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# CONFERENCE

10th Anniversary Edition

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# Early-Phase Research on Complex Interventions

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# What is a Complex Intervention?

**AN INTERVENTION THAT INVOLVES ONE OR MORE OF THE FOLLOWING:**

TYPE	DEFINITION	EXAMPLE
Multi-Component	Targeting the individual with >1 behavioral component	Diet plus physical activity intervention for cancer survivors
Multi-Level	Intervening simultaneously on ≥2 sources of influence	Intervening on both cancer survivors and their caregivers
Stepped Care Adaptive Treatments	Starting with basic treatment and stepping up only if needed	Providing education to cancer survivors and adding self-management skills training to the subgroup for whom education is insufficient

**COMPLEX INTERVENTIONS ARE MOST LIKELY NEEDED TO INTERVENE ON COMPLEX OR DIFFICULT PROBLEMS  
AND PRODUCE A BENEFIT ON IMPORTANT HEALTH OUTCOMES**

# What is Early-Phase Research?

Research on developing an intervention before proceeding to a randomized efficacy trial.

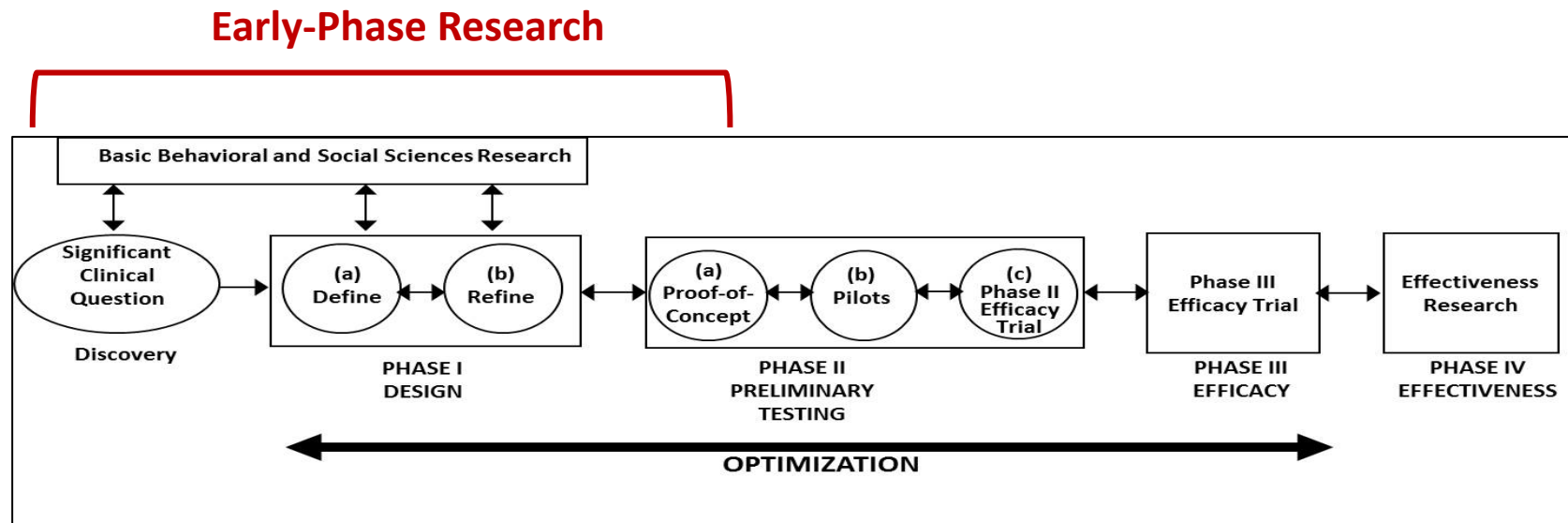
Progressive development is most important when developing complex interventions.

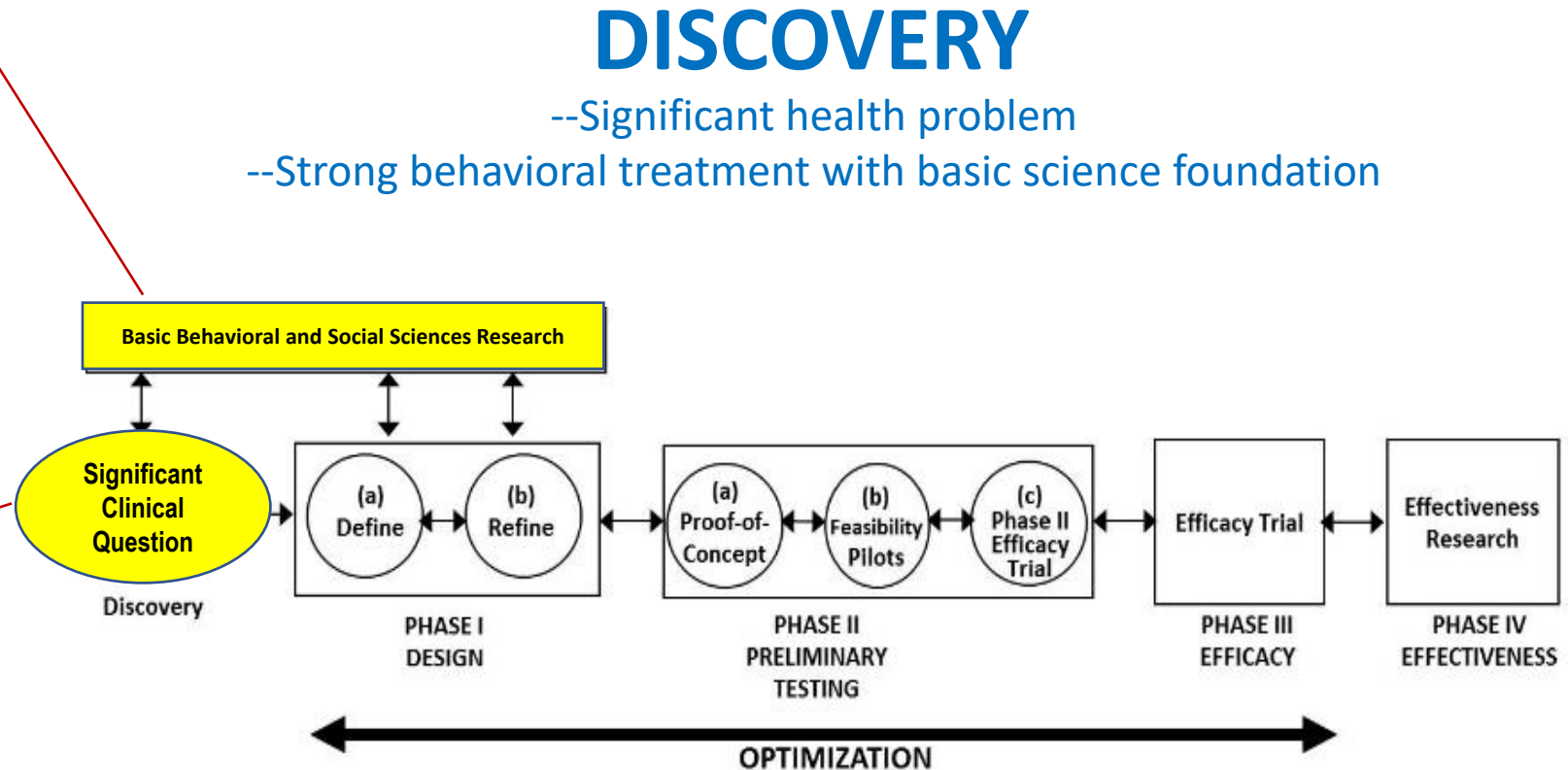
In the ORBIT Model, it includes:

Discovery

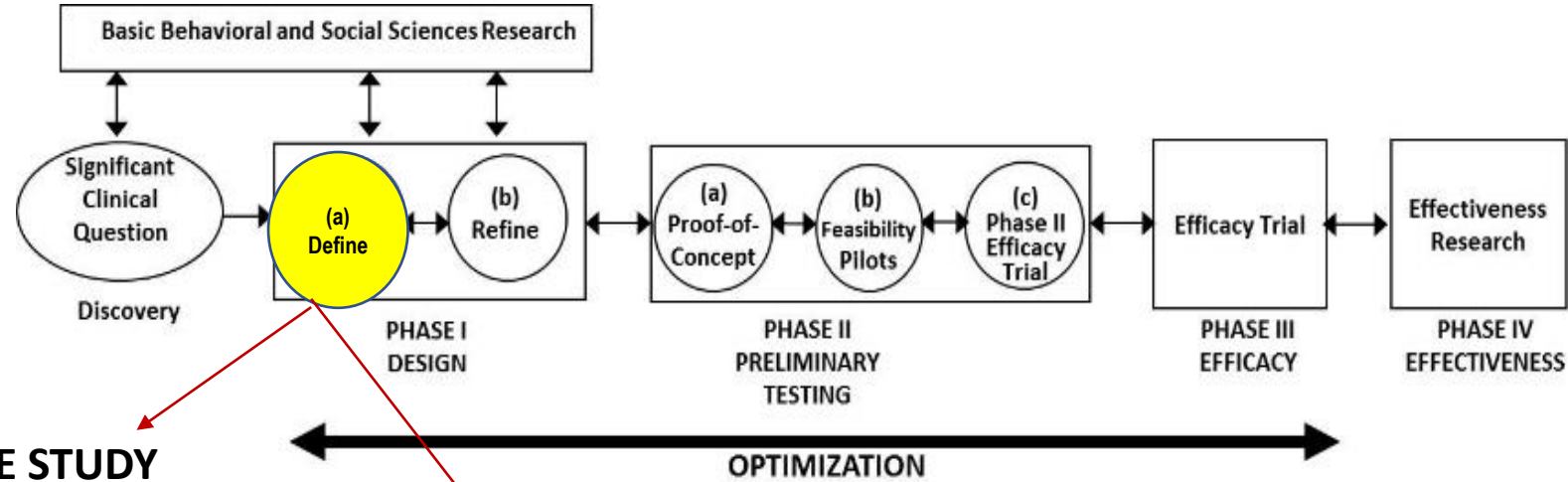
*Phase I:* Design

*Phase IIa:* Proof of Concept



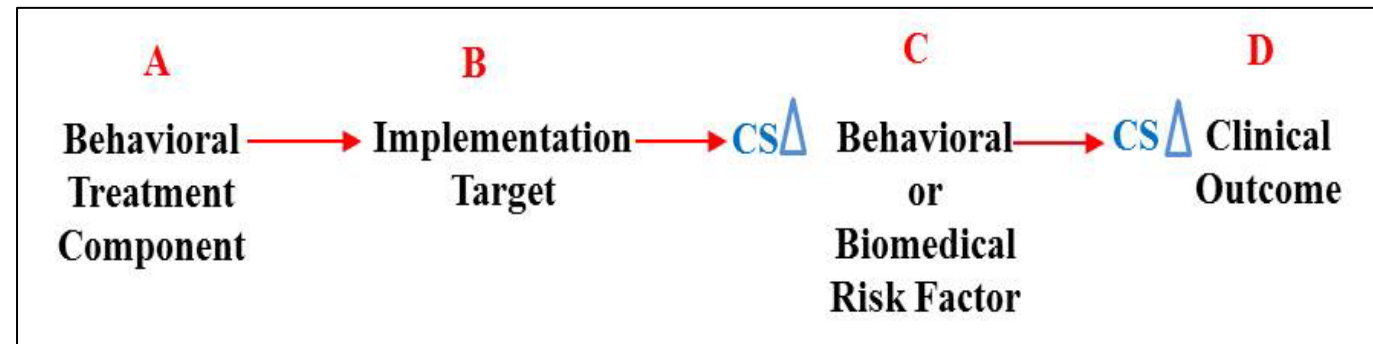


## Explore, Tinker, Assemble



**QUALITATIVE STUDY**  
*Sustained improvement in health?*  
**3 Components**  
**Metabolic Syndrome**

### Hypothesized Pathway

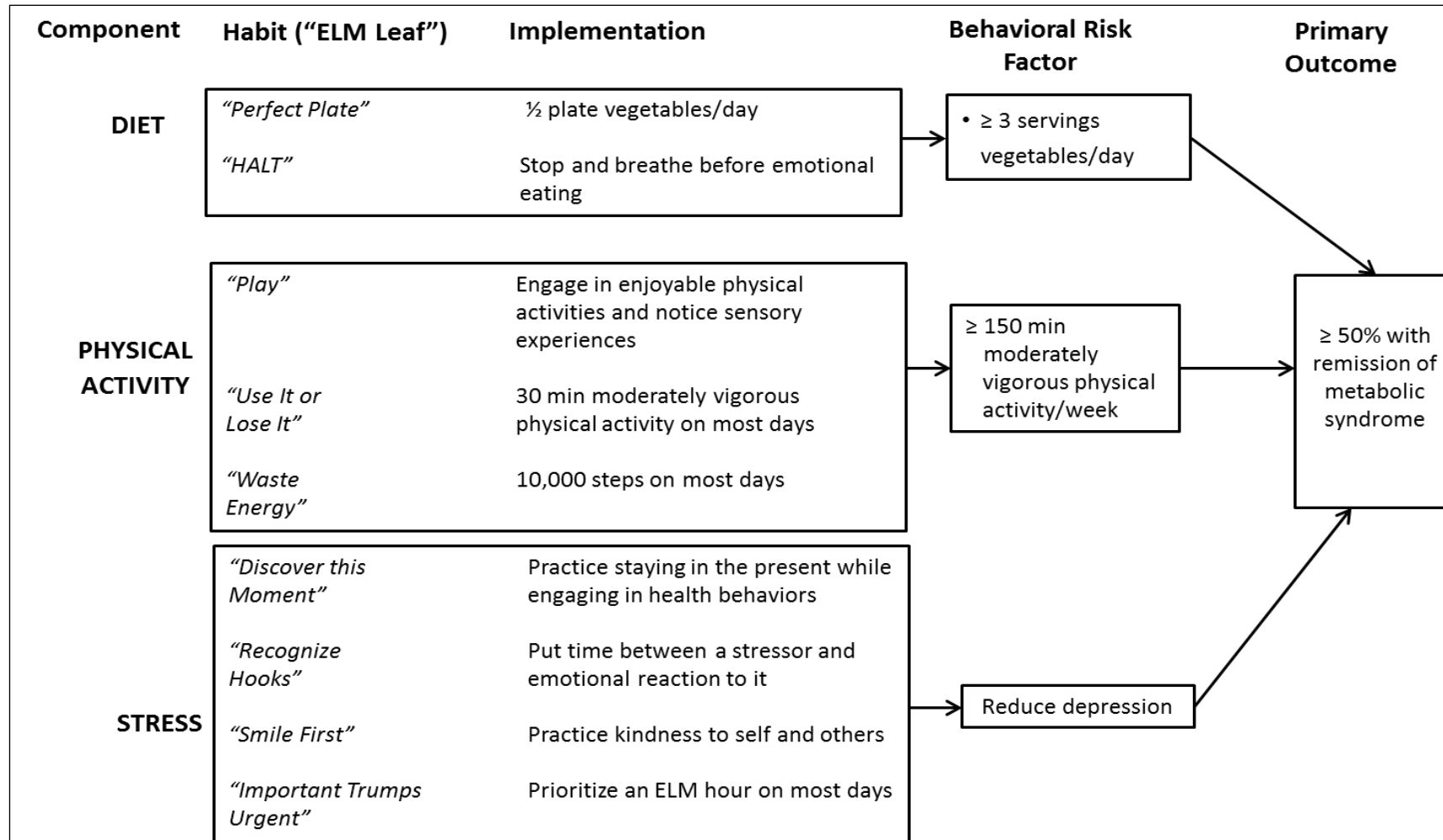


### Interdisciplinary Brainstorming



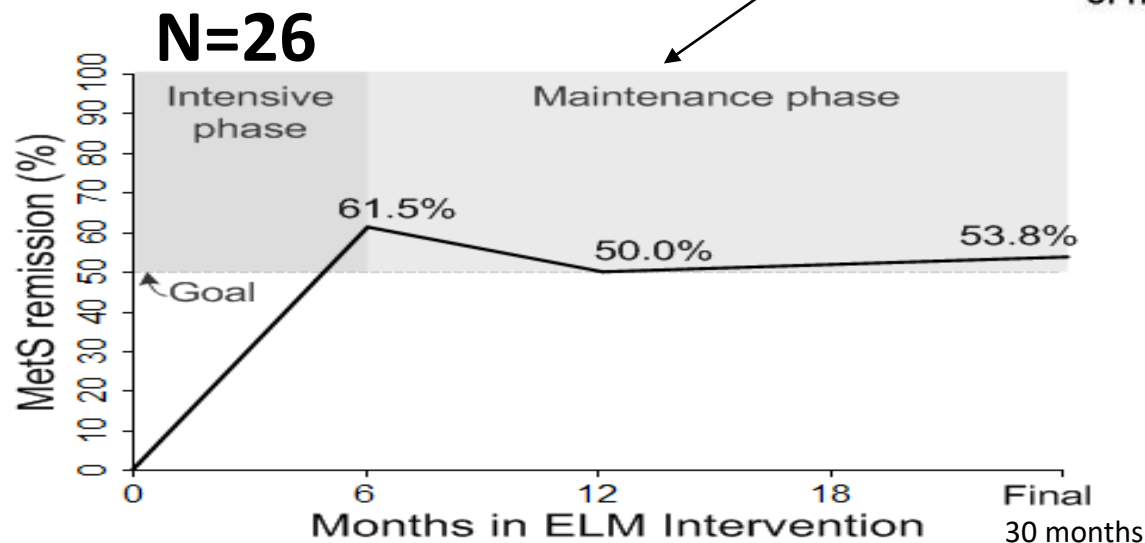
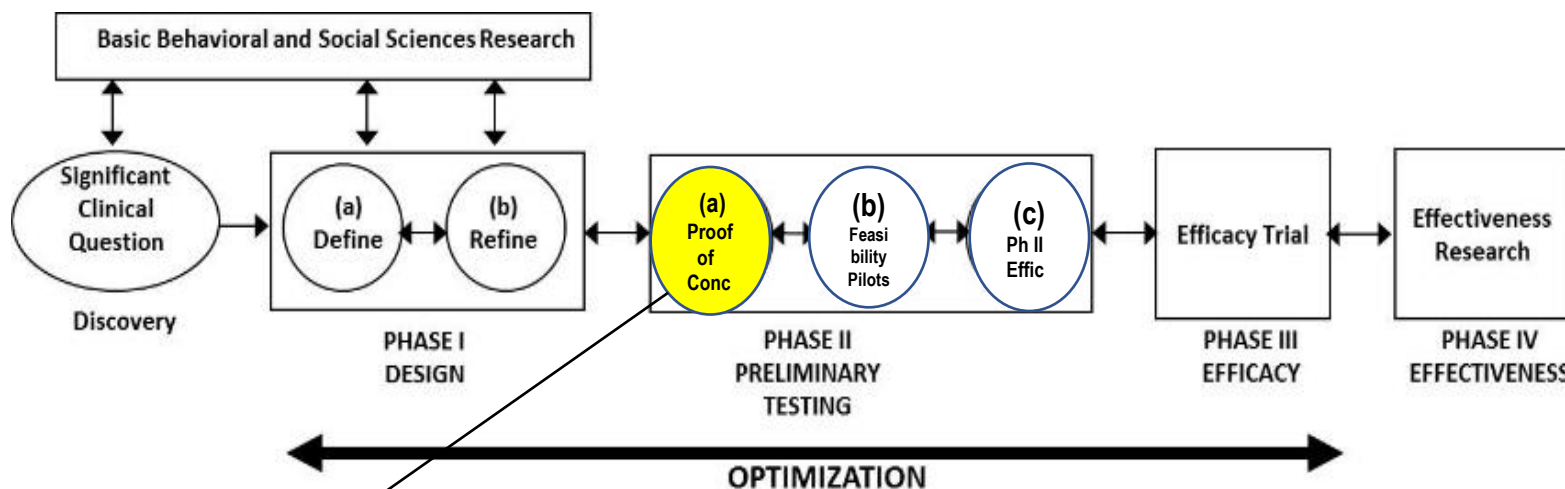
*“Begin with the  
end in mind.”*

## Hypothesized Pathway (first draft)





# Proof of Concept Plausible Health Benefit



## Hallmark:

Clinically significant milestone for success  
Go or No Go decision

## Common Features:

Quasi-experimental “treatment only” design  
No statistical hypothesis testing  
Small N  
Accessible sample

**Does NOT Control For Threats to Internal or External Validity**

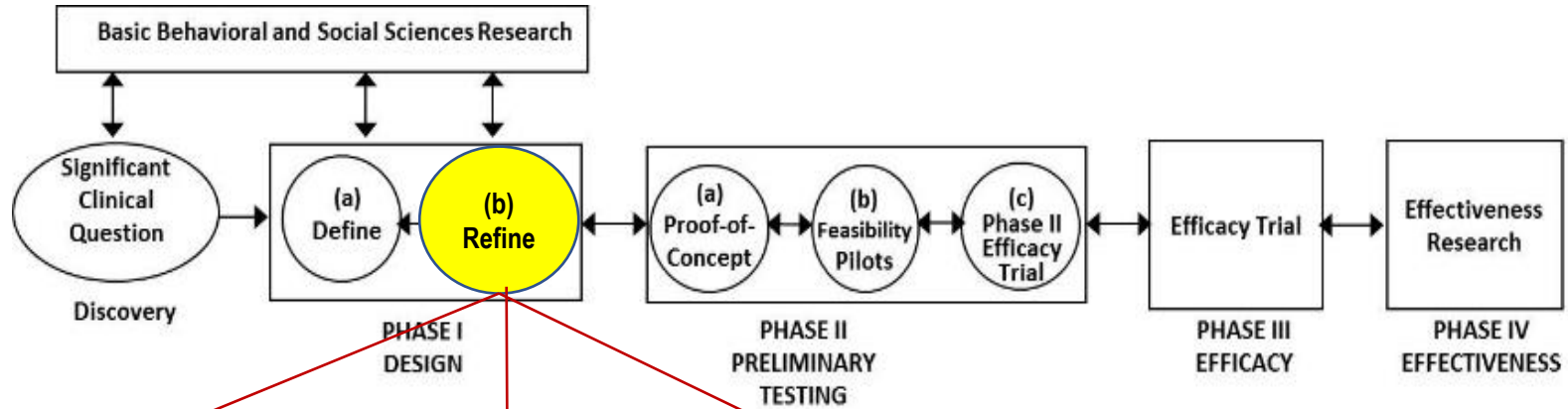


Tinkering



# REFINE

## For Strength and Efficiency



### Components Analysis of Proof of Concept:

	Remission	No Remission
≥5% weight loss	57%	17%

**Follow-Up After 7 Years:**  
*Habit Most Helpful?*

Not reacting to stress



# REFINE

## For Strength and Efficiency

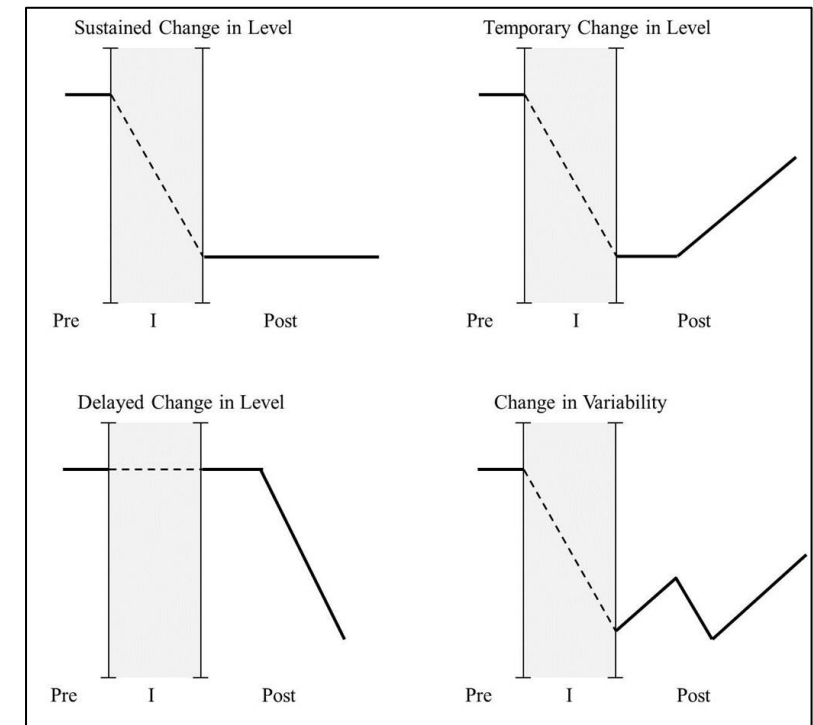
## Optimal Number of Components?

### Factorial Design

GROUP	Component 1	Component 2
1	Yes	Yes
2	Yes	No
3	No	Yes
4	No	No

## Optimal Timing of Assessment?

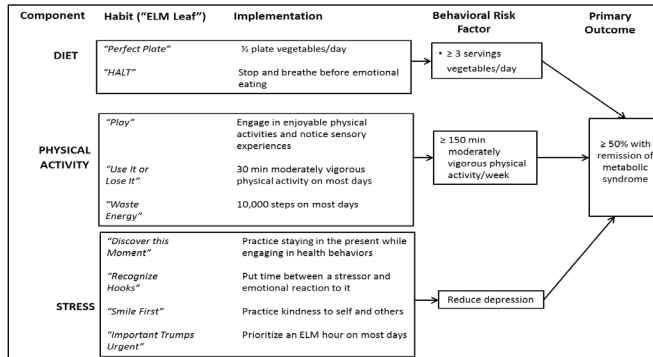
### Small N Time Series Design



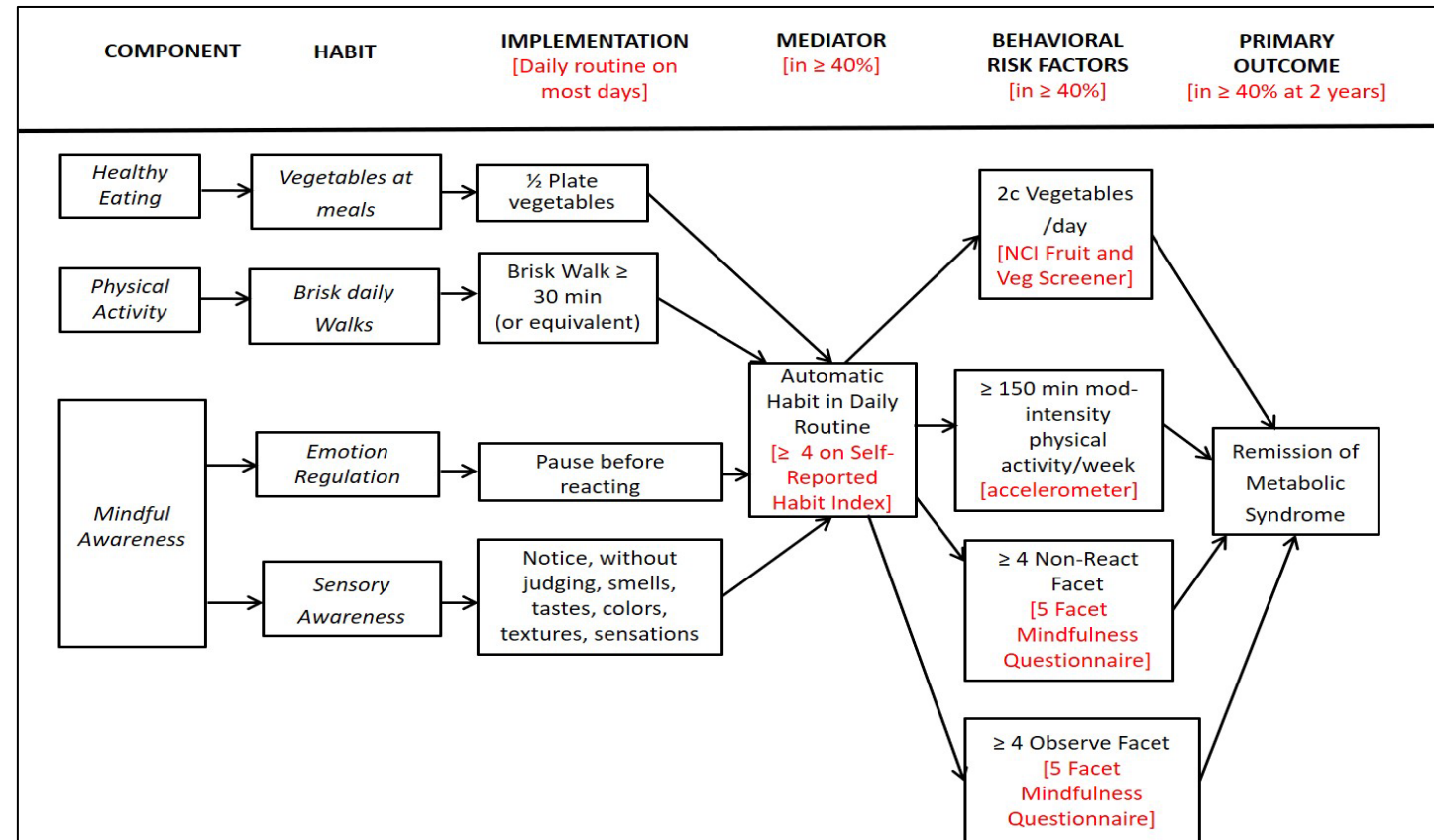
# REFINE

## For Strength and Efficiency

### Hypothesized Pathway (first draft)



### Hypothesized Pathway (second draft)



### REFINEMENT

- Changed Stress component to Mindfulness component
- Reduced number of habits from 9 to 4
- Added a Mediator
- Quantified clinically significant targets

# *“I do not have a treatment.”*

## Find a Medical/Community Partner

- Ask them about their biggest challenges
- Shadow them as they go throughout their day
- Discover a need a behavioral treatment could fill

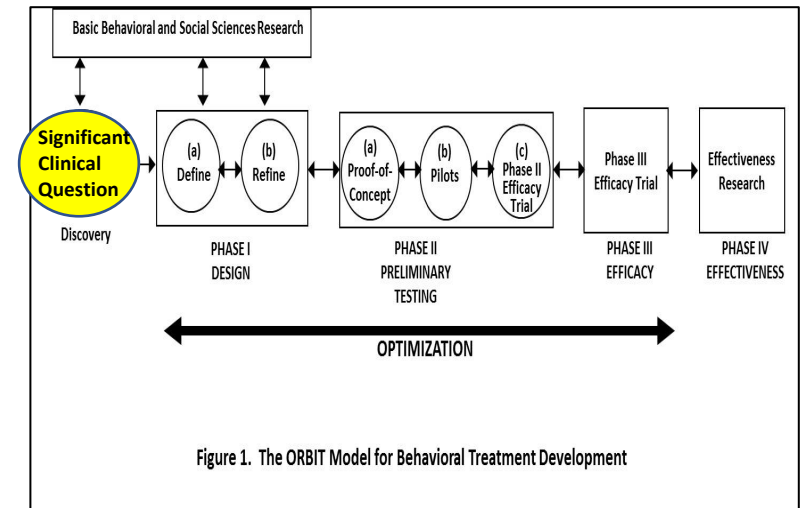
## Literature Search

- Is the health problem increasing? Increasing in subgroup? Not decreasing?
- Is the treatment for it effective? Expensive? Side-effects? Poor adherence?

## Social and Mass Media

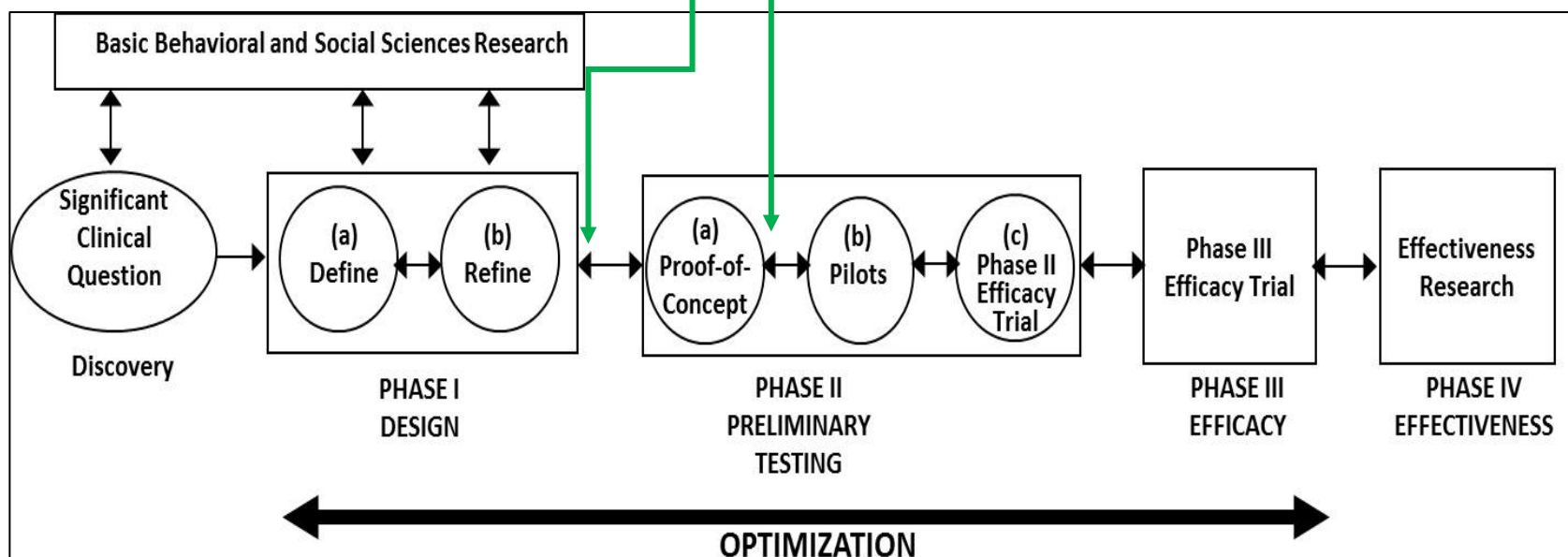
- Journalists are excellent at identifying looming health problems.

## ORBIT Discovery: Significant Clinical Question



# ***“My treatment did not work. Now what?”***

**Keep Trying**



## Accept Failures

- They happen early and often.
- Do not walk away.
- Failures breed success.



# *“How do I keep trying?”*

## Explore Cause

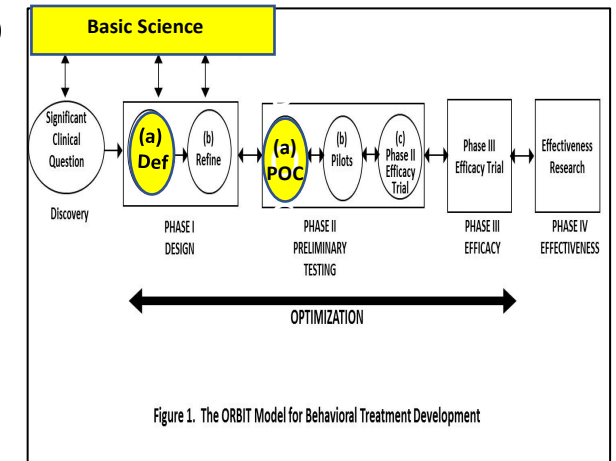
- Qualitative: Ask the participants what helped; what did not help
- Quantitative: Examine data for subgroups who did not benefit

## Decide How to Refine

- Strengthen behavior change strategy (**Discovery: Basic Science**)
- Add a new component (**Phase Ia: Define**)

## After Refinement, Try Another Proof of Concept

- Can refined treatment achieve a clinically significant target (**Phase IIa: Proof-of-Concept**)





# *How do I know if my treatment worked?*

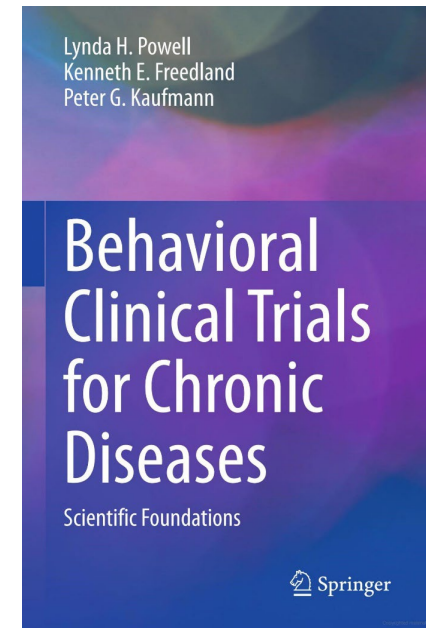
## **Do a Proof of Concept with a Clinically Significant:**

### **TARGET**

- Epidemiology
- Practice Guidelines
- Stakeholder needs  
assessment

### **SUCCESS RATE**

- Other treatments
- Similar treatments
- Stakeholder judgments
- Guidelines



**Chapter 3: Treatment Development**  
**Chapter 5: Clinical Significance**  
**Chapter 9: Outcomes**



## Early-Phase Research on Complex Interventions

- **Complex behavioral interventions:**
  - Are needed to intervene on complex health problems
  - Are needed to improve clinically important health outcomes
  - Must be developed progressively
- **Multi-Component interventions targeting the individual**
  - Are identified in the early **Define Phase Ia** of Orbit (*“everything but the kitchen sink”*)
  - Are simplified in the **Refine Phase Ib** of Orbit (maintain strength but increase efficiency)
  - The treatment package, with all components, is tested in the **Proof of Concept Phase IIa** of Orbit
- **In ORBIT,**
  - Arrows go both ways.
  - Failure is common, particularly in complex interventions.
  - Welcome failure as an opportunity for growth.