ROYBAL
Center For
Translational
Research

Welcome to the 2023 Annual Meeting

Edward R. Roybal Centers for Translational Research in the Behavioral and Social Sciences of Aging

March 14-15, 2023

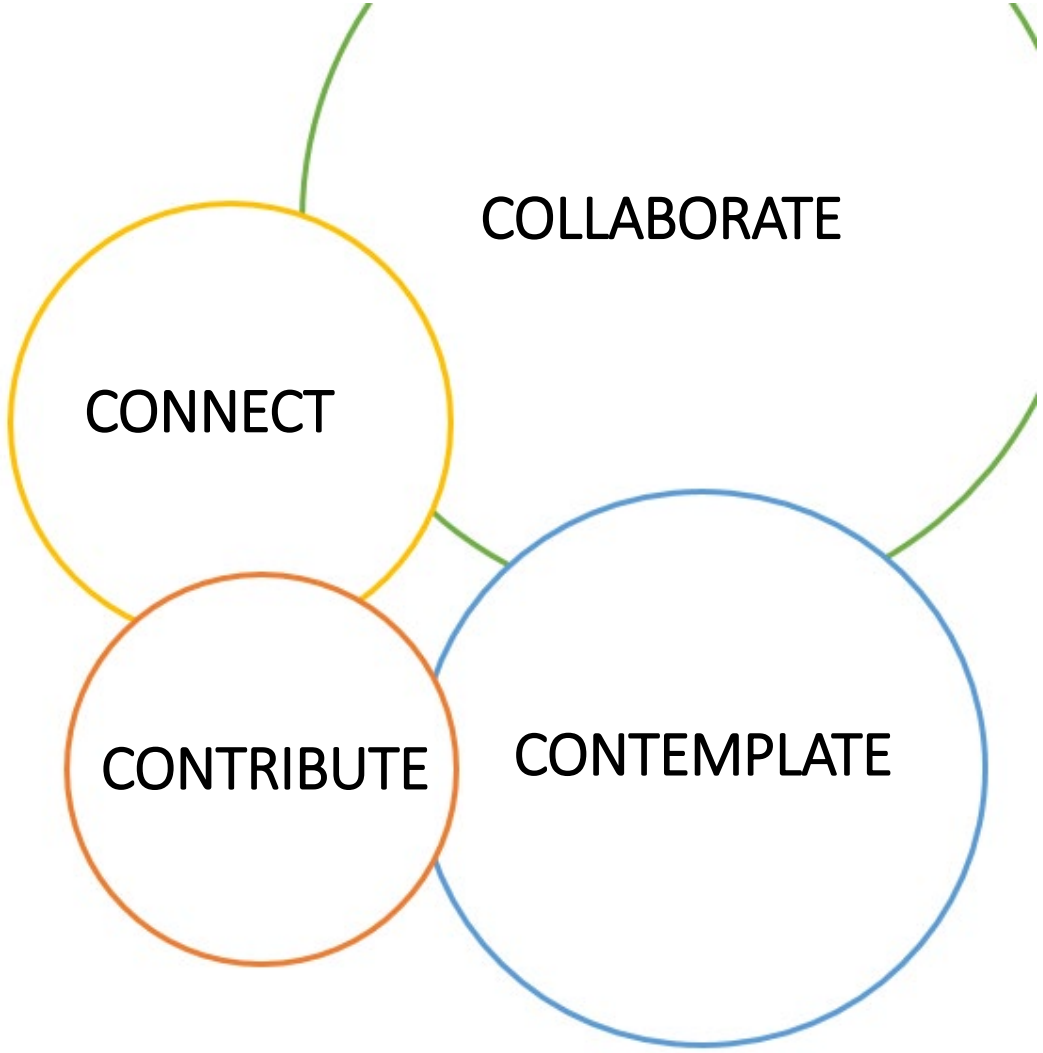
Day 1

Welcome

KARINA DAVIDSON, PHD, MASC

ROYBAL COORDINATING CENTER PI

NORTHWELL HEALTH



Meeting Goals

Day 1 Meeting Agenda

ROYBAL Center For Translational Research

- 10:00am-10:20am – **NIA Welcome**
- 10:20am-11:10am – **Recommendations for Early-Stage Trials**
- 11:10am-11:30am – **BREAK**
- 11:30am-12:00pm – **Approaches to Intervention Optimization**
- 12:00pm-1:30pm – **LUNCH**
- 1:30pm-2:30pm – **Multimodal and Multilevel Adaptive Interventions**
- 2:20pm-2:50pm – **Panel Discussion: Intervention Optimization**
- 2:50pm-3:10pm **BREAK**
- 3:10pm-4:30pm **Innovative Strategies for Enhancing Retention in Clinical Trials**
- 4:30pm-5:00pm **General Discussion**
- 5:00pm **Day 1 Adjourn**
- 6:00pm-7:00pm **Cocktail Hour**
- 7:00pm-9:00pm **Dinner Reception**

Housekeeping for Today's Meeting

BE FULLY PRESENT

TURN OFF CELL PHONES, CLOSE YOUR EMAIL, ETC.

DON'T BE LATE

PLEASE RETURN FROM LUNCH AND BREAKS ON TIME

SPEAK OFTEN AND LOUDLY

PLEASE BE SURE TO SPEAK INTO THE MICROPHONES LOCATED AT EACH TABLE

ROYBAL
Center For
Translational
Research

Welcome from the NIA

Edward R. Roybal Centers for Translational Research in the Behavioral and Social Sciences of Aging

Lisbeth Nielsen, PhD
Director, Division of Behavioral and Social Research
National Institute on Aging

Lisa Onken, PhD
Director, Behavior Change and Intervention Program
National Institute on Aging

Recommendations for Pilot Trials in Health-Related Behavioral Intervention Research

Kenneth E. Freedland, PhD
Professor of Psychiatry and Psychology
Washington University School of Medicine
St. Louis, Missouri

Washington University in St. Louis
School of Medicine

Disclosure

- Research funding: NHLBI, NIMH.

- Other relevant financial interests: None

Preface

- I’ve reviewed hundreds (thousands?) of pilot study and RCT proposals and reports as a:
  - grant reviewer
  - journal editor or reviewer
  - consultant or co-investigator
  - Summer Institute faculty member
- Through all of this, I’ve found that:
  - Many pilot studies have similar weaknesses.
  - Reviewers often overlook or disagree about them.

Preface

- Roybal pilot study proposals and plans:
  - Great ideas -- promising interventions for significant problems. ☺
  - Despite their strengths, many have similar weaknesses. ☹
  - Roybal FOAs promote some of them. ☹ ☹
- This presentation will include:
  - An honest critique.
    - You may disagree or find it difficult to accept.
    - You may be right, and I may be wrong.
    - But please keep an open mind about it.
  - Recommendations
    - Would help to improve Roybal-funded research if adopted.

Background

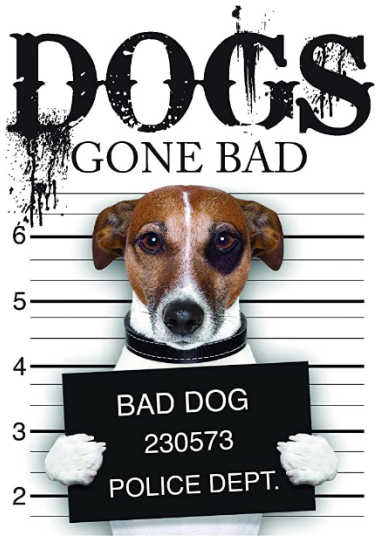
- "Pilot" is used informally to label many kinds of studies.
- "Pilot" is defined in the Roybal FOAs as follows:
  - For the purposes of this FOA, Stage I studies and small-scale Stage 0, II, III, and IV studies will be referred to as "pilot" studies.
  - All applications must include Stage I studies, in which a principle-driven intervention and the intervention's associated materials are created, refined, adapted, and pilot tested for feasibility, acceptability and efficacy.
- *Inconsistent with current methodological guidance on pilot studies.*

Background

- Across many disciplines and fields of intervention research:
  - Most "pilot" studies have been **preliminary efficacy trials (PETs).**
  - Miniature, severely underpowered, randomized controlled efficacy trials.
    - (Severely underpowered by design, not due to underenrollment.)

PETs

- Disappointing PETs typically:
  - Kill innovative interventions in their cribs.
    - Including ones that are very promising.
  - Don’t get published.



PETs

- Pleasing PETs:
  - Often get published.
  - Are used to support claims of
    - "preliminary evidence of efficacy" or
    - "a signal of efficacy."
  - Are often used to justify a larger RCT proposal.
  - Provide the effect size for the proposal's power analysis.

PETs

- Most of us thought this was the right way to do intervention research – it seemed obvious, and we didn't question it.
- Until this mind-boggling paper was published:
  - Kraemer HC et al. Caution regarding the use of pilot studies to guide power calculations for study proposals. *Archives of General Psychiatry* 2006;63(5):484-489.
- It had profound implications for:
  - The purposes, specific aims, and design of interventional pilot studies.
  - Other types of early-phase intervention research.
  - The purposes and outcomes of full-fledged RCTs.

Kraemer et al. (2006): Some Key Points

- The most likely outcomes of PETs are that:
  - RCTs that would be worth performing will be aborted instead.
  - RCTs that are not aborted will be underpowered.
- Why?
  - PETs yield highly inaccurate & biased effect size estimates.
  - But even if PETs yielded accurate estimates, PET effect sizes would still be the wrong ones to use in power analyses for larger RCTs.
- What's the right effect size to use?
  - The minimum clinically important difference (MCID).
- Valid MCID values almost never emerge from pilot studies.
  - Other kinds of studies are needed to establish valid MCIDs.

PETs With Long Lives

- Only around 5% of PET publications are ever followed by the publication of a full-fledged RCT.
- When larger efficacy trials *are* conducted, they usually produce smaller effects than PETs, or even null results.
- But PET publications live forever.
  - They inject what Paul Krugman calls "zombie ideas" – erroneous ideas that never die – into the behavioral treatment literature.
  - Despite the glaring weaknesses of the evidence they provide, they are often cited as supporting the efficacy or superiority of the intervention.
  - More rigorous confirmatory or contradictory evidence may never appear.
- Thus, PETs do much more harm than good for the cause of evidenced-based behavioral intervention research & practice.

PETs With Long Lives

APA's 89 journals published more than 5,500 articles in 2022.
This PET was #4 on APA's list of the top 10 most widely read articles.

AMERICAN PSYCHOLOGICAL ASSOCIATION

Society for the Advancement of Psychotherapy

Psychotherapy

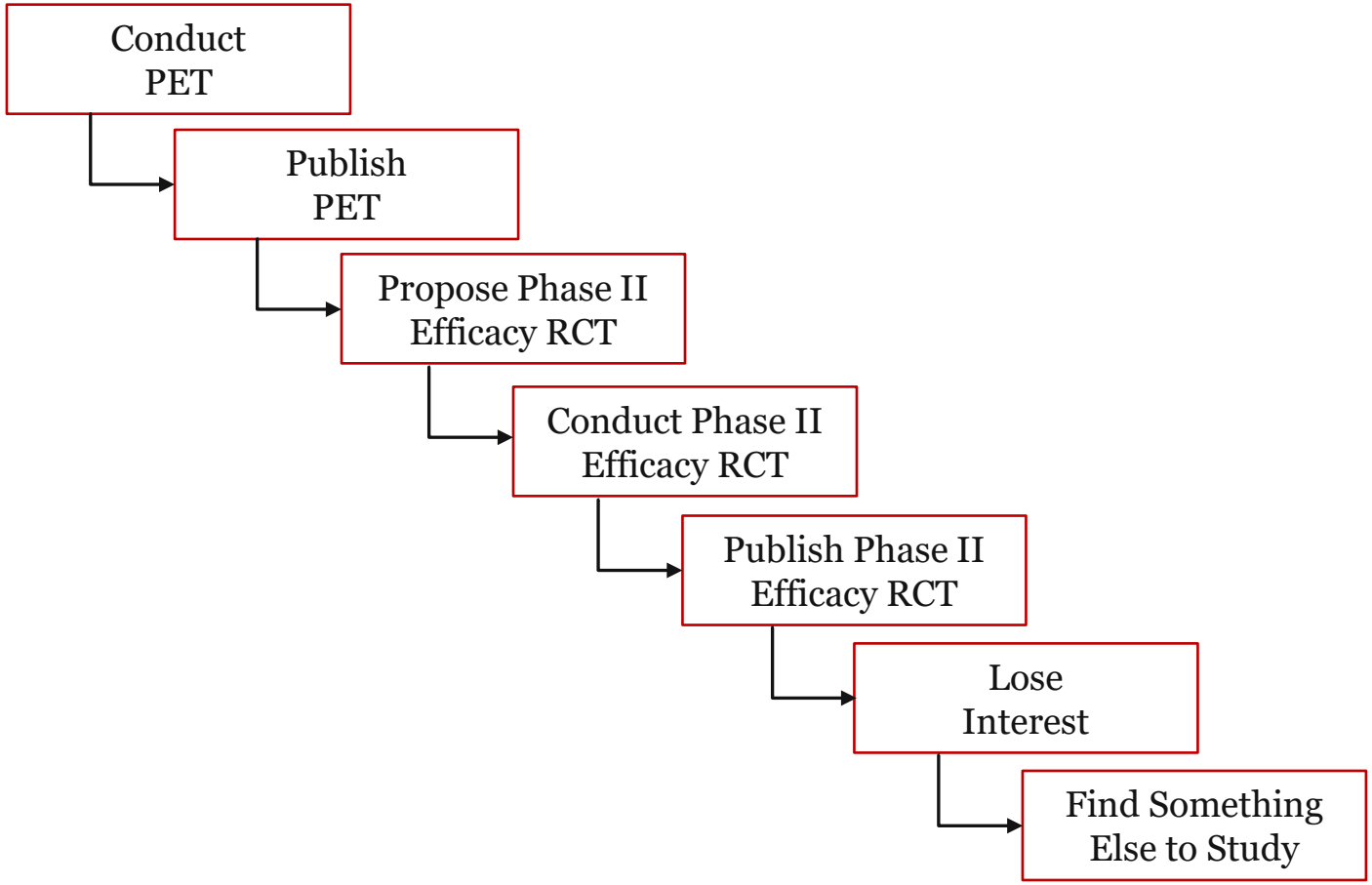
ISSN: 0033-3204

2022, Vol. 59, No. 1, 84–95
https://doi.org/10.1037/pst0000427

A Comparison of Emotion-Focused Therapy and Cognitive-Behavioral Therapy in the Treatment of Generalized Anxiety Disorder: Results of a Feasibility Randomized Controlled Trial

Ladislav Timulak[1], Daragh Keogh[1], Craig Chigwedere[1], Charlotte Wilson[1], Fiona Ward[2], David Hevey[1], Patrick Griffin[2], Louise Jacobs[2], Suzanne Hughes[1], Christina Vaughan[1], Kea Beckham[1], and Shona Mahon[1]

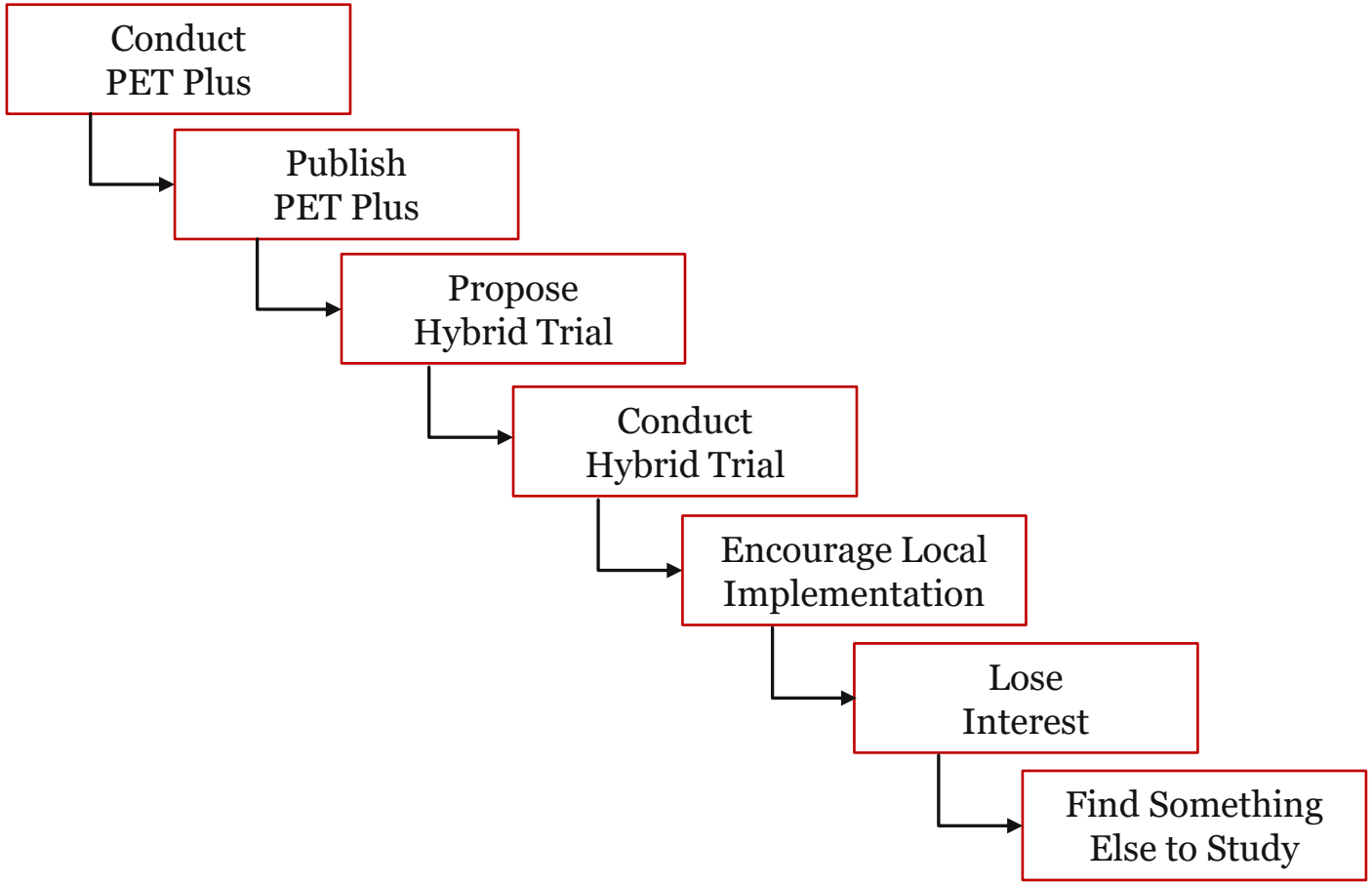
Traditional Trajectory



PET Plus

- Many researchers know that something's wrong with PETs but
  - they don't fully understand their drawbacks, and
  - they don't know enough about alternative approaches, so
  - they propose a PET but bury it under a pile of other aims and analyses.
- They've also heard that pilot studies are supposed to have something to do with feasibility and that they should be thinking ahead about scalability and implementation.
  - So, they add aims concerning feasibility, acceptability, etc.
- These "PET Plus" studies often launch investigators on a different trajectory.

Emerging Trajectory



Another Major Development

- Kramer et al. hit many of us like a big earthquake.
- Eldridge et al. hit us like a major aftershock.

CONSORT 2010 statement: extension to randomised pilot and feasibility trials

Sandra M Eldridge,[1] Claire L Chan,[1] Michael J Campbell,[2] Christine M Bond,[3] Sally Hopewell,[4] Lehana Thabane,[5] Gillian A Lancaster[6] on behalf of the PAFS consensus group

British Medical Journal 2016;355:i5239

Definitions

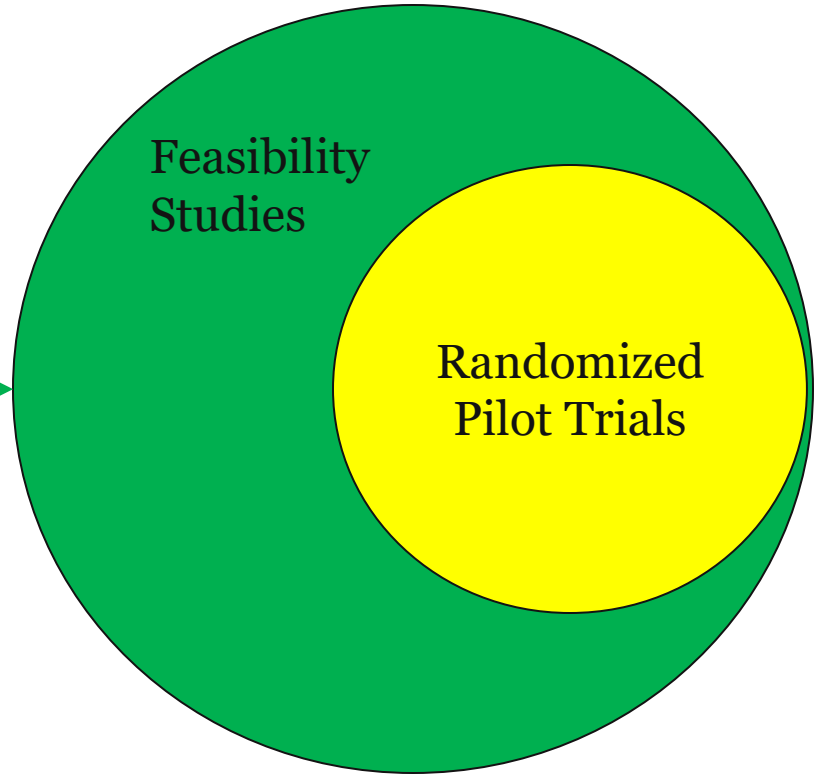
- Before developing the CONSORT guideline, Eldridge et al. established consensus definitions of "feasibility" and "pilot" and established a conceptual framework for these studies.
- They based their definitions and framework on:
  - An extensive literature review.
  - A Delphi survey of clinical trial experts.
  - Discussion sessions at methodology conferences.
  - An international consensus meeting.
    - Eldridge SM et al. *PLOS One* 2016;11(3):e0150205.

Definitions

- **Feasibility studies**:
  - are done before an RCT to assess: **"Is this RCT doable?"**
  - address recruitment, retention, delivery of the intervention, etc.
  - i.e., critical factors for the successful conduct of the future RCT.
- **Randomized pilot trials:** a special type of feasibility study.
  - **Key design feature:** A pilot trial is a smaller version of the main trial.
    - Same intervention and control groups, same measures, etc.
    - Much smaller sample.
  - **Aims** do *not* include a preliminary efficacy analysis.

Feasibility Studies and Randomized Pilot Trials

- Single-arm trials
- Quasi-experimental (non-randomized) trials with two or more arms.
- Data mining studies (e.g., analyses of EMR data)
- Stakeholder surveys or focus groups
- Experimental tests of alternative trial procedures



All of the above can address questions about ***whether a future RCT is doable.***

Added Value of Randomized Pilot Trials

- There are many kinds of feasibility studies.
- So why conduct a randomized pilot trial?
  - (Either instead of *or* in addition to other kinds of feasibility studies.)
- They address questions that other feasibility studies can't, e.g.,
  - Will our randomization and concealment procedures work?
  - Will participants accept randomization?
  - Can we prevent differential attrition?
- Pilot trials can also address a variety of other RCT feasibility questions, including questions about the control group.

RCT Reviewer's Perspective

- Reviewers of proposals for relatively large, complex, and/or expensive trials (including single-site trials) want to know:
  - Is this trial doable by these investigators, at this site (or these sites), with these resources, within this budget, etc.?
- They usually look for certain kinds of feasibility data.
  - e.g., how large is the pool of potentially eligible patients at this center?
- They may want to see randomized pilot trial data.
  - Unless the need is obviated by previous RCTs or favorable circumstances.
- Reviewers also look elsewhere for evidence of RCT feasibility.
  - E.g., How much clinical trial experience does this team have?
  - E.g., Do they have the necessary expertise and institutional support?
  - E.g., Is the protocol unduly complicated or burdensome?

When "Feasibility" ≠ CONSORT Feasibility

- Many pilot grant applicants misunderstand feasibility.
  - They believe that the purpose of a feasibility study is to establish the feasibility of the *intervention* rather than the feasibility of a future RCT.
- Problematic for two reasons:
  - Their pilot study will not establish the feasibility of the future RCT.
    - Seriously jeopardizes the chances of funding for their future RCT.
  - "Feasibility" is not an inherent property of behavioral interventions.
    - Intervention feasibility is almost always *context-dependent*.
      - An intervention may be feasible in one setting but not another.
    - Context-dependent intervention feasibility is a proper question for optimization trials in the MOST framework and for implementation research, but usually not for pilot trials.

Intervention Data in Randomized Pilot Trials

- But certain questions about the intervention can and should be addressed in a pilot trial and/or in other feasibility studies.
  - E.g., is the intervention *acceptable* to people who would be eligible to participate in the future RCT?
  - E.g., do our therapist training, supervision, & fidelity procedures work?
  - E.g., do most participants adhere to the intervention protocol?
- There are other questions about interventions that should *not* be asked in pilot trials.
  - They should be asked in other kinds of studies.
  - More on this later.

A Rare Bit of Wisdom From Donald Rumsfeld

There are known knowns.

These are things we know that we know.

There are known unknowns.

That is to say, there are things that we know we don't know.

But there are also unknown unknowns.

There are things we don't know we don't know.

Known and Unknown Unknowns in Pilot Trials

- Favorable feasibility data can build confidence among RCT reviewers, funders, and investigators that a trial is doable.
- It can't *guarantee* that the RCT will turn out to be doable or that it will run as smoothly as one might hope.
  - E.g., recruitment often turns out to be much more difficult than anyone ever expects, even after a successful pilot trial is conducted.
- In short, "Life is full of surprises!"
  - *--Mr. Bytes, the evil ringmaster in the classic 1980 film The Elephant Man*

Known and Unknown Unknowns in Pilot Trials

- Proper pilot trials enable us to form sensible albeit fallible expectations about the feasibility of a future clinical trial.
- In contrast, the faulty logic of PETs can easily lead us astray.
  - False: Conducting a PET proves I can conduct a much larger RCT.
    - Like claiming that running a mile proves I can run a marathon.
  - False: Pleasing PET results make it very likely that the larger RCT will confirm the efficacy or superiority of my intervention.
    - Like claiming that running a mile proves I will *win* the marathon.

Known and Unknown Unknowns in Pilot Trials

- It's impossible to evaluate the feasibility of a future RCT about which nothing is known.
- Thus, ironically, it's necessary to develop a formative plan for the future RCT *before* you propose a randomized pilot trial.
- The formative plan must include such elements as:
  - the design of the trial,
  - the approximate sample size,
  - the primary outcome measure and occasion,
  - the durations of the recruitment, intervention, and follow-up phases,
  - etc.

Known and Unknown Unknowns in Pilot Trials

- The formative plan makes it possible to design a smaller version of the future RCT, i.e., a randomized pilot trial.
- Also makes it possible to set "*go/no-go" feasibility criteria.*
  - If the criteria are met: Proceed with the RCT proposal.
  - If not: Refine the trial procedures and try again.
- Example:
  - Big RCT will require enrollment of ~200 patients over 24 months.
    - ~8.3 patients per month.
  - Pilot trial target: 9 patients per month for 4 months (n=36)
    - If actual enrollment <9/month: no-go.
    - If actual enrollment ≥9/month: go (if other criteria are also met).

I Miss My PET

- Favorable CONSORT-style pilot trial results reassure RCT grant reviewers that the proposed trial is doable.
- They *don't* provide some of the other preliminary data that a pleasing PET supposedly yields, especially:
  - a "preliminary signal of efficacy"
  - an effect size for the RCT power analysis

I Miss My PET

- What can RCT applicants provide instead of PET results?
  1. **A suitable minimum clinically important difference (MCID).**
  2. ***Design & refine* data to bolster the intervention's *credibility*.**
  3. ***Proof-of-concept* data to support the *plausibility* of its benefits.**

MIDs and MCIDs

- The primary effect in an RCT is a **between-group difference.**
  - **How big of a difference is big enough?**
- **MCID** is the answer to that question if the primary outcome of the RCT is clinically important.
- **MID** is the answer in earlier phases of intervention research when focusing not on clinical outcomes but instead on:
  - intermediate outcomes
  - intervention components or mechanisms
  - MID: How big of a between-group difference in this variable do we need to move forward in our translational research program?
- (Surrogate or intermediate outcome effects may be described either as MIDs or as MCIDs, depending on the circumstances.)

Treatment Model Example

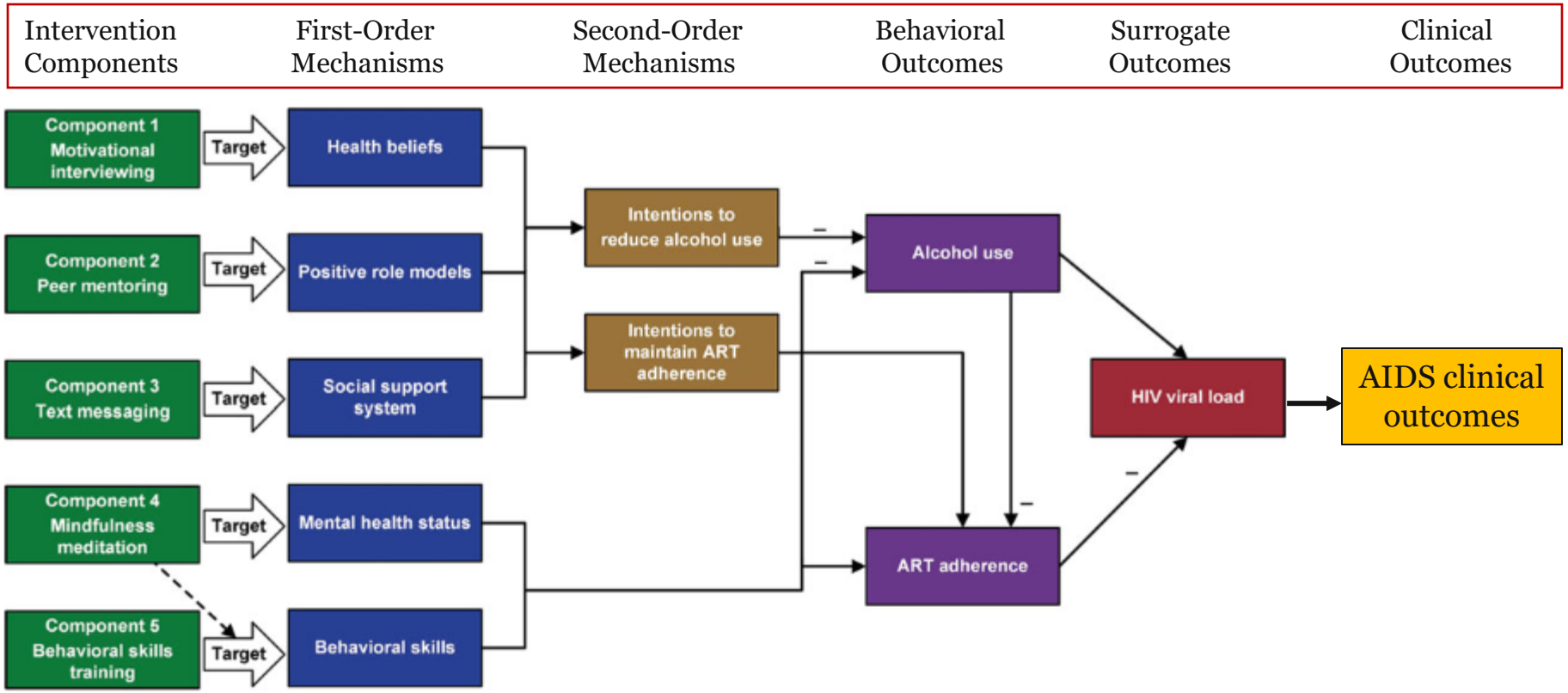


Fig. 2.1 Conceptual model for a hypothetical behavioral intervention to reduce viral load in HIV-positive individuals who are heavy drinkers (Adapted from model in Collins et al. (2016))

Adapted from Collins LM. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST).* Springer Nature. Cham, Switzerland

MID & MCID Examples

- MID
  - How big of a between-group difference in health beliefs does it take to change intentions to reduce alcohol use in excessive alcohol users with HIV?
- MCIDs
  - How big of a difference in alcohol use and ART adherence is big enough to make a clinically meaningful difference in HIV viral load?
  - How big is big enough to change clinical practices?
  - How big of a between-group difference in HIV viral load is big enough to make a difference in AIDS clinical outcomes?

MIDs & MCIDs

- Early-phase MIDs often concern "how big of an effect on this variable do we need to move on to later-phase studies of behavioral or surrogate outcomes?"
- Later-phase MCIDs concern "how big of an effect is big enough to conclude that the intervention is clinically superior to a specific alternative?"
- Use MIDs or MCIDs, not PET results, in RCT power analyses.
- Meaningful MCIDs emerge from risk factor research, clinical research, clinical practice guidelines, public health goals, cost-effectiveness considerations, stakeholder engagement, etc.
  - Seldom if ever from pilot trials.

Behavioral Treatment Models

- Treatment models for complex behavioral interventions can reveal needs for a variety of early-phase studies.
  - Some studies may be qualitative, observational, or quasi-experimental.
  - **Others may be randomized controlled trials.**
    - Relatively small samples are often adequate for early-phase investigations of components, mechanisms, or behavioral variables.
    - They're affordable within the limits of many pilot grant opportunities.
    - Roybal pilot grant applicants can propose productive, early-phase randomized trials *without* having to propose PETs.

Systematic Design & Refine Data to Establish the Intervention's *Credibility*.

- Few grant reviewers want to bet on interventions that are based on unclear rationales, vague theories, fads, etc.
  - They tend to be more enthusiastic about ones that build on:
  - basic behavioral and social science research
  - rigorous clinical research
  - systematic intervention "design and refine" research, e.g.,
    - Patient & clinician input via survey studies, focus groups, etc.
    - Clinically-relevant tests of techniques derived from lab studies.
    - Dose-finding studies (Voils et al., *Ann Behav Med* 2014).
    - Intervention optimization in the MOST framework.
    - Mechanistic findings in the SOBC or MOST framework.
- There may be needs and opportunities for a *variety* of early-phase studies on intervention components, mechanisms, intermediate outcomes, etc.

Proof-of-Concept Data to Support the *Plausibility* of the Intervention's Benefits.

- "Proof of concept" means different things to different people.
- The ORBIT Model defines a proof-of-concept (PoC) study as:
  - A small-scale test of an intervention or complex intervention package.
  - Conducted only *after* the team thinks that they're done tinkering with it.
  - Asks "will most participants reach a *clinically significant target?"*
  - Doesn't require a control group.
  - Doesn't produce "preliminary efficacy" findings.
- Favorable results speak to the *plausibility* of benefit.
  - Used in RCT proposals to argue that an effect as large or larger than the MCID is a *plausible* outcome of the trial.

Proof of Concept in ORBIT

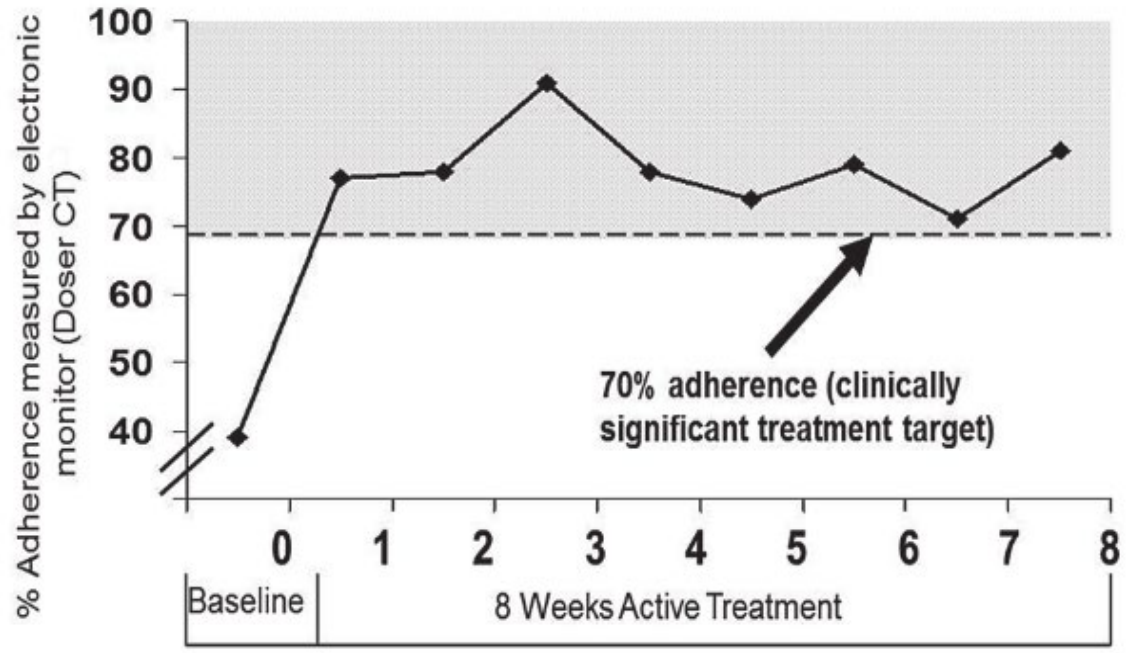


Fig. 3.3 Adherence to drug therapy during run-in and after introduction of treatment, in four subjects

- n=10 might be more persuasive than n=4
- n=20 might be more persuasive than n=10
- Bigger is better, within limits.
- **High success rate** is what's essential. e.g.
  - 8/10 patients reached the target: Great!
  - 4/10 reached the target: Not so great!

Source: Powell, Freedland, & Kaufmann (2021)

Proof of Concept in MOST

- To the best of my knowledge, the MOST framework doesn't include proof-of-concept studies.
- However, optimization trials can provide a form of PoC.
  - Which combination of components gives us the best chance of establishing efficacy in our future RCT?
  - Helps to establish the plausibility of a between-group effect $\geq$ MCID.
  - Different kind of proof-of-concept data than ORBIT, but persuasive.
    - And it should be possible to extract ORBIT-style PoC data from optimization trials conducted in the MOST framework.
- Optimization trials can also help to bolster the scientific *credibility* of interventions.

PETs as Proof of Concept

- "Preliminary efficacy" is a kind of proof of concept.
  - But it's a bad one.
- PET effects are much less trustworthy than they may seem.
- The harms of PETs greatly outweigh their perceived value.
  - Short-term harms to the investigator's research program.
  - Longer-term harms to the cause of evidence-based practices.
- Some reviewers still favor PETs.
  - But grant applicants don't have to go along with them.
  - Successful RCT proposals can build on other kinds of preliminary data.

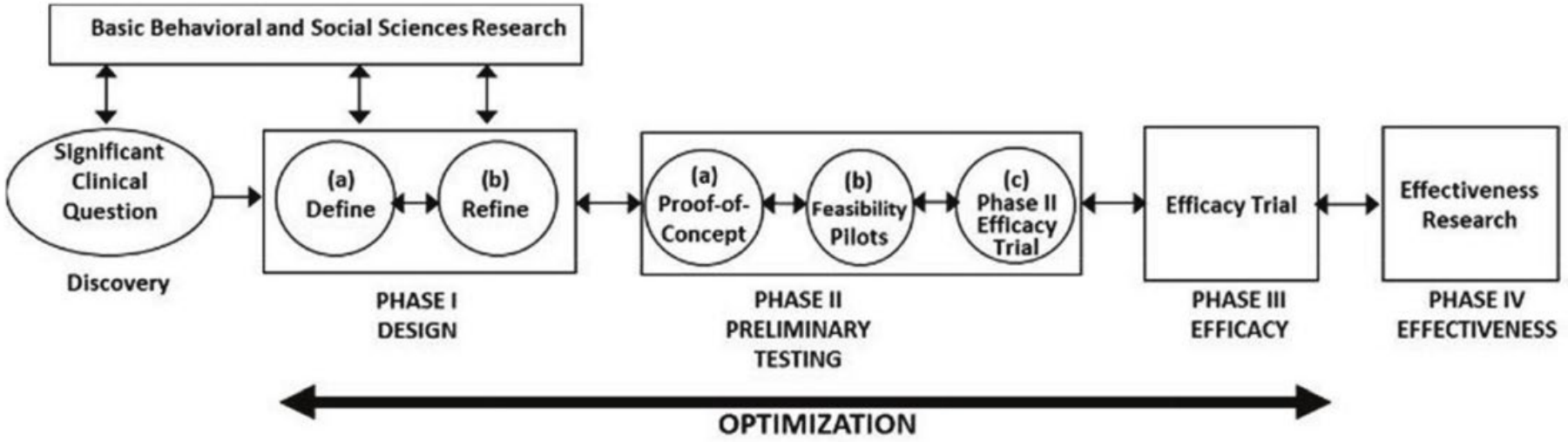
Recap: Alternatives to PETs

- Support the *credibility* of the intervention by, for example:
  - obtaining stakeholder input,
  - translating basic science findings into clinical intervention techniques,
  - conducting early-stage studies to develop & refine the intervention.
- Use a well-chosen, well-justified MID or MCID as the between-group effect size for the RCT power analysis.
  - Caution: clinical significance in RCTs is a complicated subject.
- Support the *plausibility* of obtaining an effect ≥MID or ≥MCID by providing *proof of concept* data.
  - And/or other supporting evidence from previous research.

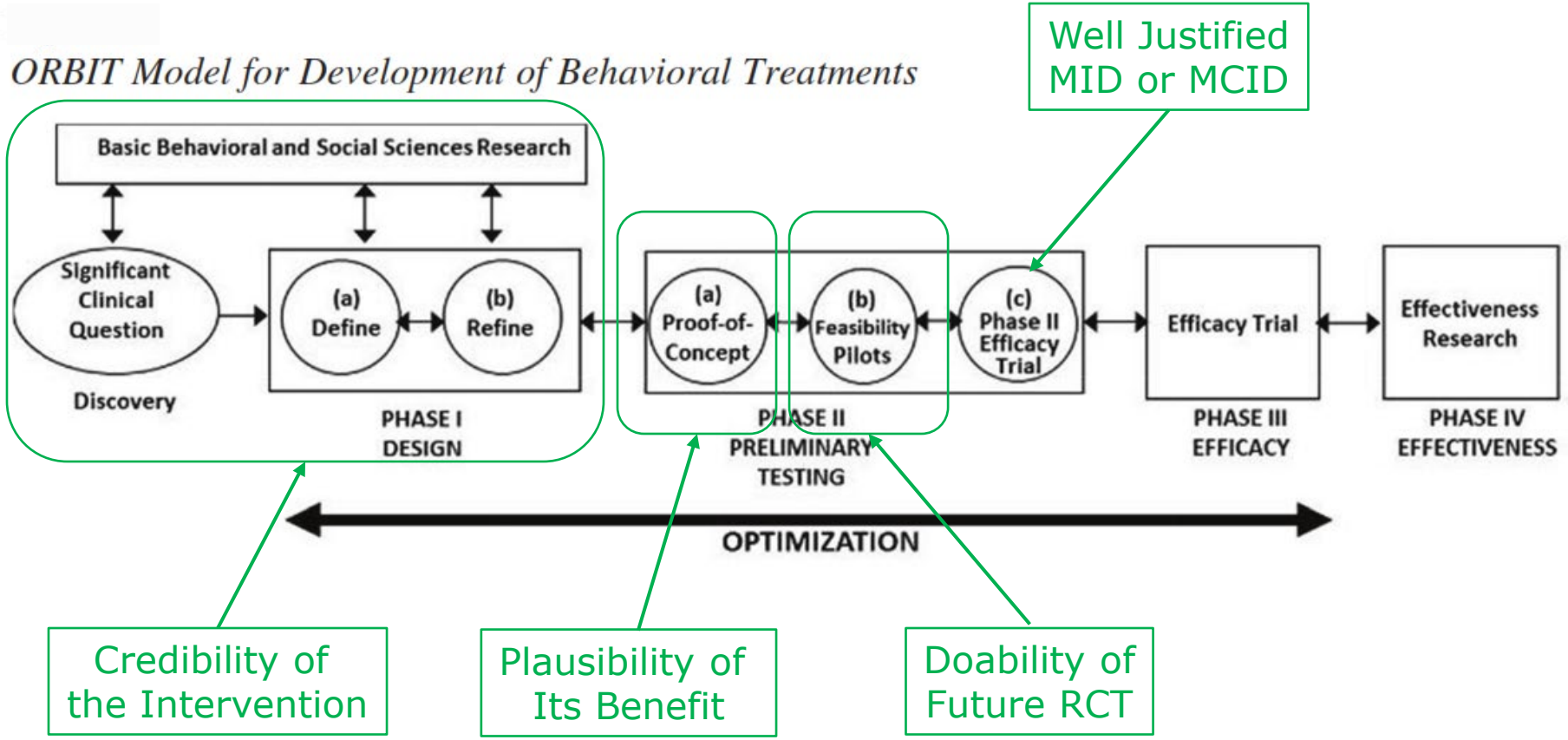
Alternatives to PETs

Figure 8

ORBIT Model for Development of Behavioral Treatments



Alternatives to PETs



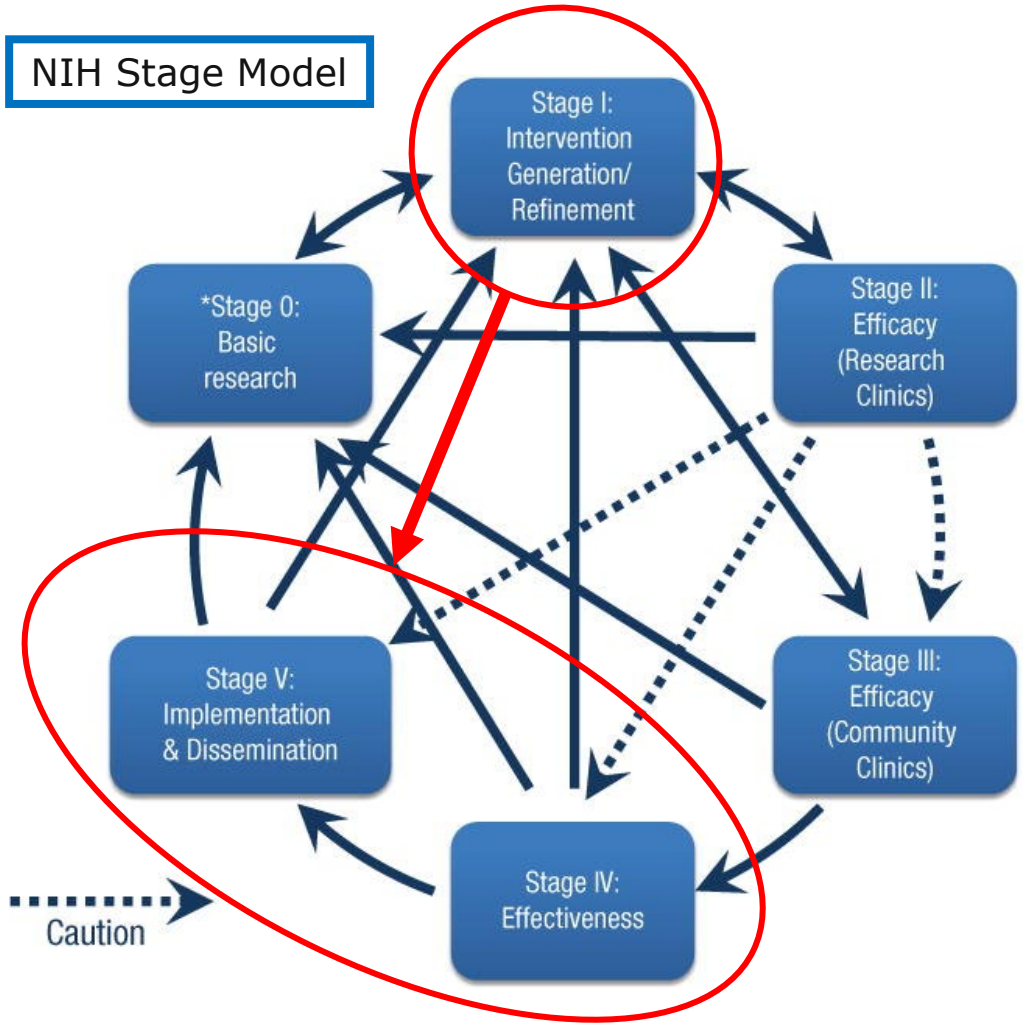
Proof of Concept in Pilot Trials

- Some investigators hesitate (perhaps with good reason) to propose *only* feasibility aims in a pilot trial grant proposal.
  - May seem too dull and/or like a missed opportunity to do more.
- So they insert some proof-of-concept aims into their proposal.
  - Let's assume they're *not* proposing a "PET plus" trial.
  - They're proposing to use intervention arm data for ORBIT-style PoC.
- Might be a good strategy, but only if they've *already* demonstrated proof of concept in a previous study!
  - Why propose to assess your readiness to conduct a large RCT if you haven't already established that the intervention is worth testing?
  - *Additional* proof-of-concept data collected in the context of a CONSORT-style pilot trial might help to strengthen the future RCT proposal.

Pilot Trials and Subsequent Research Plans

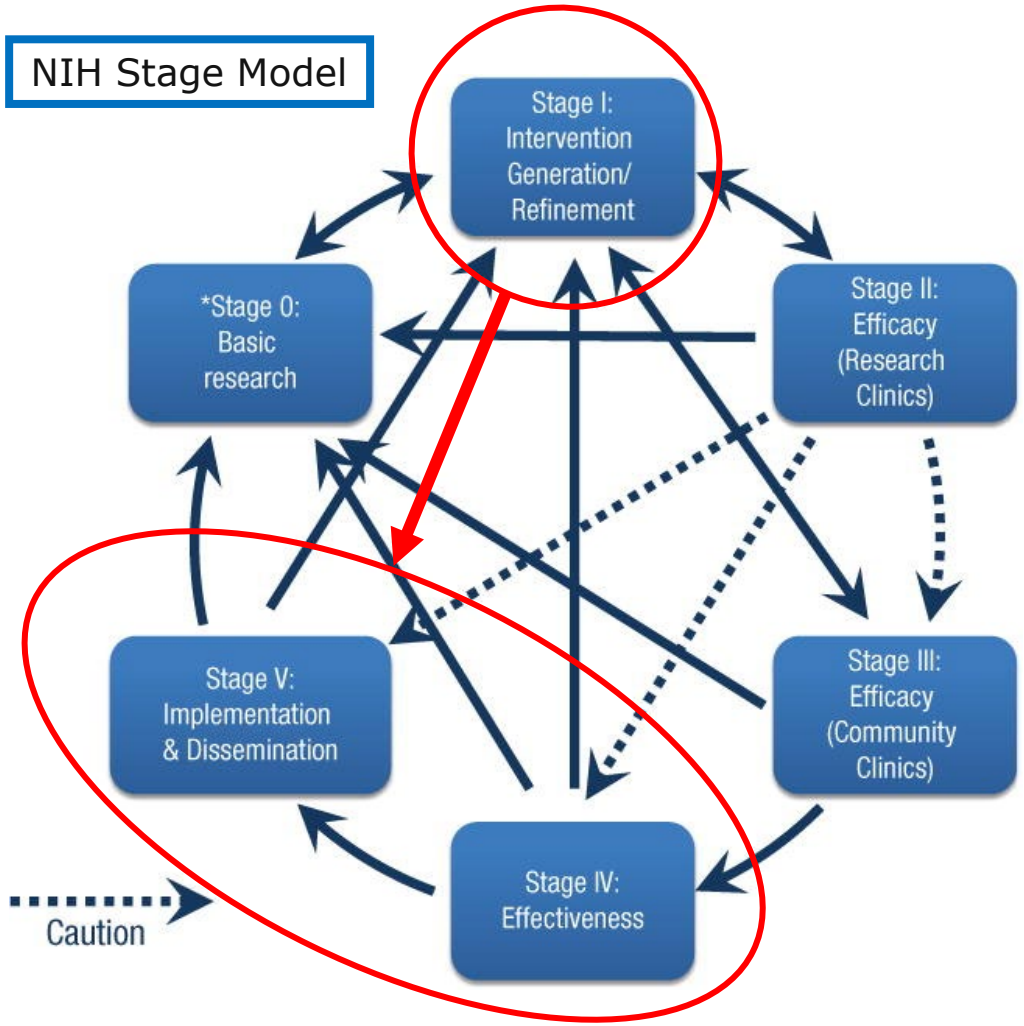
- Roybal pilot study applicants are expected to think ahead about real-world **implementation** of their intervention.
  - Makes obvious sense.
- But this may be contributing to a couple of interrelated problems in some of the Roybal research plans that I've seen.
  - Hasty progression to hybrid trials
  - Localism

Hasty Progression to Hybrid Trials



Shortcuts from pilot trials to NIH Model Stages IV & V can lead to counterproductive efforts to implement poorly developed and inadequately tested behavioral interventions.

Hasty Progression to Hybrid Trials



Inadvertently Encouraged by the FOAs?

"Multiple Stage I studies…are often are needed to lay the groundwork for Stage III and Stage IV studies that can serve as necessary steps toward ultimate implementation."

Omits Stage II

Might be interpreted as greenlighting a direct

Stage I ⟶ Stage IV / V path

Localism

- Localism: Limiting implementation goals to wherever you're doing your intervention research. e.g.,
  - Formative intervention research is done at a community center.
  - Implementation goal is sustainable uptake at this community center.
  - Implementation on a much wider scale is unlikely, even if hoped for.
- This is a small "i" implementation goal.
- Examples of implementation goals with a capital "I":
  - Intervention incorporated into healthcare policies, covered by payers, etc.
  - Widespread adoption of the intervention in clinical practice.
- Thinking small about implementation makes sense sometimes.
  - But bigger is better in many lines of research.

Implementation with a Capital "I"

- The road to Implementation with a capital "I" runs though:
  - Rigorous Stage II and/or Stage III efficacy trials.
  - Meta-analyses confirming clinically significant benefits in rigorous Stage II and/or Stage III efficacy trials.
  - Evidence that is strong enough to change major clinical practice guidelines, USPSTF recommendations, etc.

Implementation with a Capital "I"

- Even the best efficacy trials have limitations.
  - Including questions about generalizability to "real world" settings.
- But practice guideline writers yearn for definitive efficacy data.
  - High grades of evidence and strong recommendations in practice guidelines tend to be driven by rigorous efficacy data.
- "Voltage drop" is common in pragmatic effectiveness trials.
  - It's good to know how effective an intervention can be under favorable conditions before testing it under more challenging circumstances.
- Small "i" implementation research can be valuable, but it rarely affects practice guidelines or healthcare policies.
- If Implementation is the ultimate goal, hybrid trials should wait until after successful Stage II and/or III efficacy trials.

Conclusions

- CONSORT-style randomized pilot trials primarily concern the feasibility of a future RCT.
  - Not preliminary efficacy, and not the "feasibility" of the intervention.
- Other kinds of early-stage studies (including early-stage randomized trials) can have *other* aims.
  - It may take *multiple* preliminary studies, not just a single "pilot trial," to lay the groundwork for a successful (R01- or R61/R33-level) RCT.
  - If it's needed, a proper feasibility pilot trial should be the *last* preliminary study before an RCT proposal – and usually not the first or only one.
- Pilot study weaknesses affect more than the pilot study itself.
  - They're closely connected to problems in subsequent stages of research.

Recommendations

- The NIH Stage Model is wonderful, but…
  - it could be improved by updating its conceptualizations of pilot studies, feasibility, and preliminary efficacy.
- Roybal FOAs incorporate these (outdated) conceptualizations.
  - Nevertheless, most of the following recommendations could implemented without deviating from the FOAs.
  - The rest are actionable within the spirit if not the letter of the FOAs.

Recommendations

- Discourage
  - context-independent research on intervention “feasibility.”
  - preliminary efficacy trials (PETs).
  - hasty progression to hybrid trials.
  - localism in implementation goals except where it truly makes sense.
- Encourage
  - Programmatic intervention development and refinement research.
  - Proof-of-concept (plausibility) evidence instead of “preliminary efficacy.”
  - Proper feasibility studies & CONSORT-style pilot trials, when needed.
  - Progression through the efficacy stages of the NIH Stage Model.
  - Thinking big about the long-term goals of intervention research.

Thank you!

Kenneth E. Freedland, PhD
Professor of Psychiatry and Psychology
Washington University School of Medicine
St. Louis, Missouri

NYU | SCHOOL OF GLOBAL PUBLIC HEALTH

Approaches to intervention optimization: The multiphase optimization strategy (MOST)

Linda M. Collins

Presented at the 2023 Roybal Collaborative Meeting

March 14, 2023

cadio

Outline

- Why consider an alternative framework for intervention development and evaluation?
- An application of MOST in weight loss
- The argument room
- Fixed and adaptive intervention strategies

The goal of the Roybal Center program is the translation and integration of basic behavioral and social research findings into interventions to improve the lives of older people and the capacity of institutions to adapt to societal aging.

From the NIA website 3/4/23

Intervention science objectives:

1. Build a **coherent knowledge base** about what intervention strategies work, for whom, and why

2. Use this knowledge to develop interventions that have **immediate public health impact**

3. Keep making **improvements** in these interventions over time

WHAT HAS 30+ YEARS OF THIS APPROACH DELIVERED?

Objective 1: Coherent knowledge base

- When an intervention demonstrates a detectable effect, **we don't know why or how** it worked

- When an intervention does not show a significant effect, **we don't know why** it didn't work

- **Conclusion: Not making good progress toward a coherent knowledge base**

Objective 2: Immediate public health impact

- Many interventions developed empirically are **too expensive, complex, or burdensome to be implemented**
- No way to fix this without risking making them ineffective
- **Conclusion: No implementation = zero public health impact**

Objective 3: Improvements

- **We do not know which are the strong and weak components** in an intervention

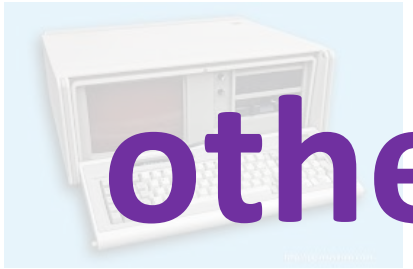
- Next steps to make improvements unclear

- **Conclusion: Not set up to make ongoing improvements**

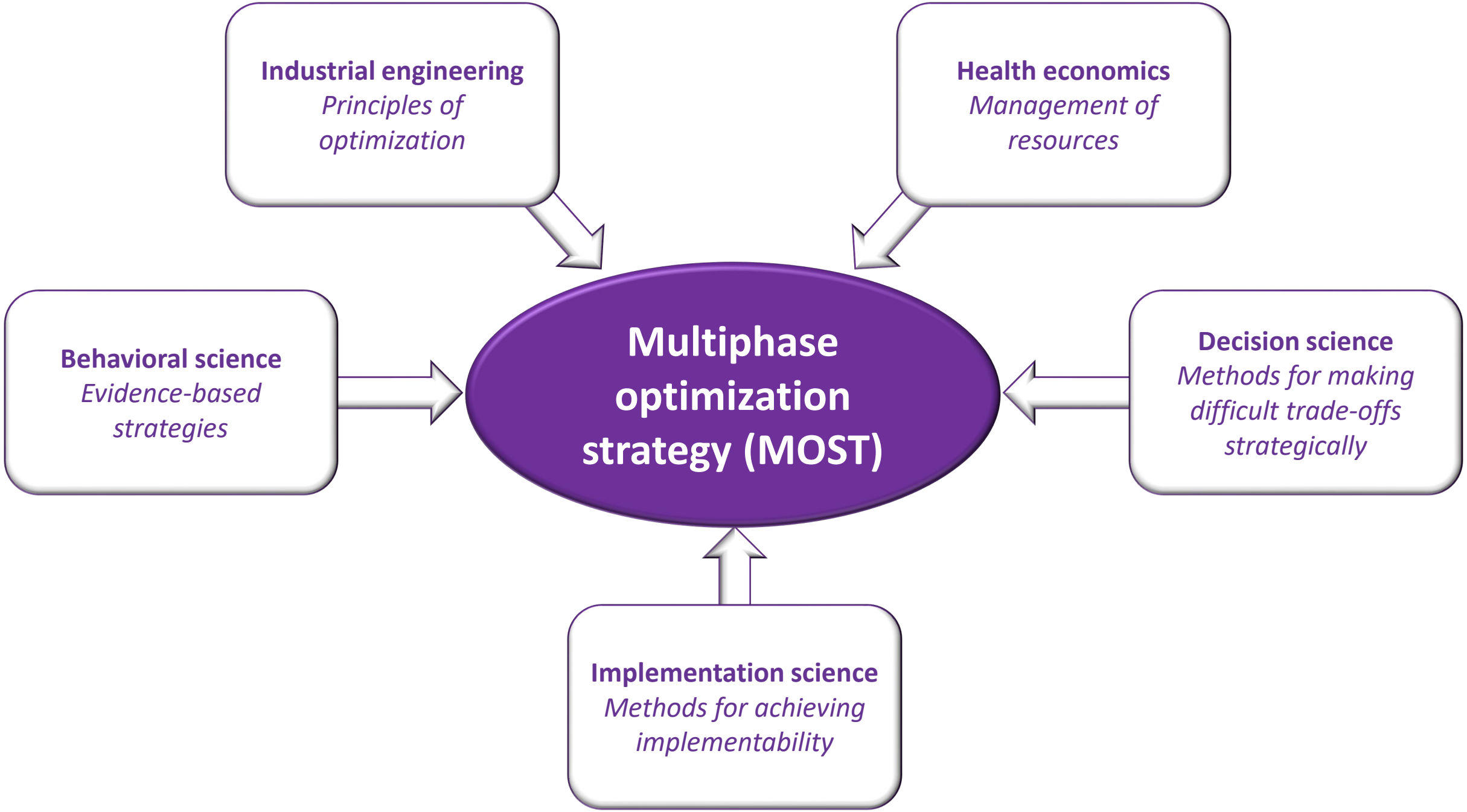
Late 20th century (mid 1980's)

Early 21st century (today)

Meanwhile, in other fields…



Maybe we need to consider a different approach


Industrial engineering
Principles of optimization
Health economics
Management of resources
Behavioral science
Evidence-based strategies
Multiphase optimization strategy (MOST)
Decision science
Methods for making difficult trade-offs strategically
Implementation science
Methods for achieving implementability

Intervention *EASE*: A strategic balance of *E*ffectiveness, *A*ffordability, *S*calability, and *E*fficiency

EASE **is achieved by BALANCING**

Effectiveness

BUT HOW?

OPTIMIZATION VIA MOST

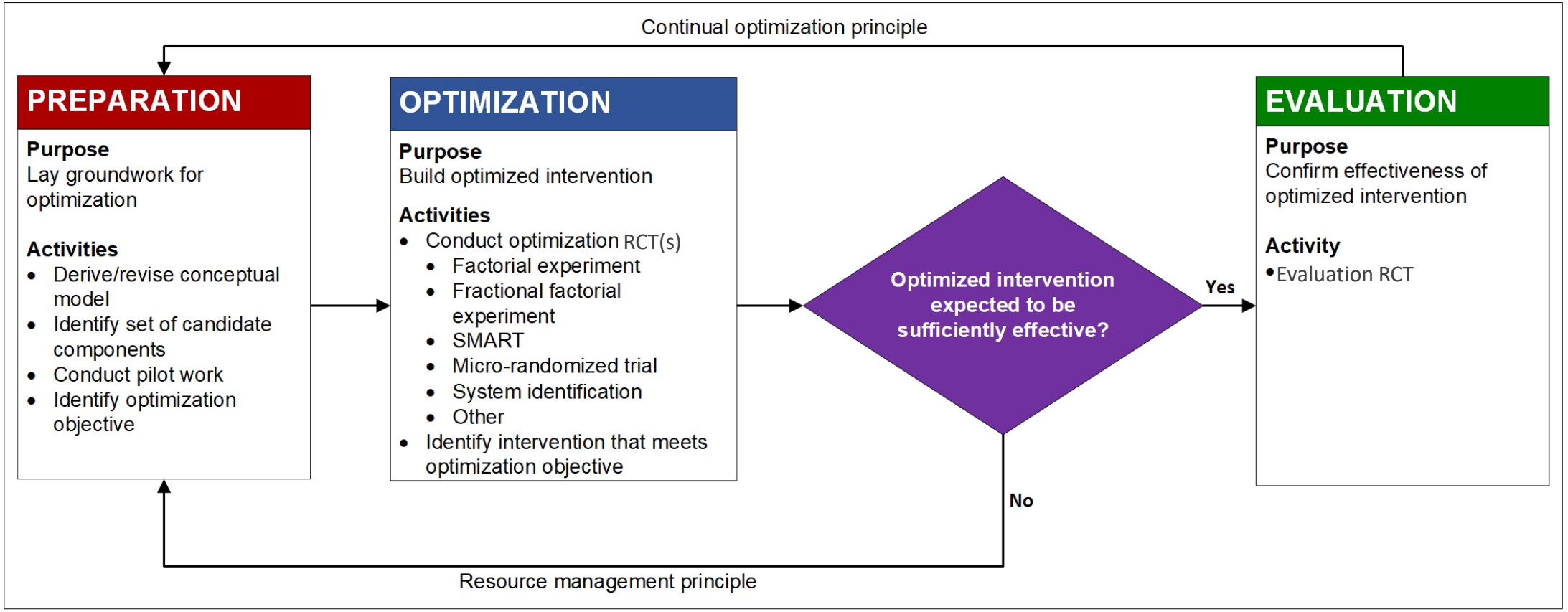
AGAINST

Affordability

Scalability

Efficiency

Multiphase optimization strategy (MOST)



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

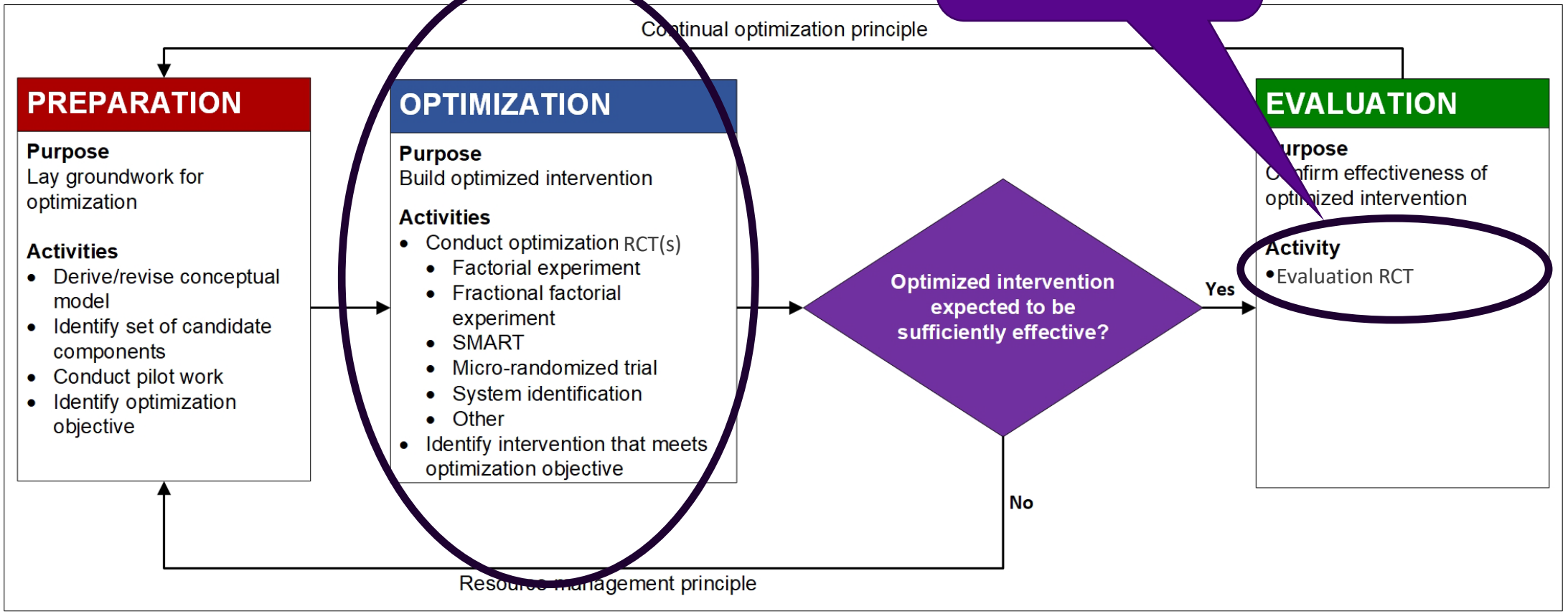
Figure taken from Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST).* New York: Springer.

The multiphase optimization strategy (MOST)

Using MOST it is possible to engineer an intervention to meet a specific objective, e.g.:

- Best expected outcome < $300 per person
- Best expected outcome < 30 minutes staff time
- Most cost-effective

Multiphase optimization s…OST)



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

Figure taken from Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST).* New York: Springer.

Outline

- Why consider an alternative framework for intervention development and evaluation?
- An application of MOST in weight loss
- The argument room
- Fixed and adaptive intervention strategies

Example: Opt-IN (funded by NIDDK: B. Spring & L. Collins, MPIs)

Original Article
CLINICAL TRIALS AND INVESTIGATIONS

Obesity

A Factorial Experiment to Optimize Remotely Delivered Behavioral Treatment for Obesity: Results of the Opt-IN Study

Bonnie Spring [1], Angela F. Pfammatter[1], Sara H. Marchese [1], Tammy Stump[1], Christine Pellegrini [2], H. Gene McFadden[1], Donald Hedeker[3], Juned Siddique[1], Neil Jordan[1,4,5], and Linda M. Collins[6,7]

Objective: Intensive behavioral obesity treatments face scalability challenges, but evidence is lacking about which treatment components could be cut back without reducing weight loss. The Optimization of Remotely Delivered Intensive Lifestyle Treatment for Obesity (Opt-IN) study applied the Multiphase Optimization Strategy to develop an entirely remotely delivered, technology-supported weight-loss package to maximize the amount of weight loss attainable for ≤$500.

Study Importance

What is already known?

- Effective behavioral treatment packages for obesity impose a burden and cost that impede scalability, but evidence is lacking about which components could be reduced or eliminated

Obesity (2020) **28**, 1652-1662.

What is the objective of optimization in Opt-IN?

Objective: Intensive behavioral obesity treatments face scalability challenges, but evidence is lacking about which treatment components could be cut back without reducing weight loss. The Optimization of Remotely Delivered Intensive Lifestyle Treatment for Obesity (Opt-IN) study applied the Multiphase Optimization Strategy to develop an entirely remotely delivered, technology-supported weight-loss package to maximize the amount of weight loss attainable for ≤$500.

Components* being examined in optimization trial

Candidate component	Higher level	Lower level
Coaching calls (10-15 min calls from a health coach)	24	12
Text messages	Yes	No
Meal replacement recommendation	Yes	No
PCP reports (report about weigh-loss progress sent to PCP)	Yes	No
Buddy training	Yes	No

*All participants received a core intervention based on a custom-designed smartphone app showing personalized goals for diet, PA, and weight and enabling self-monitoring

Comparison of three alternative approaches

Design	Approximate N to achieve power≥.80 (Cohen's *d*=.28)	Number of experimental conditions	Can interactions be examined?
Option A: Five individual experiments	2,560	10	No

Comparison of three alternative approaches

Design	Approximate N to achieve power≥.80 (Cohen's *d*=.28)	Number of experimental conditions	Can interactions be examined?
Option A: Five individual experiments	2,560	10	No
Option B: Comparative treatment	1,536	6	No

Comparison of three alternative approaches

Design	Approximate N to achieve power≥.80 (Cohen's *d*=.28)	Number of experimental conditions	Can interactions be examined?
Option A: Five individual experiments	2,560	10	No
Option B: Comparative treatment	1,536	6	No
Option C: Factorial experiment	512	32	Yes, all

When used to address suitable research questions, balanced factorial experimental designs often require many FEWER participants than alternative designs.

Don't believe me? Try reading:

Chakraborty, B., Collins, L.M., Strecher, V., and Murphy, S.A. (2009). Developing multicomponent interventions using fractional factorial designs. *Statistics in Medicine*, *28,* 2687-2708.

Collins, L.M., Dziak, J.J., Kugler, K.C., & Trail, J.B. (2014). Factorial experiments: Efficient tools for evaluation of intervention components. *American Journal of Preventive Medicine*, *47*, 498-504.

Collins, L.M., Dziak, J.J., & Li, R. (2009). Design of experiments with multiple independent variables: A resource management perspective on complete and reduced factorial designs. *Psychological Methods*, *14*, 202-224.

Chapter 3 in Collins, L.M. (2018), *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST)*. New York: Springer.

Optimize based on results of optimization trial

- Analyze data, obtain estimates of effects of each of the components
- Use this information to select components
  - Discard components that do not perform adequately
  - If desired, based on predicted outcomes and estimated costs, select components that will make up optimized intervention

Objective: Intensive behavioral obesity treatments face scalability challenges, but evidence is lacking about which treatment components could be cut back without reducing weight loss. The Optimization of Remotely Delivered Intensive Lifestyle Treatment for Obesity (Opt-IN) study applied the Multiphase Optimization Strategy to develop an entirely remotely delivered, technology-supported weight-loss package to maximize the amount of weight loss attainable for ≤$500.

TABLE 6 Predicted 6-month weight change and cost of candidate component combinations (i.e., interve n packages)

						Estimated effects			
No.	Calls	Text message	Meal replacement	PCP report	Buddy training	6-month weight change (kg)	Achieving 5% weight loss (%)	Achieving 7% weight loss (%)	Cost
21	12	No	No	Yes	Yes	−6.1112	57.13	51.77	$427
1	12	No	No	Yes	No	−3.3966	34.48	25.86	$337
5	12	No	No	No	Yes	−5.0540	46.56	31.02	$414
17	12	No	No	No	No	−5.2389	52.95	41.17	$324

2nd best weight loss

Least expensive

Outline

- Why consider an alternative framework for intervention development and evaluation?
- An application of MOST in weight loss
- The argument room
- Fixed and adaptive intervention strategies

"MOST takes too long!"

- RESPONSE: Too long to accomplish… what exactly?

- Is the objective SOLELY to get a significant effect in an evaluation RCT without
  - Understanding why the intervention works
  - Ensuring it is implementable
  - Laying groundwork for ongoing improvement?

- If this is your objective, MOST is not for you

“MOST takes too long!”

- OR is the objective to
  - Build a coherent base of knowledge that can be used to…
  - …develop interventions with high public health impact and…
  - …keep improving the interventions over time?

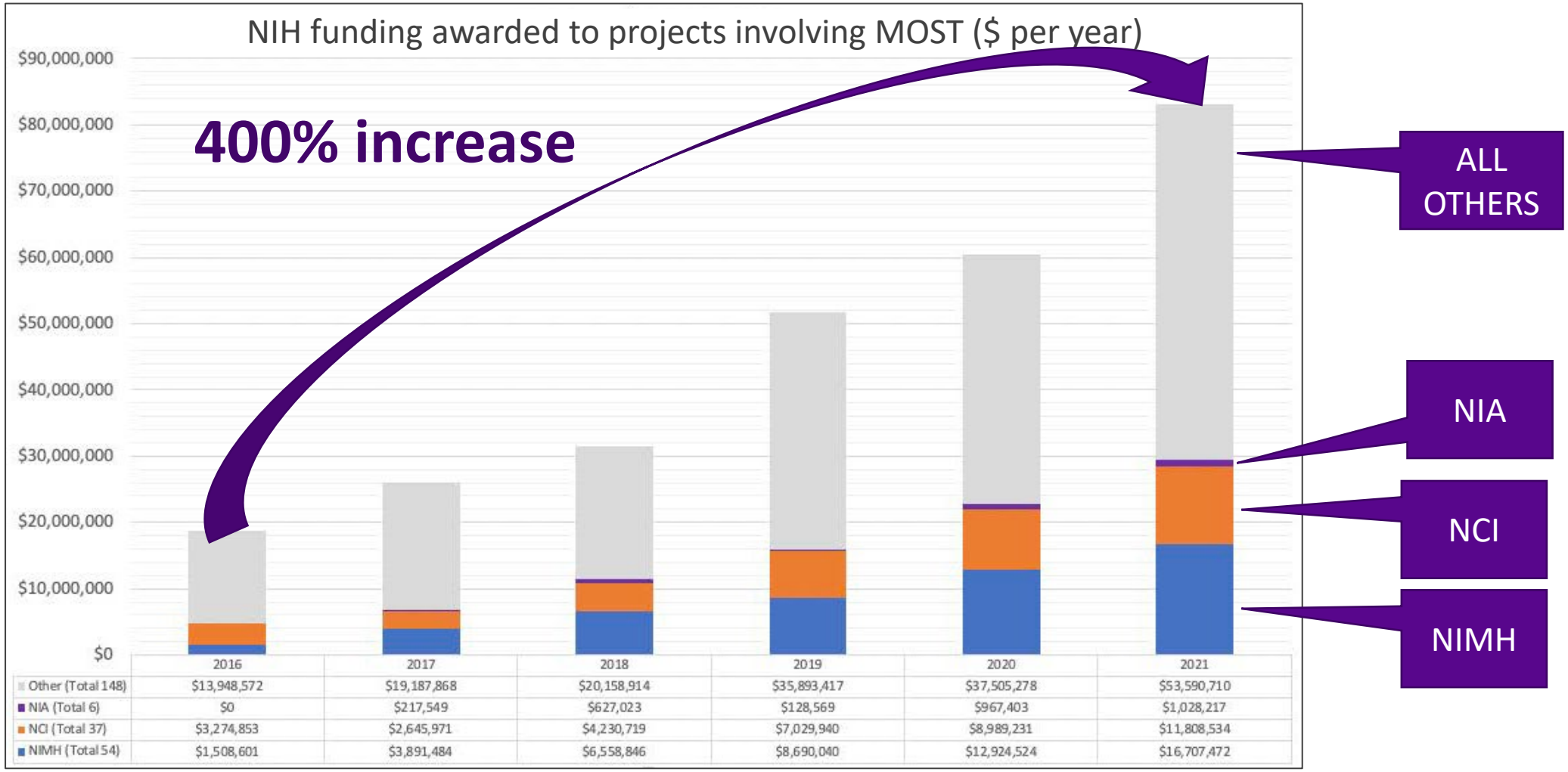
- I would argue MOST is much faster than the classical approach

"Nice ideas, but you will never get them through an NIH review committee."

"…*conformity is anathema to scientific progress*."

Neil deGrasse Tyson, *Starry Messenger: Cosmic Perspectives on Civilization* (2022)

“Nice ideas, but you will never get them through an NIH review committee.”



	2016	2017	2018	2019	2020	2021
Other (Total 148)	$13,948,572	$19,187,868	$20,158,914	$35,893,417	$37,505,278	$53,590,710
NIA (Total 6)	$0	$217,549	$627,023	$128,569	$967,403	$1,028,217
NCI (Total 37)	$3,274,853	$2,645,971	$4,230,719	$7,029,940	$8,989,231	$11,808,534
NIMH (Total 54)	$1,508,601	$3,891,484	$6,558,846	$8,690,040	$12,924,524	$16,707,472

Outline

- Why consider an alternative framework for intervention development and evaluation?
- An application of MOST in weight loss
- The argument room
- Fixed and adaptive intervention strategies

Two types of intervention strategies

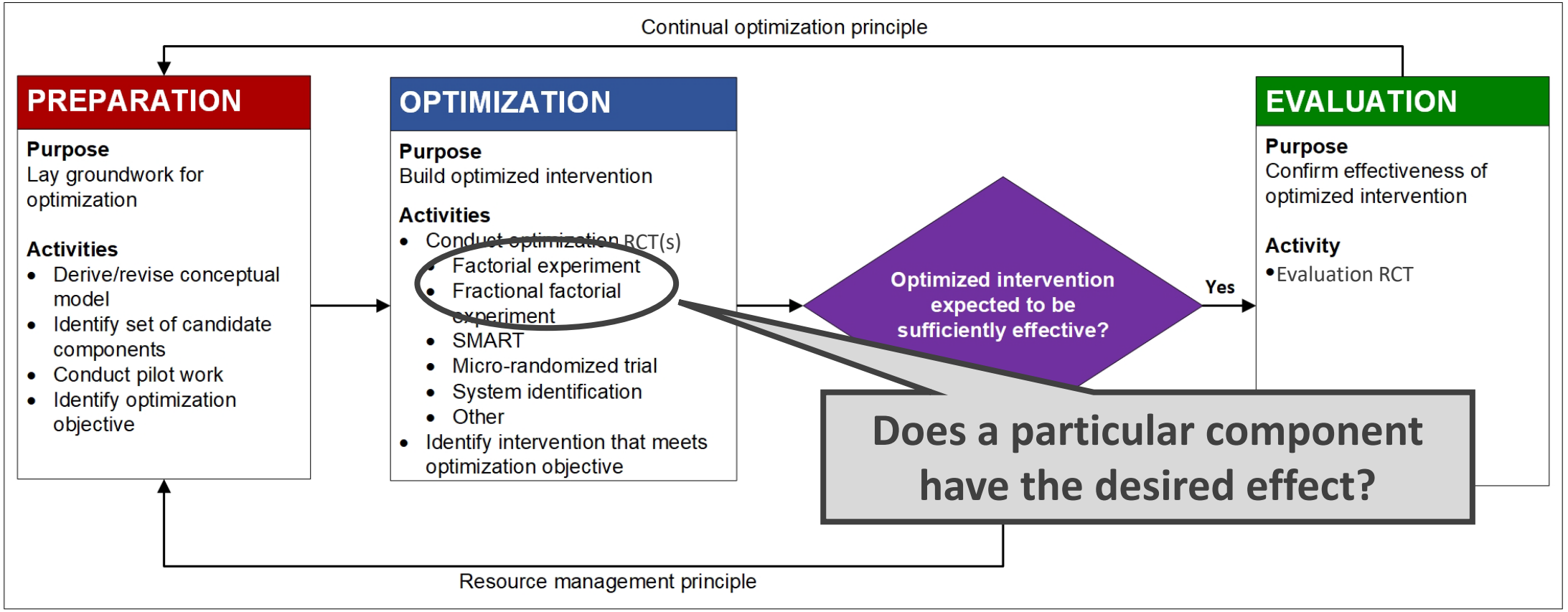
- **Fixed**: all participants offered the same treatment
- **Adaptive**: treatment is strategically varied
- An intervention may use both strategies

Why strategically vary treatment?

- To **produce good outcomes for all individuals** by providing each individual with the appropriate treatment…

- …and **make efficient use of resources** by providing only what treatment is needed and no more

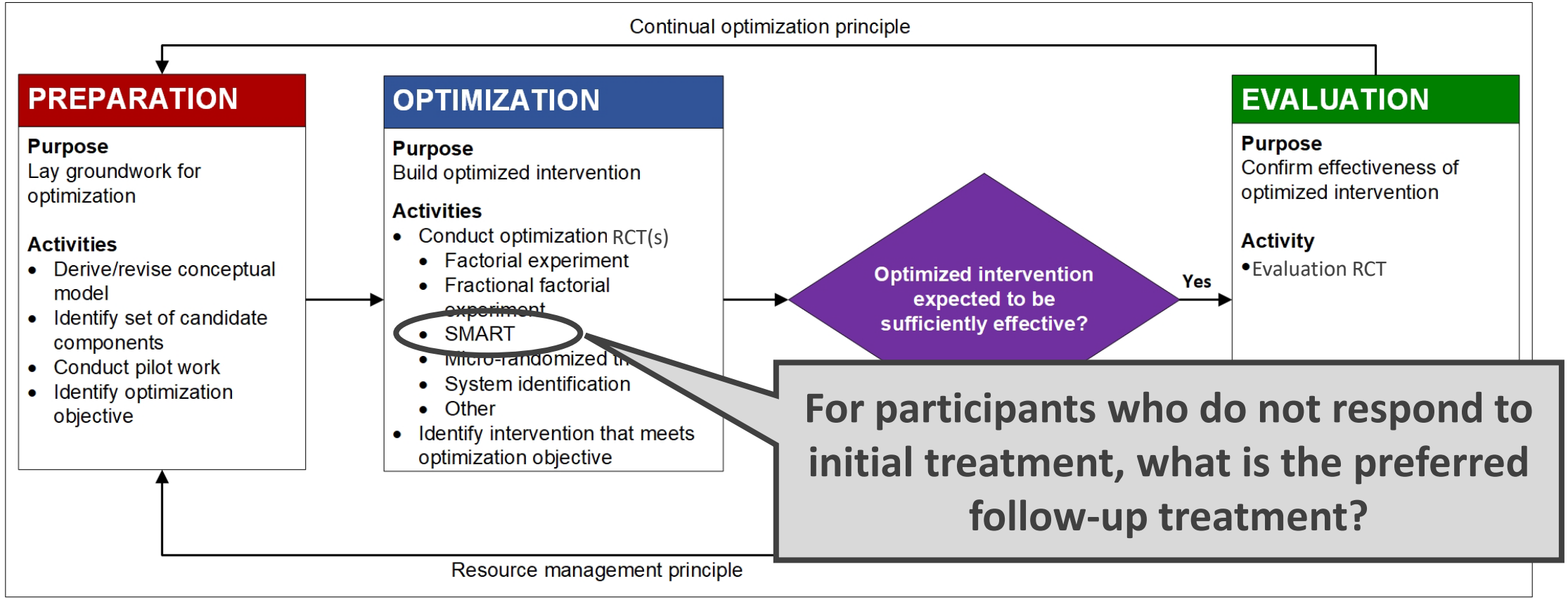
Different research questions require different optimization trial designs



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

Figure taken from Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST).* New York: Springer.

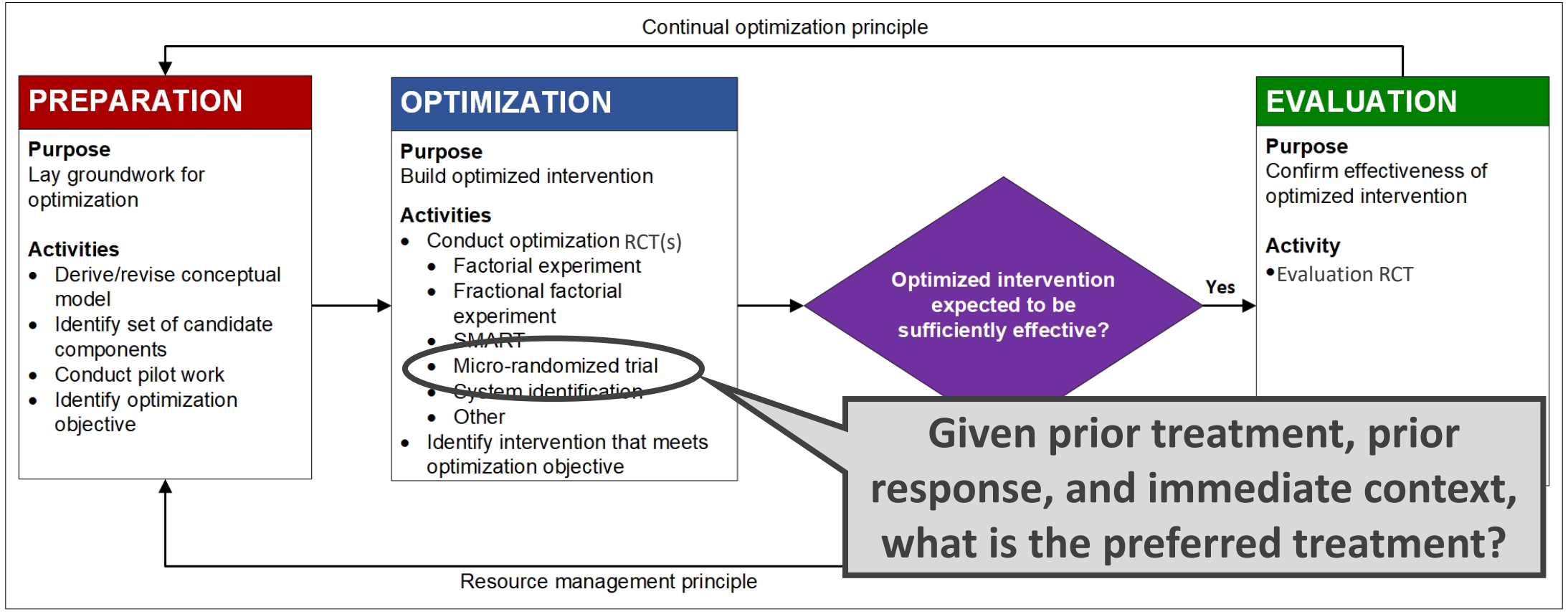
Different research questions require different optimization trial designs



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

Figure taken from Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST).* New York: Springer.

Different research questions require different optimization trial designs



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

Figure taken from Collins, L.M. (2018). *Optimization of Behavioral, Biobehavioral, and Biomedical Interventions: The Multiphase Optimization Strategy (MOST).* New York: Springer.

Virtual training on MOST
May 22-25, 2023

https://cadio.org/cadio-academy

Brief application due **March 24**

Browse our online resources.

d3c

Resources on adaptive interventions.

Browse learning resources.

Sign up for our newsletter.

Search open-source software.

cadio

Resources on intervention optimization.

Browse learning resources.

Sign up for our newsletter.

Register for webinars.
Wednesdays from 1-2 pm Eastern

APPENDIX

Detour: Brief refresher on factorial experiments

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

	Factor (Component) A	
Factor (Component) B	Off	On
Off	A,B off	A on, B off
On	A off, B on	A,B on

Experimental Condition	Factor A	Factor B
1	Off	Off
2	Off	On
3	On	Off
4	On	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

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

Opt-IN experimental design

TABLE 1 Opt-IN factorial design with 32 conditions

Intervention target	Individual		Environment		
Combination	Coaching calls	Texts	Meal replacement	PCP reports	Buddy training
1	12	No	No	Yes	No
2	12	No	Yes	Yes	Yes
3	12	Yes	No	Yes	Yes
4	12	Yes	Yes	Yes	No
5	12	No	No	No	Yes
6	12	No	Yes	No	No
7	12	Yes	No	No	No
8	12	Yes	Yes	No	Yes
9	24	No	No	Yes	No
10	24	No	Yes	Yes	Yes
11	24	Yes	No	Yes	Yes
12	24	Yes	Yes	Yes	No
13	24	No	No	No	Yes
14	24	No	Yes	No	No
15	24	Yes	No	No	No
16	24	Yes	Yes	No	Yes
17	12	No	No	No	No
18	12	No	Yes	No	Yes
19	12	Yes	No	No	Yes
20	12	Yes	Yes	No	No
21	12	No	No	Yes	Yes
22	12	No	Yes	Yes	No
23	12	Yes	No	Yes	No
24	12	Yes	Yes	Yes	Yes
25	24	No	No	No	No
26	24	No	Yes	No	Yes
27	24	Yes	No	No	Yes
28	24	Yes	Yes	No	No
29	24	No	No	Yes	Yes
30	24	No	Yes	Yes	No
31	24	Yes	No	Yes	No
32	24	Yes	Yes	Yes	Yes

Opt-IN experimental design

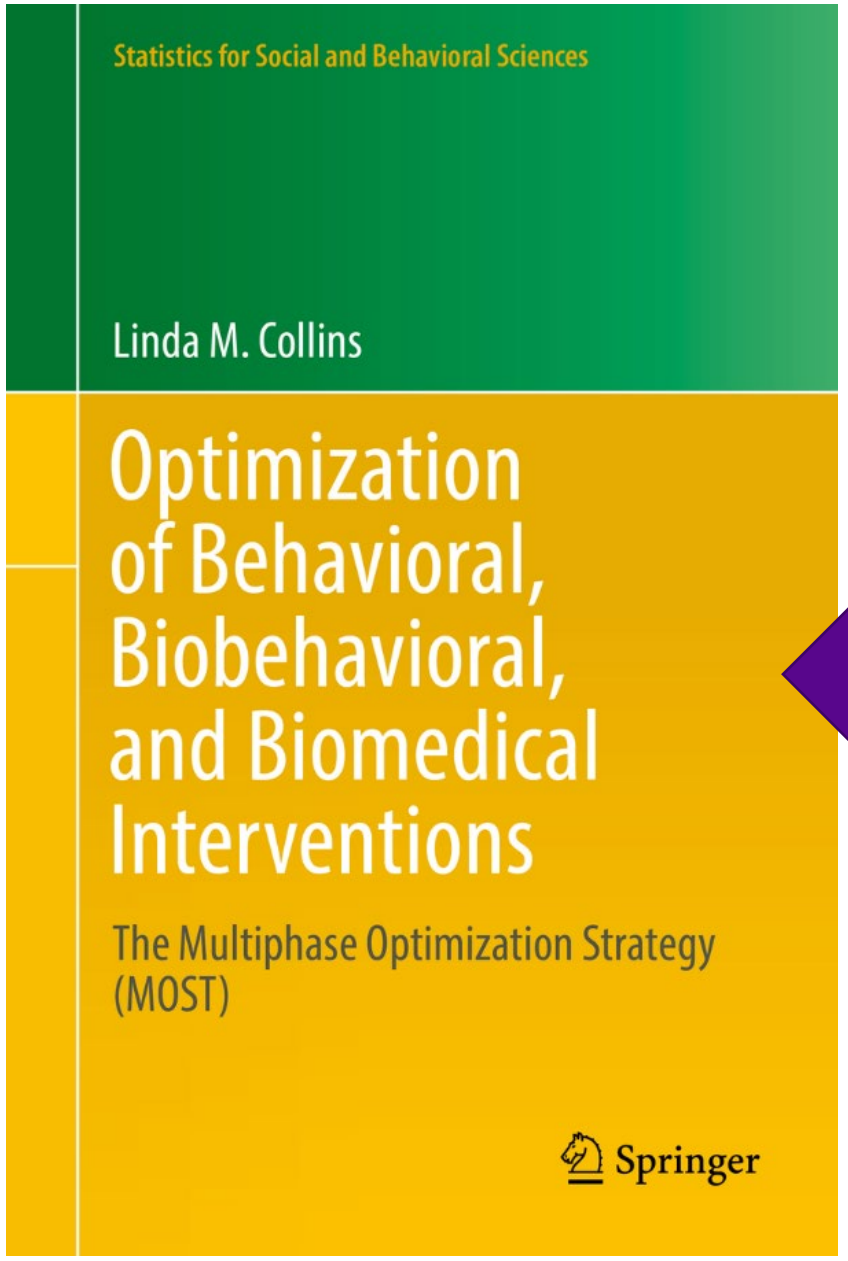
TABLE 1 Opt-IN factorial design with 32 conditions

Intervention target	Individual		Environment		
Combination	Coaching calls	Texts	Meal replacement	PCP reports	Buddy training
1	12	No	No	Yes	No
2	12	No	Yes	Yes	Yes
3	12	Yes	No	Yes	Yes
4	12	Yes	Yes	Yes	No
5	12	No	No	No	Yes
6	12	No	Yes	No	No
7	12	Yes	No	No	No
8	12	Yes	Yes	No	Yes
9	24	No	No	Yes	No
10	24	No	Yes	Yes	Yes
11	24	Yes	No	Yes	Yes
12	24	Yes	Yes	Yes	No
13	24	No	No	No	Yes
14	24	No	Yes	No	No
15	24	Yes	No	No	No
16	24	Yes	Yes	No	Yes
17	12	No	No	No	No
18	12	No	Yes	No	Yes
19	12	Yes	No	No	Yes
20	12	Yes	Yes	No	No
21	12	No	No	Yes	Yes
22	12	No	Yes	Yes	No
23	12	Yes	No	Yes	No
24	12	Yes	Yes	Yes	Yes
25	24	No	No	No	No
26	24	No	Yes	No	Yes
27	24	Yes	No	No	Yes
28	24	Yes	Yes	No	No
29	24	No	No	Yes	Yes
30	24	No	Yes	Yes	No
31	24	Yes	No	Yes	No
32	24	Yes	Yes	Yes	Yes

Opt-IN experimental design

TABLE 1 Opt-IN factorial design with 32 conditions

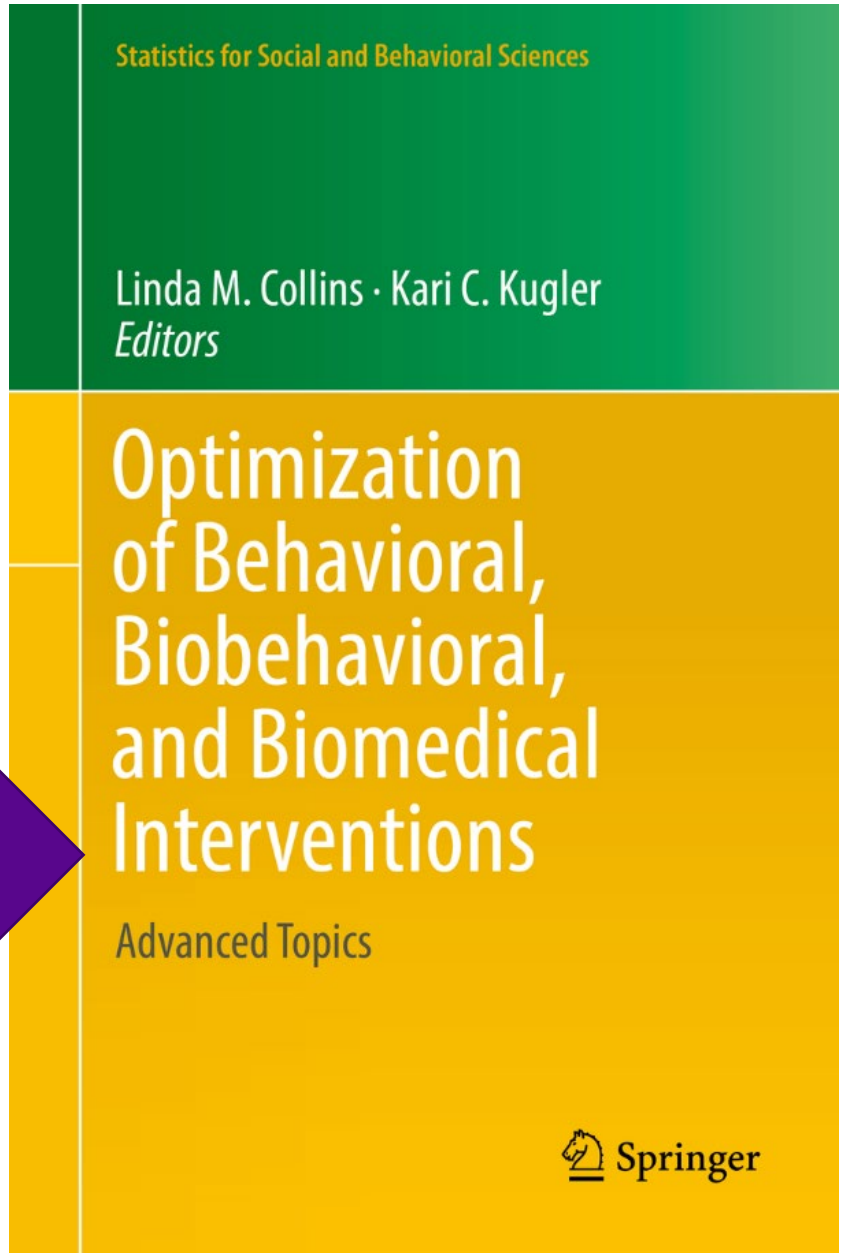
Intervention target	Individual		Environment		
Combination	Coaching calls	Texts	Meal replacement	PCP reports	Buddy training
1	12	No	No	Yes	No
2	12	No	Yes	Yes	Yes
3	12	Yes	No	Yes	Yes
4	12	Yes	Yes	Yes	No
5	12	No	No	No	Yes
6	12	No	Yes	No	No
7	12	Yes	No	No	No
8	12	Yes	Yes	No	Yes
9	24	No	No	Yes	No
10	24	No	Yes	Yes	Yes
11	24	Yes	No	Yes	Yes
12	24	Yes	Yes	Yes	No
13	24	No	No	No	Yes
14	24	No	Yes	No	No
15	24	Yes	No	No	No
16	24	Yes	Yes	No	Yes
17	12	No	No	No	No
18	12	No	Yes	No	Yes
19	12	Yes	No	No	Yes
20	12	Yes	Yes	No	No
21	12	No	No	Yes	Yes
22	12	No	Yes	Yes	No
23	12	Yes	No	Yes	No
24	12	Yes	Yes	Yes	Yes
25	24	No	No	No	No
26	24	No	Yes	No	Yes
27	24	Yes	No	No	Yes
28	24	Yes	Yes	No	No
29	24	No	No	Yes	Yes
30	24	No	Yes	Yes	No
31	24	Yes	No	Yes	No
32	24	Yes	Yes	Yes	Yes



Do not buy these books!* You can download pdf versions from the Springer portal at your university library.

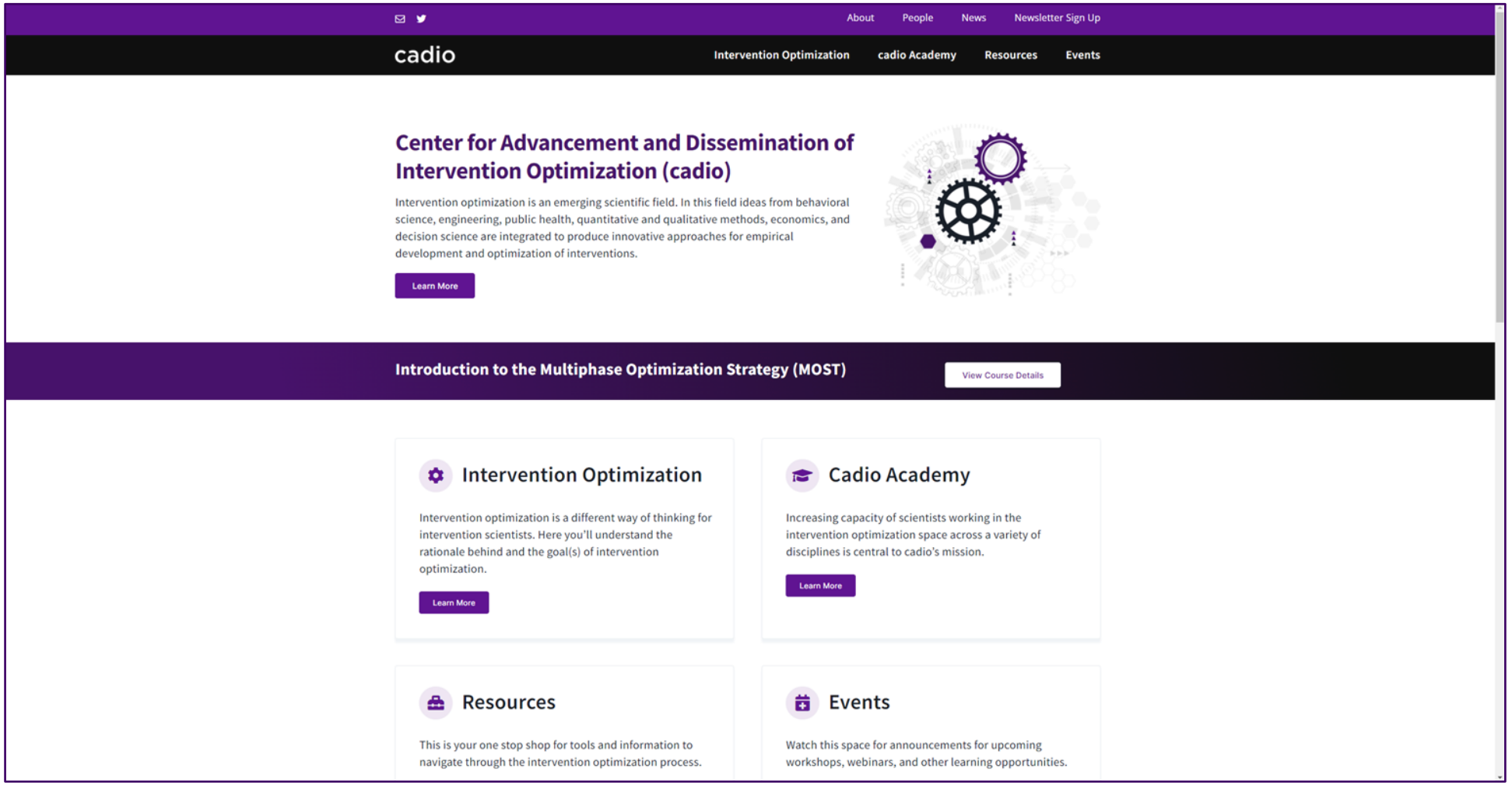
Comprehensive intro

Advanced topics



*unless you want a hard cover version

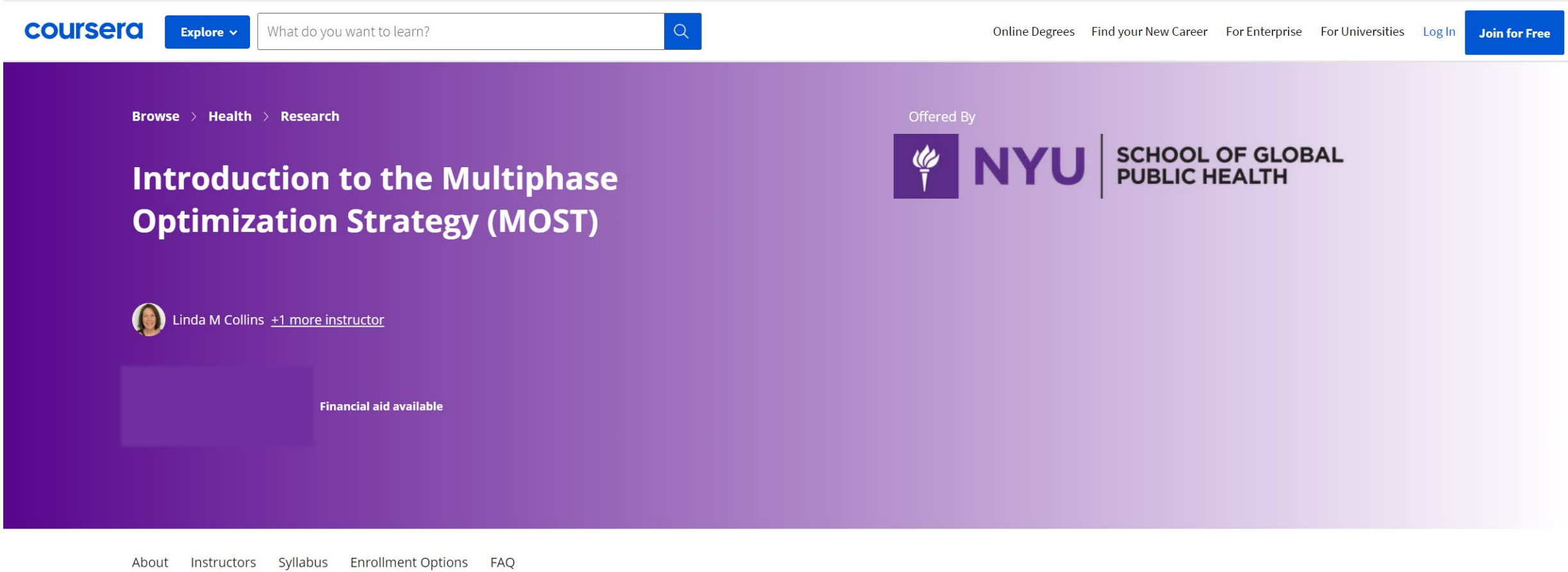
Resources at https://cadio.org/



cadio is supported by the NYU School of Global Public Health and the National Institute on Drug Abuse

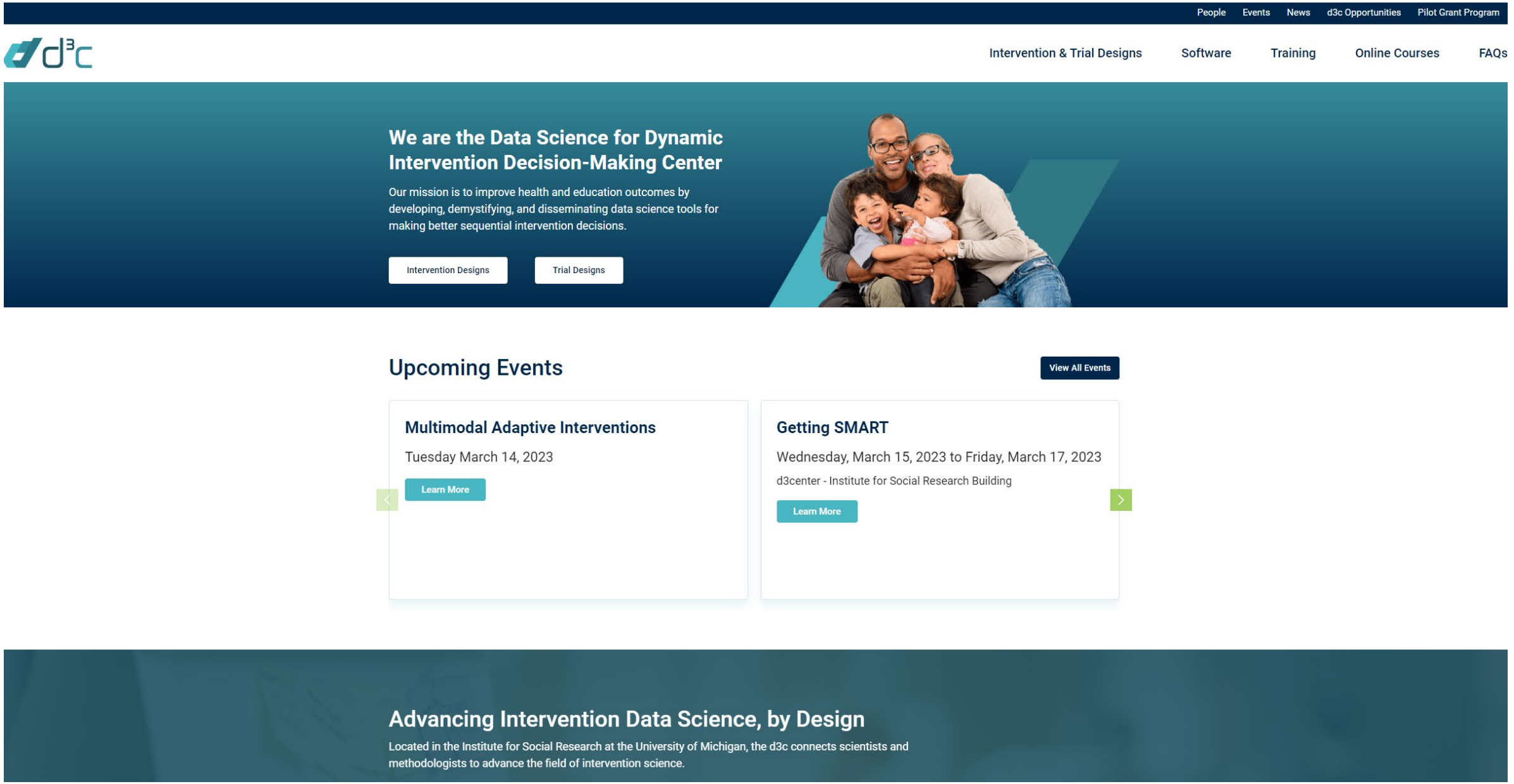
Cadio academy https://cadio.org/cadio-academy/

Asynchronous and synchronous online training



Preparation supported by R25 DA049699

Resources at https://d3c.isr.umich.edu/



SIGN UP FOR OUR NEWSLETTER!

https://cadio.org/newsletter-sign-up/

REGISTER FOR WEBINARS!

(all are Wednesdays 1-2 pm Eastern)

https://cadio.org/events/webinars/

Linda M. Collins

Department of Social & Behavioral Sciences
Department of Biostatistics
Center for Advancement and Dissemination of Intervention Optimization (cadio)

School of Global Public Health
New York University

Email: linda.m.collins@nyu.edu
Twitter: @collins_most

Break

REFRESHMENTS LOCATED OUTSIDE OF MEETING ROOM

PLEASE RETURN BY 11:25AM

Lunch

LUNCH WILL BE SERVED IN THE WISCONSIN ROOM

PLEASE RETURN BY 1:25PM

Multimodal & Multilevel Adaptive Interventions

Innovations in Intervention and Experimental Designs

Inbal Billie Nahum-Shani · Daniel Almirall

Data Science for Dynamic Decision-Making Center · University of Michigan

Collaborators and Funding

John Dziak · UIC
Maureen Walton · UM
Walter Dempsey · UM
Linda Collins · NYU
Susan Murphy · Harvard
Catherine Stanger · Dartmouth
Sylvie Naar · FSU
Amy Kilbourne · UM
Elizabeth Connors · Yale
Andrew Quanbeck · UWisc
Aaron Lyon · UWash

P50 DA054039 · NIH, NIDA
R01 DA039901 · NIH, NIDA
U01 CA229437 · NIH, NCI
R324B210001 · IES
R305B210004 · IES

Examples are based on
R01 AA026574 · PI: Walton
R01 MH114203 · PI: Kilbourne
R01 HD095973 · PI: Kasari
K08 MH116119 · PI: Connors
R01DA047279 · PI: Quanbeck

Some examples are modified for illustrative purposes.

Outline

The future of adaptive interventions is multi-modal & multi-level

Multimodal Adaptive Interventions

Hybrid Experimental Designs

Multilevel Adaptive Interventions

Multilevel SMART Design

The Future

Prevention and treatment requires addressing people's changing needs

Adaptive interventions play an important role

Digital technology offers opportunities to adapt at different timescales and different levels

To leverage these opportunities, we need—

Multimodal Adaptive Interventions

MADIS

Multilevel Adaptive Interventions

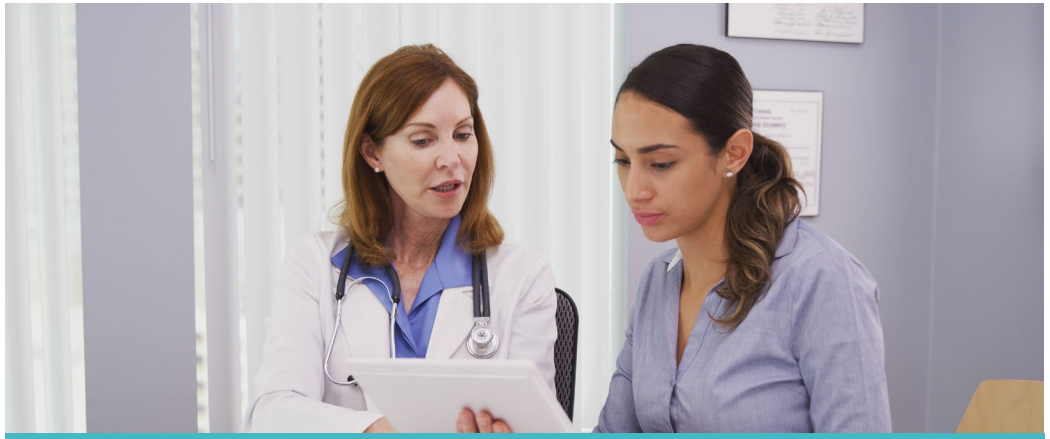
MAIST S

Multimodal Adaptive Interventions

Inbal Billie Nahum-Shani · University of Michigan

A Gap

Leveraging technology requires high-quality integration of human-delivered and digital components



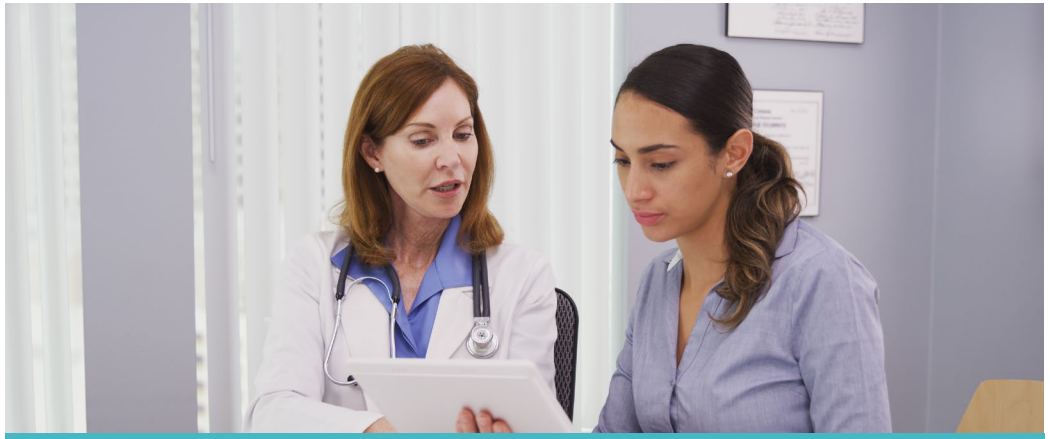
Human Support can combat disengagement in digital services

Digital components can extend therapeutic contact beyond the clinic

A Gap

Leveraging technology requires high-quality integration of human-delivered and digital components

We don't know how best to sequence and adapt human-delivered and digital components



Human Support can combat disengagement in digital services

Digital components can extend therapeutic contact beyond the clinic

What tools do we have?

Components	Time Scale for Adaptation	Intervention Framework	Experimental Design
Human-delivered	*Slow*	Adaptive Interventions	SMART
Digital	*Fast*	Just-in-Time Adaptive Interventions	MRT
Human-delivered & Digital	*Multiple Time Scales*	Multimodal Adaptive Interventions	

What tools do we have?

Components	Time Scale for Adaptation	Intervention Framework	Experimental Design
Human-delivered	*Slow*	Adaptive Interventions	SMART
Digital	*Fast*	Just-in-Time Adaptive Interventions	MRT
Human-delivered & Digital	*Multiple Time Scales*	Multimodal Adaptive Interventions	HED

What tools do we have?

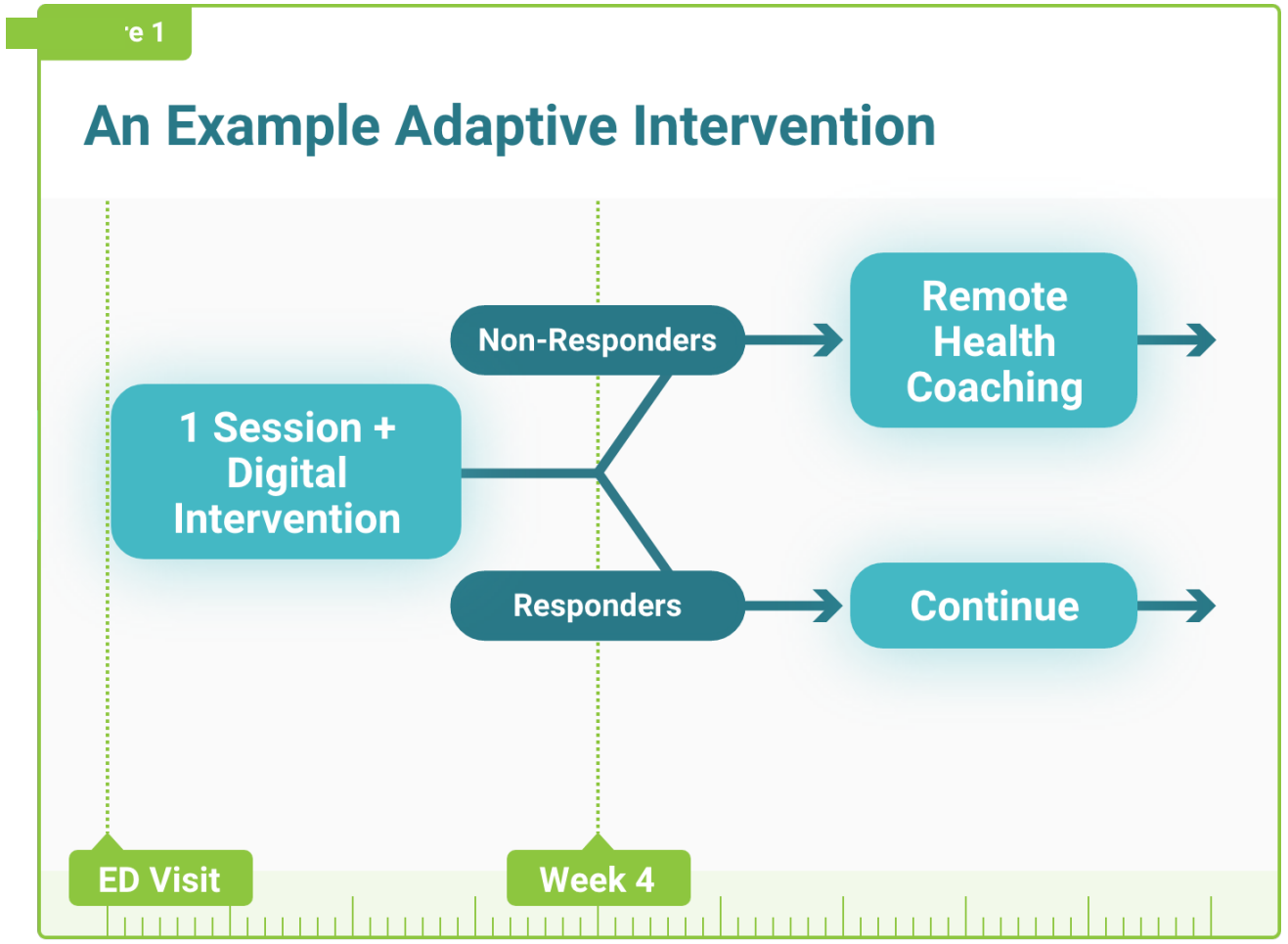
Components	Time Scale for Adaptation	Intervention Framework	Experimental Design
Human-delivered	*Slow*	Adaptive Interventions	SMART
Digital	*Fast*	Just-in-Time Adaptive Interventions	MRT
Human-delivered & Digital	*Multiple Time Scales*	Multimodal Adaptive Interventions	HED

What tools do we have?

Components	Time Scale for Adaptation	Intervention Framework	Experimental Design
Human-delivered	*Slow*	Adaptive Interventions	SMART
Digital	*Fast*	Just-in-Time Adaptive Interventions	MRT
Human-delivered & Digital	*Multiple Time Scales*	Multimodal Adaptive Interventions	HED

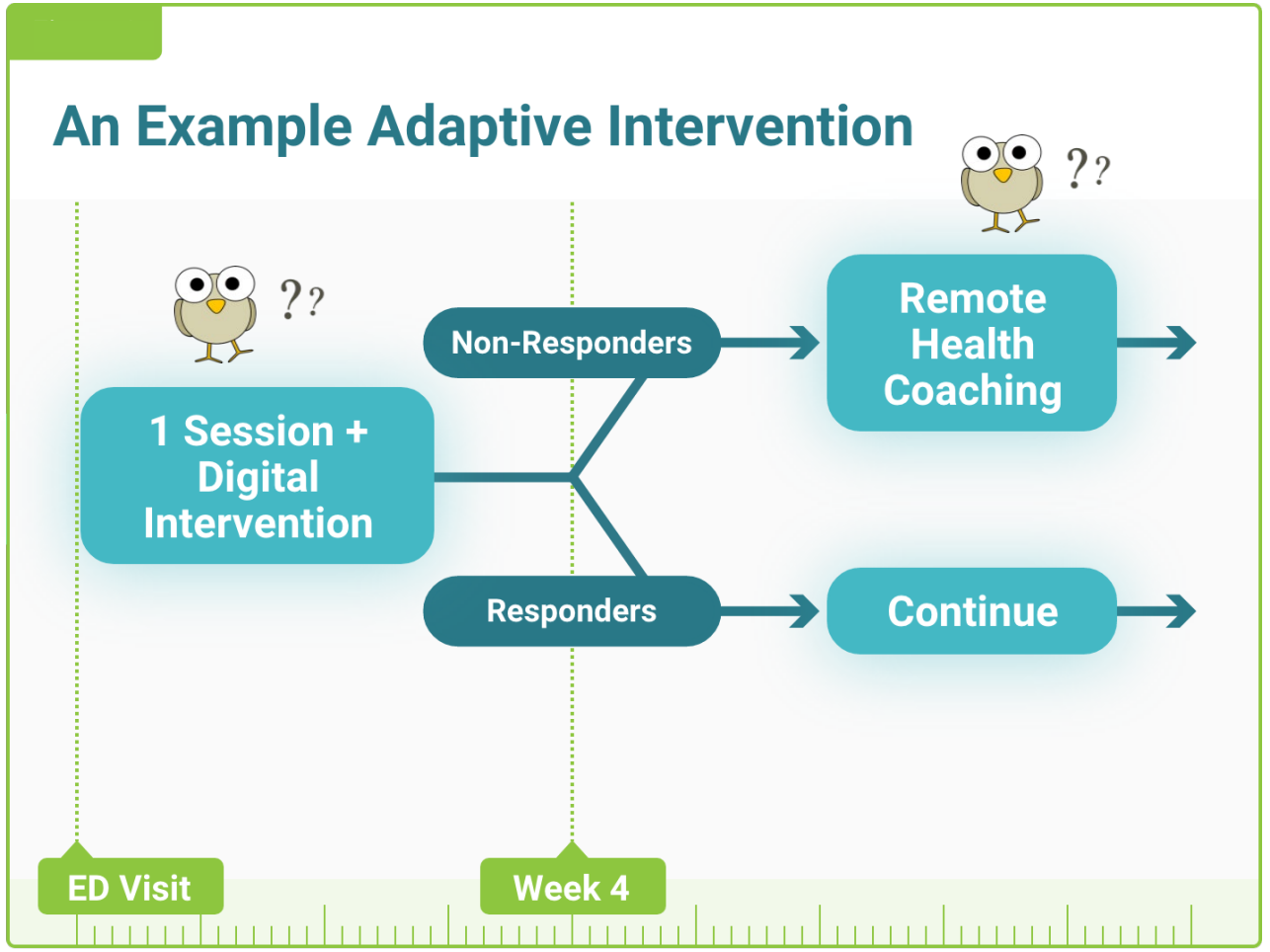
Adaptive Interventions

- Intervention delivery framework
- Use ongoing information about the person to decide whether and how to intervene
- Address conditions that change relatively slowly
- Guide the adaptation of human-delivered components



Adaptive Interventions

- At ED visit—is it beneficial to start with or without RHC?
- At Week 4—is it beneficial to step up the intensity or continue for non-responders?



Beneficial = reducing number of substance use days by week 16

Sequential Multiple Assignment Randomized Trial (SMART)

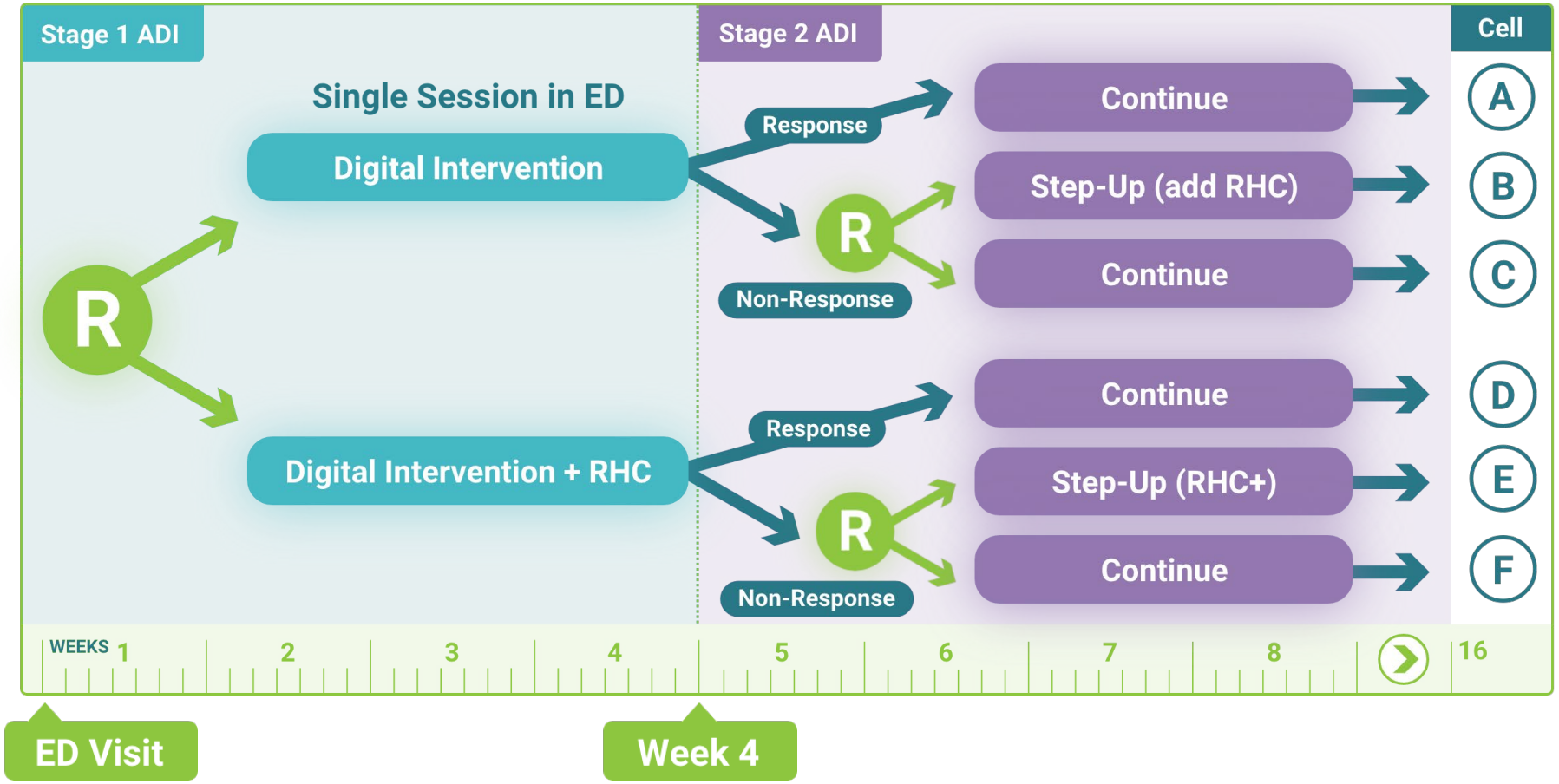
- Randomized Trial
  - **Multiple stages of randomization**
  - **Each stage corresponds to a point in time**
  - **—at which we have scientific questions about the selection and adaptation of components**

Lavori PW, Dawson R. A design for testing clinical strategies: biased adaptive within-subject randomization. Journal of the Royal Statistical Society: Series A (Statistics in Society). 2000;163(1):29-38.

Murphy SA. An experimental design for the development of adaptive treatment strategies. Statistics in Medicine. 2005;24(10):1455-1481.

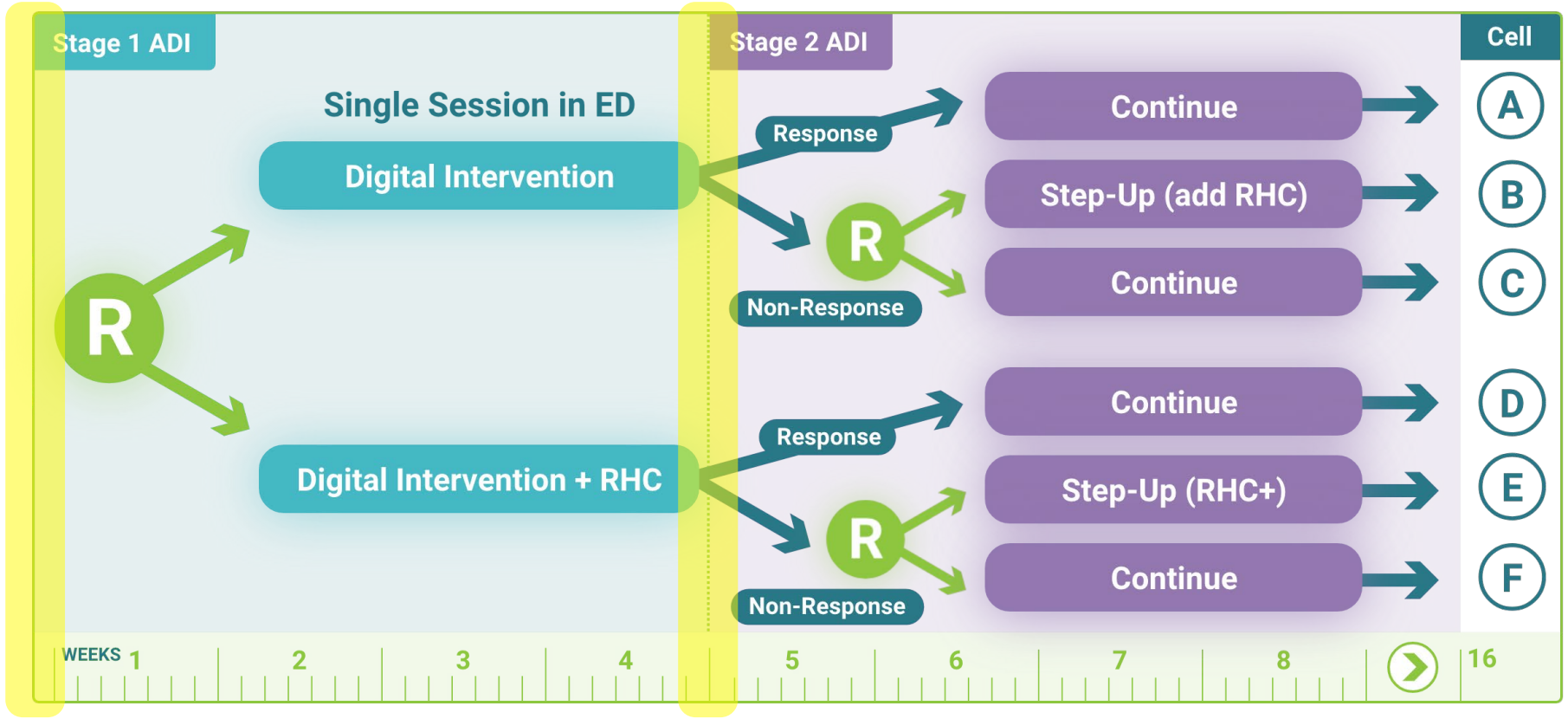
The SMART

- At ED visit—is it beneficial to start with or without RHC?
- At Week 4—is it beneficial to step up the intensity or continue for non-responders?



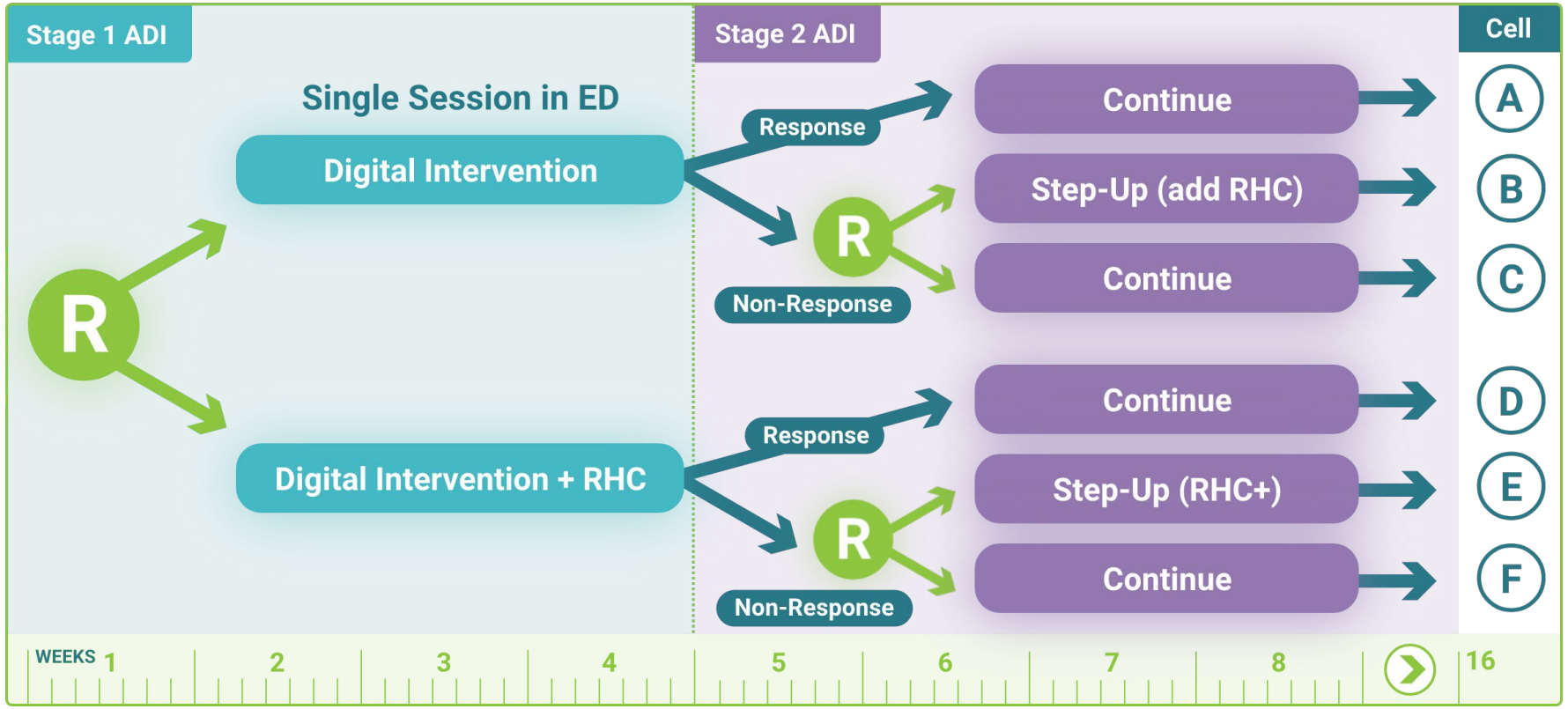
The SMART

- Time scale for randomization: slow
- Questions: sequencing and adaptation at slow time scales



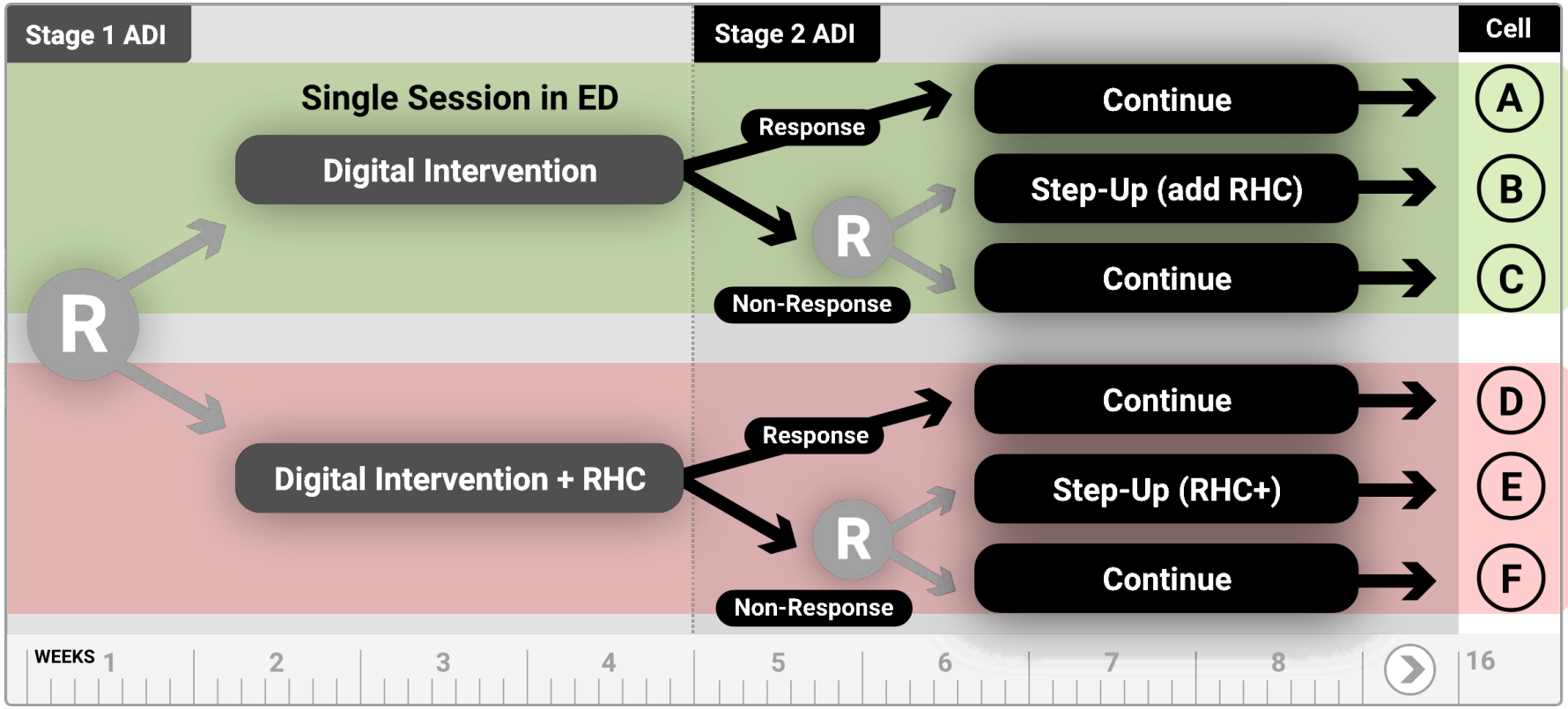
The SMART

- How to answer scientific questions about adaptive intervention development?



The SMART

- At ED visit—is it beneficial to start with or without RHC?
- At Week 4—is it beneficial to step up the intensity or continue for non-responders?



Week 16 Substance Use Across A-C

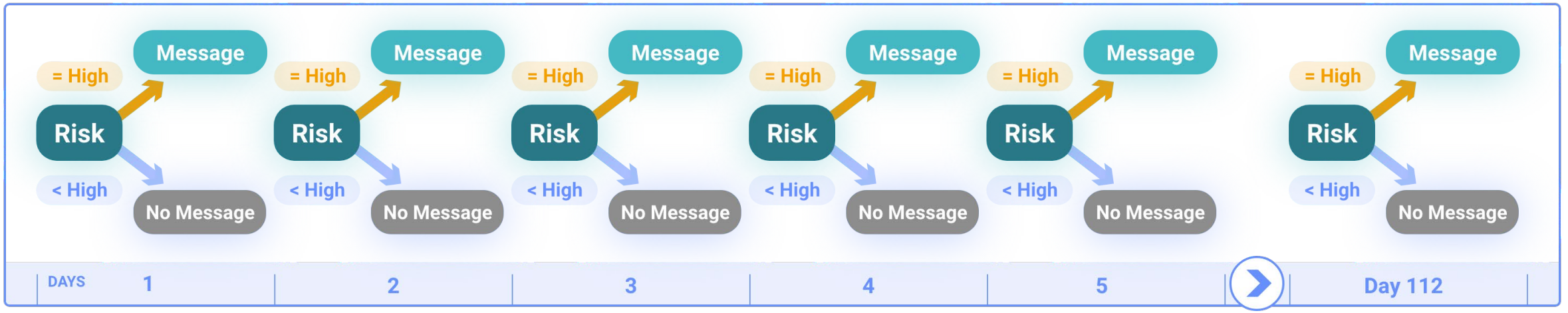
Week 16 Substance Use Across D-F

What tools do we have?

Components	Time Scale for Adaptation	Intervention Framework	Experimental Design
Human-delivered	*Slow*	Adaptive Interventions	SMART
Digital	*Fast*	Just-in-Time Adaptive Interventions	MRT
Human-delivered & Digital	*Multiple Time Scales*	Multimodal Adaptive Interventions	HED

Just-in-Time Adaptive Interventions (JITAI)

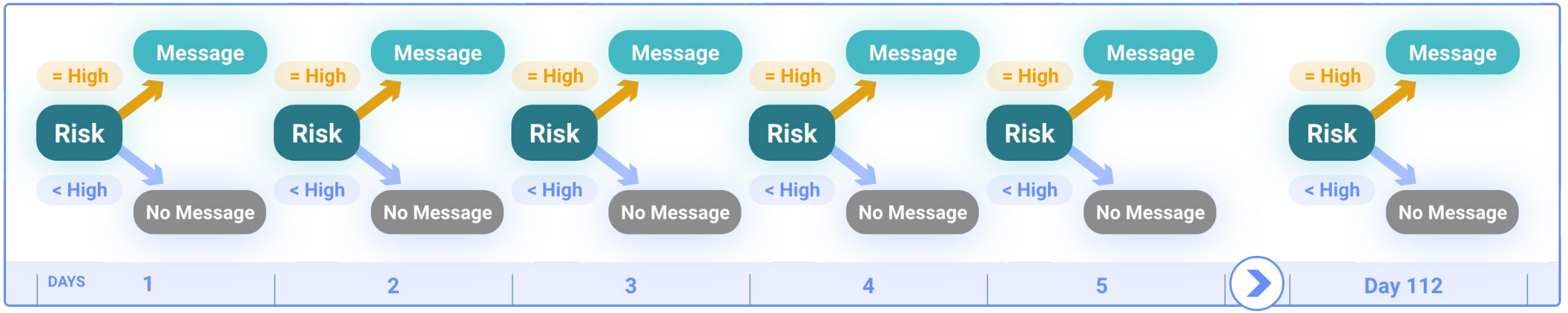
- Use ongoing information about the person to decide whether and how to intervene
- Address conditions that change relatively rapidly
- Guide the adaptation of digital interventions



Just-in-Time Adaptive Interventions (JITAI)

- On average, is it beneficial to deliver (vs. not deliver) a message?
- Under what conditions would delivering a message be beneficial?

Beneficial = reducing next day substance use



Micro-Randomized Trial (MRT)

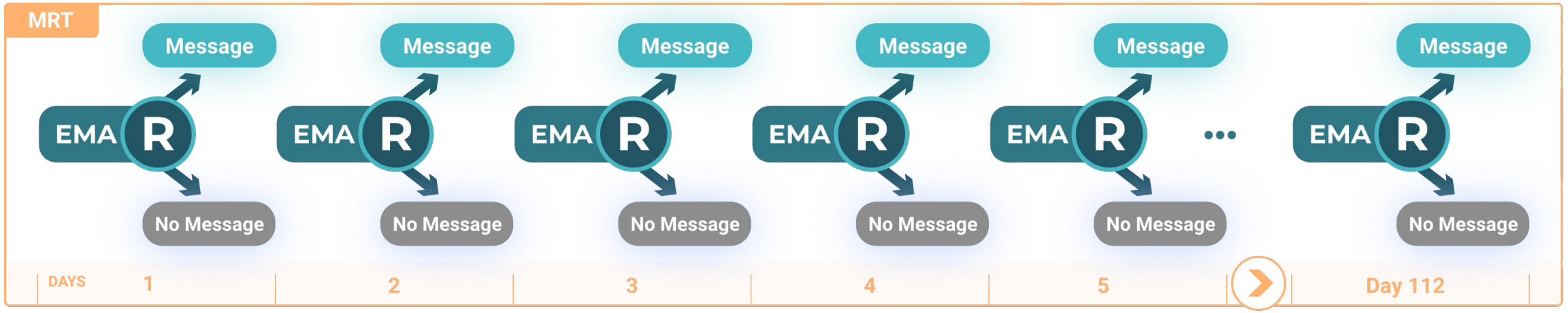
- Randomized Trial
  - **Sequential randomizations: each participant randomized between intervention options at each decision point**
  - **Each person may be randomized 100s or 1000s of times, multiple times per day**

Liao P, Klasnja P, Tewari A, Murphy SA. Sample size calculations for micro-randomized trials in mHealth. Statistics in Medicine. 2016;35(12):1944–1971.

Qian T, Walton AE, Collins LM, ... , Murphy SA. The Micro-Randomized Trial for Developing Digital Interventions: Experimental Design and Data Analysis Considerations. Psychological Methods.

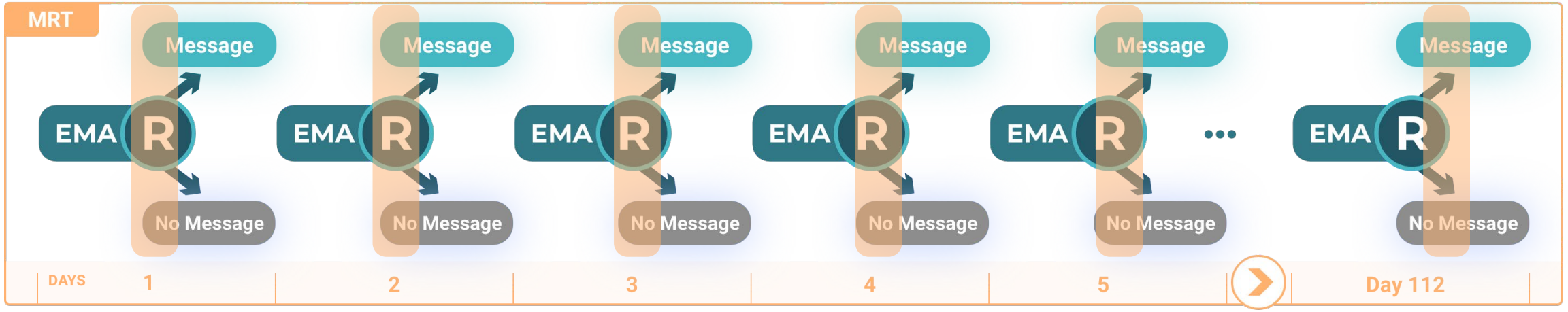
Micro-Randomized Trial (MRT)

- Is it beneficial to deliver a message in terms of reducing next-day substance use?
- Under what conditions would delivering a message be beneficial?



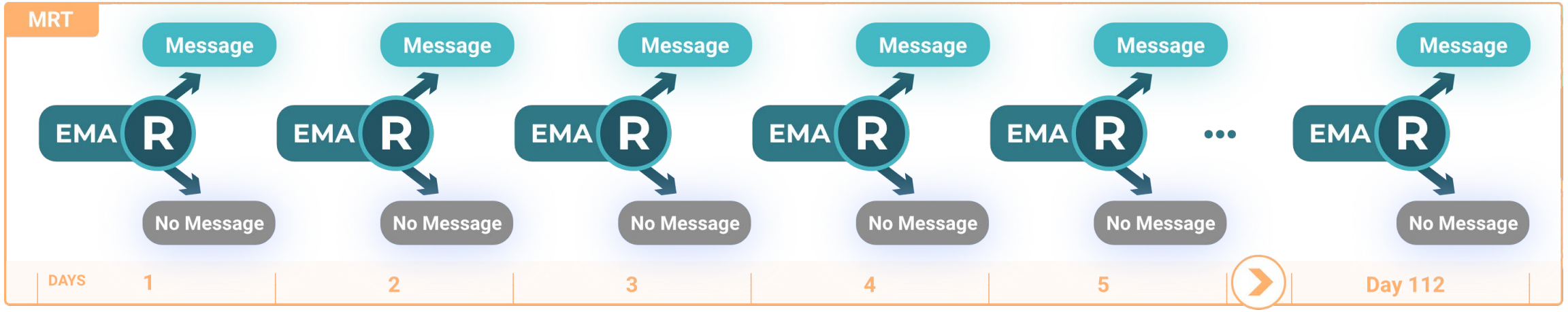
Micro-Randomized Trial (MRT)

- Time scale for randomization: fast
- Questions: sequencing and adaptation at fast time scales



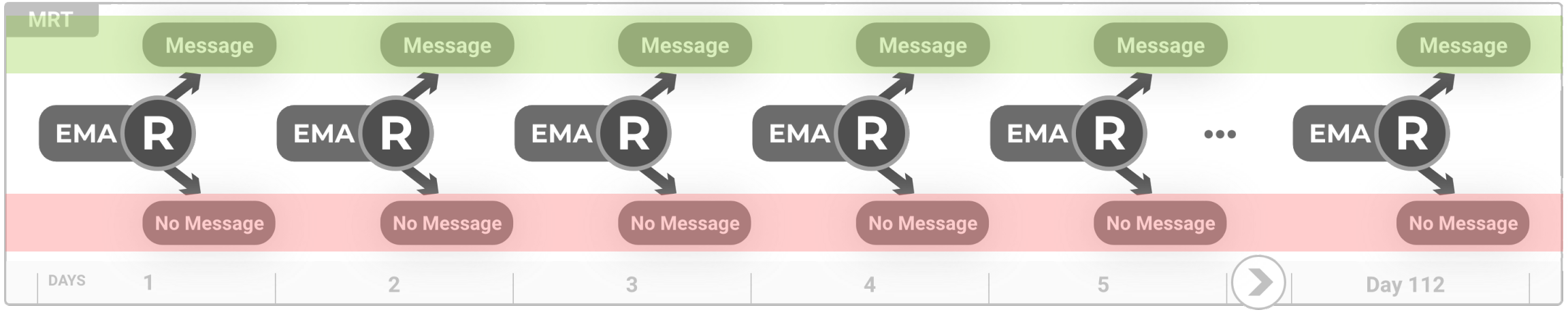
Micro-Randomized Trial (MRT)

- How to answer scientific questions about JITAI development?



Micro-Randomized Trial (MRT)

- Is it beneficial to deliver a message in terms of reducing next-day substance use?
- Under what conditions would delivering a message be beneficial?



Next day substance use across all days in which a message was delivered.

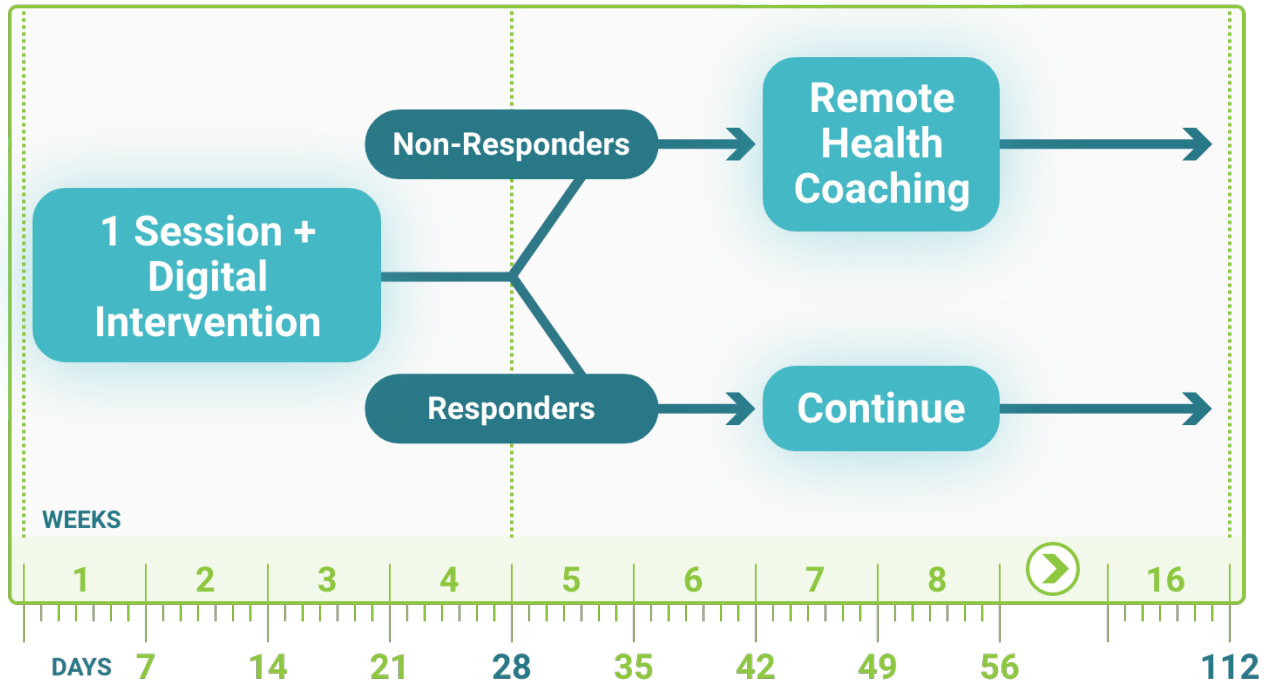
Next day substance use across all days in which a message was not delivered.

What tools do we have?

Components	Time Scale for Adaptation	Intervention Framework	Experimental Design
Human-delivered	*Slow*	Adaptive Interventions	SMART
Digital	*Fast*	Just-in-Time Adaptive Interventions	MRT
Human-delivered & Digital	*Multiple Time Scales*	Multimodal Adaptive Interventions	HED

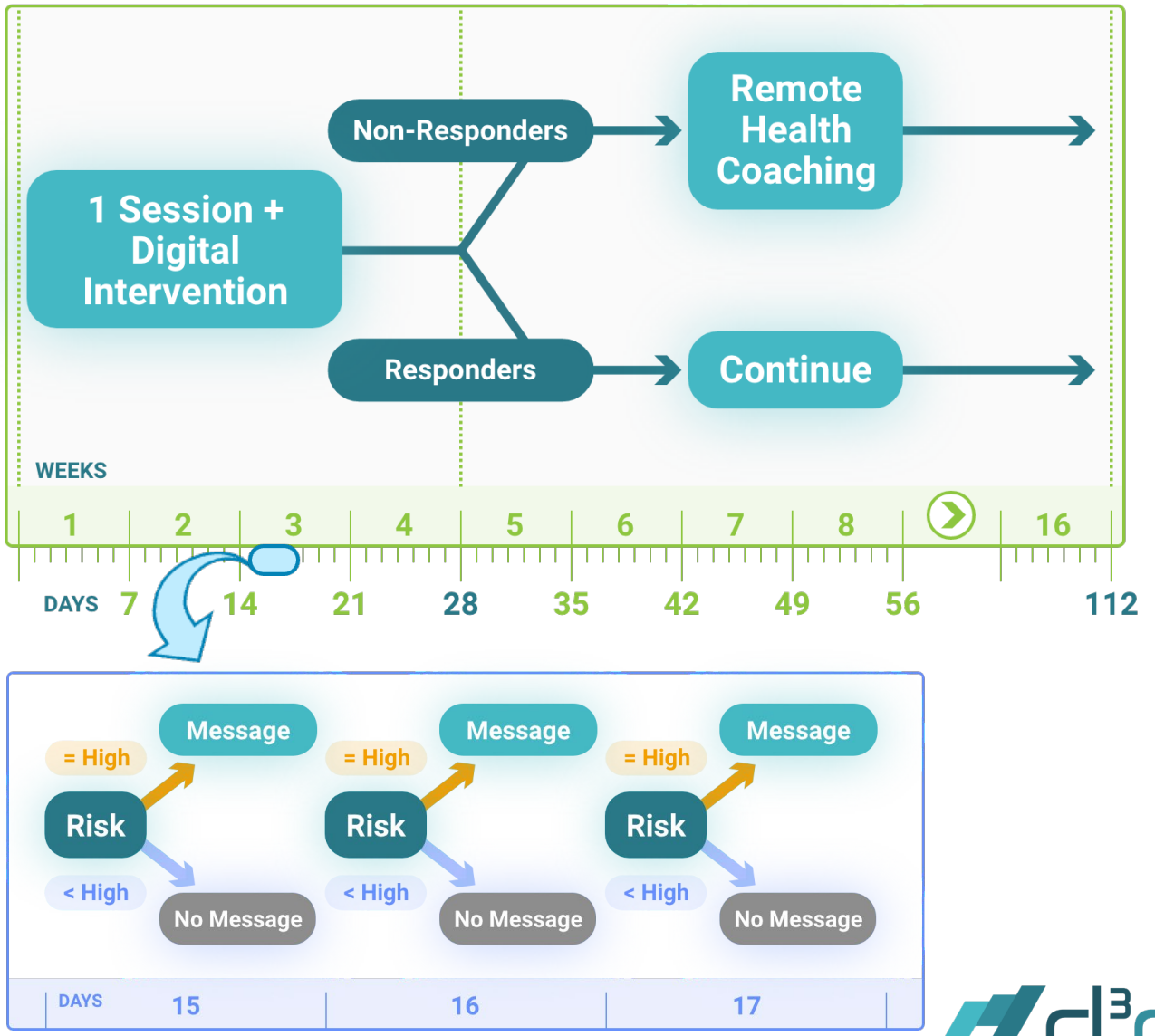
Multimodal Adaptive Intervention

(MADI)



Multimodal Adaptive Intervention

(MADI)

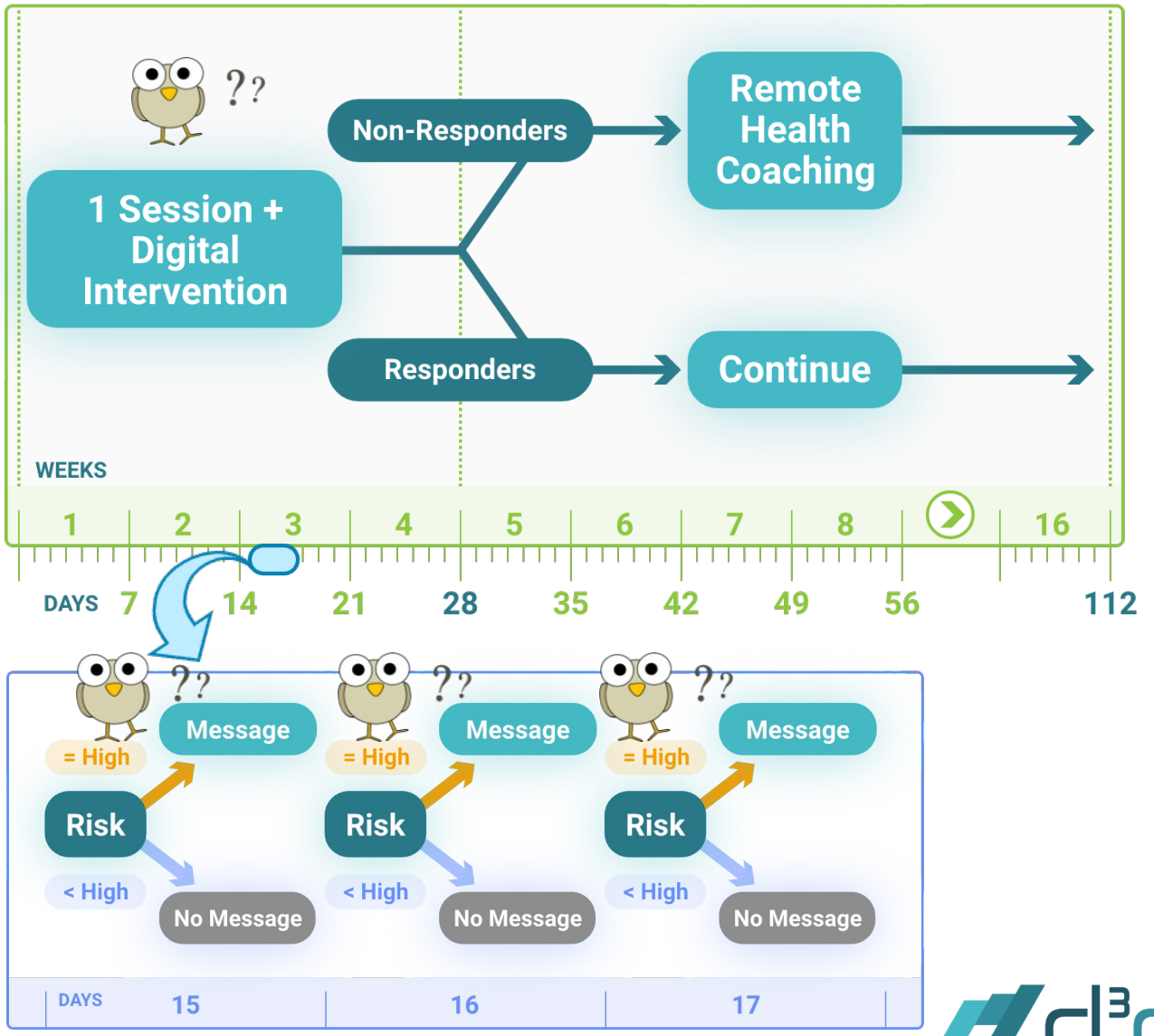


Multimodal Adaptive Intervention (MADI)

- Intervention delivery framework
- Both human-delivered and digital components are sequenced and adapted over time, at different time scales
- Can be operationalized as the integration between an adaptive intervention and a JITAI

Multimodal Adaptive Intervention

(MADI)



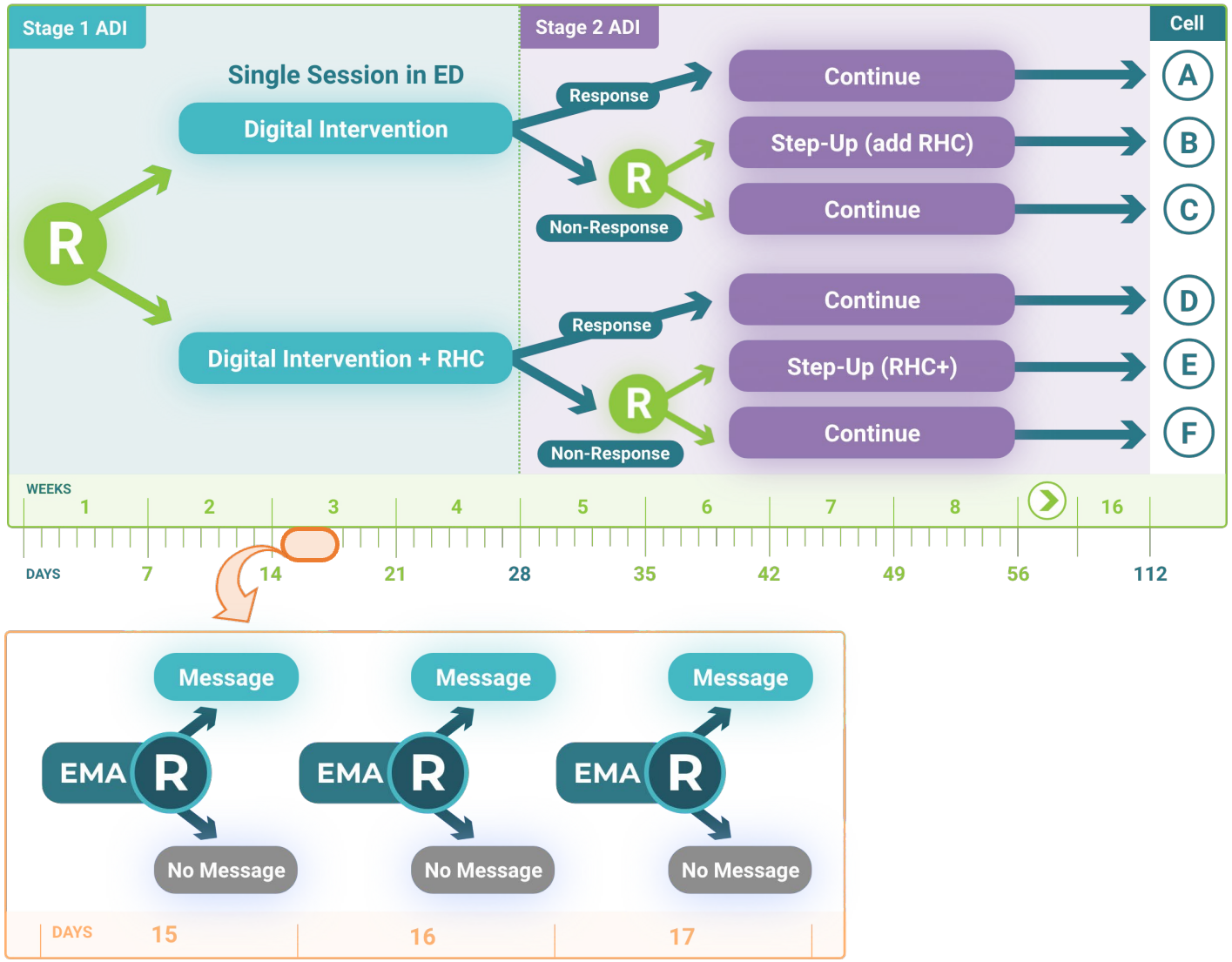
Hybrid Experimental Design (HED)

- Randomized Trial
  - **Sequential randomizations**
  - **At multiple time scales**

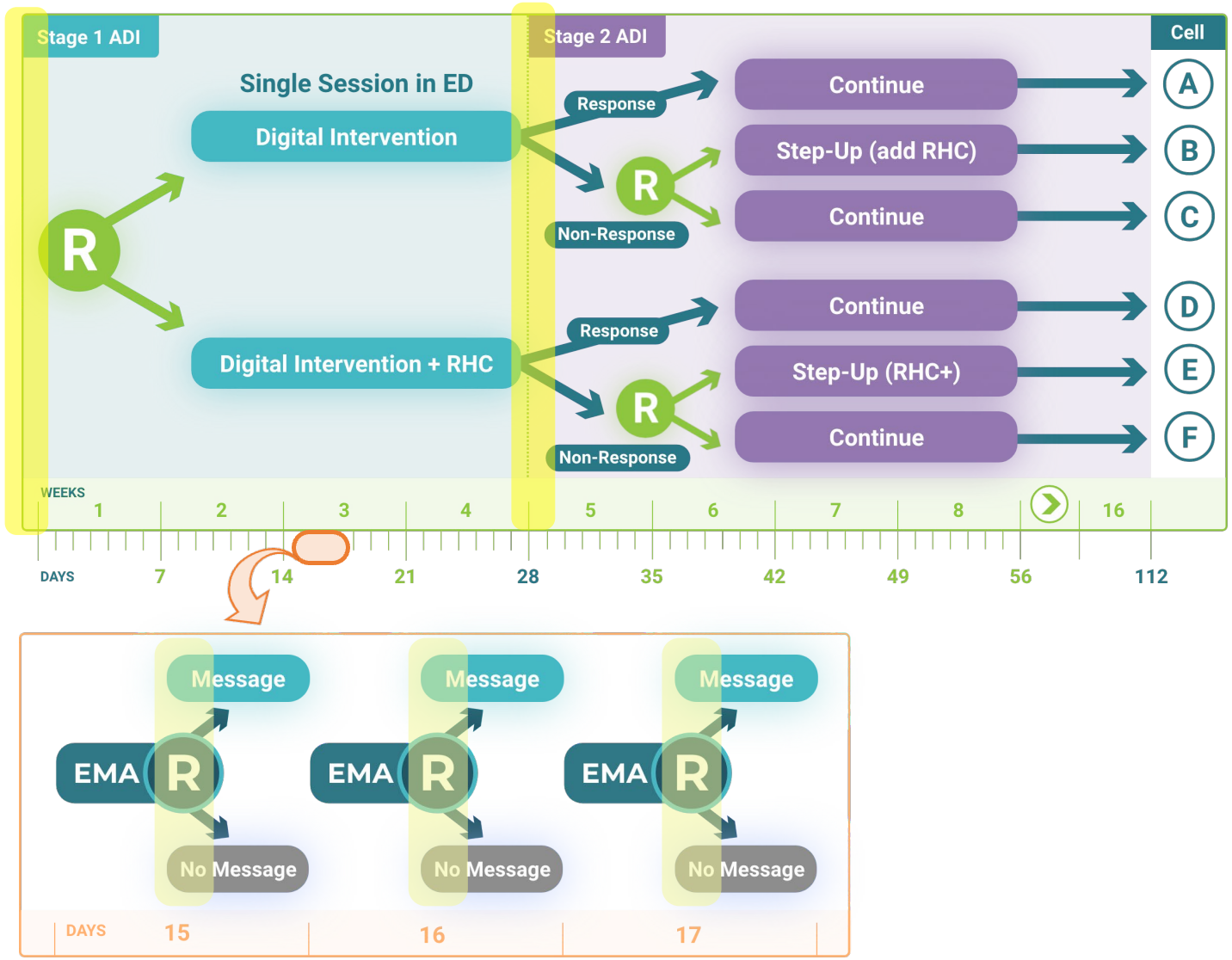
Nahum-Shani, I., Dziak, J. J., Walton, M. A., & Dempsey, W. (2022). Hybrid Experimental Designs for Intervention Development: What, Why and How. *Advances in Methods and Practices in Psychological Science, 5*(3), 1–15.

Nahum-Shani, I., Dziak. J.J., Venera., H., Pfammatte, A.F., Spring, B., & Dempsey, W. (2023). Design of Experiments with Sequential Randomizations on Multiple Timescales: The Hybrid Experimental Design. https://arxiv.org/abs/2302.09046

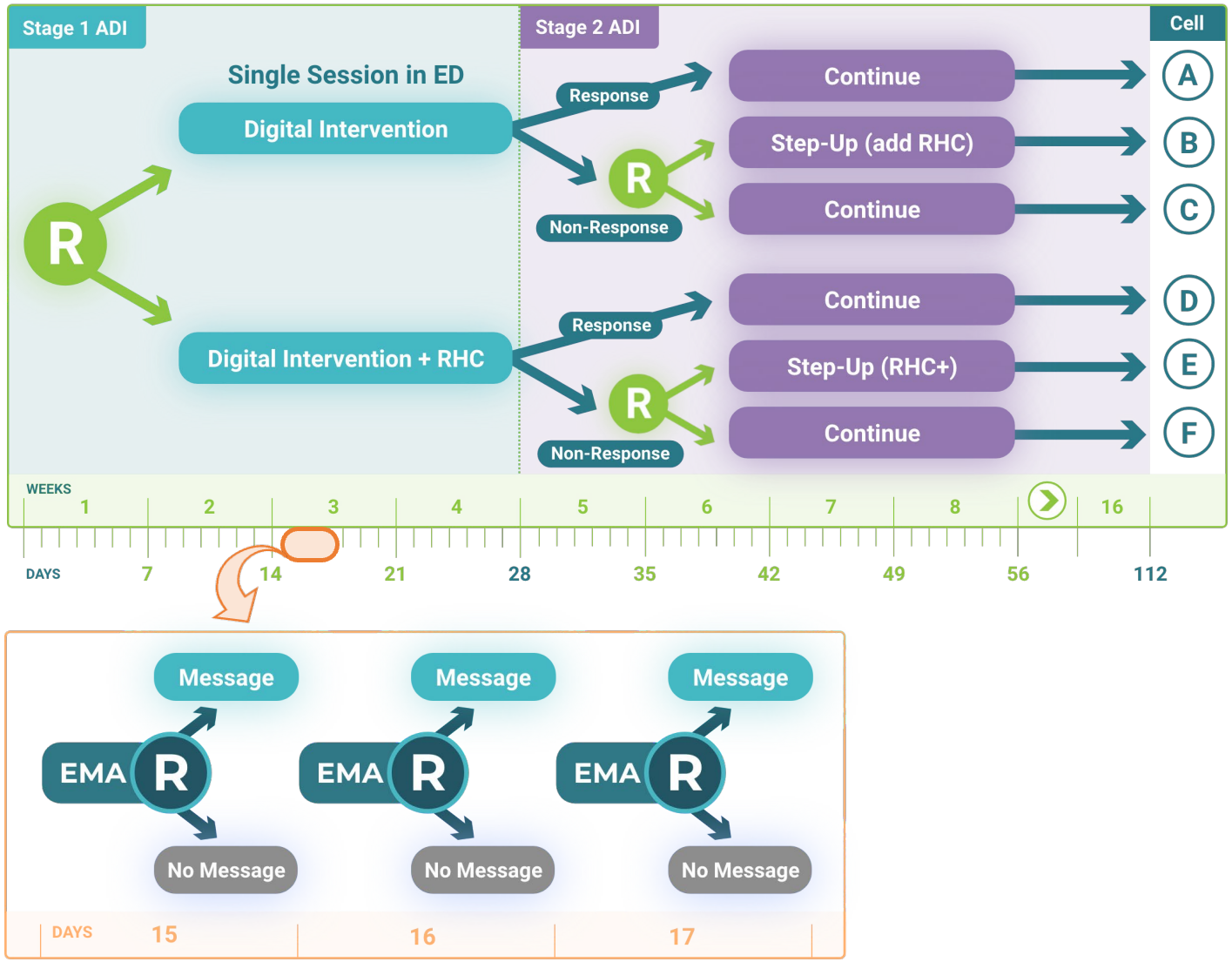
Hybrid Experimental Design (HED)



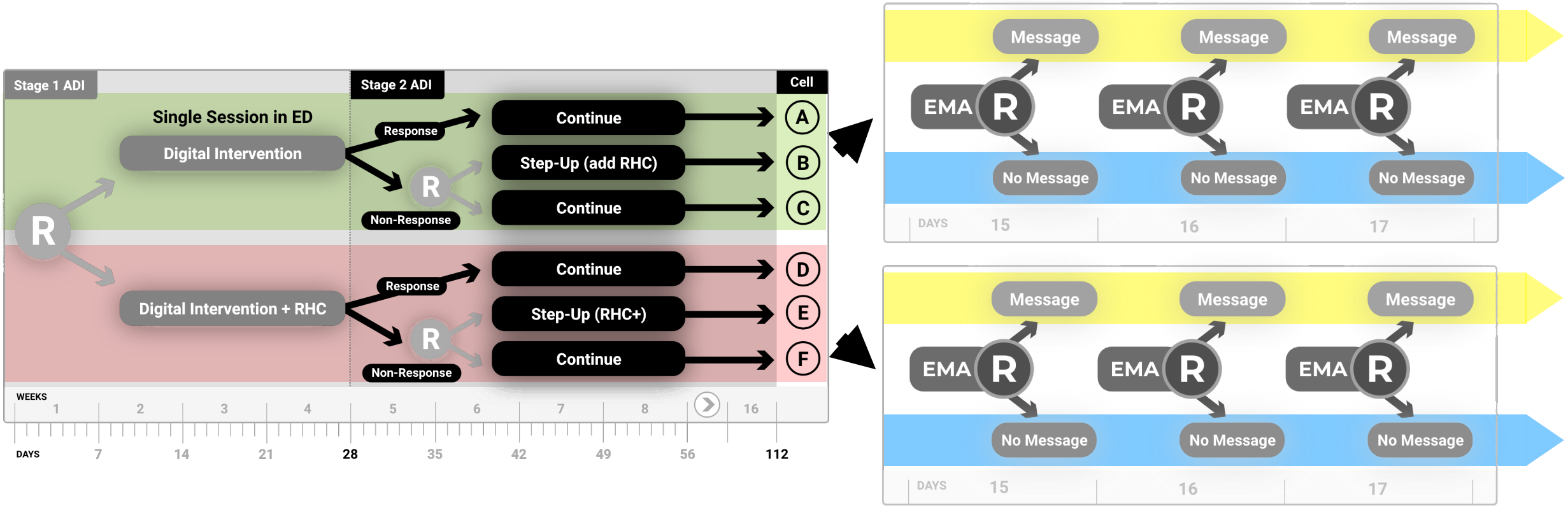
Hybrid Experimental Design (HED)



How to use this design to answer scientific questions about MADIs?



Does the proximal effect of delivering (vs. not delivering) a daily message on next day substance use vary by whether coaching was delivered initially?



Hybrid Experimental Design (HED)

1. Nahum-Shani, I., Dziak, J. J., Walton, M. A., & Dempsey, W. (2022). Hybrid Experimental Designs for Intervention Development: What, Why and How. *Advances in Methods and Practices in Psychological Science*, 5(3), 1–15.

    - Appendix A: Models for Analyzing Data from a HED
    - Appendix B: Sample Size Simulations
    - Appendix C: Power Calculation for HEDs: A User Guide for MC Simulations
    - Appendix D: Annotated Analysis Code for Example HED

2. Nahum-Shani, I., Dziak. J.J., Venera., H., Pfammatte, A.F., Spring, B., & Dempsey, W. (2023). Design of Experiments with Sequential Randomizations on Multiple Timescales: The Hybrid Experimental Design. *https://arxiv.org/abs/2302.09046*

Multilevel Adaptive Interventions

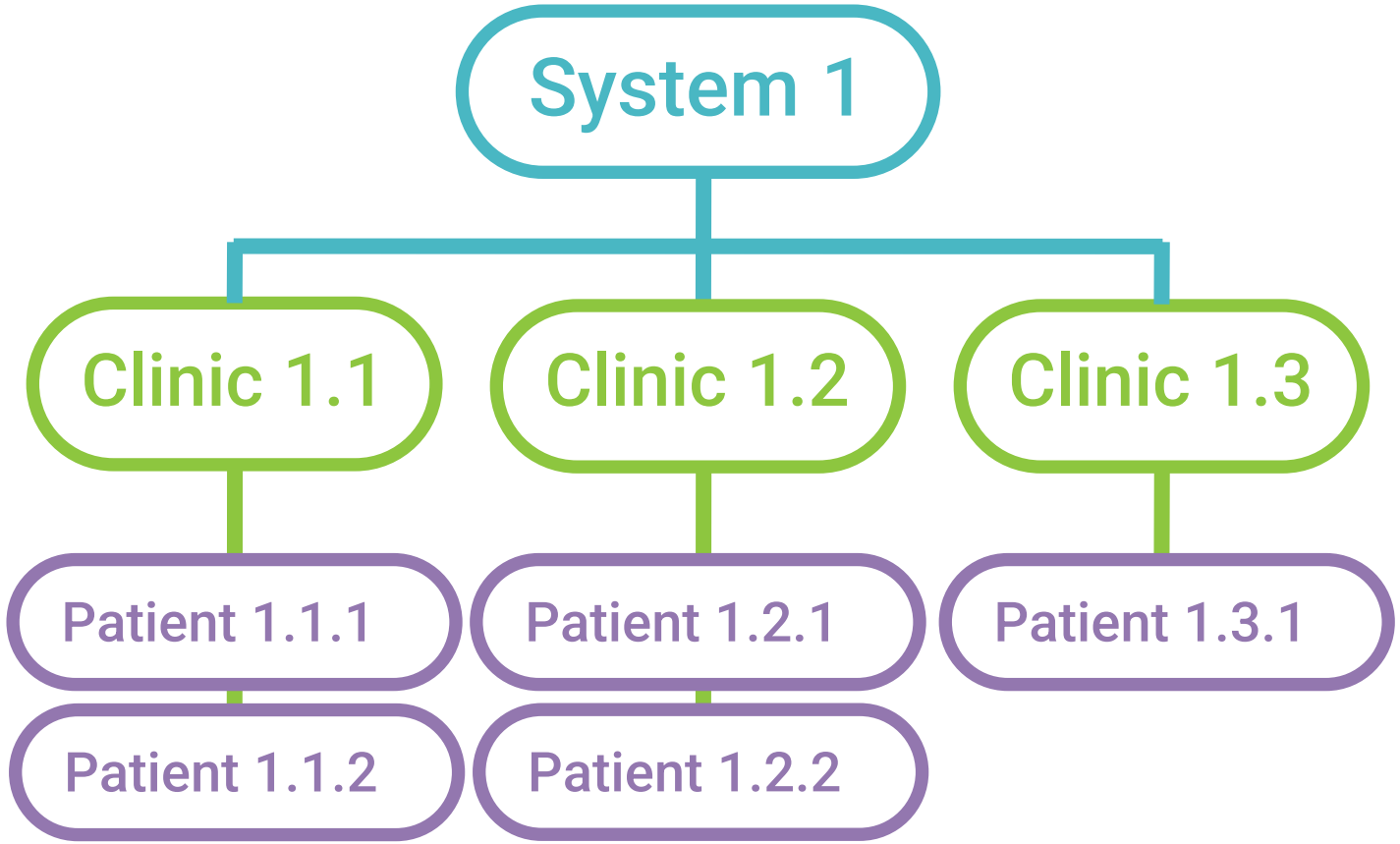
Daniel Almirall and many colleagues · University of Michigan and beyond

Another Gap

Some interventions have components at multiple levels.

Implementation strategies are a prototypical example.

But we don't know how best to sequence and adapt interventions at multiple levels.



Outline

Multilevel Adaptive Interventions

Some optimization questions

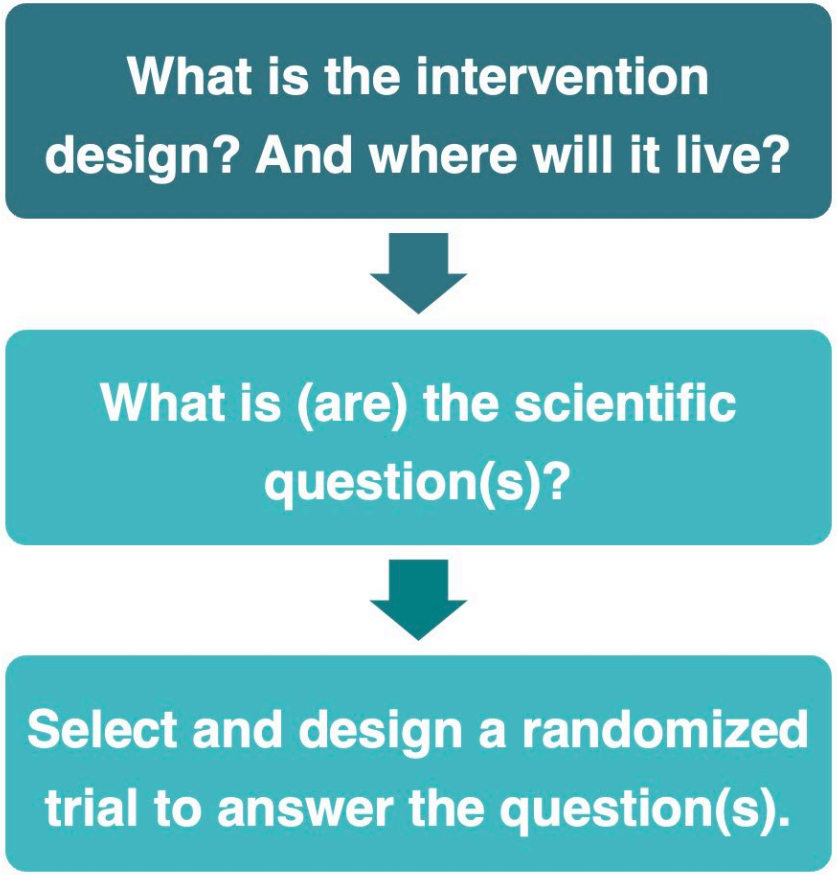
Randomized trial design to answer the questions

Outline

Multilevel Adaptive Interventions

Some optimization questions

Randomized trial design to answer the questions

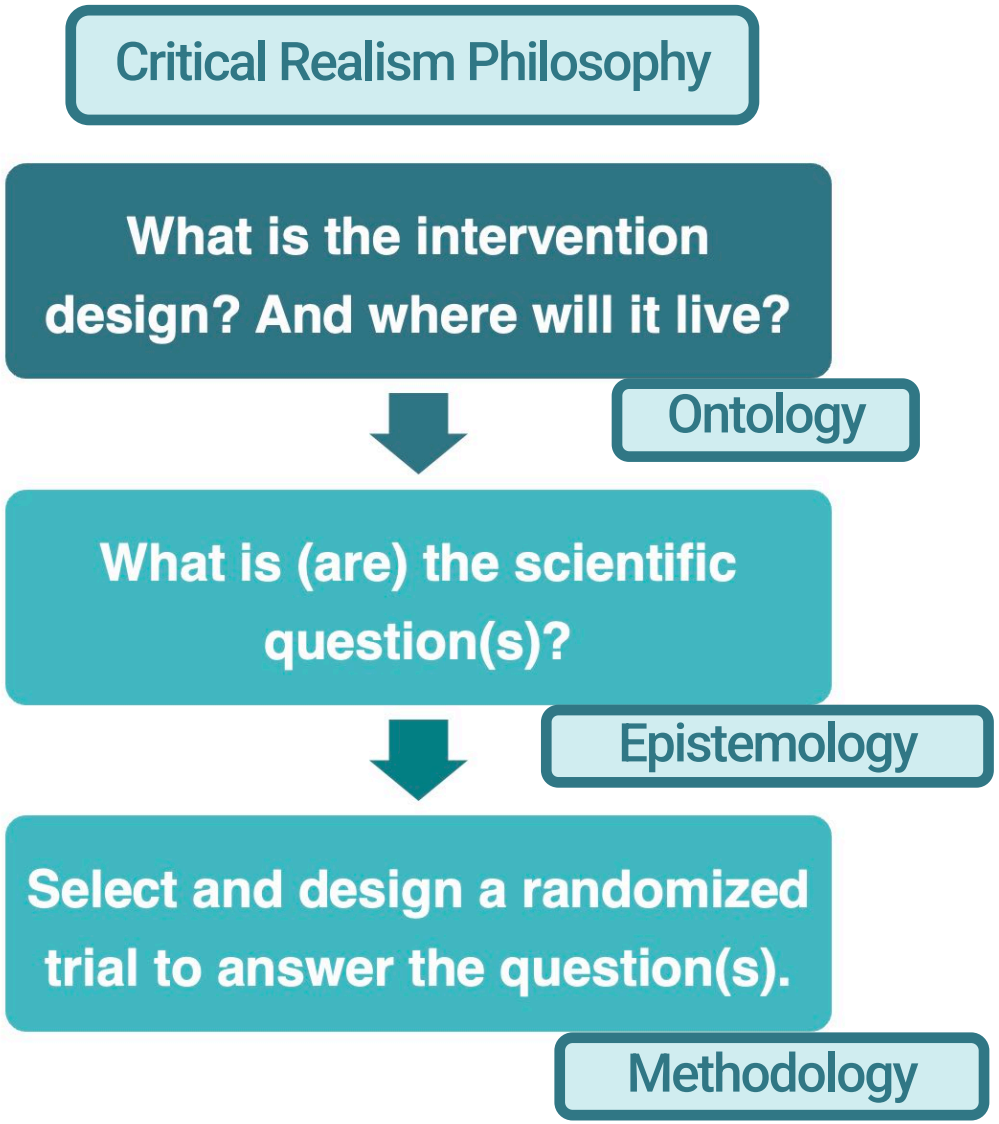


Outline

Multilevel Adaptive Interventions

Some optimization questions

Randomized trial design to answer the questions



Outline

Multilevel Adaptive Interventions

Some optimization questions

Randomized trial design to answer the questions

So put on your clinician or implementer hats.

What is a Multilevel Adaptive Intervention?

Multilevel Adaptive Intervention

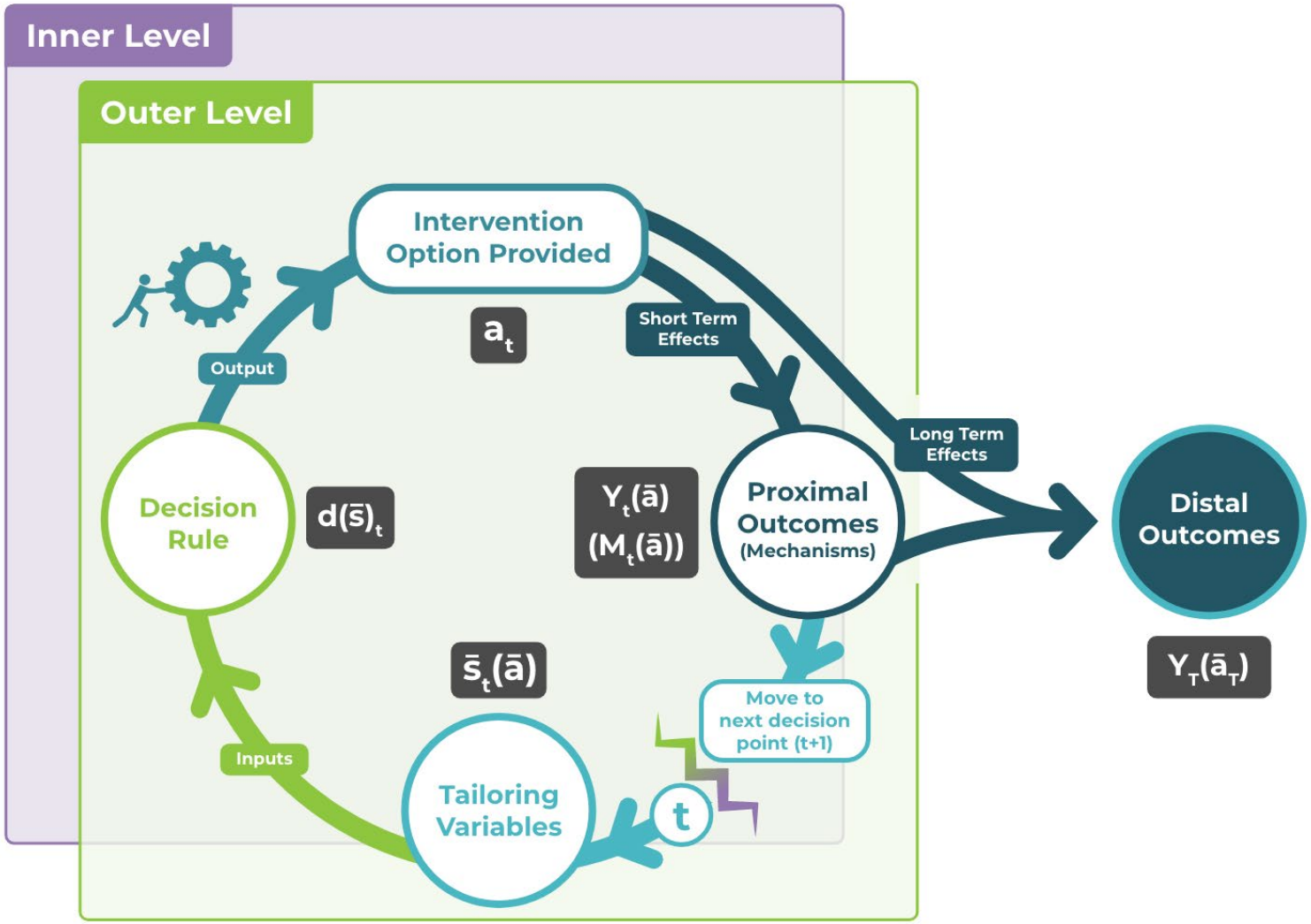
A sequence of decision rules used to guide how best to adapt the provision of intervention…

At critical decision points

Across multiple levels

Based on both baseline + ongoing / changing status of targets within the different levels of intervention

Multilevel Adaptive Intervention



Examples will be Drawn from Implementation Science

Adaptive implementation strategy at the clinic-level

\+

Adaptive implementation strategy at the clinician-level

=

Multilevel Adaptive Implementation Strategy (MAISY)

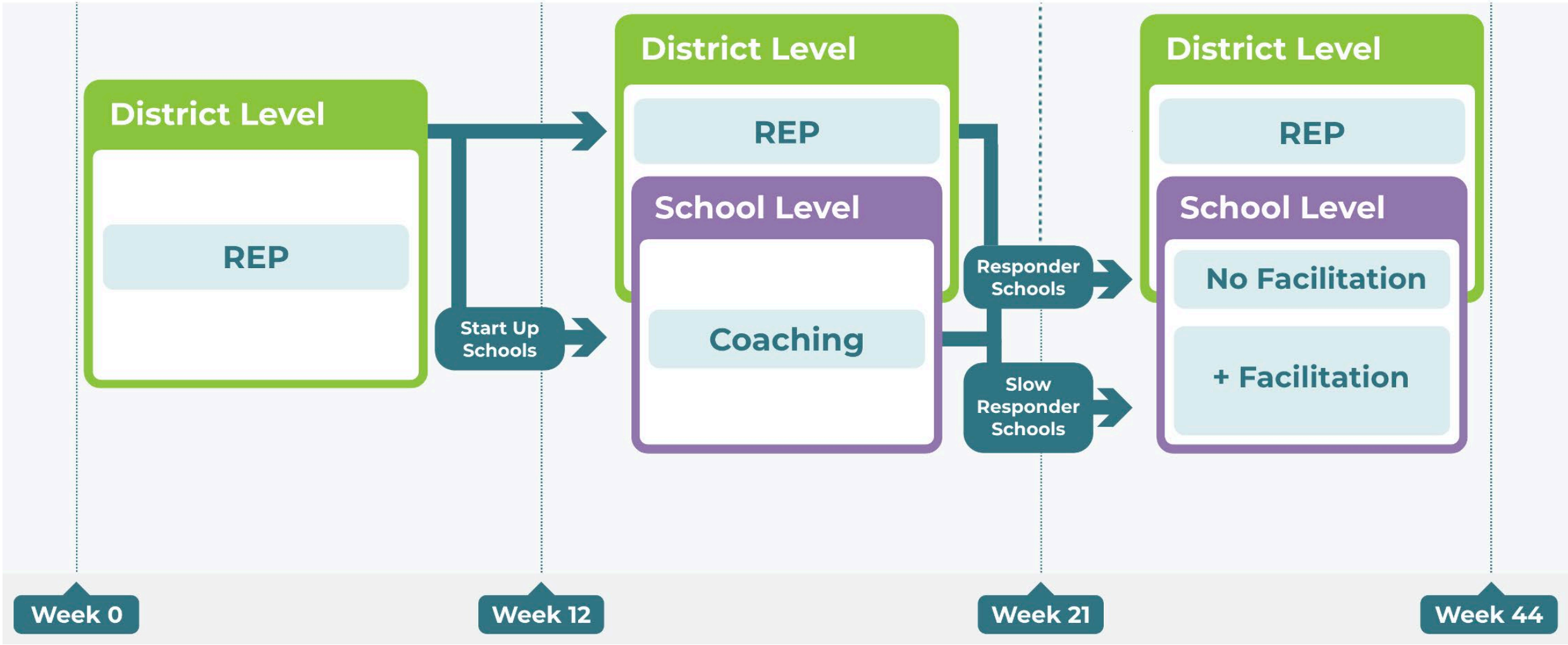
A MAISY is a specific type of multilevel adaptive intervention.

MAISY Example 1

Principal Investigator: Amy Kilbourne

Adaptive School-Based Implementation of CBT (ASIC)

EBP: Cognitive Behavioral Therapy in Michigan Schools

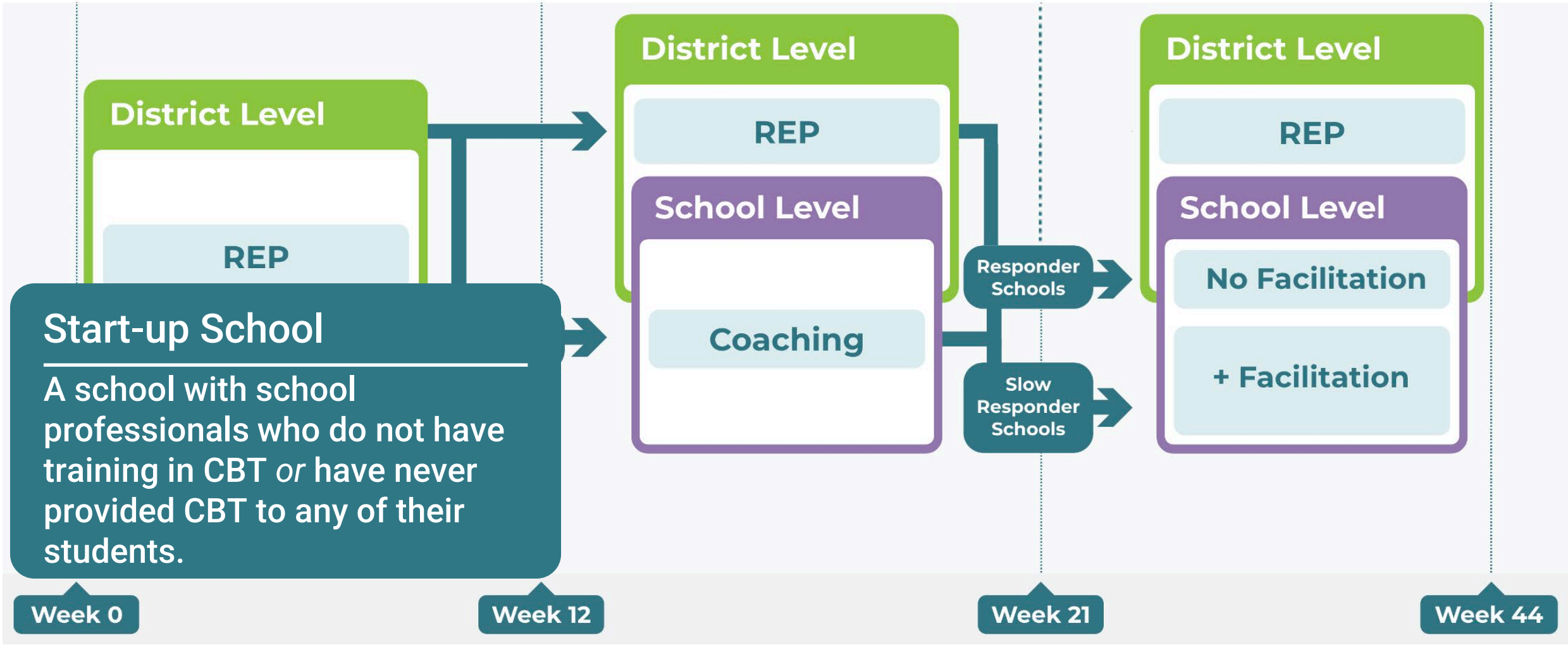


MAISY Example 1

Principal Investigator: Amy Kilbourne

Adaptive School-Based Implementation of CBT (ASIC)

EBP: Cognitive Behavioral Therapy in Michigan Schools

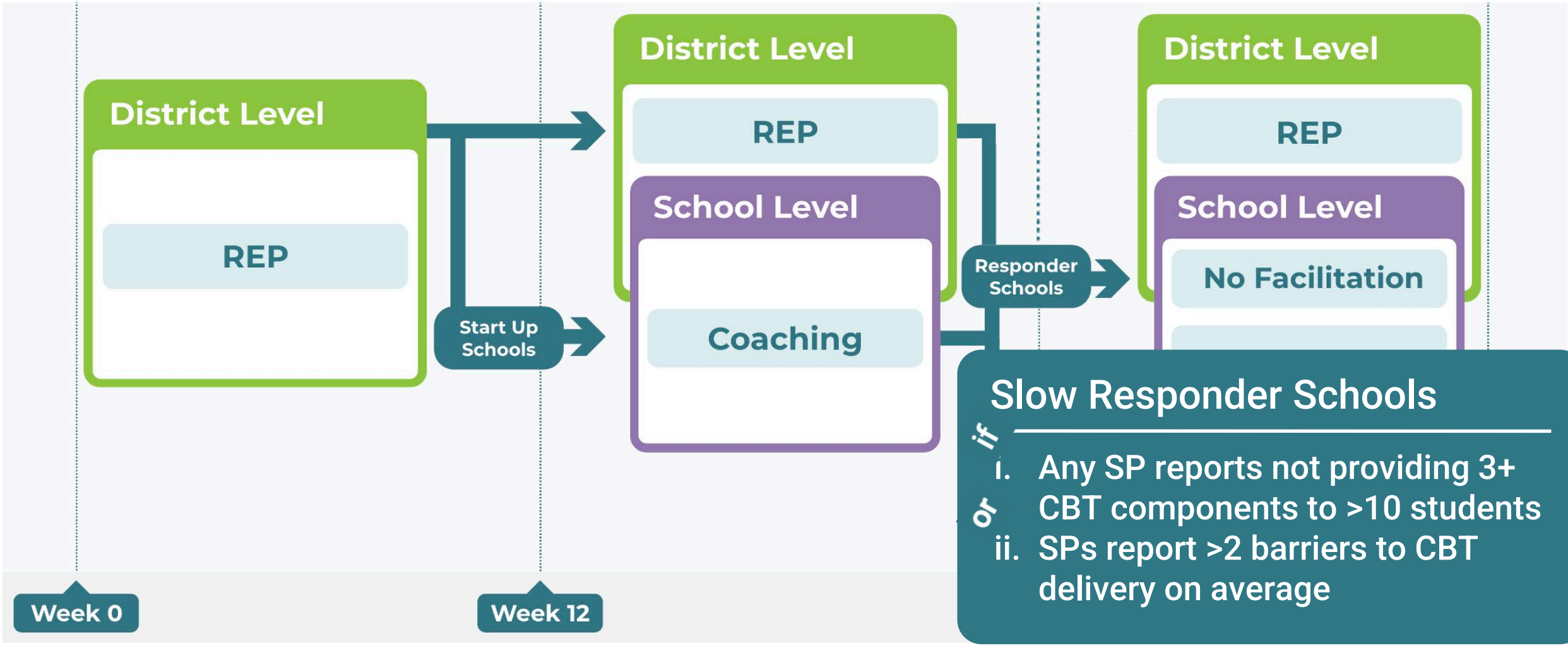


MAISY Example 1

Principal Investigator: Amy Kilbourne

Adaptive School-Based Implementation of CBT (ASIC)

EBP: Cognitive Behavioral Therapy in Michigan Schools

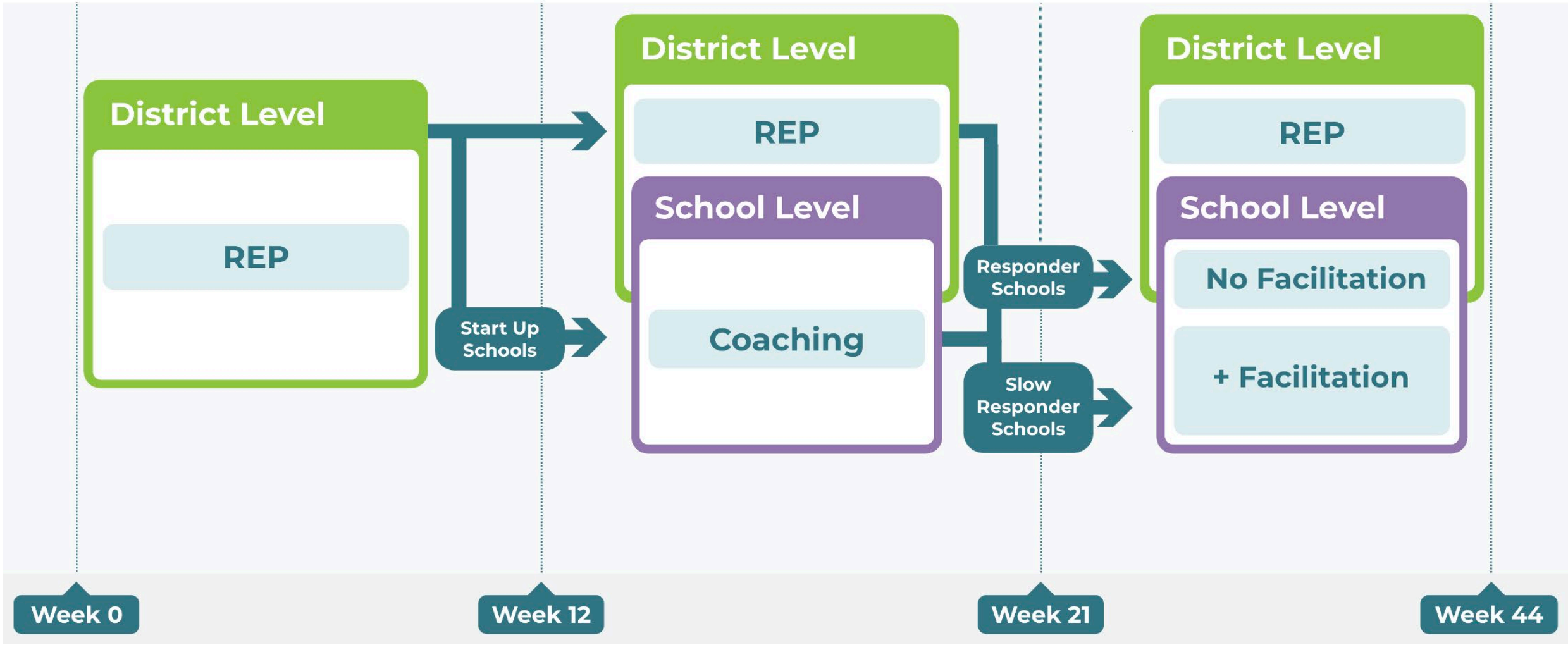


MAISY Example 1

Principal Investigator: Amy Kilbourne

Adaptive School-Based Implementation of CBT (ASIC)

EBP: Cognitive Behavioral Therapy in Michigan Schools

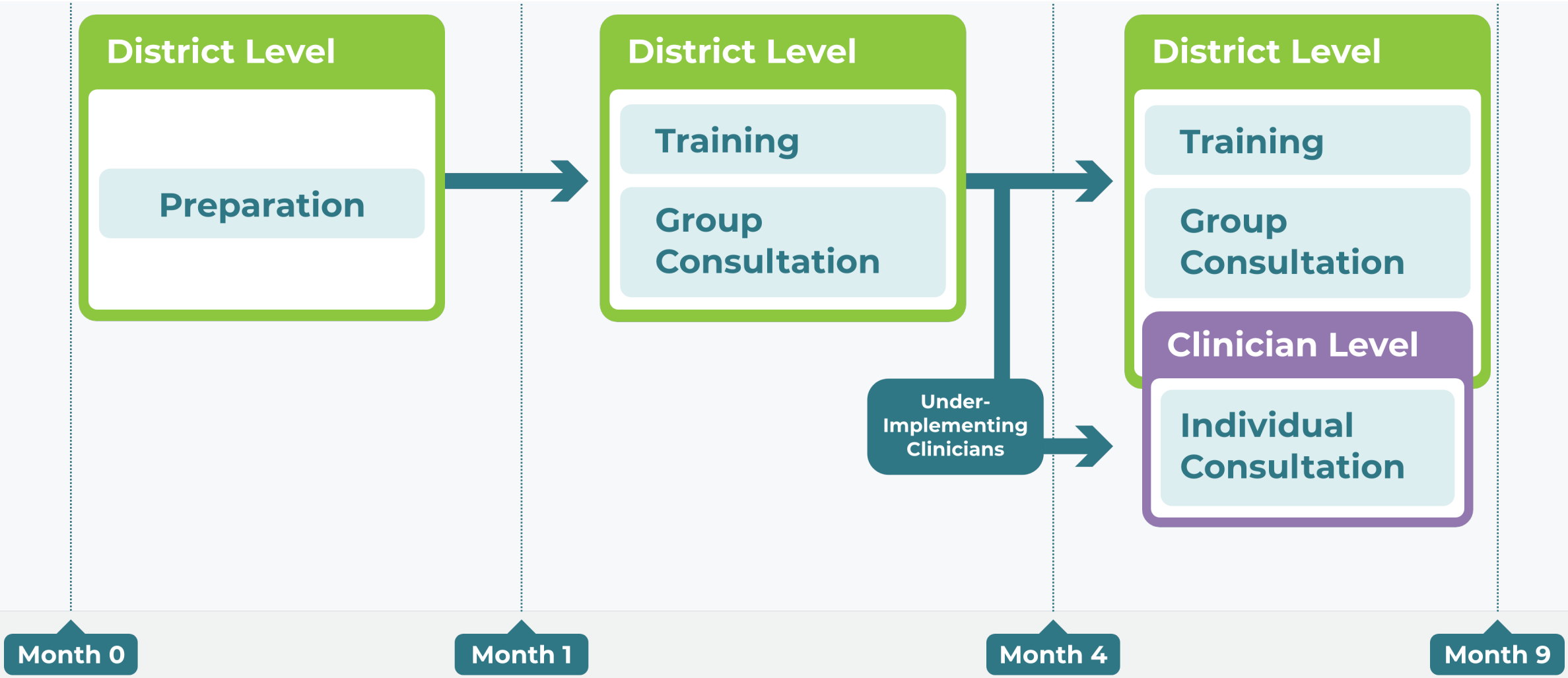


MAISY Example 2

Principal Investigator: Elizabeth Connors

Feedback & Outcomes for Clinically Useful Student Services (FOCUSS)

EBP: Measurement-Based Care in Connecticut Schools

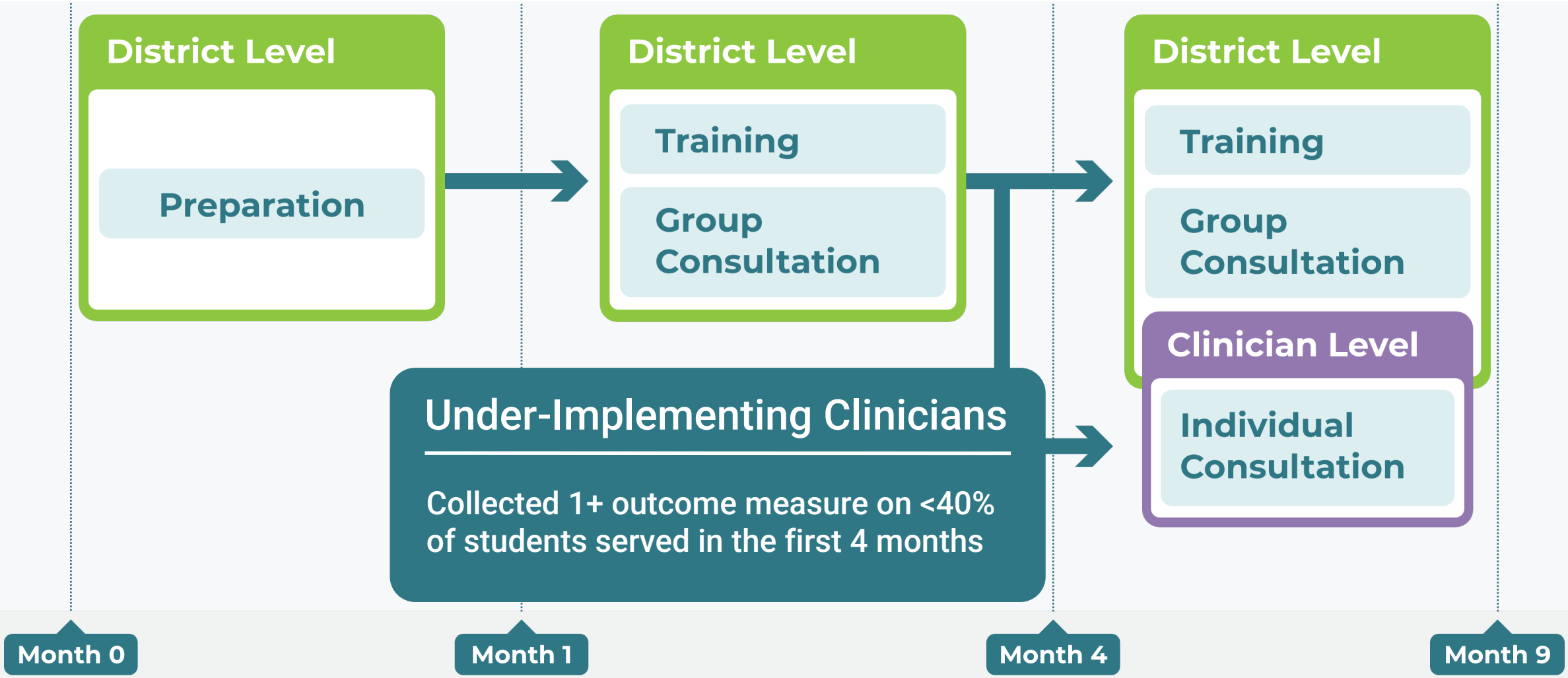


MAISY Example 2

Principal Investigator: Elizabeth Connors

Feedback & Outcomes for Clinically Useful Student Services (FOCUSS)

EBP: Measurement-Based Care in Connecticut Schools

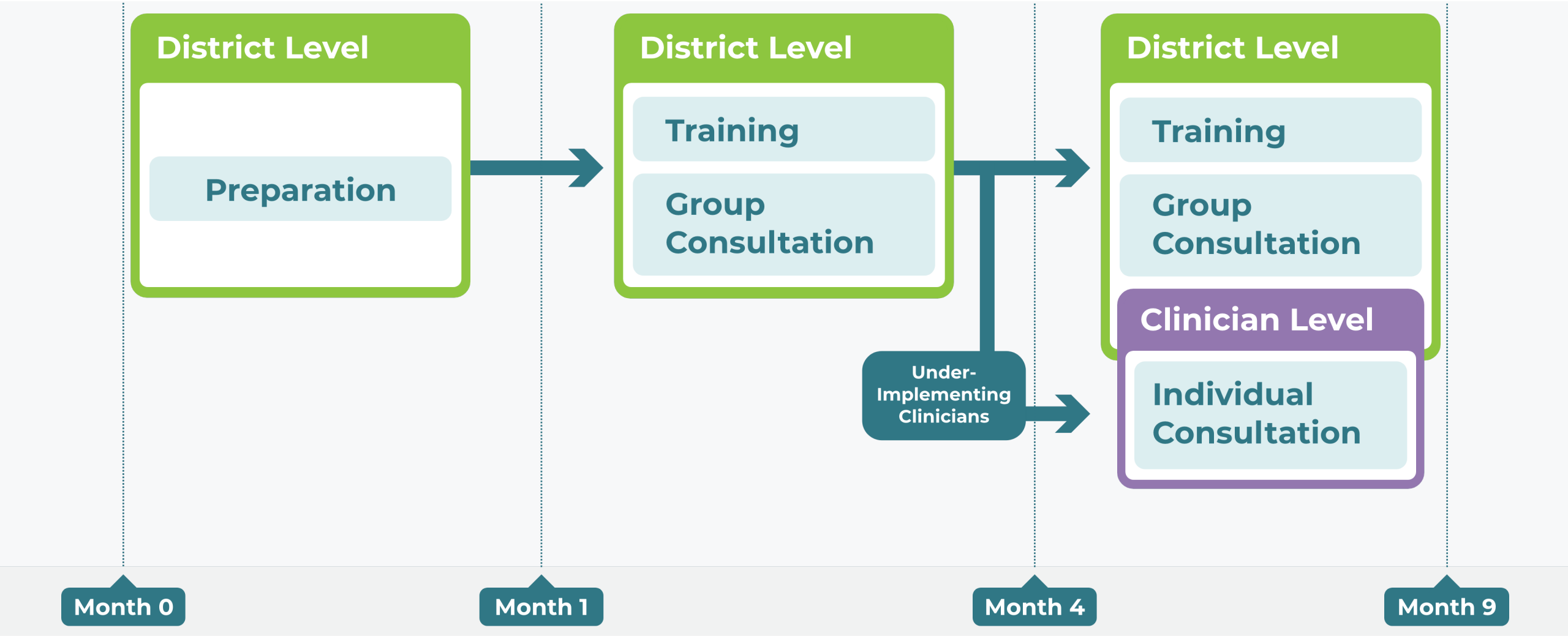


MAISY Example 2

Principal Investigator: Elizabeth Connors

Feedback & Outcomes for Clinically Useful Student Services (FOCUSS)

EBP: Measurement-Based Care in Connecticut Schools



Why do we need Multilevel Adaptive Interventions?

Timing is important	Speed of adoption varies across levels. Not all targets are ready to take on more.
Strategic sequencing	Lay a strong foundation for subsequent strategies, if needed
Health equity	Can be part of operationalizing vertical health equity principles at different levels

Why do we need Multilevel Adaptive Interventions?

Engagement is critical	One level might focus primarily on engagement effect; another primarily on therapeutic effect
Often more is not better	Kitchen sink strategies can be suboptimal, especially when there are multiple levels
Resource/Cost Efficiency	Step-up for targets that need it; step-down for targets doing well; but this may differ across levels

A Multilevel Adaptive Intervention is not a Research Method

Not an experimental design

There are no randomizations in a MAISY!

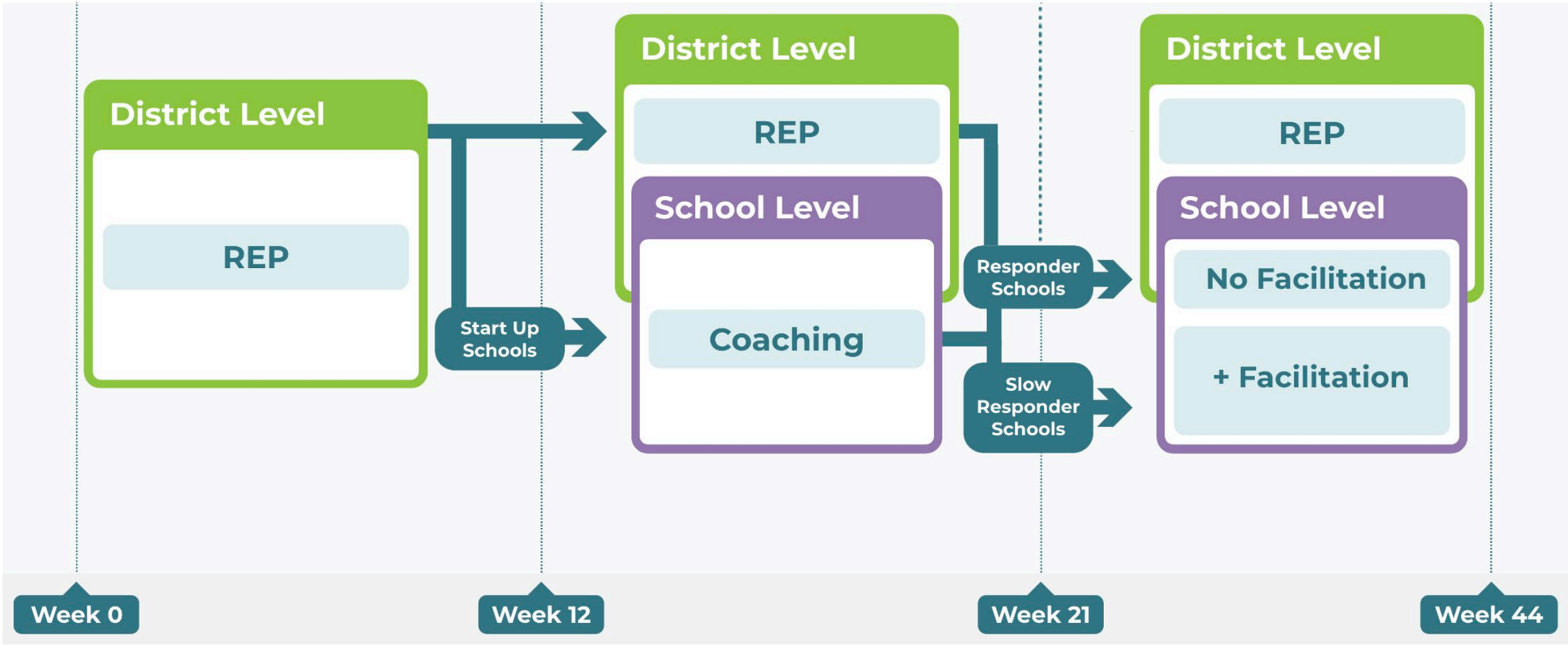
Not an approach to conducting pilot studies

Not an approach to data analysis

Not an adaptive trial design

Recall MAISY Example 1

Adaptive School-Based Implementation of CBT (ASIC)



Other Considerations

Pre-specified (i.e., pre-planned) decisions

Mechanisms can be tailoring variables

The tailoring variables are part of the multilevel adaptive intervention

Outline

Multilevel Adaptive Interventions: What? Why? Who?

Using randomization to develop an optimized multilevel adaptive intervention

Now put your researcher hats back on!

Optimization Questions

Basic, but important!

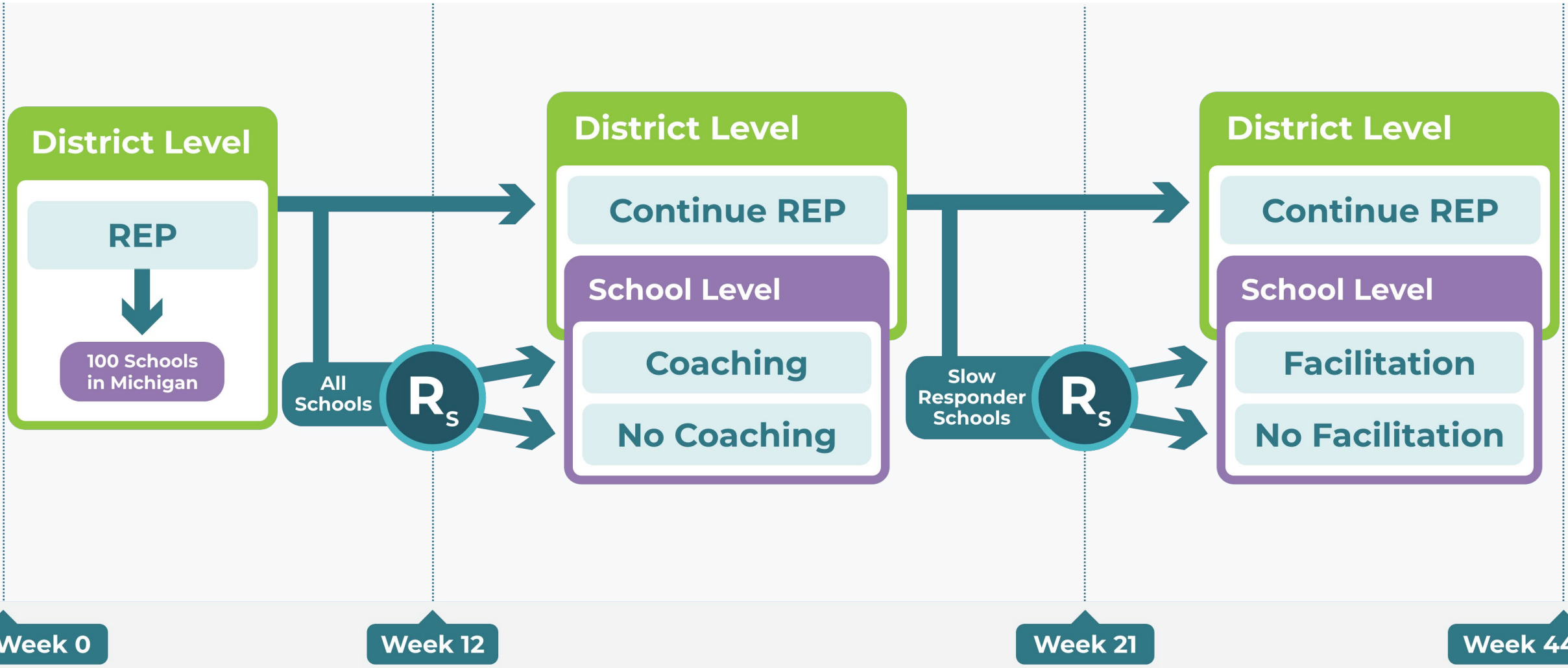
	Type	In the context of ASIC
1	First-Stage Strategies	What is the effectiveness of Coaching?
2	Later-Phase Strategies	What is the effect of Facilitation among schools that are slower responders?
3	Interaction	Do Coaching and Facilitation interact to produce beneficial outcomes?
4	Adaptive vs. Not Adaptive	What is the effect of the MAISY shown earlier vs. only Coaching (not adaptive)?

SMART Example

Principal Investigator: Amy Kilbourne

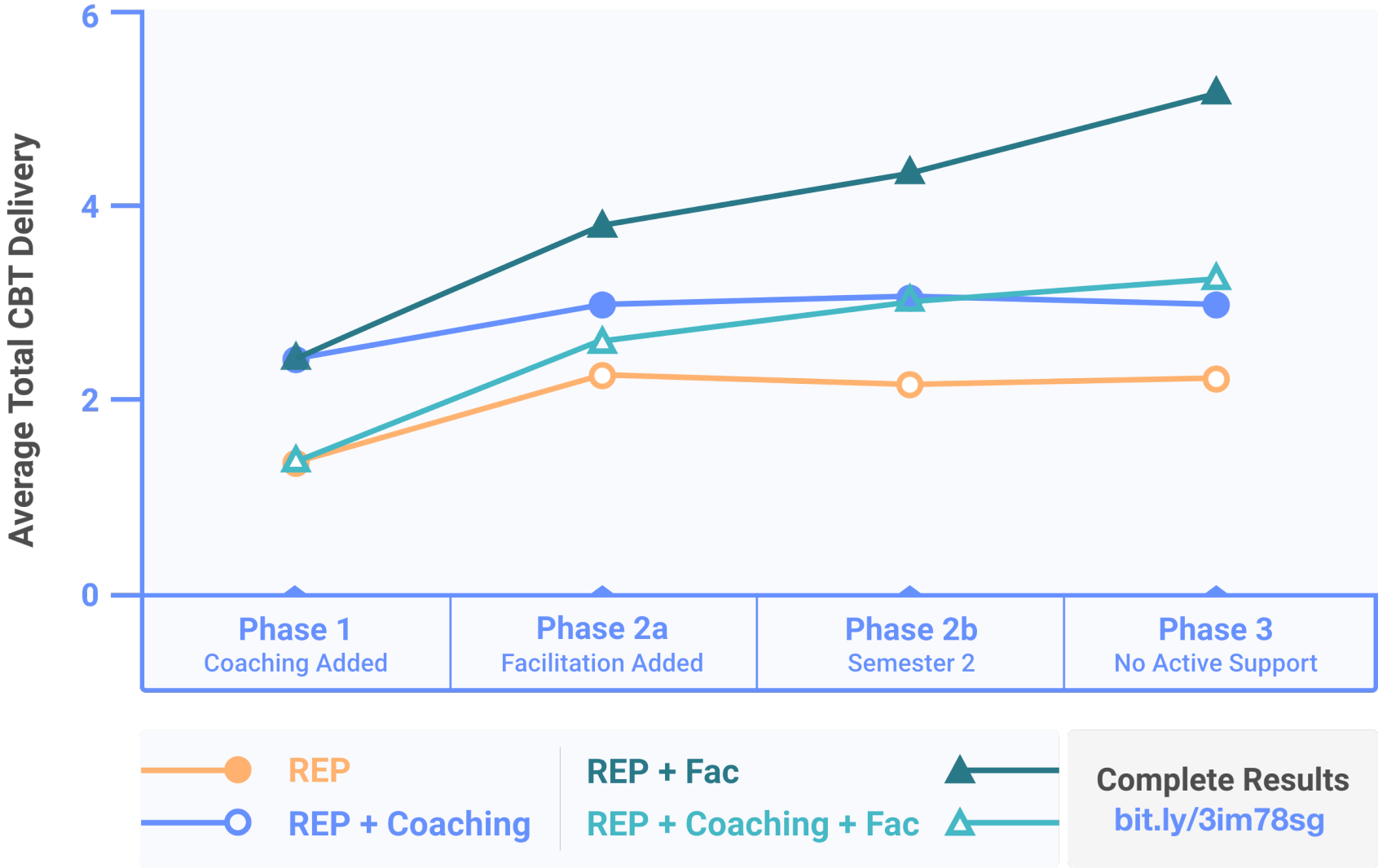
The ASIC Sequential Multiple Assignment Randomized Trial

EBP: Cognitive Behavioral Therapy in Michigan Schools



Sneak Peek at Surprising Results

ASIC



Optimization Questions

All About Tailoring

	Type	In the context of ASIC
5	Better Way to Define Non-Response?	Should we use a more lenient definition (a lower cut-off) for “Responding School”?
6	Other Baseline Tailoring Variables?	Perhaps only start-up schools require Coaching?
7	Other Ongoing Tailoring Variables?	Perhaps Facilitation should only be offered to sub-optimally responding schools that did not engage in Coaching?

Optimization Questions

More About Tailoring

	Type	In the context of ASIC
8	Other Multilevel Tailoring Variables?	Perhaps Facilitation should only be offered to sub-optimally responding schools within the lowest-resourced school districts?
9	Does the putative mechanism aide in decision making?	Is Facilitation necessary in sub-optimally responding schools delivering higher-quality CBT as a result of Coaching?

Optimization Questions

Some Novel Ones

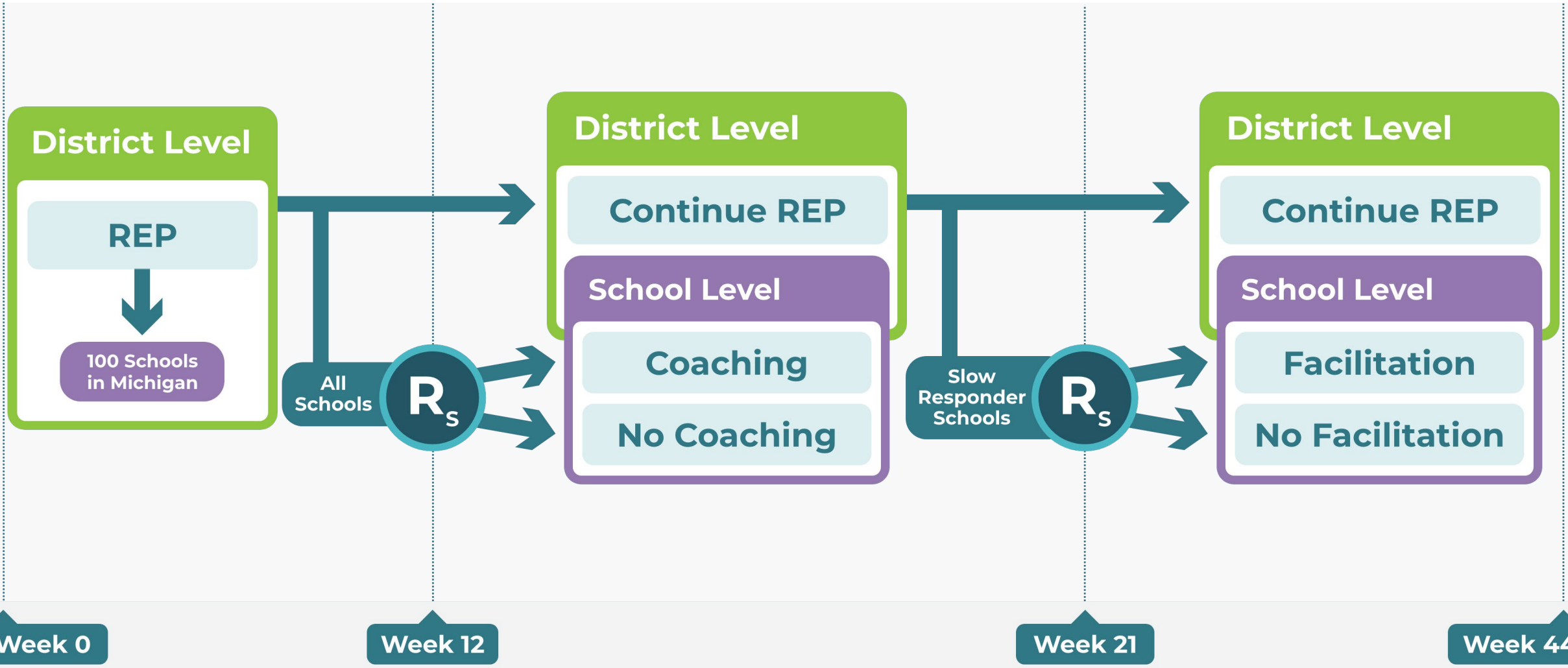
	Type	In the context of ASIC
10	Sleeper effects of prior stage strategies?	Is it possible that first-stage strategies have no effect in the short-run but have beneficial effects in the long-run when followed by a particular second-stage strategy?
11	Prescriptive effects?	Did we learn something from Coaching that can help decide whether to do Facilitation?

SMART Example

Principal Investigator: Amy Kilbourne

The ASIC Sequential Multiple Assignment Randomized Trial

EBP: Cognitive Behavioral Therapy in Michigan Schools

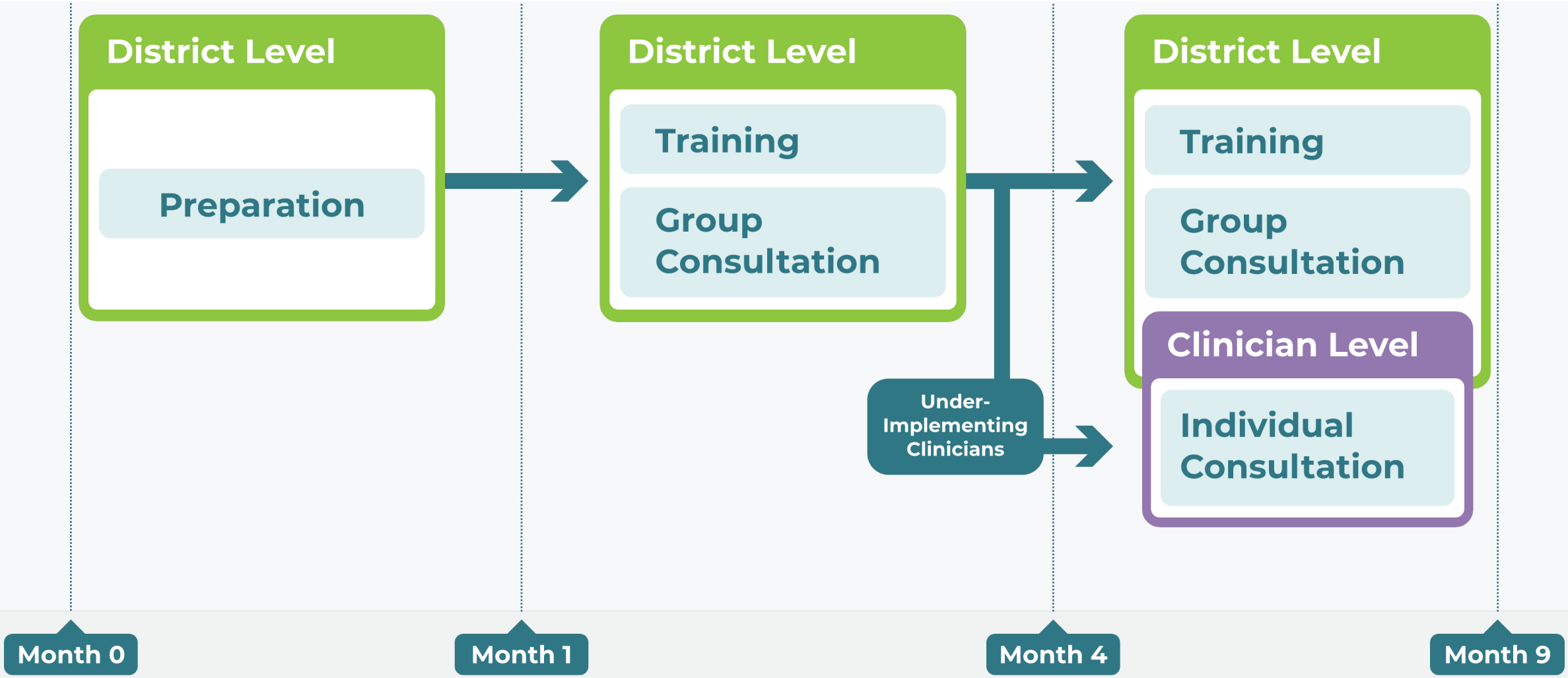


MAISY Example 2

Principal Investigator: Elizabeth Connors

Feedback & Outcomes for Clinically Useful Student Services (FOCUSS)

EBP: Measurement-Based Care in Connecticut Schools



Optimization Questions

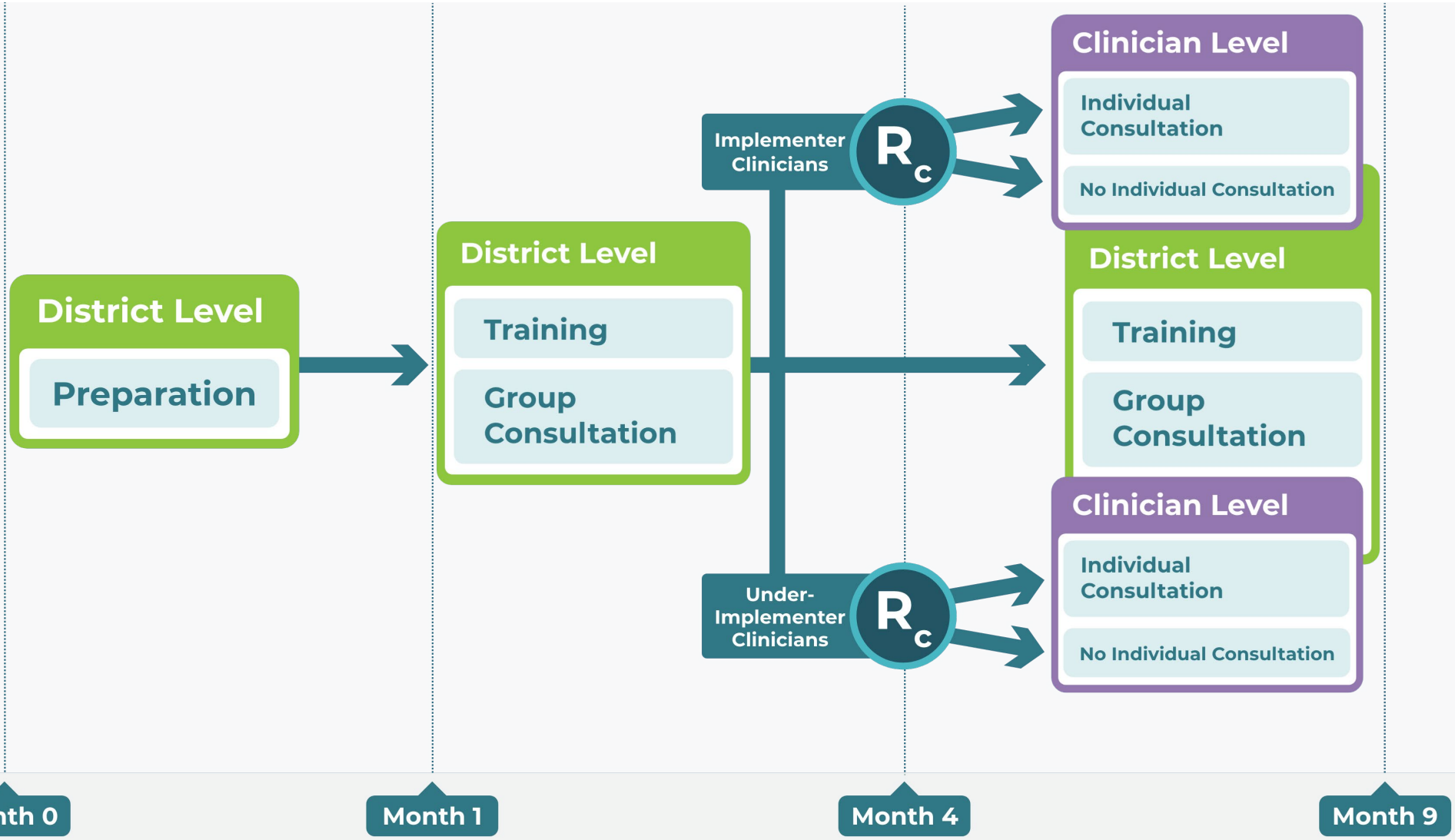
Back to Questions 2 & 7

	Type	In the context of FOCUSS
2	Later-Phase Strategies	What is the average effect of clinician-level Individual Consultation?
7	Ongoing Tailoring Variables	How do we define “under-implementing clinician”?

The FOCUSS Study

Two-arm Optimization Randomized Trial

Principal Investigator: Elizabeth Connors



Optimization Questions

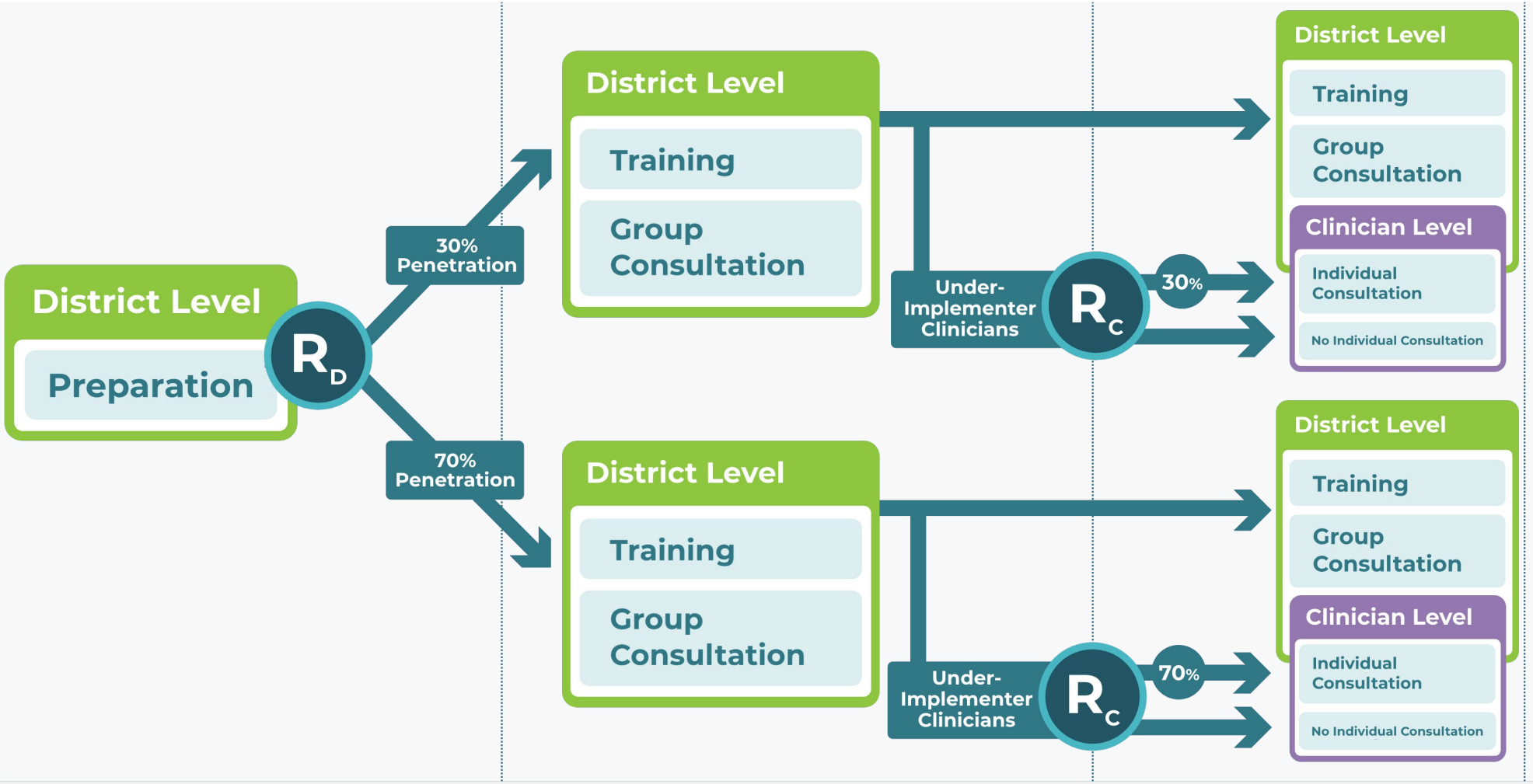
Concerning Spillover

	Type	In the context of FOCUSS
2	Optimal tipping point effect?	Effect of providing Individual Consultation to 30% vs. 70% of under-implementers in a district?
7	Outer-level strategies that engender beneficial spillover?	Target a random 1/2 of under-implementing clinicians vs. up to 1/2 on a first-come first-serve basis?

Illustrated Using FOCUSS

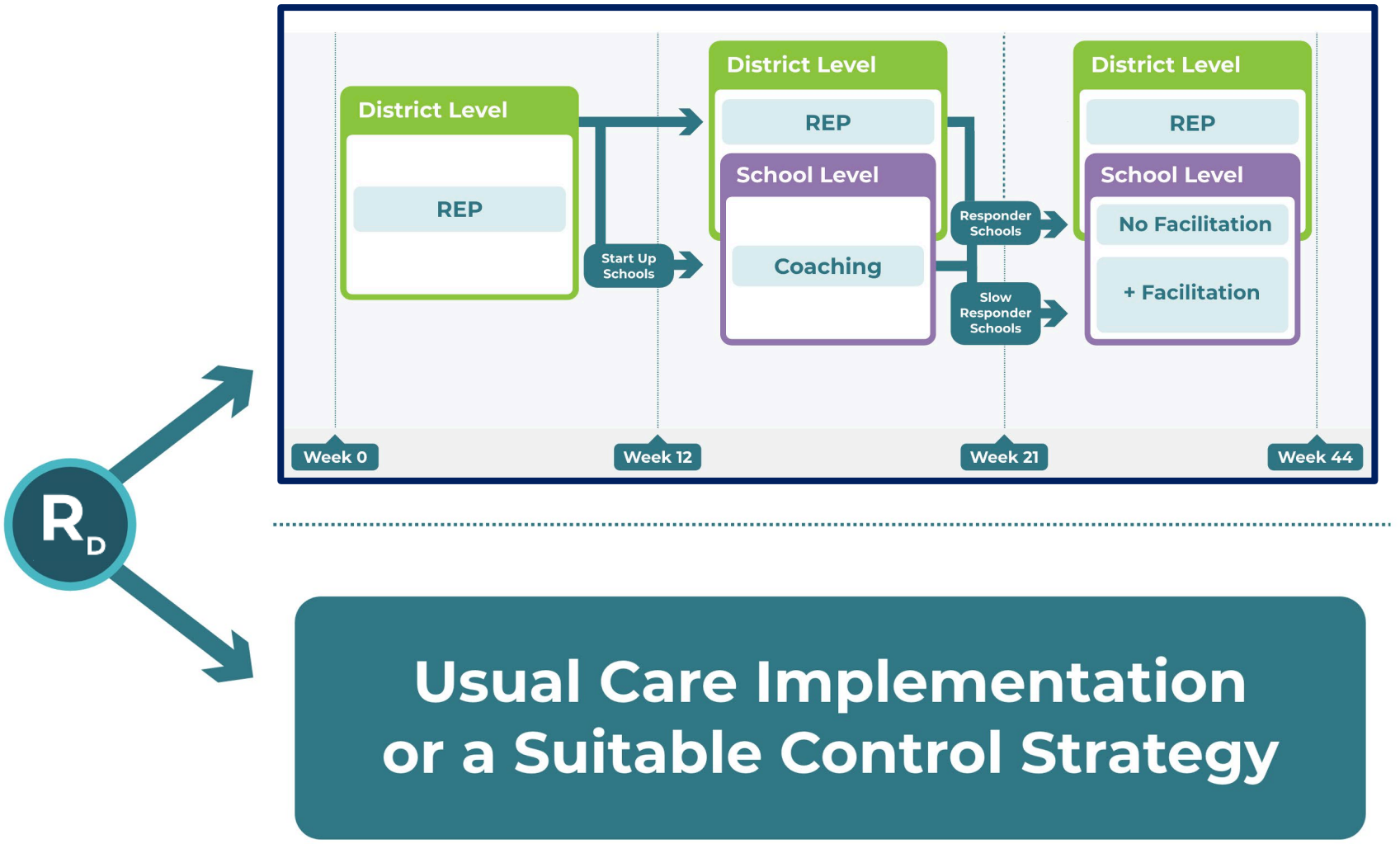
A Hypothetical, Multilevel SMART

Principal Investigator: Elizabeth Connors



Evaluation and optimization questions are different.

An evaluation randomized trial looks like this.



Browse our online resources.

d3c

Resources on adaptive interventions.

Browse learning resources.

Sign up for our newsletter.

Search open-source software.

cadio

Resources on intervention optimization.

Browse learning resources.

Sign up for our newsletter.

Register for webinars.
Wednesdays from 1-2 pm Eastern

Break

REFRESHMENTS LOCATED OUTSIDE OF MEETING ROOM

PLEASE RETURN BY 3:05PM

ROYBAL
Center For
Translational
Research

Innovative Strategies to Enhance Retention in Clinical Trials

MICHAELA KIERNAN, PHD

General Discussion

FACILITATED BY KARINA DAVIDSON, PHD, MASC

ROYBAL COORDINATING CENTER PI

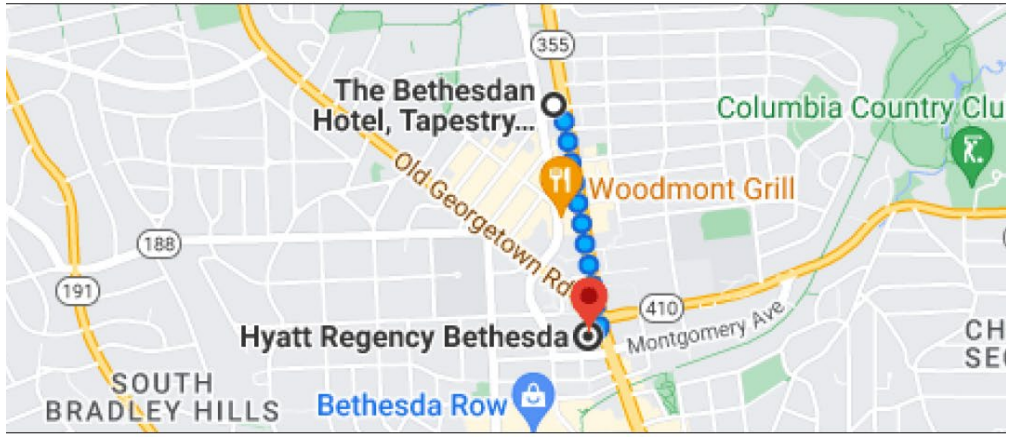
NORTHWELL HEALTH

We welcome you to join us for an evening reception!

Morton's Steakhouse

Hyatt Regency Hotel
7400 Wisconsin Ave, Bethesda, MD

Cocktail Reception	**6pm-7pm**
Seated Dinner	**7pm-9pm**



Located within walking distance from The Besthesdan Hotel

Day 1 Adjourn

ENJOY THE EVENING!

WE LOOK FORWARD TO SEEING YOU FOR DAY 2!

ROYBAL
Center For
Translational
Research

Welcome to the
2023 Annual Meeting

Edward R. Roybal Centers for Translational Research in the Behavioral and Social Sciences of Aging

March 14-15, 2023
Day 2

Day 2 Agenda

ROYBAL Center For Translational Research

8:30am-9:45am	**BREAKFAST**
10:00am-10:55am	**Panel Discussion: Lessons Learned from the Conduct of Clinical Trials**
11:00am-11:50am	**Panel Discussion: Best Practices for Mentoring Investigators Conducting Clinical Trials and Behavioral Interventions**
11:50am-12:10pm	**BREAK**
12:10pm-1:00pm	**Improving Representation in Clinical Trials: Recommendations from the 2022 NASEM Report**
1:00pm-1:15pm	**Closing Remarks**
1:30pm	**Adjourn**

Boxed lunch available

Housekeeping Reminders

BE FULLY PRESENT

TURN OFF CELL PHONES, CLOSE YOUR EMAIL, ETC.

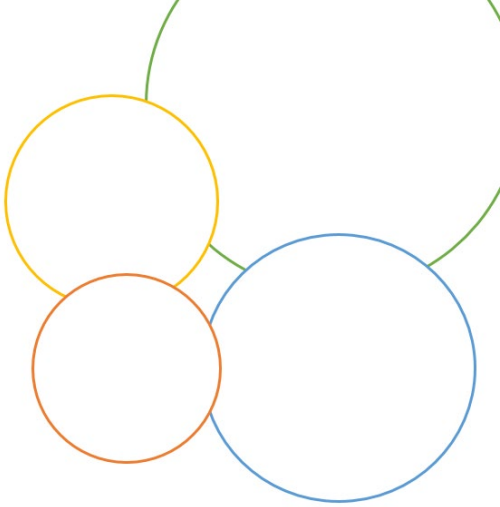
DON’T BE LATE

PLEASE RETURN FROM LUNCH AND BREAKS ON TIME

SPEAK OFTEN AND LOUDLY

PLEASE BE SURE TO SPEAK INTO THE MICROPHONES LOCATED AT EACH TABLE

ROYBAL
Center For
Translational
Research



Panel Discussion:
Lessons Learned from the Conduct of Clinical Trials

MODERATOR

NITEESH CHOUDHRY, MD, PHD

Professor, Harvard Medical School
Professor, Department of Health Policy & Management
Harvard T.H. Chan School of Public Health
Director, Roybal Center for Therapeutic Optimization using Behavioral Science
Brigham and Women's Hospital

PANELISTS

MARY BUTLER, PHD, MBA

Associate Professor,
School of Public Health Division of Health Policy and Management
University of Minnesota

MINA SEDRAK, MD, MS

Associate Professor, Medical Oncology
Deputy Director, Center for Cancer and Aging
City of Hope Comprehensive Cancer Center

JASMIN TIRO, PHD

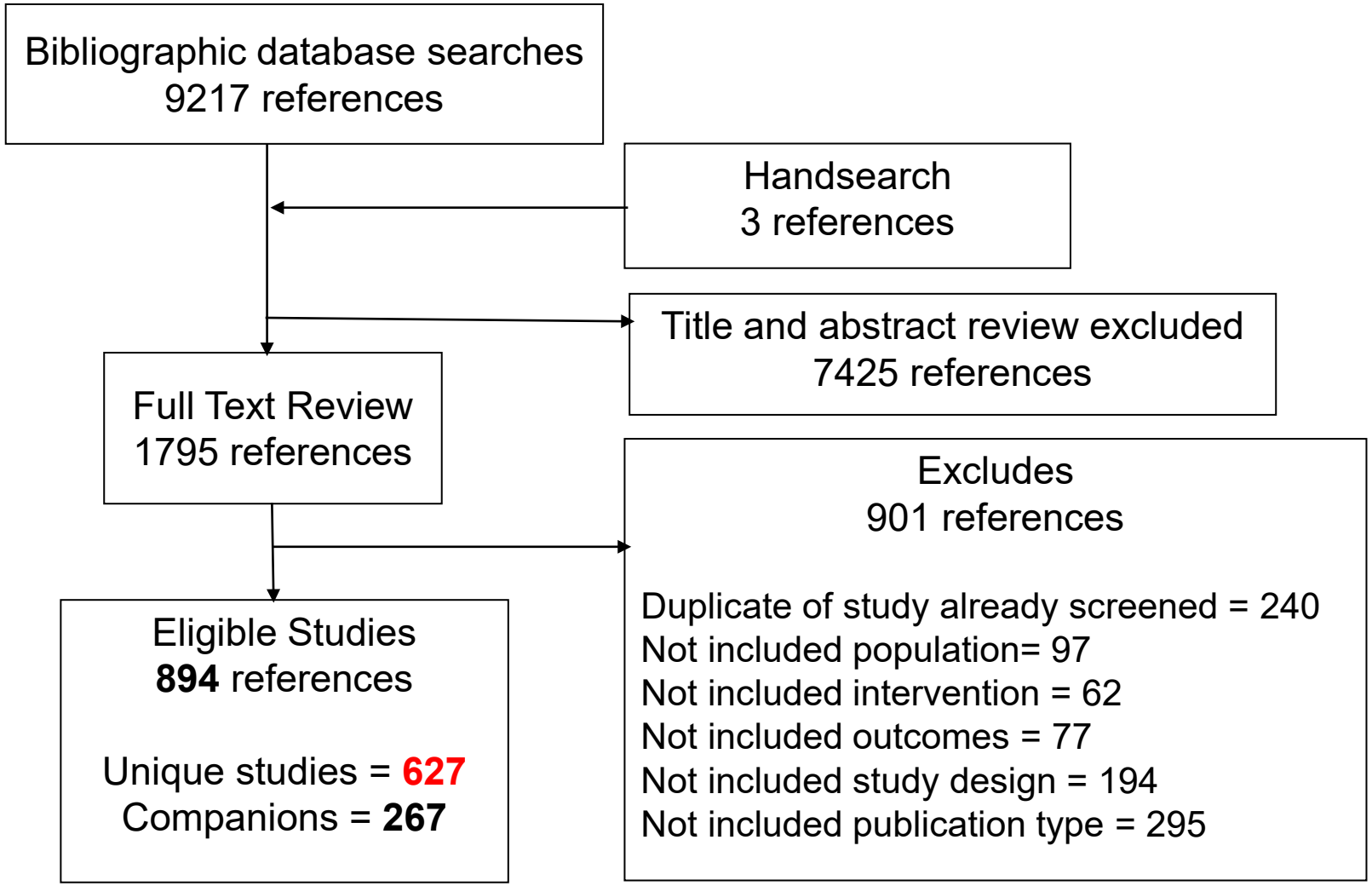
Professor
Division of Biological Sciences
Associate Director, Cancer Prevention and Population Science
The University of Chicago

The Report's Objective

To assess the evidence for care interventions for people living with dementia (PLWD) and their informal and formal caregivers for potential broad dissemination and implementation.

But systematic reviews like this are also the basis for evidence-based research.

Results - Eligible Studies (March 2020)



Results – Eligible Studies (continued)

- **100** studies in the **analytic set:** the set of studies not judged to be pilots or have a high potential for bias that might have interfered with the ability of the study to answer its research question.

- **527** studies in the **evidence map:** the set of studies that did not undergo synthesis. Summarizes what has been studied and facilitates identifying future research needs.

Implication of Analytic Set vs Evidence Map Set

Not using pilot, small sample, and high risk of bias studies in analysis allowed for a high-level assessment of the state of the science.

Results

Despite a lot of work and often compelling rationales, the available evidence could not yet provide clear answers about which interventions (or interventions components) offer consistent benefits.

- Low-strength evidence for collaborative care models for select outcomes
- Low-strength evidence for REACH II for select outcomes
- Insufficient evidence for 191 comparisons for 36 other interventions

Clarification

An assessment of insufficient evidence does not mean that the intervention is determined to be of no value. Rather, it means that due to the uncertainty of the evidence we could not draw meaningful conclusions at this time.

Lessons Learned For Research

- Weaknesses of the evidence base can be addressed by attending to study design and conduct
  - Risk of inflated effect sizes
    - Small study bias is reduced or eliminated with larger studies (but opens door to finding significant differences that are not minimally important)
  - Risk of study bias largely due to problems with
    - Selection
    - Attrition
    - Fidelity

Lessons Learned for Research

- Lack of consensus on intervention taxonomies and terms hampers aggregation – the basis of evidence-based research

- Fidelity to interventions is not commonly addressed adequately

How do we classify a spork?

Lessons Learned for Research

- Quality of life still often lacking as outcome, as were harms (especially including unintended consequences of complex interventions)

- Many populations of interest, especially as related to health equity, were not represented in the literature

Bigger Thoughts for Future Research

- Research questions related to dissemination and implementation at the outset of intervention design may help prepare dementia care and caregiver interventions for rapid implementation in real-world settings.

- Complex interventions for complex systems are hard to do. Initiatives to creatively redesign research processes in other fields may provide opportunities to learn from and experiment with other ways of doing this science.

Additions From Public Comments

"Many aspects of care interventions for PLWD and their caregivers need more thorough exploration. We hesitated to give an exhaustive list for fear of overwhelming the readers. **We are instead guided by peer and public comments on the draft version** of this report **to mention the following areas**: functional and health status limitations, access to care and intervention services and supports as well as accessibility, transportation, culture, racial/ethnic, and related factors.

Discussion, page 114

Additions From Public Comment (cont.)

People living with dementia urgently requested more research on interventions that support personhood, purpose and meaning, social and peer supports, proactive approaches to living with a chronic, progressive illness, and lifestyle and spirituality interventions."

ROYBAL
Center For
Translational
Research

Panel Discussion:

Best Practices for Mentoring Investigators Conducting Clinical Trials and Behavioral Interventions

MODERATOR

KENNETH HEPBURN, PHD

Professor, Nell Hodgson Woodruff School of Nursing
Emory University
Co-Director, Emory Roybal Center

PANELISTS

BONNIE SPRING, PHD

Professor of Preventive Medicine, Psychology & Psychiatry, Director, Institute for Public Health and Medicine's Center for Behavior and Health
Northwestern University

WENDY DEMARK-WAHNEFRIED, PHD, RD

Professor & Webb Endowed Chair of Nutrition Sciences
Associate Director, Cancer Prevention & Control
University of Alabama at Birmingham

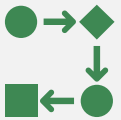
Objective

Engage in a Conversation about Best Practices and Challenges in Mentoring Investigators

(Roybal Pilot Investigators and Others)

In the “idea stage” (pre-application)

In Medias Res – conducting the work



In taking the “next step:”

- Moving along the Stage Model
- Disseminating Findings

The Mentorship Education of Bonnie Spring, PhD

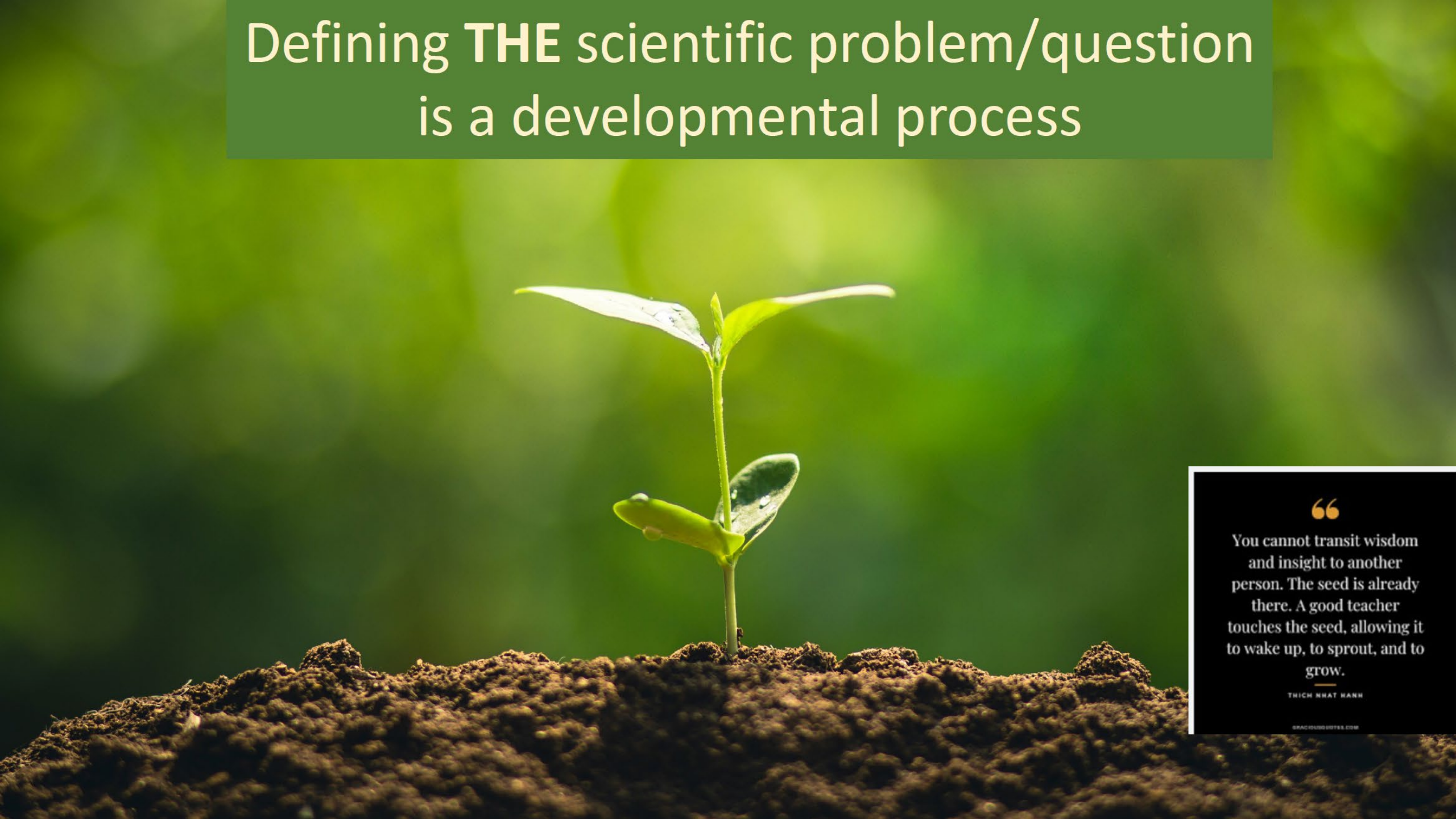
Professor of Preventive Medicine

Director, Institute for Public Health and Medicine – Center for Behavior and Health,

Northwestern University, Feinberg School of Medicine


3 Lessons Learned

Defining **THE** scientific problem/question is a developmental process



Failure is Part of the Process of Getting to Success

“I have not failed. I've just found 10,000 ways that won't work.”
Thomas A. Edison

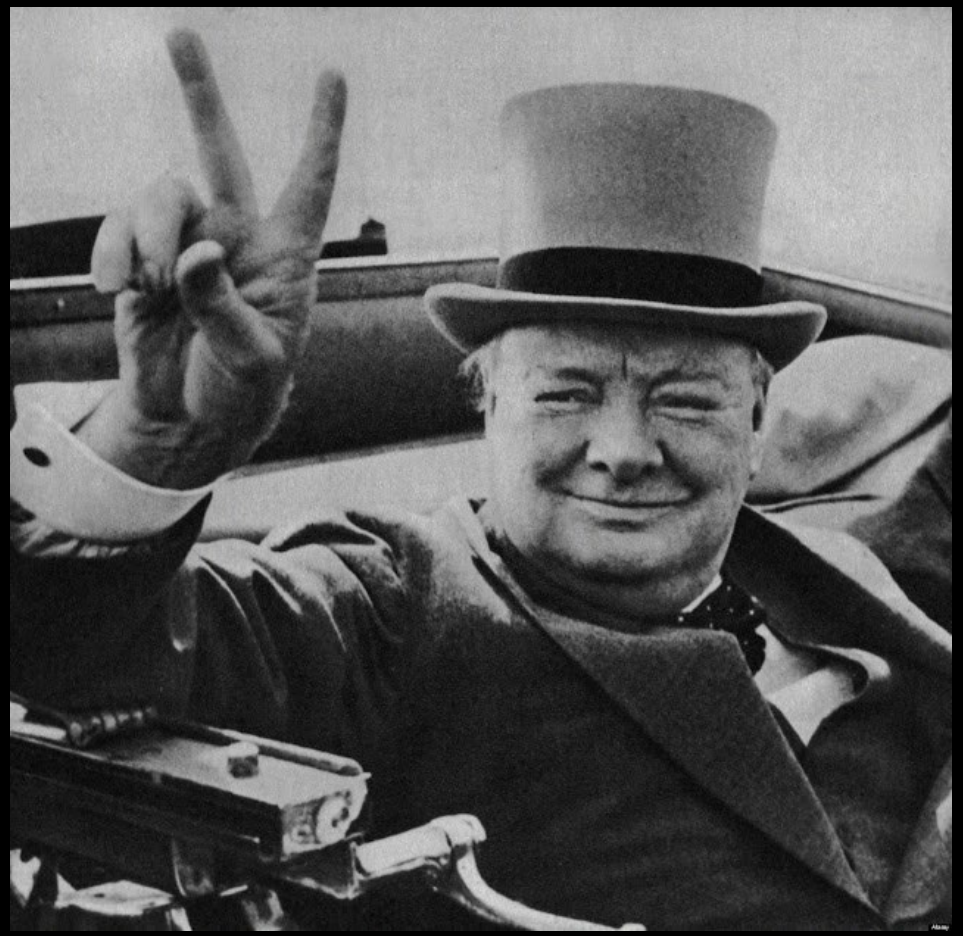

Mentoring
Up
Down
and Sideways

Thank you.

bspring@northwestern.edu

Some Tips for Mentoring Investigators Conducting Clinical Trials and Behavioral Interventions

Wendy Demark-Wahnefried, PhD, RD
Professor and Webb Endowed Chair of Nutrition Sciences
University of Alabama at Birmingham (UAB)
Associate Director of Cancer Prevention and Control
O'Neal Comprehensive Cancer Center at UAB



“We make a living by what we get, but we make a life by what we give."
Winston Churchill

Being a mentor is fiercely rewarding and when it goes right…it’s great!

…but, when it goes wrong…it stinks!

Simple Formulaic Advice:
3 A's of Mentoring

- **Availability**
- **Active listening, and**
- **Analysis** (encouragement, feedback, and advice)

…but, it's a heck of a more complicated than that.

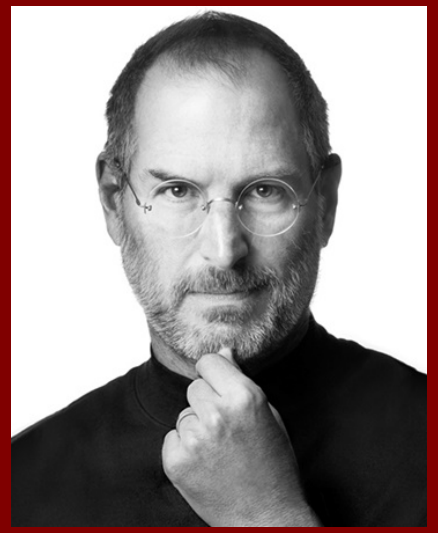
- One part matchmaking
- One part behavioral theory (Expectation Management)
- Iterative use of proven tools (IDPs)
- Patience and forgiveness

Honest Appraisals are Critical

Mentor(s)

"Advice is like snow; the softer it falls, the longer it dwells, and the deeper it sinks "
Samuel Taylor

Mentee



“My job is not to be easy on people. My job is to take the great people we have and push them to make them even better.”

Individual Development Plan (IDP)

Adapt it and Use it As a Working Document

Mentor Role

Is relationship working? Replace - Add

Point-out/Provide Opportunities

- Set Incremental Goals
- Regulatory Approvals/Protocols
- Recruitment
- Sample/Data Processing
- Date Analysis
- Abstracts, Manuscripts, New Grants

Set Project Timeline and Meeting Schedule

Review Progress (What's working - what's not)

Revise strategies to overcome obstacles

Mentee Role

Is relationship working? Unmet Needs?

Seek-out Opportunities Obtain Mentor Input

“My mistakes have been my greatest mentors" - Steve Maraboli

Case Study:

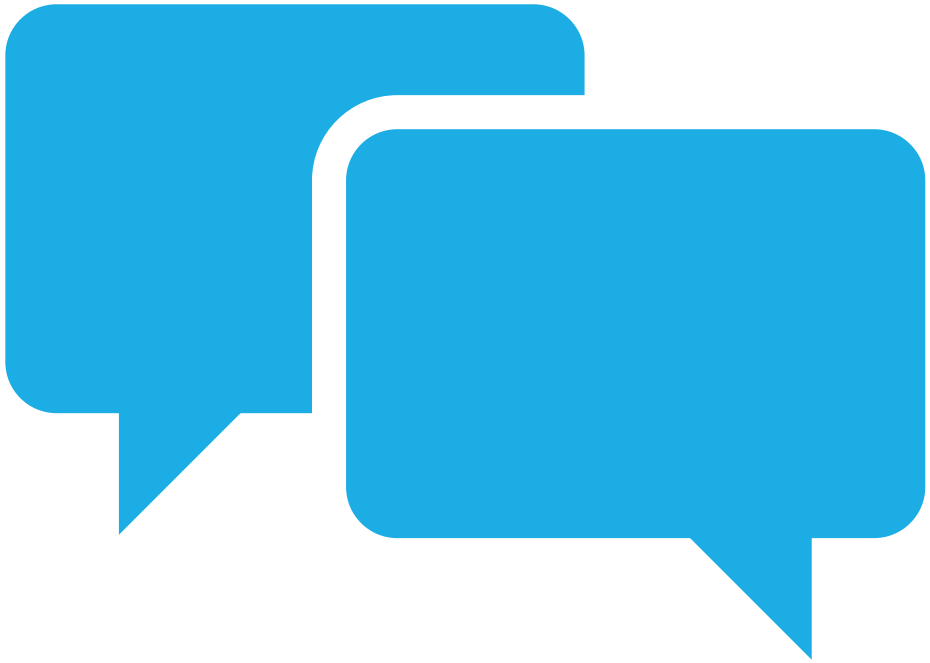
- **Dr. X interviews for an entry level faculty position (great cv, bad interview)**
- **Department willing to offer post-doc appt**

- **Professor W just awarded a pilot project**
- **Resonates with background of candidate**
- **Sees opportunity to help – potential benefit**

- **Dr. X comes on as a post-doc**
- **Weekly meetings transpire**
- **Professor W shares survey study – attempts to offer guidance**
- **Dr X unreceptive to guidance**
- **Survey study fails – requires rescue**
- **Heated exchange occurs**

- **Dr. X files grievance**
- **Is paired with another mentor**

- **Professor W feels unjustly accused, embarrassed and generally awful**
- **Professor W makes sure that outcome expectations are managed from the start**



Open Discussion

KENNETH HEPBURN, PHD

BONNIE SPRING, PHD

WENDY DEMARK-WAHNEFRIED, PHD, RD

Break

REFRESHMENTS LOCATED OUTSIDE OF MEETING ROOM

PLEASE RETURN BY 12:05PM

ROYBAL
Center For
Translational
Research

Increasing representation in clinical trials: Findings and Recommendations from the 2022 NASEM Report

CARLOS DEL RIO, MD

ROYBAL

Center For Translational Research

Closing Remarks

KARINA DAVIDSON, PHD, MASC

ROYBAL COORDINATING CENTER PI

NORTHWELL HEALTH

Acknowledgments

PRESENTERS

Kenneth Freedland

Linda Collins

Billie Nahum-Shani

Daniel Almirall

Michaela Kiernan

Niteesh Choudhry

Mary Butler

Jasmin Tiro

Mina Sedrak

Kenneth Hepburn

Bonnie Spring

Wendy Demark-Wahnefried

Carlos del Rio

NIA PERSONNEL

Lis Nielsen

Lisa Onken

Partha Bhattacharyya

Ama Donkor

Acknowledgments

ROSE LI AND ASSOCIATES

Stephanie Tiller

Sabira Mohamed

John Sarmiento

Damon Kane

Rebecca Lazeration

ROYBAL COORDINATING CENTER

Nicole Donoghue

June Marro

ROYBAL
Centers For
Translational
Research

Day 2
Adjourn

SAFE TRAVELS!

Boxed lunch available in the Wisconsin room