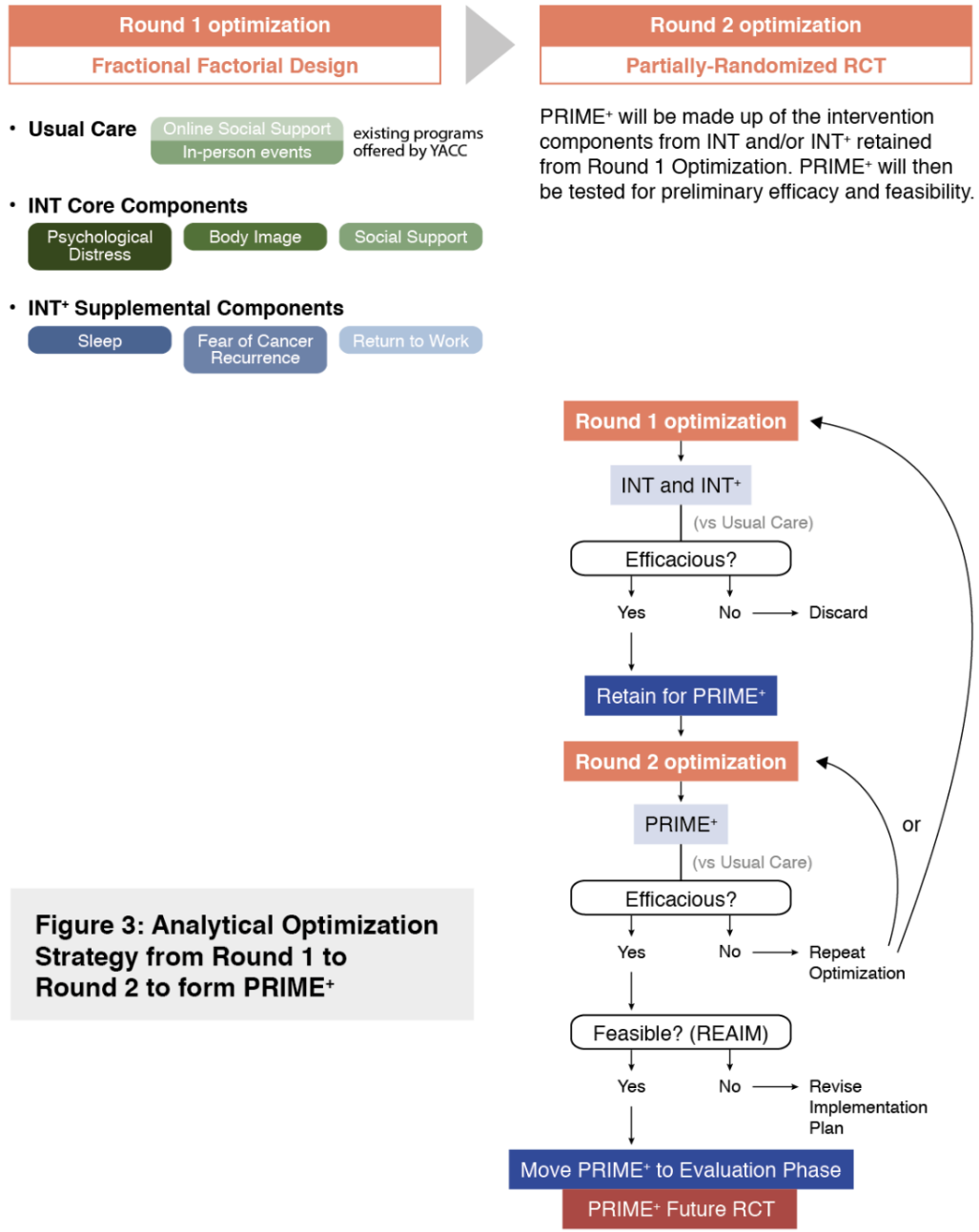


Figure 3: Analytical Optimization Strategy from Round 1 to Round 2 to form PRIME+

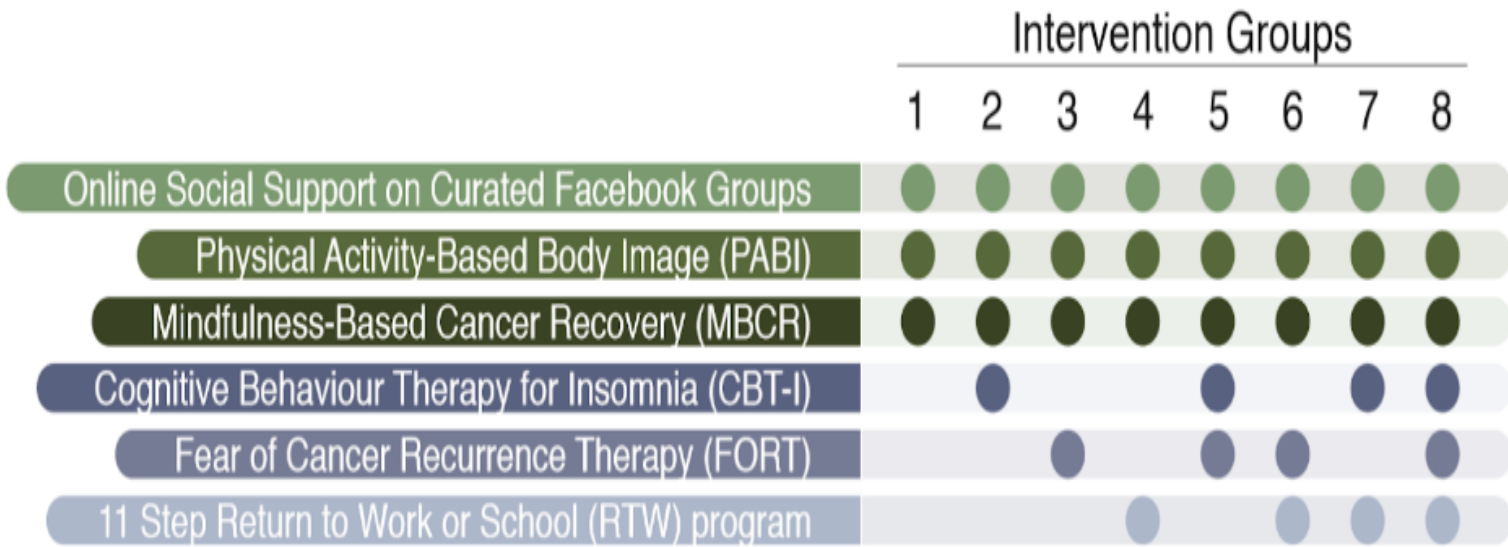


Figure 6: Round 1 Optimization: Fractional factorial design

8 intervention groups + 1 control group (Usual Care, UC).

Table 1: PRIME+: RE-AIM Data collection Plan Round 2 Optimization

RE-AIM Component	Definition
Reach	- Percentage of individuals who participate based on valid denominator - Characteristics of participants compared to nonparticipants or to target population - Exclusion criteria- Report numbers excluded
Effectiveness	- Measure of primary outcome: Feasibility (Loss to follow-up (<30%)) - Measure of primary outcome: Intervention (Post-Traumatic Growth): Posttraumatic Growth Inventory (PTGI) collected over time - Measure of broader outcomes: Feasibility (*e.g.*, attendance, adherence) - Measure of secondary outcomes: Intervention (*e.g.*, quality of life) a. Participant-level: Demographics (study-specific tool); b. Distress: Kessler Psychological Distress Scale (K10); c. Quality of Life: short-Form Health Survey 12 (SF-12); d. Body Image Scale (BIS); e. Fear of Cancer Recurrence Inventory; f. Sleep: Insomnia Severity Index (ISI); g. Work Productivity and Activity Impairment (WPAI); h. Social Support: Multi-dimensional Scale of Perceived Social Support (MSPSS). - Measure of short-term attrition (%) and differential rates by participant characteristics or treatment condition - Comparison of all other intervention tolerability outcomes between different cancer diagnosis groups and by sex and gender.
Adoption	- Number and type of supplemental interventions chosen by participants
Implementation	- Measure of primary outcomes at data collection points - Measure of long-term attrition (%) and differential rates by participant characteristics or treatment condition
Maintenance	- Potential for program uptake - Evaluation of all Knowledge Transfer and Mobilization activities through feedback and surveys from all participants/attendees at these activities. - Qualitative: Discussion and evaluation of alignment between YACC mission and appraisal of potential ongoing institutional support for the PRIME+ program

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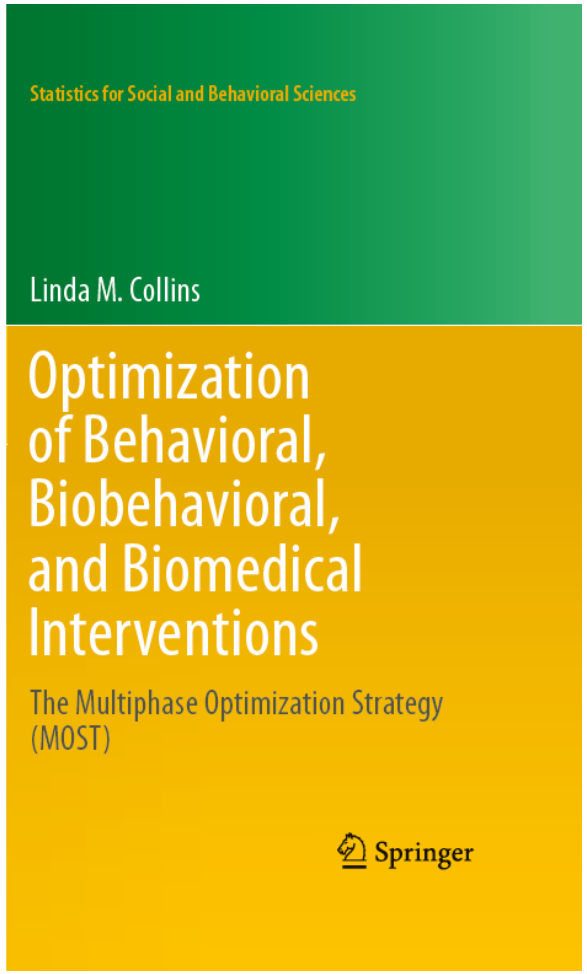
- Examples of research applications with MOST
- Resources - where can I learn more on MOST?

For more information:

- Introduction to MOST with Linda Collins
  - https://www.youtube.com/watch?v=AdXsya3mtWI

- MOST website: https://methodology.psu.edu/ra/most
  - Sign up for eNews
  - Section on MOST with
    - Suggested reading
    - FAQ
    - Advice for people writing grant proposals involving MOST
  - Apply for free consulting on MOST https://methodology.psu.edu/publications/news/most-consulting



Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy.*

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